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Occupational Intakes of Radionuclides: Part 4

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Authors on behalf of ICRP
F. Paquet, M.R. Bailey, R.W. Leggett, G. Etherington, E. Blanchardon, T. Smith, D. Melo, T.P. Fell, V. Berkovski, D. Nosske, J.D. Harrison

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Occupational Intakes of Radionuclides: Part 4

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Abstract- The 2007 Recommendations (ICRP, 2007) introduced changes that affect the calculation of effective dose, and implied a revision of the dose coefficients for internal exposure, published previously in the *Publication 30* series (ICRP, 1979, 1980, 1981, 1988b) and *Publication 68* (ICRP, 1994b). In addition, new data are now available that support an update of the radionuclide-specific information given in *Publications 54* and *78* (ICRP, 1988a, 1997b), for the design of monitoring programmes and retrospective assessment of occupational internal doses. Provision of new biokinetic models, dose coefficients, monitoring methods and bioassays data was performed by Committee 2 and its Task Groups INDOS and DOCAL.

A first report in a series of documents replacing the *Publication 30* series and *Publications 54, 68* and *78* has been issued (OIR Part 1). This first report describes the assessment of internal occupational exposure to radionuclides, biokinetic and dosimetric models, methods of individual and workplace monitoring, and general aspects of retrospective dose assessment.

The following reports of the series (Parts 2 to 5) provide data on individual elements and their radioisotopes, including information on chemical forms encountered in the workplace; a list of principal radioisotopes and their physical half-lives and decay modes; the parameter values of the reference biokinetic model; and data on monitoring techniques for the radio-isotopes most commonly encountered in workplaces. For most of the elements, reviews of data on inhalation, ingestion and systemic biokinetics are also provided.

Dosimetric data provided in the printed reports of the series include tables of committed effective dose per intake (Sv per Bq intake) for inhalation and ingestion, tables of committed effective dose per content (Sv per Bq measurement) for inhalation, and graphs of retention and excretion data per Bq intake for inhalation. These data are provided for all absorption types and for the most common isotope(s) of each element section.

The electronic annex that accompanies this series of reports contains a comprehensive set of committed effective and equivalent dose coefficients, committed effective dose per content functions, and reference bioassay functions. Data are provided for inhalation, ingestion and for direct input to the blood.

This fourth report in the series provides the above data for the following elements : Cerium (Ce), Praseodymium (Pr), Neodymium (Nd), Promethium (Pm), Samarium (Sm), Europium (Eu), Gadolinium (Gd), Terbium (Tb), Dysprosium (Dy), Holmium (Ho), Erbium (Er), Thulium (Tm), Ytterbium (Yb), Lutetium (Lu), Actinium (Ac), Protactinium (Pa), Neptunium (Np), Plutonium (Pu), Americium (Am), Curium (Cm), Berkelium (Bk), Californium (Cf), Einsteinium (Es) and Fermium (Fm).

Keywords: Occupational exposure; Internal Dose Assessment; Biokinetic and Dosimetric models; Bioassays interpretation

CONTENTS

PREFACE

The 2007 Recommendations (*Publication 103*, ICRP, 2007) introduced changes to the radiation weighting factors used in the calculation of equivalent dose to organs and tissues and also changes to the tissue weighting factors used in the calculation of effective dose. In addition, an important development was the adoption of reference computational models, in place of the ad-hoc composite mathematical models that have been used by ICRP for all previous internal dose assessments. *Publication 103* also clarified the need for separate calculation of equivalent dose to males and females and sex-averaging in the calculation of effective dose (ICRP, 2007).

These changes implied a revision of the dose coefficients provided in the *Publication 30* series (ICRP, 1979, 1980, 1981, 1988b) and *Publication 68* (ICRP, 1994b). In addition, there was a need to update the radionuclide-specific information given in *Publications 54* and *78* (ICRP, 1988a, 1997b), for the design and planning of monitoring programmes and retrospective assessment of occupational internal doses. This work was performed by Committee 2 and its Task Groups INDOS, DOCAL and IDC and is published now as a series of documents providing revised dose coefficients for occupational intakes of radionuclides (OIR) by inhalation and ingestion.

The first report of this series (OIR Part 1, ICRP, 2015) provided general information on control of occupational exposures, biokinetic and dosimetric models, monitoring methods, monitoring programmes and retrospective dose assessment. The subsequent reports provide data on individual elements and their radioisotopes, including information on chemical forms encountered in the workplace; a list of principal radioisotopes and their physical half-lives and decay modes; reviews of data on inhalation, ingestion and systemic biokinetics; the structure and parameter values of the reference systemic biokinetic model; and data on monitoring techniques for the radio-isotopes most commonly encountered in workplaces.

Dosimetric data provided in the printed reports of the series include tables of committed effective dose per intake (Sv per Bq intake) for inhalation and ingestion, tables of commited effective dose per content (Sv per Bq measurements) for inhalation, and graphs of retention and excretion data per Bq intake for inhalation. These data are provided for all absorption types and for the most common isotope(s) of each element section.

The electronic annex that accompanies this series of reports contains a comprehensive set of committed effective and equivalent dose coefficients, committed effective dose per content functions, and reference bioassay functions for inhalation, ingestion and for direct input to the blood.

The second report in the series (ICRP, 2016a) provided data for the following elements : Hydrogen (H), Carbon (C), Phosphorus (P), Sulphur (S), Calcium (Ca), Iron (Fe), Cobalt (Co), Zinc (Zn), Strontium (Sr), Yttrium (Y), Zirconium (Zr), Niobium (Nb), Molybdenum (Mo) and Technetium (Tc).

The third report (ICRP, 2016b) provided data for the following elements: Ruthenium (Ru), Antimony (Sb), Tellurium (Te), Iodine (I), Caesium (Cs), Barium (Ba), Iridium (Ir), Lead (Pb), Bismuth (Bi), Polonium (Po), Radon (Rn), Radium (Ra), Thorium (Th) and Uranium (U).

This report provides data on the actinide and lanthanide series. (Please note that Th and U data are given in Part 3). The elements included are: Cerium (Ce), Praseodymium (Pr), Neodymium (Nd), Promethium (Pm), Samarium (Sm), Europium (Eu), Gadolinium (Gd), Terbium (Tb), Dysprosium (Dy), Holmium (Ho), Erbium (Er), Thulium (Tm), Ytterbium (Yb), Lutetium (Lu), Actinium (Ac), Protactinium (Pa), Neptunium (Np), Plutonium (Pu), Americium (Am), Curium (Cm), Berkelium (Bk), Californium (Cf), Einsteinium (Es) and Fermium (Fm).

Part 5 will provide data for most of the other elements.

Four Task Groups participated in the completion of this report. INDOS and DOCAL were involved until 2014 and then were replaced by the newly formed IDC and CPRT.

The membership of Task Group 21 on Internal Dosimetry (INDOS) was:

Members:

F Paquet (Chair)	G Etherington	J L Lipsztein
E Ansoborlo	A Giussani	D Melo
M R Bailey	R A Guilmette	
E Blanchardon	J D Harrison	
H Doerfel	R W Leggett	

Corresponding Members:

A Bouville	A Luciani	D Whillans
C-M Castellani	D Newton	
R Cruz-Suarez	D Nosske	
C Hurtgen	D M Taylor	

The membership of Task Group 4 on Dose Calculations (DOCAL) was:

Members:

W E Bolch (Chair)	A Endo	N Ishigure
M Zankl	V Berkovski	T P Fell
D Nosske	L Bertelli	N E Hertel
N Petoussi-Henss	K F Eckerman	J G S Hunt
M Pelliccioni		

Corresponding Members:

A Birchall	H Schlattl
G Gualdrini	M Stabin
D Jokisch	R Tanner
C Lee	X G Xu

The membership of Task Group 95 on Internal Dose Coefficients (IDC) was:

Members:

F Paquet (Chair)	V Berkovski	R W Leggett
M R Bailey	G Etherington	
E Blanchardon	T P Fell	

Corresponding Members:

E Ansoborlo	D Gregoratto	M Puncher
L Bertelli	J Marsh	T Smith
E Davesne	D Melo	G Ratia
A Giussani	D Nosske	

The membership of Task Group 96 on Computational Phantoms and Radiation Transport (CPRT) was:

Members:

W Bolch (Chair)	A Endo	M Zankl
J Hunt	N Petoussi-Henss	C Lee
CH Kim		

Corresponding Members:

D Jokisch	H Schlattl,	KP Kim
J Li		

The membership of Committee 2 was:

(2013-2017)

J D Harrison (Chair)	M Degteva	D Noβke
M R Bailey	A Endo	F Paquet
V Berkovski	JG Hunt	N Petoussi-Henss
L Bertelli	C Hyeong Kim	F Wissmann
W E Bolch	R Leggett	
D Chambers	J Ma	

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1. INTRODUCTION

(1) The present report is Part 4 of a series which provides revised dose coefficients for occupational intakes of radionuclides (OIR) by inhalation and ingestion. It also presents radionuclide-specific information for the design and planning of monitoring programmes and retrospective assessment of occupational internal doses.

(2) This OIR report series replaces the *Publication 30* series (ICRP, 1979, 1980, 1981, 1988b), and *Publications 54*, *68* and *78* (ICRP, 1988a, 1994b, 1997). The revised dose coefficients, dose per content values and reference bioassay functions have been calculated using the *Publication 100* (ICRP, 2006) Human Alimentary Tract Model (HATM) and a revision of the *Publication 66* (ICRP, 1994a) Human Respiratory Tract Model (HRTM) which takes account of more recent data. The revisions made to the HRTM are described in OIR Part 1 (ICRP, 2015). Revisions have also been made to many models for the systemic biokinetics of radionuclides, making them more physiologically realistic representations of uptake and retention in organs and tissues and of excretion.

(3) Data are given for elements of the lanthanide and actinide families, apart for uranium and thorium which were presented in OIR Part 3. Due to the lack of information in the literature on the biokinetics of many of the 15 elements of the lanthanide series, ^{57}La to ^{71}Lu, individual development of meaningful biokinetic models to describe the behaviour of each of the elements in humans was not feasible. Available data have been utilised to construct a generic lanthanide biokinetic model and to define element-specific parameters for each element in the series.

(4) A generic model is also presented for the actinide family since most data showed a similar behaviour in the body of all actinide elements except uranium. Additional data are presented in the respective element section.

1.1. Methodology used in this report series

(5) The general methodology for producing the biokinetic and dosimetric models is given in OIR Part 1 (ICRP, 2015). For each element, detailed reviews of the literature were carried out to identify experimental studies and human contamination cases that provide information to quantify absorption to blood from the respiratory and alimentary tracts, and the biokinetics following systemic uptake. These reviews, and the analyses of the data obtained from them, are summarised in each element section.

(6) In the case of inhalation, chemical forms are usually addressed in order of decreasing solubility in the lungs. Where information was available, HRTM absorption parameter values were derived from experimental data from both *in vivo* and *in vitro* studies. For *in vitro* studies, estimation of the dissolution parameter values (rapidly dissolved fraction, f_r, rapid and slow dissolution rates, s_r and s_s) was usually straightforward. For *in vivo* studies, however, simulation modelling was often needed to derive them from the data available: typically retention in organs and excretion in urine and faeces: for further information see Supporting Guidance 3 (ICRP, 2002).

(7) In some recent publications, the authors derived HRTM parameter values: if so they are reported. In most cases, parameter values were derived by the ICRP Task Group (INDOS or IDC) members and their colleagues. This is indicated in the text by wording such as "analysis carried out here...": the first such occurrence for each element is given as "analysis carried out here (i.e. by the Task Group)...".

(8) Material-specific rates of absorption have been adopted (and dose coefficients and bioassay functions provided for them in the accompanying electronic annex) for a limited number of selected materials, i.e., those for which:

- There are *in vivo* data from which specific parameter values can be derived;
- Results from different studies are consistent;
- It was considered that occupational exposure to the material is likely;
- The specific parameter values are sufficiently different from default Type F, M or S parameter values to justify providing additional specific dose coefficients and bioassay functions.

(9) Other materials were assigned to default HRTM absorption Types, using the criteria described in *Publication 71* (ICRP, 1995) and Supporting Guidance 3 (ICRP, 2002) for making such assignments using experimental data. Type M is assumed for particulate forms of most elements "by default", i.e. in the absence of such information. A material is assigned to Type F if the amount absorbed into blood by 30 d after intake is greater than the amount absorbed over the same period from a hypothetical material with a constant absorption rate corresponding to a half-time of 10 d, under identical conditions. Similarly, a material is assigned to Type S if the amount absorbed into blood by 180 d is less than the amount absorbed over the same period from a hypothetical material with a constant rate of absorption to blood of 0.001 d^{-1} (extrapolation was used in some cases, as indicated in the text). For studies where it was possible to apply the criteria, a statement is made to the effect that results “are consistent with” (or “give”) assignment to Type F (M or S). For studies where the results point towards a particular Type, but there was insufficient information to apply the criteria, a statement is made to the effect that the results "indicate" or "suggest" Type F (M or S) behaviour.

(10) Assignments are not made here on the basis of the known solubility of chemical forms in aqueous media, because this is not considered to be a reliable guide to absorption from the respiratory tract (Section E.2.2.1 in ICRP, 1994a). If it is considered appropriate in a particular situation, it would need to be carried out with caution. In practice, it might well be possible to assign a radionuclide, to which workers have been exposed, to an absorption Type without knowing its chemical form, e.g. from environmental and/or bioassay measurements. These could include in-vitro dissolution tests on air filters or swabs; in-vivo measurements (chest compared to whole body); or excretion measurements (urine compared to fecal). Nevertheless, for each element, a default absorption Type is recommended for use in the absence of information on which the exposure material can be assigned to Type F, M or S. For most elements Type M is recommended by default.

(11) For soluble (Type F) forms of each element, estimates are made of the overall rate of absorption from the respiratory tract to blood, where information is available. In general this results from dissolution of the deposited material, and also transfer through lining fluids and epithelium into blood. Nevertheless, for simplicity this is usually represented by the rapid dissolution rate, s_r, (see Section 3.2.3 in OIR Part 1). Because of the wide range of the estimated values of s_r, element-specific values are adopted in this series of documents for those elements for which estimates could be made. Justification of the value chosen for an element is given in the subsection headed: "Rapid dissolution rate for *element*".

(12) For some elements, a significant fraction of the dissolved material is absorbed slowly. In some cases this can be represented by formation of particulate material (which is subject to clearance by particle transport). In others, some dissolved material appears to be attached to lung structural components, and removed only by absorption to blood. To represent the latter type of time-dependent uptake, it is assumed that a fraction, f_b, of the dissolved

material is retained in the 'bound' state, from which it goes into blood at a rate s_b. Evidence for retention in the bound state, rather than by transformation into particulate material may be in one or more forms: e.g. systemic uptake rather than faecal clearance of the retained material; slower clearance than for insoluble particles deposited in the same region of the respiratory tract; or autoradiography showing diffuse rather than focal retention of activity.

(13) The bound state was included in the HRTM mainly to take account of slow clearance of dissolved materials from the alveolar-interstitial region. Applying the same bound state parameter values in all regions could lead, unintentionally, to high calculated doses to the bronchial (BB) and bronchiolar (bb) regions. Hence in this series of documents it is assumed that for those elements for which a bound state is adopted ($f_b > 0$), it is applied in the conducting airways (ET_2, BB and bb regions) only if there is supporting experimental evidence. Justification of the values chosen for an element is given in the subsection headed: "Extent of binding of *element* to the respiratory tract".

1.2. Data presented in this report series

(14) Data presented in this report series are in a standard format for each element and its radioisotopes. Each element section provides information on chemical forms encountered in the workplace; principal radioisotopes, their physical half-lives and decay modes; reviews of data on inhalation, ingestion and systemic biokinetics; the structure and parameter values for the systemic biokinetic model; monitoring techniques and detection limits typically achieved in a practical monitoring programme. The detection limits presented in this report were derived from a compilation of data from laboratories in Europe, Asia, North America and South America that perform routine monitoring of the specified radionuclide. The sensitivity of the measurements depends on the technique, the counting time and other factors. For example *in vivo* detection limits depend on the detection system (type, quality and number of detectors), counting geometry, and shielding and design of the installation. Those details are outside the scope of this report.

(15) Dosimetric data are provided in the printed reports of the series and in electronic annexes. The methodology for dose calculation is described in OIR Part 1 (ICRP, 2015) and in *Publication 134* (ICRP, 2016c). Due to the amount of data to be provided, the printed reports provide tables and graphs restricted to tables of committed effective dose per intake (Sv per Bq intake) for inhalation and ingestion; tables of committed effective dose per content (Sv per unit activity measurements (Bq)) for inhalation, and graphs of retention and excretion data per Bq intake for inhalation.

(16) Data in the printed reports are provided for all absorption Types of the most common isotope(s) and for an Activity Median Aerodynamic Diameter (AMAD) of 5 µm. In cases for which sufficient information is available (principally for actinide elements), lung absorption is specified for different chemical forms and dose coefficients and bioassay data are calculated accordingly. The dose coefficients and dose per content values presented in this report series are given for a Reference Worker at light work (ICRP, 2015).

(17) The electronic annex that accompanies this series of reports contains a comprehensive set of committed effective and equivalent dose coefficients, dose per content functions, and reference bioassay functions for almost all radionuclides included in *Publication 107* (ICRP, 2008) that have half-lives equal to or greater than 10 min, and for other selected radionuclides. Data are provided for a range of physico-chemical forms and for aerosols with median sizes ranging from an Activity Median Thermodynamic Diameter (AMTD) of 0.001 µm to an AMAD of 20 µm. Data for ingestion and injection (i.e. direct entry to the blood) are

provided to allow the interpretation of bioassay data for cases of inadvertent ingestion (e.g. of material on contaminated skin) or rapid absorption through intact or damaged skin (injection).

(18) The dose coefficients and other radionuclide-specific data are provided as a set of data files which may be accessed by the user directly or by using the accompanying Data Viewer. The Data Viewer permits rapid navigation of the dataset and visualisation of the data in tabulated and graphical formats, such as graphs of the time series of dose per content coefficients or predicted activity content per unit dose (Bq Sv^{-1}) as a function of time after intake. Graphical presentations of decay chains and nuclear decay data from Publication 107 (ICRP, 2008) are also included.

(19) Part 2 (ICRP, 2016a) provided the data above on: Hydrogen (H), Carbon (C), Phosphorus (P), Sulphur (S), Calcium (Ca), Iron (Fe), Cobalt (Co), Zinc (Zn), Strontium (Sr), Yttrium (Y), Zirconium (Zr), Niobium (Nb), Molybdenum (Mo) and Technetium (Tc).

(20) Part 3 (ICRP 2016b) provided the data above on the following elements: Ruthenium (Ru), Antimony (Sb), Tellurium (Te), Iodine (I), Caesium (Cs), Barium (Ba), Iridium (Ir), Lead (Pb), Bismuth (Bi), Polonium (Po), Radon (Rn), Radium (Ra), Thorium (Th) and Uranium (U).

(21) Part 4 provides data on the actinides and lanthanide series. (Please note that Th and U data are given in Part 3). The elements included are: Cerium (Ce), Praseodymium (Pr), Neodymium (Nd), Promethium (Pm), Samarium (Sm), Europium (Eu), Gadolinium (Gd), Terbium (Tb), Dysprosium (Dy), Holmium (Ho), Erbium (Er), Thulium (Tm), Ytterbium (Yb), Lutetium (Lu), Actinium (Ac), Protactinium (Pa), Neptunium (Np), Plutonium (Pu), Americium (Am), Curium (Cm), Berkelium (Bk), Californium (Cf), Einsteinium (Es) and Fermium (Fm). Due to the similartities between the elements in a series, generic biokinetic models are provided for the lanthanides and the actinides. Specific individual data are given, when relevant, in the element sections.

(22) Part 5 will provide data for most of the remaining elements.

REFERENCES

ICRP, 1979. Limits for intake of radionuclides by workers. ICRP Publication 30, Part 1. Ann. ICRP 2(3/4).

ICRP, 1980. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 2. Ann. ICRP 4(3/4).

ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6(2/3).

ICRP, 1988a. Individual monitoring for intakes of radionuclides by workers: design and interpretation. ICRP Publication 54, Ann. ICRP 19(1-3).

ICRP, 1988b. Limits for intakes of radionuclides by workers: An Addendum. ICRP Publication 30, Part 4. Ann. ICRP 19(4).

ICRP, 1994a. Human respiratory tract model for radiological protection. ICRP Publication 66. Ann. ICRP 24(1-3).

ICRP, 1994b. Dose coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

ICRP, 1997. Individual monitoring for internal exposure of workers – Replacement of ICRP Publication 54. ICRP Publication 78. Ann. ICRP 27(3/4).

ICRP, 2006. Human alimentary tract model for radiological protection. ICRP Publication 100. Ann. ICRP 36(1-2).

ICRP, 2007. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Ann. ICRP 37(2-4).
ICRP, 2008. Nuclear decay data for dosimetric calculations. ICRP Publication 107. Ann. ICRP 38(3).
ICRP, 2015. Occupational intakes of radionuclides. Part 1. ICRP Publication 130. Ann. ICRP 44(2).
ICRP, 2016a. Occupational intakes of radionuclides. Part 2. ICRP Publication 135. Ann. ICRP (In Press).
ICRP, 2016b. Occupational intakes of radionuclides. Part 3. ICRP Publication 1XX. Ann. ICRP ICRP (To come)
ICRP, 2016c. The ICRP Computational framework for internal dose assessment for Reference workers : Specific absorbed fractions. ICRP Publication 134. Ann. ICRP (In Press).

2. A GENERIC BIOKINETIC MODELING SCHEME FOR THE LANTHANIDES

(23) Information on the biokinetics of several of the 15 elements of the lanthanide series, ^{57}La to ^{71}Lu, is too limited to develop well-supported biokinetic models based on element-specific data. However, the lanthanides show a regular gradation in chemical properties across the series, and animal studies indicate that this is reflected in reasonably predictable changes across the lanthanide family in their deposition in the liver and skeleton as well as in their excretion patterns. These regular differences in chemical and biological behaviour have been used to construct a generic lanthanide biokinetic model and, where specific information is not available, to assign element-specific parameter values for each of the lanthanides.

(24) This section describes the basis for the generic modeling scheme, the common model structure applied, and the generic and element-specific parameter values assigned to each element in the series. Subsequent element sections expand on specific data or assumptions for each of the lanthanides.

2.1. Lanthanide physico-chemistry

(25) The fifteen elements from lanthanum (Z=57) to lutetium (Z=71) form the lanthanide series. The term 'rare earths' has also been used to refer to this group of elements, and at times to a larger group, including yttrium (Z=39) and scandium (Z=21). The International Union of Pure and Applied Chemistry (IUPAC) prefers the term lanthanoid to lanthanide (IUPAC, 2005) but this terminology is not adopted in this document.

(26) There are strong similarities in the chemical behaviour of the lanthanide elements (Durbin, 1960, 1962; Vidaud et al., 2012).

Sources and production

(27) Lanthanides may be encountered in industry in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, sulphates, carbonates and citrates). The most common lanthanides minerals are monazite (sand-composed of phosphates of thorium, cerium, neodymium and lanthanum) and bastnäsite (mixed fluorocarbonate of various lanthanides).

(28) The radio-lanthanides from lanthanum (La) through dysprosium (Dy) are produced in significant yield (representing about 40% of fission product mass) in the fission of ^{235}U/^{239}Pu in light water reactors. The mutual separation of fission product lanthanides from transplutonium actinides in used nuclear fuel reprocessing is motivated by the desire to reduce long-term radiotoxicity of used fuel (Nash et al., 2012).

Uses

(29) Lanthanides are increasingly employed in electronic (e.g. superconductors), catalytic, ceramic, glass polishing, magnetic technologies… Lanthanide ions are used as the active ions in luminescent materials for optoelectronics applications (e.g. Nd:YAG laser) and as co-dopants in doped-fiber optical amplifiers. The radio-lanthanides (e.g. ^{153}Sm, ^{177}Lu, ^{166}Ho…) are also considered as excellent candidates for radiotherapy because of their desirable physical characteristics and ready availability. They have also been investigated for different potential therapeutic applications such as: i) palliative treatment of pain from bone cancer (^{153}Sm); ii) microspheres and colloids for radiation synovectomy (^{165}Dy, ^{166}Ho, ^{153}Sm); iii) labeled monoclonal antibodies for radioimmunotherapy (^{177}Lu, ^{166}Ho). Common polyaminocarboxylate

chelating agents such as ethylene diamine tetraacetic acid (EDTA) and diethylene triamine pentaacetic acid (DTPA) are currently used to form strong and stable *in vivo* complexes.

Physico-Chemistry

(30) The fifteen elements of the lanthanide series (Ln), also called f-transition metals or 4f elements, exhibit basically similar chemical properties. The electronic structure of the lanthanide elements is $[Xe]6s^2 4f^n$, except for lanthanum (La), gadolinium (Gd) and lutetium (Lu) which are $[Xe]\ 5d^1 6s^2 4f^n$. Lanthanide ions are usually stable and mainly present in aqueous solution as trivalent ions Ln(III) with few exceptions such as cerium (Ce), praseodymium (Pr), terbium (Tb) and dysprosium (Dy) that can also exist at valence IV, and samarium (Sm), europium (Eu) thulium (Tm) and ytterbium (Yb) that can be also present at valence II (Table 2.1).

(31) In aqueous solutions, the properties of the lanthanides are usually ruled by the ionic radii decreasing, the so-called lanthanide contraction, regularly from 1.16 Å for La(III) to 0.98 Å for Lu(III) (Fig. 2.1) at coordination number VI (Shannon, 1976). The coordination numbers for $[Ln(H_20)_n]^{3+}$ in aqueous solution are up to IX for the early lanthanides and VIII for the later members.

(32) In terms of oxido-reduction potentials, the Ln (0/3+) couples are nearly the same for all the family ranging from +2.28 V (Lu) to +2.52 V (La) (Charlot, 1958) which means that these metals are strongly electropositive or highly reducing and thus are classified as hard acidic cations in the Pearson theory of Hard and Soft Acids and Bases (HSAB) (Pearson, 1963). One important property of Ln(III) is that, whatever the ligand, they form ionic bonds rather than covalent bonding. Their high hydrophilicity leads to a competition between any chelating or extracting agent and water molecules. Because the different lanthanide ions have slightly different radii, the lattice energy of their salts and hydration energies of the ions are slightly different, leading to small differences in solubility.

(33) Lanthanides in aqueous solution are mainly present as Ln^{3+} ions and as hard acidic cations, readily form stable complexes with O-donor ligands. They react slowly and can form either hydroxides $Ln(OH)_{3aq}$ or precipitated $Ln(OH)_{3s}$ (Klungness at al., 2000; Cotton, 2006), with stability constant (log β) ranging from -8.8 to -7.3 and solubility product (log Ks) ranging from -20.1 to -25.0 in the series. Moreover, solubility product (log Ks) of two basic mineral anions such as phosphates (PO_4^{3-}) (-26.2 to -25.4) and carbonates (CO_3^{2-}) (-29.9 to -32.2) can be dominant and play a major role within different biological and environmental media (Leggett et al., 2014). Some specific ligands which are good complexing agents such as EDTA with log β ranging from 15.5 to 19.8 (Smith et Martell, 1989) and DTPA with log β ranging from 19.5 to 22.5 (Anderegg et al., 2005), are commonly used in separation chemistry and radiotherapy.

Table 2.1. Oxidation states for the lanthanide elements[a].

Element	Oxidation state
La	**III**
Ce	**III,** IV
Pr	**III,** IV
Nd	**III**
Pm	**III**
Sm	II, **III**
Eu	II, **III**

Gd	**III**
Tb	**III**, IV
Dy, Ho, Er, Tm	**III**
Yb	II, **III**
Lu	**III**

[a] In bold font are the most stable oxidation states under aqueous conditions.

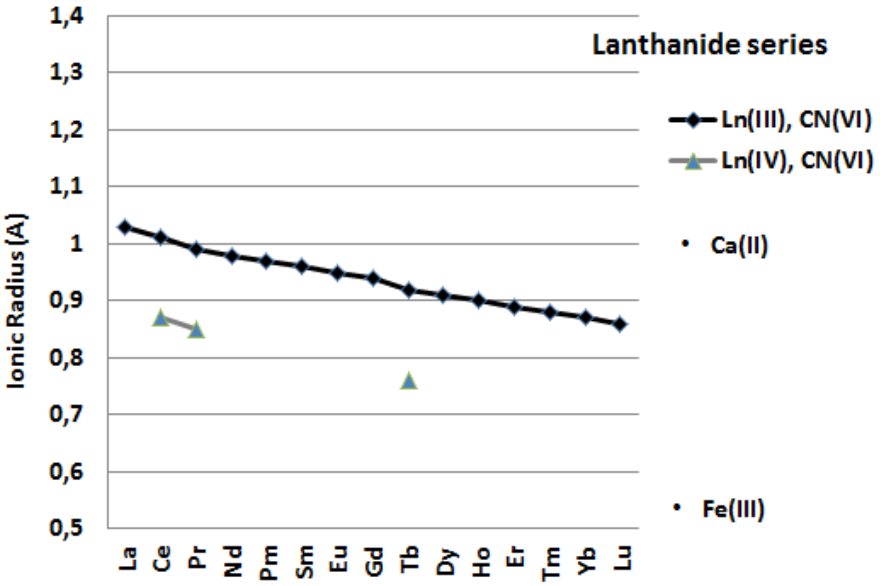


Fig. 2.1. Ionic radii of lanthanide series for the two main oxidation states (III and IV) and for a coordination number (CN = VI). Ca(II) and Fe(III) radii are given as a comparison.

Behaviour within biological media

(34) The biochemical properties of lanthanides have been described by several authors (e.g. Evans, 1983). Elements of the lanthanide series occur in only trace amounts in organisms and play no biological role. However, it may be expected that they find their way into the food chain, water and air, and that the human body contain a natural, or 'base load', of the elements (e.g. Zhu et al, 2010).

(35) Speciation of lanthanides within biological media is driven mainly by hydrolysis and precipitation with basic mineral anions such as phosphates (PO_4^{3-}) and carbonates (CO_3^{2-}), as a function of pH conditions (Leggett et al., 2014).

(36) Trivalent lanthanides have been shown to substitute for metal ions such as Ca^{2+}, and, to a lesser extent, Mg^{2+}, Fe^{3+} and Mn^{2+} (Evans, 1983).Trivalent lanthanides therefore interact with many proteins which either have an absolute dependence on Ca^{2+} or whose activity is stimulated by Ca^{2+}. Trivalent lanthanide can for example replace Ca^{2+} in Conconavalin A and bind to many proteins such as transferrin, IgG, albumin and calmodulin and to acetylcholine receptors (Evans, 1983). Trivalent lanthanides also promote polymerization of collagen and some individual elements such as Tb^{3+} promote aggregation of haemocyanin (Evans and Drouven, 1983). Stability constants of lanthanides with different amino acids are relatively

weak (log β ranging from 3.0-6.5) (Smith and Martell, 1989) compared to classical organic complexes.

(37) Trivalent lanthanides are known to bind to the cellular membrane but not penetrate it. They also bind tightly to cartilage, which explains their use for investigations on arthritis (Evans, 1983). Additional characteristics of tissue binding and on the behaviour in the body are given in the paragraphs below.

2.2. Routes of Intake

2.2.1. Inhalation

(38) The behaviour of ionic (water-soluble) lanthanides following deposition in the respiratory tract is difficult to determine because ionic solutions (e.g. chloride) are unstable at neutral pH and in many biological media, resulting in colloid formation. For example, cerium hydroxide precipitates from nitrate solution at pH 8.1 (NCRP, 1978). As discussed in the cerium inhalation section, this may account, in part at least, for the wide range in lung clearance kinetics observed following deposition of cerium chloride in the lungs.

(39) There is extensive information on the behaviour of cerium following its deposition in the respiratory tract, but relatively little for other lanthanides, and for several of them there are no experimental studies at all. Because of the lack of information on the lung clearance characteristics of most lanthanides other than cerium, and the similarities in the chemical behaviour of the lanthanides, the behaviour of cerium is used in this document as a model for other lanthanide elements.

(40) As described in the cerium section, there have been many studies of the behaviour of cerium deposited in the respiratory tract as chloride (more than for any other water-soluble form of any lanthanide). It appears that the absorption characteristics of cerium following deposition of the chloride depend strongly on the methods used to prepare and administer the material. In particular, the fraction dissolved rapidly (f_r) varied from 0.02 to 0.96 and seems to decrease with increasing mass administered and increasing pH.

(41) In the analysis of the data and the determination of absorption parameter values carried out here (*i.e.*, by the Task Group), the following biokinetic data and models were used:

- For deposition in the respiratory tract of each species, data from the literature, e.g. Snipes et al. (1983), Raabe et al. (1988), and information relating to the study (e.g. early excretion).
- For particle transport from the alveolar-interstitial region of the respiratory tract in each species, clearance rates from the literature (e.g. Snipes et al., 1983; Bailey et al., 1985).
- For transit through the alimentary tract and for systemic biokinetics, the cerium model for dogs developed by Shyr et al. (1991); changes were made to the rates, but not to the structure, for other species (rats, mice, hamsters).
- Rates for the respiratory tract, alimentary tract or systemic models were also adapted when no information was available for the particular species or strain, or when the fit with "default" values was not considered sufficiently good.

(42) The most comprehensive studies of cerium chloride deposited in the lungs involved complementary experiments in which ^{144}Ce was inhaled by dogs as carrier-free ^{144}Ce in a CsCl vector, in a mixture of CsCl and $CeCl_3$, or in $CeCl_3$ (Boecker and Cuddihy 1974; Cuddihy et al., 1975, 1976). Analysis was carried out here by simultaneously fitting data from these experiments: values of s_r, f_b, s_b, and s_s were assumed to be the same in each experiment, while f_r

was allowed to vary between them. The results could be fit well, with absorption parameter values of s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1} and s_s = 0.0015 d^{-1}. (Values of f_r were ~0.95 for carrier-free ^{144}Ce in a CsCl vector; 0.84 for ^{144}Ce in a mixture of CsCl and $CeCl_3$; and 0.52 for ^{144}Ce in $CeCl_3$.)

(43) These parameter values were applied in the analysis of the results of other lanthanide studies carried out here. The bound fraction parameter values were applied in all cases. The rapid and slow dissolution rates were usually applied to water-soluble forms.

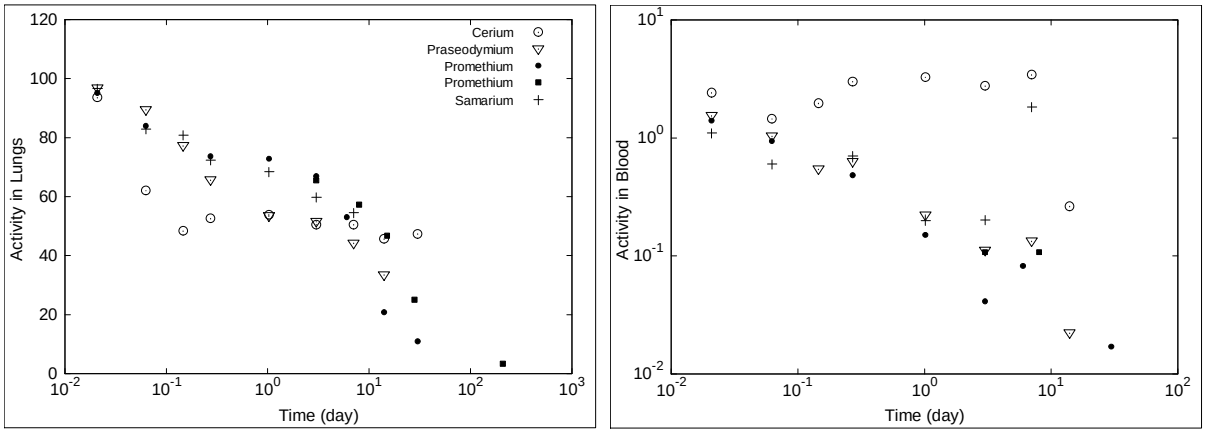
(44) These results were also used to select the bound state parameter values for cerium; specific parameter values for water-soluble forms of cerium; and were a major input to selecting the rapid dissolution rate for cerium. These parameter values were then applied to the rest of the lanthanides. See the section below on Absorption Types and parameter values, and for more details, the cerium inhalation section.

2.2.1.1. Comparisons of respiratory tract clearance of lanthanides

(45) Comparisons that could be made between the clearance characteristics of lanthanides deposited in the respiratory tract under similar conditions are described in the next paragraphs. Ideally, comparisons would have been made between elements administered simultaneously e.g. 'dual-isotope' experiments, or at least as part of the same study, but there are very few such experiments reported. Comparisons are therefore made here between studies carried out by the same research group under apparently similar conditions. However, as noted above, the clearance kinetics of cerium deposited as chloride in the respiratory tract seem to be sensitive to the conditions under which it is administered. Hence observed differences could be due to differences in experimental conditions or to differences between elements. In this section, emphasis is placed on comparing the biokinetics of different lanthanides following deposition in the respiratory tract. Further information on the experiments and derivation of parameter values is given in the corresponding element sections.

Cerium, praseodymium, promethium and samarium chlorides inhaled by mice

(46) Similar studies were carried out in which the biokinetics were followed after inhalation of the chlorides (pH 3.5) of ^{144}Ce, ^{143}Pr, ^{147}Pm, and ^{153}Sm by mice (Gensicke and Spode, 1962; Gensicke and Nitschke, 1964, 1965, 1970; Gensicke et al., 1973). The results are compared in Fig. 2.2.



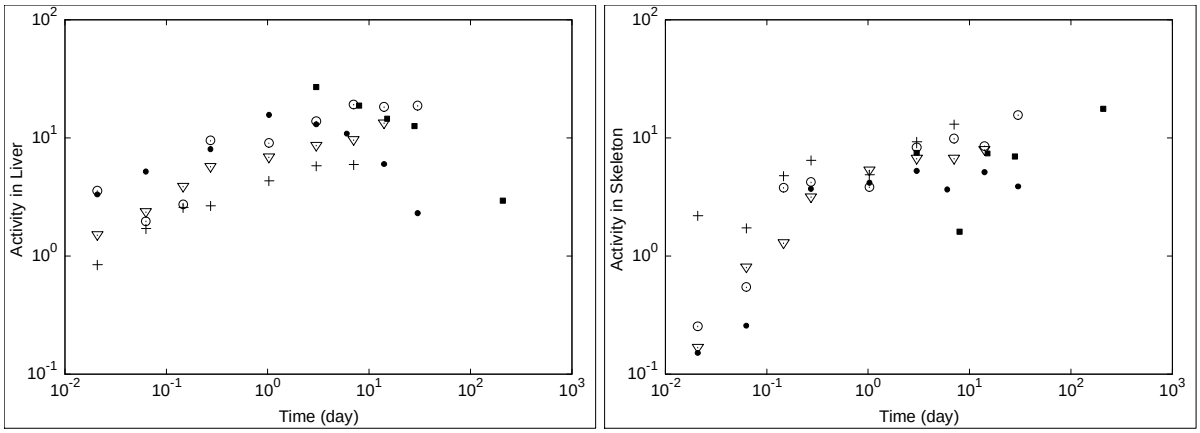


Fig. 2.2. Comparison of biokinetics of lanthanides inhaled by mice as chlorides. Data (decay-corrected) normalised to sum of contents of lungs, trachea, and systemic organs at end of inhalation (t = 30 minutes).

(o) ^{144}Ce Gensicke and Spode (1962); (∇) ^{143}Pr Gensicke and Nitschke (1964); (●) ^{147}Pm Gensicke and Nitschke (1965); (■) ^{153}Sm Gensicke and Nitschke (1970); (+) ^{147}Pm Gensicke et al. (1973).

(47) Broadly similar behaviour is seen, except for greater retention of ^{144}Ce (than of other lanthanides) in the lungs beyond 1 d, and greater retention of ^{144}Ce in the blood beyond 1 hour. The very low lung clearance of ^{144}Ce is surprising, but the data are difficult to interpret (see cerium section). Even for insoluble particles, clearance from the lungs of mice would normally be readily observable over this period, suggesting that a considerable fraction is bound. As noted above, there is great variation between studies in lung clearance of cerium deposited in the lungs as chloride. The fraction dissolved rapidly seemed to decrease with increasing mass administered and increasing pH. However, it was administered in this experiment at pH 3.5, and the avid retention was not observed with the other lanthanides administered under similar conditions.

(48) Analyses were carried out here, considering together the four experiments which showed similar behaviour: one each for ^{143}Pr and ^{153}Sm and two for ^{147}Pm. Assuming (as above) that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, fits were obtained with values of f_r = 0.3 for ^{147}Pm and 0.4 for ^{153}Sm and ^{143}Pr.

(49) As an alternative, the value of the slow dissolution rate was optimised for the results of these four experiments simultaneously. This gave a higher value of s_s = 0.006 d^{-1}, and slightly lower values of f_r: 0.2 for ^{147}Pm, and 0.4 for ^{143}Pr and ^{153}Sm.

(50) With the same assumptions for the other parameter values (including s_s = 0.0015 d^{-1}), a fit was also made to the four datasets simultaneously, assuming that the same value of f_r applied to ^{143}Pr, ^{153}Sm and ^{147}Pm. This gave f_r = 0.4.

(51) The values of f_r derived for ^{143}Pr, ^{153}Sm and ^{147}Pm administered as chlorides, with various assumptions, ranged from 0.2 to 0.4. These are similar to those obtained for ^{140}La and ^{144}Ce administered to dogs as $LaCl_3$ and $CeCl_3$ (0.4 and 0.5 respectively, see below).

Water-soluble forms of praseodymium, europium, gadolinium, terbium and ytterbium administered to rats

(52) Moskalev et al. (1972) followed the biokinetics of ^{143}Pr (for 32 d), ^{153}Gd, ^{160}Tb, ^{169}Yb (for 64 d) and ^{152}Eu (for 128 d) after deposition in the lungs of rats. However, few details are given. The text states that following inhalation or intratracheal instillation, rare-earth nuclides, even when administered as soluble simple salts, are slowly and incompletely absorbed

from lung tissue, but the distribution of the absorbed portion is the same as after intravenous administration. Fig. 135 of Moskalev et al. (1972) shows retention (presumably in the lungs) of the five radionuclides: data read from it are given in Table 2.2. They are assumed here to be decay-corrected, although it is not stated in the original paper.

Table 2.2. Radionuclide lung retention in rats (Moskalev et al., 1972).

	% of "given dose" (initial lung deposit)				
	^{143}Pr	^{153}Gd	^{160}Tb	^{169}Yb	^{152}Eu
1 hour	72	13	–	70	68
1 d	66	9.9	34	24	41
2 d	53	7.3	28	16	33
8 d	29	3.3	13	5.7	14
32 d	12	1.1	3.2	1.4	2.7
64 d	–	0.6	1.6	0.7	1.1
128 d	–	–	–	–	0.4

(53) Results are similar for ^{160}Tb, ^{169}Yb and ^{152}Eu: lung retention falls fairly rapidly to ~10% initial lung deposit (ILD) at 8 d, and ~1% ILD remains at 64 d. Retention of ^{153}Gd falls much faster in the first hour, presumably because of greater deposition in the upper airways, and rapid mucociliary clearance (see gadolinium section). Retention of ^{143}Pr was somewhat greater.

(54) Analysis was carried out here assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1} (based on cerium, see above). The results fit well with f_r ~0.7 for ^{143}Pr; ~0.9 for ^{153}Gd; and >0.95 for ^{160}Tb, ^{169}Yb and ^{152}Eu. Thus they support the application of the cerium parameter values to these elements.

Lanthanum and cerium chlorides inhaled by dogs

(55) Cuddihy and Boecker (1970) followed the biokinetics of ^{140}La up to 8 d in beagle dogs that inhaled ^{140}La as $^{140}LaCl_3$ in a $LaCl_3$-CsCl vector. Comparison with the behaviour of cerium deposited in the respiratory tract under similar conditions was made using the results reported by Cuddihy et al. (1975) (Fig. 2). The same research team followed the biokinetics of ^{144}Ce up to 32 d, in beagle dogs that inhaled ^{144}Ce as $^{144}CeCl_3$ or as ^{144}Ce in a CsCl vector (both in 0.1N HCl). The former is more directly comparable with the ^{140}La experiment because it also involved the use of the stable element as carrier, but tissue distribution data are available only at 32 d, whereas the last ^{140}La measurement was at 8 d. As shown in Fig. 2, ^{144}Ce as $^{144}CeCl_3$ is absorbed more slowly from the lungs than for ^{144}Ce in CsCl vector, with less uptake to blood and deposition in liver and skeleton. The amounts of lanthanum in lung, liver and skeleton show similar trends with time to those of ^{144}Ce in CsCl vector, and if extrapolated to 32 d, would be reasonably consistent with the ^{144}Ce as $^{144}CeCl_3$. Measurements of activity in blood made throughout the experiment are similar for lanthanum and ^{144}Ce as $^{144}CeCl_3$. Thus the results indicate that the two elements behaved similarly.

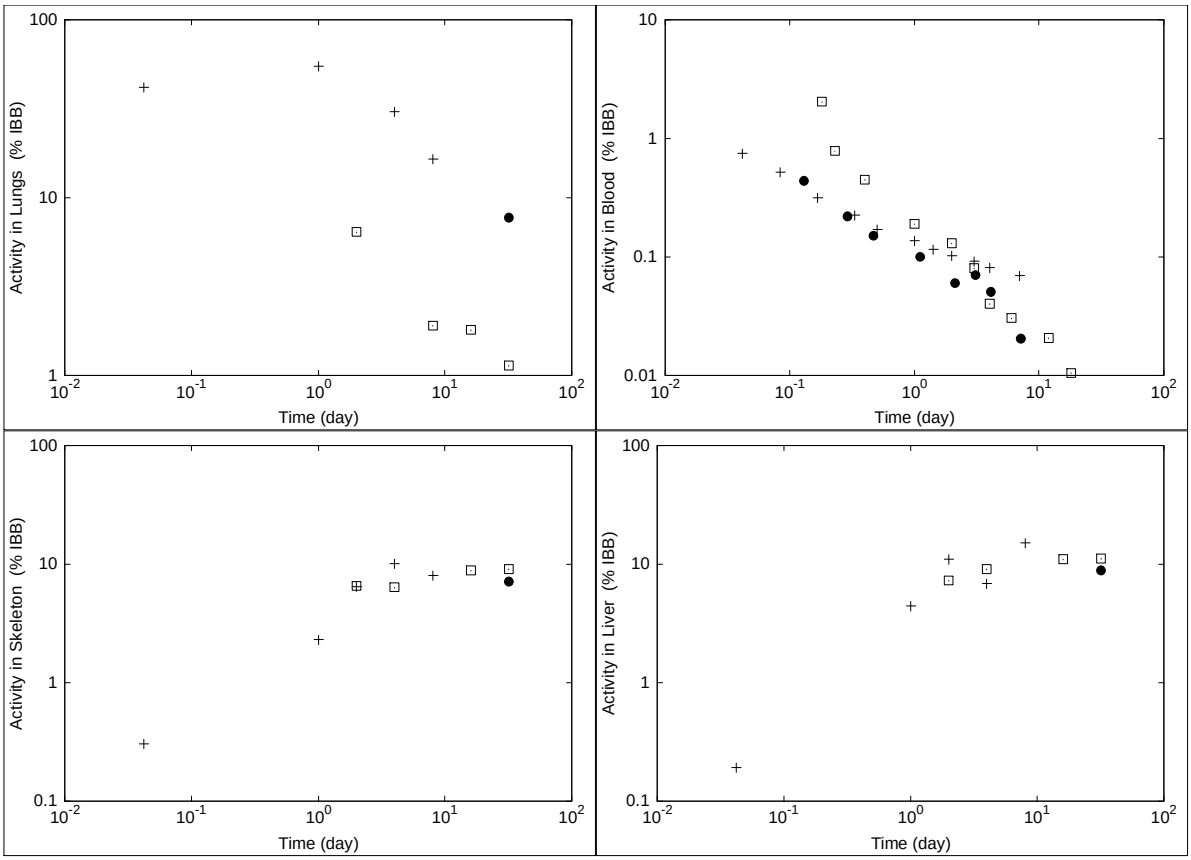


Fig. 2.3. Tissue distribution and retention of lanthanum and cerium (decay-corrected percent of initial body burden, IBB), following inhalation of chlorides by beagle dogs.
Cuddihy et al. (1970) $LaCl_3$ (+); Cuddihy et al. (1975) $CeCl_3$ (●) Cuddihy et al. (1975) $CeCl_3$ in a CsCl vector (□).

(56) It was observed that the ^{140}La concentration in the nasal turbinates was higher at all times than in other tissues, including lung. The authors noted that persistent high local concentrations of other radionuclides in the nasal turbinates had been observed following inhalation (see e.g. cerium section). Benjamin et al. (1979) noted long-term retention of ^{144}Ce and ^{91}Y but not of ^{90}Sr in the nasal cavity following inhalation of the chlorides by dogs.

Lanthanum and cerium chlorides inhaled by monkeys

(57) Ducousso and Pasquier (1974) investigated the rapid phase of absorption of ^{140}La inhaled by monkeys as $^{140}LaCl_3$ in a vector of NaCl in 0.1N HCl solution (pH 1). The fraction absorbed in 1 hour decreased with increasing mass deposited, from ~6% ILD at 0.2 µg to ~3% ILD at 9 µg. (However, it was noted that the absolute mass absorbed increased.) By 4 hours the fraction absorbed at the highest mass increased to ~6% ILD. Measurements were also made under the same conditions with ^{144}Ce inhaled as $^{144}CeCl_3$ in a vector of NaCl in 0.1N HCl solution. Broadly similar results were obtained for ^{144}Ce as for ^{140}La.

(58) Pasquier (1973) also provided evidence for binding of lanthanum in the alveolar region, as is assumed here for cerium.

Lanthanum, gadolinium and yttrium chlorides intratracheally instilled into rats

(59) Suzuki et al. (1992), Yoneda et al. (1995) and Hirano et al. (1990) followed the biokinetics of lanthanum, gadolinium, and yttrium for 168 d, 174 d and 162 d following intratracheal instillation of stable chlorides (10–100 µg) into rats. The lanthanum, gadolinium and yttrium were retained in the lungs with half-times of ~244 d, 136 d and 170 d, respectively. In all three cases the clearance was considerably slower than observed in radiotracer studies, and considerably slower than would be expected for insoluble particles in rats (ICRP, 2002), suggesting that there was considerable binding to lung structures.

2.2.1.2. Long-term lung retention following occupational exposure to rare earths

(60) Stable 'rare earth' elements have had a number of industrial applications which have resulted in worker inhalation exposures. Cerium (containing other rare earths) has been widely used in lens polishing. The electrodes of some carbon arc lamps contained a cerium fluoride core to enhance their brightness. As the electrodes burned, dust containing cerium and other rare earths was inhaled by the lamp operators, such as cinema projectionists and photo-engravers. Studies have been conducted to investigate the lung retention of rare earths and their possible role in lung disease. Table 2.3 summarises information from analyses of lung tissues and/or lung lavage fluid of exposed workers, typically many years after exposure. The table records which elements were measured at concentrations well above the range observed in subjects who were not occupationally exposed. This depends not only on their persistence in the lungs, but also on the relative concentrations in the inhaled material and the method of analysis. Insufficient information is available from such studies to assess absorption parameter values, nor is the chemical form inhaled known, but the presence of lanthanides in the lungs years after exposure indicates Type M or S behaviour.

Table 2.3. Lanthanides measured in human lung tissue or lavage fluid following occupational exposure (concentration higher than in range observed in non-occupationally observed subjects indicated by ✓).

Element								Reference
La	Ce	Nd	Sm	Eu	Tb	Yb	Lu	
✓	✓	✓	✓	✓	✓	✓	✓	Sabbioni et al. (1982)
✓	✓	✓	✓	✓	✓	✓	✓	Vocaturo et al. (1983)
✓	✓	✓	✓		✓	✓	✓	Sulotto et al. (1986)
✓	✓	✓						Waring and Watling (1990)
	✓							Pairon et al. (1994)
✓	✓							McDonald et al. (1995)
✓	✓	✓	✓		✓	✓		Porru et al. (2000)

2.2.1.3. Environmental exposure to lanthanides

(61) Zhu et al. (2010) reported measured concentrations of 60 elements in 18 major organ or tissue samples collected from autopsies of 68 adult men (20–60 years old) from four regions of China. The results include concentrations in lung for all the lanthanides except promethium, which has no stable isotopes. (Concentrations of europium were measured with a less sensitive technique than that used for the other elements, and are not strictly comparable.) Leggett et al. (2014) compared the concentrations of lanthanides (relative to that of lanthanum) in the various

tissues with their concentrations in "soil" (based on measurements in crustal rock etc.) to investigate whether transfer through the environment to tissues was similar across the lanthanides. They noted that concentrations in lung were higher than in other soft tissues, and assessed that most of the material in lungs resulted from retention of inhaled particles (presumably dust derived from rocks and soil), rather than systemic material. The concentration (relative to that of lanthanum) in lungs followed a pattern broadly similar to that in soil: an exponential decrease with increasing atomic number (Z), with the lanthanides having even numbered values of Z being more abundant than those with odd numbered Z. This suggests broadly similar behaviour of the lanthanides in terms of air concentrations, lung deposition, and lung retention. The decrease in relative concentration with increasing Z is somewhat faster in the lungs than in soils. However, this might reflect either the lanthanide profile in the inhaled material, or an increase in the rate of dissolution in the lungs with increasing Z.

Absorption Types and parameter values

Rapid dissolution rate for lanthanides

(62) By analogy with cerium, a value of 1 d^{-1} is applied here to all Type F forms of all lanthanides. Because it is lower than the general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S forms of all lanthanides.

Extent of binding of lanthanides to the respiratory tract

(63) By analogy with cerium, a bound fraction with f_b = 0.07 and a rate of uptake s_b = 0.02 d^{-1}, applied in the ET_2 and AI regions (but not in the BB and bb regions), is adopted here for all lanthanides.

(64) Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides are given in Table 2.4. As noted above, the bound fraction parameter values and rapid dissolution rates derived for cerium are applied to the other lanthanides. Table 2.4 is therefore based on the table of absorption parameter values for inhaled and ingested cerium (Table 4.2.).

(65) As described above, in most cases where comparisons could be made between the biokinetics of different lanthanides deposited in the respiratory tract under similar conditions, similar behaviour was observed. Therefore the material specific parameter values chosen for water-soluble forms of cerium are assumed here to apply to other lanthanides. Material-specific parameter values for dioxides based on cerium dioxide are also included, but oxides forms other than dioxide, are by default assigned to Type M.

For most elements (including cerium), under the heading 'Default parameter values', the corresponding table includes a list of materials for which there is *in vivo* information which is sufficient to assign the chemical form to a default absorption Type, but specific parameter values for that form are not adopted. This could be because there is insufficient information to derive parameter values, or for another reason, for example, exposure to it is unlikely. For the lanthanides, these materials are instead listed in Table 2.5.

Table 2.4. Absorption parameter values for inhaled and ingested lanthanides.

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A[b]
Specific parameter values[c]					
Water soluble forms, including chloride and citrate[d]		0.5	1	0.0015	3×10^{-4}
Dioxide		0.001	1	0.001	5×10^{-7}
Default parameter values[d,e]					
Absorption Type	Assigned forms				
F	— NB: Type F should not be assumed without evidence	1	1	–	5×10^{-4}
M[e]		0.2	1	0.005	1×10^{-4}
S	Irradiated fuel fragments	0.01	1	1×10^{-4}	5×10^{-6}
Ingested material[f]					
All compounds					5×10^{-4}

a It is assumed that for all lanthanides a bound fraction $f_b = 0.07$ with an uptake rate $s_b = 0.02\ d^{-1}$ is applied to material in the ET and AI regions, and associated lymph nodes LN_{ET} and LN_{TH}. It is assumed that $f_b = 0.0$ for material deposited in the BB and bb regions. The values of s_r for Type F, M and S forms of all lanthanides ($1\ d^{-1}$) are element-specific.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the (rounded) product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms the lanthanide (5×10^{-4} in all cases).

c See text of cerium section for summary of information on which parameter values are based, and on ranges of parameter values observed in different studies. For both water soluble forms, and dioxide, specific parameter values are used for dissolution in the lungs, but a default value of f_A (footnote b). Note that oxides forms of lanthanides other than cerium will probably not be dioxides, and so will be assigned to Type M.

d Materials are listed in Table 4 where there is sufficient information in the individual element section to assign to a default absorption Type. If specific parameter values are derived, they are not adopted here.

e Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

f Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A ($=5 \times 10^{-4}$) for ingestion of the radionuclide.

Table 2.5. Summary of information from *in vivo* studies to enable assignment of chemical forms to default absorption Types[a].

Element	Type F	Type M	Type S
La	La-DTPA	Chloride	
Ce		Chloride, citrate, fluoride, hydroxide	Irradiated fuel fragments
Pr		Chloride	
Pm		Chloride, oxide (Pm_2O_3)	
Sm		Chloride, oxide (Sm_2O_3)	
Eu		Nitrate, oxide (Eu_2O_3)	
Gd	Chloride, citrate	Oxide (Gd_2O_3)	
Tb		Oxide (Tb_4O_7)	
Tm		Oxide (Tm_2O_3)	

a See text of individual element section.

2.2.2. Ingestion

(66) Lanthanides in solution exhibit a strong tendency to hydrolyse and to form insoluble species, poorly available for intestinal absorption (Harrison, 1995).

(67) Durbin et al. (1956) investigated the biokinetics of lanthanide tracers in rats, including GI uptake of ^{144}Ce, ^{152,154}Eu, ^{160}Tb and ^{170}Tm administered intragastrically in citrate solution. Estimated fractional absorption was below $1x10^{-3}$ in all cases.

(68) Moskalev et al. (1972) summarised results of their extensive studies of the biological behaviour of radio-lanthanides (^{140}La, ^{144}Ce, ^{143}Pr, ^{147}Pm, ^{152}Eu, ^{153}Gd, ^{160,161}Tb, and ^{169}Yb) in rats, including fractional uptake from the GI tract following intragastric administration. Preparations were administered in hydrochloride, nitrate, or citrate solutions with a pH of 3.0-6.0. The investigators concluded that GI uptake of lanthanides does not exceed 5×10^{-4}.

(69) Results of other, smaller-scale studies of GI uptake of the lanthanides are reasonably consistent with the above findings for rats (Table 2.6). Estimated f_A values for La tracers were $\sim 2 \times 10^{-3}$ for administration as chloride to dogs (Cuddihy and Boecker, 1970), $< 7 \times 10^{-6}$ for administration as carbonate to dogs (Damment and Gill, 2003); and $\sim 10^{-5}$ for administration as carbonate to human subjects (Pennick et al., 2006). The estimated f_A was $<10^{-4}$ for ^{144}Ce ingested as chloride and ^{147}Pm ingested as perchlorate by miniature swine (McClellan et al., 1965). In goats, urinary ^{144}Ce and ^{147}Pm represented an estimated 0.3% and 0.08%, respectively, of the orally administered amounts over the first 7-9 d, and activity in urine was undetectable thereafter (Ekman and Åberg, 1961). In a dual stable isotope study of GI uptake of Nd in four men and four women, the estimated f_A values for individual subjects ranged from $<1.4 \times 10^{-4}$ to 3.6×10^{-3} (McAughey, 1996). The estimated mean f_A for Pm was 10^{-5} for ingestion of ^{143}Pm as chloride by adult male human subjects (Palmer et al., 1970) and 7×10^{-5} for intragastric administration of ^{147}Pm as chloride to rats (Sullivan et al., 1984). f_A for Sm was extremely low following its administration as nitrate or oxide to rats (Bruce et al., 1963) or chloride to human subjects (Fairweather et al., 1997). The estimated f_A for ^{153}Gd administered to rats as the chloride in a wide range of masses (2×10^{-2} µg to 4×10^{-2} g) was in the range 7.6×10^{-5} to 2.0×10^{-4} (Ramounet et al., 2000). The estimated f_A for Eu administered as chloride to rats was in the range 2×10^{-4} to 3×10^{-3} (Berke, 1970).

(70) In *Publication 30*, Part 3 (ICRP, 1981), a reference GI absorption fraction of 3×10^{-4} was recommended for all compounds of lanthanides. In *Publication 68* (ICRP, 1994b), a value of 5×10^{-4} was adopted by analogy with trivalent actinides. The f_A value 5×10^{-4} is adopted here for all lanthanides as a reasonably representative value based on experimental results.

Table 2.6. Fractional absorption f_A of lanthanides.

Lanthanides (Ln)	In vivo f_A	ICRP recommendations
Lanthanum (La)	$< 7 \times 10^{-6}$ to 2×10^{-3}	5×10^{-4}
Cerium (Ce)	$< 10^{-3}$	
Praseodymium (Pr)	$< 5 \times 10^{-4}$	
Neodymium (Nd)	$< 1.4 \times 10^{-4}$ to 3.6×10^{-3}	
Promethium (Pm)	10^{-5} to $< 5 \times 10^{-4}$	
Samarium (Sm)	/	
Europium (Eu)	7.8×10^{-5} to 1.6×10^{-2}	
Gadolinium (Gd)	7.6×10^{-5} to 2.0×10^{-4}	
Terbium (Tb)	$< 5 \times 10^{-4}$ to $<10^{-3}$	
Dysprosium (Dy) to Lutetium (Lu)		

	< 5 x 10^{-4} to < 10^{-3}	

2.2.3. Systemic distribution, retention and excretion of lanthanide elements

2.2.3.1. A regular distribution pattern for lanthanides observed in rat studies

(71) Durbin (1960, 1962, 1973) compared the behavior of trivalent lanthanide elements in rats following their intramuscular administration. The main sites of deposition of all lanthanides were the liver and skeleton. The initial division between liver and skeleton and the early excretion pattern appeared to be related to the ionic radius, which for the lanthanide family declines monotonically with increasing atomic number (Table 2.7). For elements with ionic radii between 92 pm and 106 pm, a decrease in ionic radius was associated overall with a decrease in uptake by liver, an increase in uptake by bone, and an increase in the early urinary excretion rate (Table 2.7. and Fig. 2.4). Little difference in the distribution or excretion through 4 d was seen for lanthanide elements with ionic radius of 92 pm or less (Tb, Dy, Ho, Er, Tm, Yb, and Lu): the content of bone and liver ranged from 58–68% and 1–7%, respectively, and cumulative urinary excretion was 16–27% of the injected amount. Elements that deposited primarily in the liver were eventually excreted largely in faeces.

Table 2.7. Distribution of trivalent lanthanide elements in rats 4 d post administration, as a function of ionic radius and atomic number.

Element	Ionic radius (pm)	Atomic number	% injected activity				
			Bone	Liver	Other tissues	Faeces	Urine
Lanthanum	106	57	18	65	11	3	3
Cerium	103	58	28	51	6	9	6
Praesodymium	101	59	27	48	9	9	7
Neodymium	100	60	31	27	10	10	22
Promethium	98	61	36	41	7	6	10
Samarium	96	62	33	35	6	13	13
Europium	95	63	36	25	11	11	17
Gadolinium	94	64	41	12	10	10	27
Terbium	92	65	60	7	10	7	16
Dysprosium	91	66	60	3	7	6	24
Holmium	89	67	56	2	8	13	21
Erbium	88	68	56	1	9	7	27
Thulium	87	69	64	2	7	5	22
Ytterbium	86	70	58	3	13	7	19
Lutetium	85	71	68	3	4	7	16

Based on data reported by Durbin (1960, 1962, 1973).

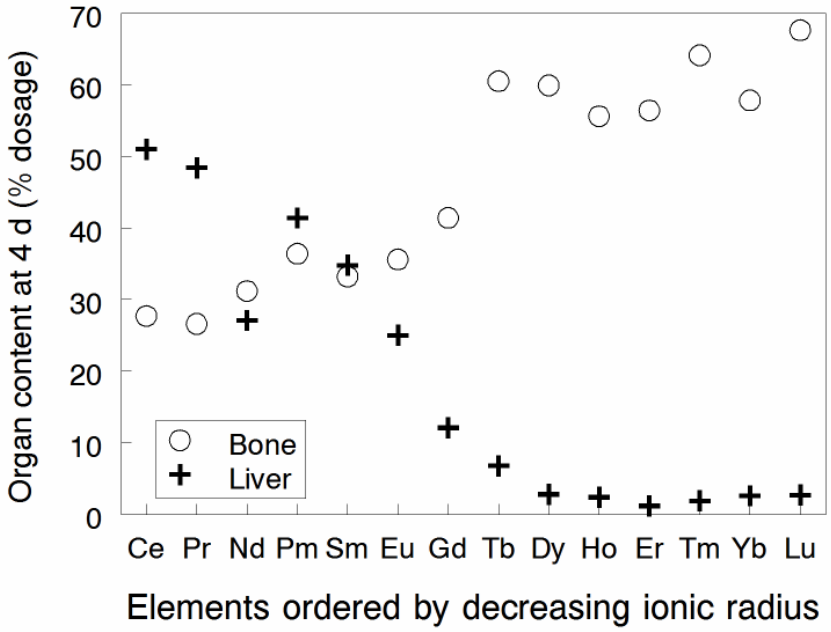
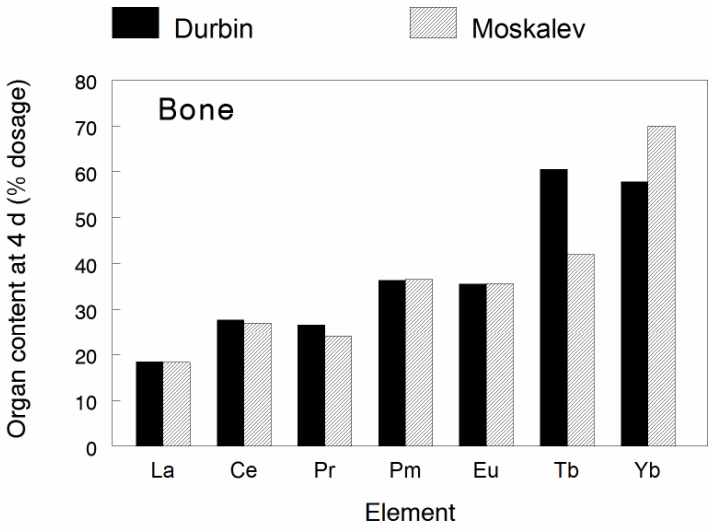


Fig. 2.4. Relation of ionic radius of lanthanide elements and their accumulation in bone and liver of rats following intramuscular injection (based on data of Durbin, 1960).

(72) Moskalev et al. (1974) reached conclusions similar to those of Durbin from their studies of the systemic behavior of the lanthanide elements La, Ce, Pr, Pm, Eu, Gd, Tb, and Yb in rats following intravenous administration (Fig. 2.5.) but described their results in terms of increasing atomic weight rather than decreasing ionic radius. They found that the lighter lanthanides La, Ce, Pr accumulated mainly in the liver (~70%) and to some extent in the skeleton (~20%); the relatively heavy lanthanides Tb and Yb accumulated mainly in the skeleton (~80%) and to some extent in the liver (<20%); and the elements Pm, Eu, and Gd with intermediate atomic weight occupied intermediate places in this scheme. Elimination of the lanthanide elements in urine and faeces also was found to depend on atomic weight. The light elements La, Ce, Pr were excreted primarily in faeces, and only a few percent was excreted in urine over the observation period. With increasing atomic number the percentage eliminated in faeces decreased proportionally to the decline in accumulation in the liver. A change in pH of solutions and presence of carriers had a substantial effect on the distribution of lanthanides due to differences in uptake by the reticuloendothial system.



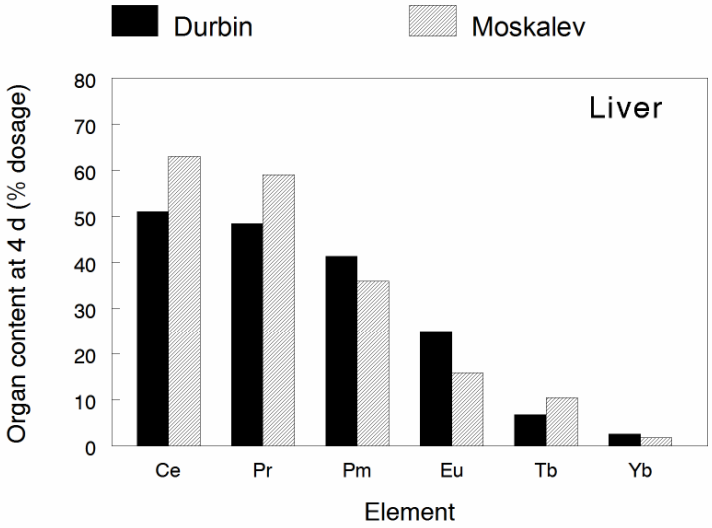


Fig. 2.5. Comparison of contents of lanthanide elements in bone and liver of rats 4 d after intramuscular or intravenous administration, as determined by Moskalev et al. (1974) and Durbin (1960).

(73) Findings of Ando et al. (1989) regarding the early systemic behavior of the lanthanide elements Ce, Sm, Gd, Tb, Tm, Yb, and Lu in rats support Durbin's conclusions that bone and liver are the dominant deposition sites for the lanthanides and that the deposition in bone tends to increase and deposition in liver tends to decrease with decreasing ionic radius (Fig. 2.6.). The data of Ando and coworkers, which were reported as activity concentrations rather than tissue contents, are normalised in Fig. 2.6. to tissue contents determined by Durbin for terbium.

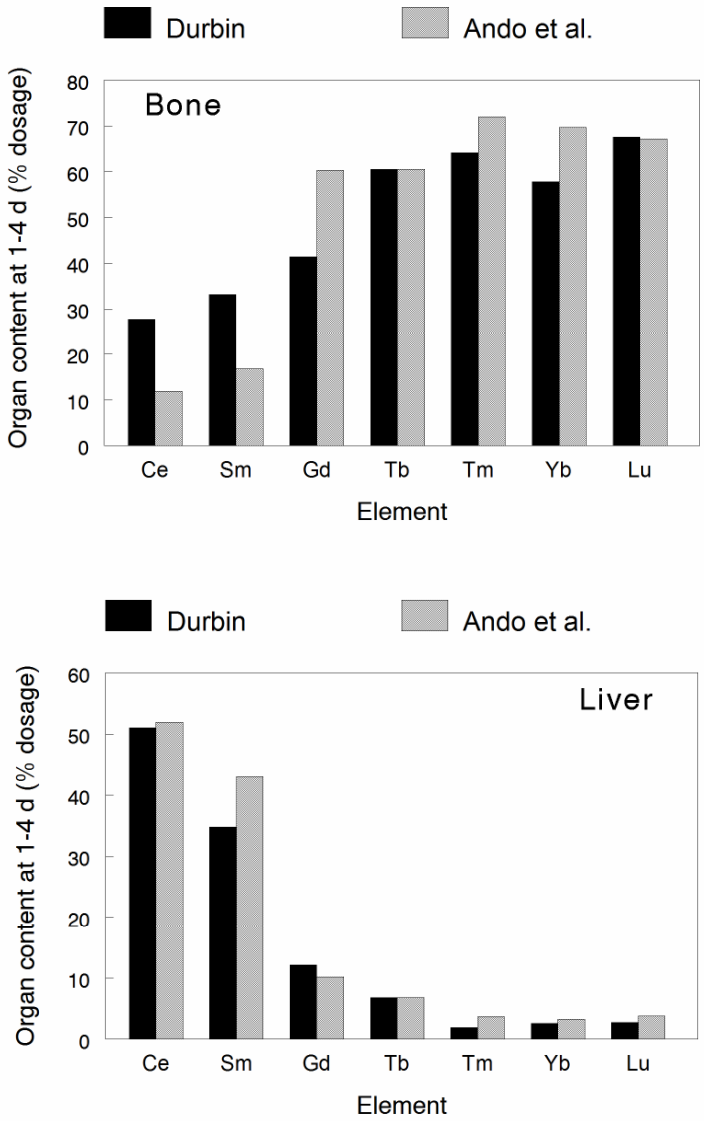


Fig. 2.6. Comparison of relative contents of lanthanide elements in bone and liver of rats at early times after administration, as determined by Ando et al. (1989) and Durbin (1960).
Tissue activity concentrations determined by Ando et al. were normalised to the organ contents of terbium at 4 d as determined by Durbin.

(74) Data on uptake of lanthanide elements in tissues other than liver and bone do not reveal any trends in the systemic behavior. For example, data reported by Ando et al. (1989) for early times after injection indicate that the relative concentrations of Ce, Sm, Gd, Tb, Tm, Yb and Lu ranged from 0.02–0.05 in blood, 1.2–2.8 in kidneys, 0.02–0.07 in skeletal muscle, and 0.2–0.8 in the spleen, with no indication of uptake being related to the ionic radius of the elements.

2.2.3.2. Systemic biokinetic models for the lanthanide elements

(75) A largely generic systemic biokinetic model for the lanthanide elements proposed by Taylor and Leggett (2003) is used in this report. The generic (element-independent) features of the model include the model structure and most but not all transfer coefficients between compartments. Transfer coefficients that are assumed to vary to some extent across the lanthanide elements include those describing transfer from blood to liver, blood to bone, blood to excretion pathways, exchange between blood and one of three compartments of other soft tissues, and the removal half-time from liver to blood.

(76) The model structure is shown in Fig. 2.7. This is a generic structure introduced in ICRP *Publication 67* (1993) and applied in the present report series to a number of elements that accumulate largely in the liver and on bone surfaces including most actinide elements.

On the basis of the apparently gradual change in the distribution and excretion of the lanthanides with decreasing ionic radius and a recognition of the uncertainty in interspecies extrapolation of the available biokinetic data, Taylor and Leggett divided the lanthanide elements into five sets of neighboring or individual elements for the purpose of assigning set-specific parameter values: (1) La, Ce, and Nd; (2) Nd, Pm, and Sm; (3) Eu; (4) Gd; (5) Tb, Dy, Ho, Eu, Tm, Yb, Lu. In the development of either generic or set-specific parameter values, preference was given to data on human subjects, dogs, and swine when available. Because biokinetic data for human subjects or laboratory animals other than rodents are sparse or absent for some lanthanide elements, the development of some generic or set-specific parameter values also relied on the assumption that the general trends in the initial distribution and urinary excretion of the lanthanides observed in rats also hold for man. In contrast to data for rats, human studies of the biokinetics of Pm and Gd in human subjects indicate relatively slow removal loss from the liver. Based on these human data as well as analogy with actinide elements, it was assumed that the lanthanide elements are tenaciously retained in the liver. The model for update and removal by other soft tissues is based on collective data on the lanthanides in laboratory animals, and analogy with the actinide elements. The model for uptake and removal by the gonads is based on analogy with the actinide elements.

(77) For all lanthanide elements, half of the skeletal deposit is assigned to trabecular surfaces and half to cortical surfaces. The subsequent behavior of skeletal deposits is then described by the generic bone model for bone-surface-seeking radionuclides. That is, activity is removed from bone surfaces at a rate proportional to the bone turnover rate. Part of the activity removed from bone surfaces is buried in bone volume and part deposits in bone marrow. Activity is removed from bone volume at the rate of bone remodeling and deposited in bone marrow. The removal half-time from bone marrow to blood is assumed to be 0.25 y by analogy with plutonium.

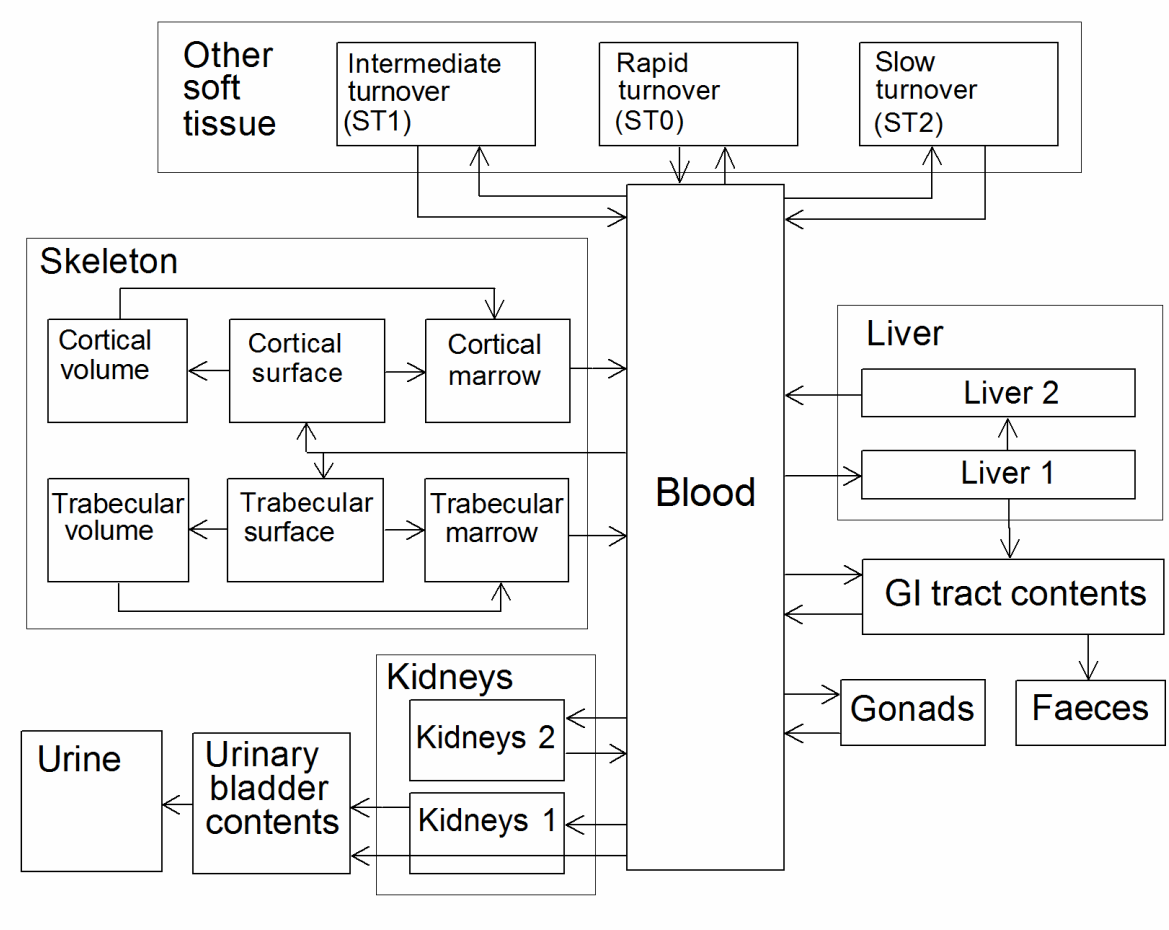


Fig. 2.7. Structure of the systemic biokinetic models for the lanthanide elements.

(78) Transfer coefficients from blood to other compartments generally are derived from a generic removal half-time from blood, together with deposition fractions for those compartments. The removal half-time from blood is assumed to be 30 min for each of the lanthanide elements. The corresponding transfer coefficient is 33.27 d^{-1}. Of activity leaving blood, 30% is assigned to a rapid-turnover soft-tissue compartment called ST0, which is assumed to be part of the circulation. Thus, the deposition fractions are relative to the remaining 70% of outflow from blood, 23.29 d^{-1} (= 0.7 x 33.27 d^{-1}). For example, if the deposition fraction for cortical bone surface is 0.2, the transfer coefficient from blood to cortical bone surface is 0.2 x 23.29 d^{-1} or 4.658 d^{-1}.

(79) The following parameter values are generic, i.e., they are applied to all lanthanide elements:

- Percentage of outflow from blood going to rapid-turnover soft tissue (ST0): 30%
- Deposition fractions for:
  a. Kidneys 1: 1.5%
  b. Kidneys 2: 0.5%
  c. ST2 (soft tissues with tenacious retention): 2%
  d. Testes: 0.035%
  e. Ovaries: 0.011%
- Removal half-time from:

a. Blood (to all destinations): 0.5 h
b. ST0 (to blood): 0.5 d
c. ST2 (to blood): 15 y
d. Kidneys 1 (to urinary bladder contents): 7 d
e. Kidneys 2 (to blood): 500 d
f. Liver 1 (to SI content + Liver 2): 30 d
g. Bone marrow compartments to blood: 0.25 y
h. Gonads to blood: 5 y

- Fractional transfer from:
  a. Liver 1 to SI content: 0.84 y^{-1} (10% of outflow from Liver 1)
  b. Liver 1 to Liver 2: 7.59 y^{-1} (90% of outflow from Liver 1)
  c. Trabecular surface to trabecular volume, 0.09 y^{-1}
  d. Cortical surface to cortical volume, 0.015 y^{-1}
  e. Trabecular surface to trabecular marrow, 0.18 y^{-1}
  f. Cortical surface to cortical marrow, 0.03 y^{-1}
  g. Trabecular volume to trabecular marrow, 0.18 y^{-1}
  h. Cortical volume to cortical marrow, 0.03 y^{-1}
  i. Trabecular or cortical marrow to blood, 2.77 y^{-1}

(80) Element- or set-specific parameter values for the lanthanide elements are listed in Table 2.8 (See sections on individual elements).

Table 2.8. Non-generic parameter values for the lanthanide elements.

Parameter value	La to Nd	Pm, Sm	Eu	Gd	Tb to Lu
Deposition fraction					
Liver 1 (0.9) + Biliary path (0.1)	0.50	0.45	0.25	0.15	0.05
Bone surface	0.30	0.35	0.35	0.45	0.55
Urinary bladder contents	0.02	0.07	0.2	0.2	0.2
Right colon contents	0.06	0.01	0.01	0.01	0.01
Soft tissues (ST1)	0.07954	0.07954	0.14954	0.14954	0.14954
$T_{1/2}$, ST1 to Blood	1 y	1 y	100 d	100 d	100 d
$T_{1/2}$, Liver 2 to Blood	2 y	2 y	1 y	1 y	1 y

Table 2.9. Transfer coefficients for the lanthanide elements (see sections on individual element).

Path[a]		Transfer coefficient (d^{-1})				
From	To	La, Ce, Pr	Nd, Pm, Sm	Eu	Gd	Tb, Dy, Ho, Er, Tm, Yb, Lu
Blood	Liver 1	11.6	10.5	5.82	3.49	11.6
Blood	Trab surf	3.49	4.08	4.08	5.24	6.41
Blood	Cort surf	3.49	4.08	4.08	5.24	6.41
Blood	Kidneys 1	0.349	0.349	0.349	0.349	0.349
Blood	Kidneys 2	0.117	0.117	0.117	0.117	0.117
Blood	UB cont	0.466	1.63	4.66	4.66	4.66
Blood	RC cont	1.4	0.233	0.233	0.233	0.233
Blood	Testes	0.00815	0.00815	0.00815	0.00815	0.00815
Blood	Ovaries	0.00256	0.00256	0.00256	0.00256	0.00256
Blood	ST0	9.98	9.98	9.98	9.98	9.98
Blood	ST1	1.85	1.85	3.48	3.48	3.48
Blood	ST2	0.466	0.466	0.466	0.466	0.466
Liver 1	SI cont	0.00231	0.00231	0.00231	0.00231	0.00231
Liver 1	Liver 2	0.0208	0.0208	0.0208	0.0208	0.0208
Liver 2	Blood	0.00095	0.00095	0.0019	0.0019	0.0019
Trab surf	Trab mar	0.000493	0.000493	0.000493	0.000493	0.000493
Trab surf	Trab vol	0.000247	0.000247	0.000247	0.000247	0.000247
Trab vol	Trab mar	0.000493	0.000493	0.000493	0.000493	0.000493
Trab mar	Blood	0.0076	0.0076	0.0076	0.0076	0.0076
Cort surf	Cort mar	0.0000821	0.0000821	0.0000821	0.0000821	0.0000821
Cort surf	Cort vol	0.0000411	0.0000411	0.0000411	0.0000411	0.0000411
Cort vol	Cort mar	0.0000821	0.0000821	0.0000821	0.0000821	0.0000821
Cort mar	Blood	0.0076	0.0076	0.0076	0.0076	0.0076
Kidneys 1	UB cont	0.099	0.099	0.099	0.099	0.099
Kidneys 2	Blood	0.00139	0.00139	0.00139	0.00139	0.00139
Testes	Blood	0.00038	0.00038	0.00038	0.00038	0.00038
Ovaries	Blood	0.00038	0.00038	0.00038	0.00038	0.00038
ST0	Blood	1.39	1.39	1.39	1.39	1.39
ST1	Blood	0.0019	0.0019	0.00693	0.00693	0.00693
ST2	Blood	0.000128	0.000128	0.000128	0.000128	0.000128

[a]Trab = trabecular; Cort = cortical; surf = surface; vol = volume; mar = marrow; UB = urinary bladder; RC = right colon; cont = content; ST0, ST1, ST2 are compartments of Other soft tissues with fast, intermediate, and slow turnover, respectively.

2.2.3.3. Treatment of radioactive progeny

(81) Chain members addressed in the derivation of dose coefficients for radioisotopes of lanthanide elements are also lanthanides, except that caesium and barium isotopes appear in a few lanthanum or cerium chains. A radioactive progeny produced in a systemic compartment following intake of a lanthanide is assumed to follow the characteristic model of the progeny from its time of production, insofar as this assumption is unambiguous. This assumption is always straightforward if the progeny is a lanthanide because the characteristic models for all lanthanides were developed within a common model structure, so that the site of production of a lanthanide progeny is always identifiable in the progeny's systemic model. Because the

structures of the characteristic models for caesium and barium differ from that of the lanthanides, however, caesium or barium may be produced by radioactive decay at systemic sites not identifiable with the model structures for these two elements. In such cases caesium or barium is assumed to transfer to the central blood compartment of its characteristic model at the rate 1000 d^{-1} if produced in a soft tissue compartment or bone surface compartment and at the rate of bone turnover if produced in a bone volume compartment. The subsequent behavior of caesium or barium is assumed to be described by its characteristic model.

REFERENCES

Anderegg, G., 1982. Critical survey of stability constants of NTA complexes. Pure & Appl. Chem. 54, 2693–2758.

Anderegg, G., 2005. Critical evaluation of stability constants of metal complexes of complexones for biomedical and environmental applications. Pure & Appl. Chem. 77, 1445–1495.

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Bailey, M.R., Hodgson, A., Smith, H., 1985. Respiratory tract retention of relatively insoluble particles in rodents. J. Aerosol Sci. 16, 279–293.

Benjamin S. A., Boecker B. B., Cuddihy R. G., McClellan R. O., 1979. Nasal carcinomas in beagles after inhalation of relatively soluble forms of beta emitting radionuclides. J. Natl. Cancer Inst. 63, 133–139.

Berke, H. L., 1968. The metabolism of the rare earths. 1. The distribution and excretion of intravenous $^{152\text{-}154}$Europium in the rat. Health Phys. 15, 301–312.

Boecker, B. B., Cuddihy, R. G., 1974. Toxicity of 144Ce inhaled as 144CeCl3 by the Beagle: Metabolism and dosimetry. Radiat. Res. 60, 133–154.

Boyd, H.A., Thomas, R. L., 1970. Preparation of aerosols of thulium and americium by thermal degradation. In Fission Product Inhalation Program Annual Report 1969–1970, LF-43, pp. 25–30. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Bruce, D.W., Hietbrink, B.E., Dubois, K.P., 1963. The acute mammalian toxicity of rare earth nitrates and oxides. Toxicol. Appl. Pharmacol. 5, 750–759.

Bünzli, G., Pecharsky, V., 2013. Handbook rare-earth 2013 Volume 43, Pages 2–601.

Charlot, G., 1958. Tables of constants and numerical data. Selected constants: oxydo-reduction potentials. Pergamon press.

Cotton, S., 2006. Lanthanide and actinide chemistry. Inorganic chemistry. Eds John Wiley & Sons, Sussex, England.

Cuddihy, R. G., Becker, B. B., 1970. Kinetics of lanthanum retention and distribution in the beagle dog following administration of $^{140}LaCl_3$ by inhalation, gavages and injection. Health Phys. 19, 419–426.

Cuddihy, R. G., Boecker, B. B., McClellan, R. O., Kanapilly, G. M., 1976. 144Ce in tissues of beagle dogs after inhalation of CeCl3 with special emphasis on endocrine glands and reproductive organs. Health Phys. 30, 53–59.

1199 Cuddihy, R. G., Gomez, S. R., Pfleger, R. C., 1975. Inhalation exposures of beagle dogs to
1200 cerium aerosols: Physical chemical and mathematical analysis. Health Phys. 29, 257–
1201 265.
1202 Damment, S. J. P., Gill, M., 2003. The pharmacokinetics and tissue distribution of lanthanum
1203 carbonate (Fosrenol®), a new non-aluminium, non-calcium phosphate binder. J. Am.
1204 Soc. Nephrol. 14, 204A.
1205 Damment, S. J. P., Pennick, M., 2007. Systemic lanthanum is excreted in the bile of rats.
1206 Diakonov, I.I., Ragnarsdottir, K.V., Tagirov, B.R., 1998. Standard thermodynamic properties
1207 and heat capacities equations of rare earth hydroxides: Ce, Pr, Sm, Eu, Gd, Tb, Dy, Ho,
1208 Er, Tm, Yb, and Y hydroxides. Comparison of thermochemical and solubility data.
1209 Chem. Geol. 151, 327–347.
1210 Ducousso, R., Pasquier, C., 1974. Lung contamination by Ce and La evolution of the early
1211 spontaneous absorption as a function of the initial lung burden. Health Phys. 26, 519-
1212 524.
1213 Durbin, P. W., Williams, M.H., Gee, M., Newman, R. H., Hamilton, J. G., 1956. Metabolism
1214 of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.
1215 Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225–
1216 238.
1217 Durbin, P. W., 1962. Distribution of the transuranic elements in mammals. Health. Phys. 8,
1218 665–671.
1219 Durbin, P. W., 1973. Metabolism and biological effects of the transuranium elements. In:
1220 Uranium, Plutonium and Transplutonic Elements. Eds. H. C. Hodge, J. N. Stannard and
1221 J. B. Hursh. Handbook of Experimental Pharmacology. (Berlin, Springer-Verlag)
1222 pp.739-896.
1223 Ekman, L., Åberg, B., 1961. Excretion of niobium-95, yttrium-91, and promethium-147 in
1224 Goats. Res. Vet. Sci. 2, 100–105.
1225 Evans, C. H., 1983. Interesting and useful biochemical properties of lanthanides. TIBS 445–
1226 449.
1227 Evans, C. H., Drouven, B. J., 1983. The promotion of collagen polymerization by lanthanide
1228 and calcium ions. Biochem J. 213, 751–758.
1229 Ewaldsson, B., Magnusson, G., 1964. Distribution of radiocerium and radiopromethium in
1230 mice. Acta Radiol. Ther. Phys. Biol. 2, 65–72.
1231 Fairweather, S.J., Minihane, AM., Eagles, J., Owen, L., Crews, HM., 1997. Rare earth
1232 elements as nonabsorbable fecal markers in studies of iron absorption. Am. J. Clin.
1233 Nutr. 65, 970–976.
1234 Firshing, F.H., Brune, S.N., 1986. Solubility products of the trivalent rare-earth carbonates. J.
1235 Chem. Eng. Data, 31, 40–42.
1236 Firshing, F.H., Brune, S.N., 1991. Solubility products of the trivalent rare-earth phosphates. J.
1237 Chem. Eng. Data, 36, 93–95.
1238 Gensicke, F., Hölzer, F., Nitschke, HW., 1973. The behaviour of inhaled radiopromethium in
1239 the organism and the effect of hexametaphosphate on the excretion of the nuclide. [Das
1240 Verhalten von inhaliertem Radiopromethium im Organismus und die Wirkung von
1241 hexametaphosphat auf die Ausscheidung des Nuklids.]. Radiobiol. Radiother. 14, 199–
1242 211.
1243 Gensicke, F., Nitschke, HW., 1964. On the problem of radiopraseodymium metabolism after
1244 inhalation. [Zur Frage des Stoffwechsels von Radiopraseodym (143Pr) nach Inhalation
1245 von Flüssigkeitaerosolen bei der weissen Maus.] Strahlentherapie 123, 259–266.

Gensicke, F., Nitschke, HW., 1970. Metabolism of inhaled radiosamarium (153Sm) in mice [Der Stoffwechsel von inhaliertem Radiosamarium bei Mausen.] Radiobiol. Radiother. 11 57–61.

Gensicke, F., Spode, E., 1962. On the problem of the metabolism of inhaled radiocerium (Ce-144 to Pr-144). [Zur Frage der Stoffwechsels von inhalierten Radiocer (Ce-144 bis Pr-144)] Radiobiol. Radiother. 3, 147–151.

Gensicke, F., Nitschke, H.W., 1965. Metabolism of radiopromethium (^{147}Pm) following inhalation of liquid aerosols in mice [Der Stoffwechsel von Radiopromethium (^{147}Pm) nach Inhalation von Flüssigkeitsaerosolen bei Mäusen.] Strahlentherapie, 128, 288–295.

Hahn, F. F., Boecker, B. B., Griffith, W. C., Muggenburg, B. A., 1997. Biological effects of inhaled $^{144}CeCl_3$ in beagle dogs. Radiat. Res. 147, 92–108.

Harrison, JD., 1995. Ingested radionuclides. In: Radiation and Gut. Eds., Potten, C.S. and Hendry J.H. (Oxford, Elsevier). 253-289.

Hirano, S., Kodama, N., Shibata, K., Suzuki, K.T., 1990. Distribution, localization, and pulmonary effects of yttrium chloride following intratracheal instillation in the rat. Toxicol. Appl. Pharmacol. 104, 301–311.

Hölzer, F., Gensicke, F., 1965. Investigations of the microdistribution of inhaled radiopromethium (^{147}Pm) [in German]. Strahlentherapie 128, 396–405.

ICRP, 1979. Limits for intake of radionuclides by workers. ICRP Publication 30, Part 1. Ann. ICRP 2(3/4).

ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6(2/3).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: part 2 ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).

ICRP, 1994. Dose coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. Supporting Guidance 3. Ann. ICRP 32(1/2).

IUPAC, 2005. International Union of Pure and Applied Chemistry Nomenclature. Nomenclature of inorganic chemistry. Connelly, N.G., Hartshorn, R.M., Damhus, T., Hutton, A.T..

Klungness, G.D., Byrne, R.H., 2000. Comparative hydrolysis behavior of the rare earths and yttrium: the influence of temperature and ionic strength. Polyhedron 19, 90–107.

Leggett, R.W., Ansoborlo, E., Bailey, et al., 2014. Biokinetic data and models for occupational intake of lanthanoids. Int. J. Radiat. Biol. 90, 996–1010.

McAughey, JA., 1996. Assessment of internal dose from plutonium and other radionuclides using stable isotope tracer techniques in man. Contract report N° BI3P-CT920048, Commission of the European Communities radiation protection programme 1992–1994.

McClellan, R. O., Bustad, L. K., Keough, R. F., 1965. Metabolism of some SNAP radionuclides in miniature swine. Aerospace Med. 36, 16–20.

McConnon, D., Cole, C. R., 1971. The comparative metabolism of intravenously injected promethium in swine and humans. Health Phys. 21, 61.

McDonald, J. W., Ghio, A. J., Sheehan, C. E., Bernhardt, P. F., Roggli, V. L., 1995. Rare earth (cerium oxide) pneumoconiosis: analytical scanning electron microscopy and literature review. Mod. Patho. 8, 859–865.

Moskalev, Yu. I., 1961. Distribution of lanthanum-140 in the animal organism. In: Raspredelenie biologischeskoe deistvie I migratsiya radioaktivnykh izotopov, (eds.)

Lebedinskii, A. V. and Moskalev, Yu. I. (Translated in Distribution, biological effects and migration of radioactive isotopes. AEC-tr-7512, pp. 45-59).

Moskalev, Yu. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: Biologicheskoye deystviye vneshnikh i vnutrennikh istochnikov radiastsii pp183-190 (eds. Moskalev, Yu. I., and Kalistratova, V. S.). Moscow. Translated in Biological effects of radiation from external and internal sources. AEC-tr-7457 (1974) pp. 278-287.

Moskalev, Yu. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of Distribution in the Organism of Radioactive Isotopes of Lanthanide Elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

Nash, N.L., Madic, C., Mathur, J.N., Lacquement, J., 2006. Actinide separation science and technology. In The chemistry of actinide and transactinides elements. 2622–2798.

NCRP, 1978. Physical, chemical, and biological properties of radiocerium relevant to radiation protection guidelines. NCRP Report No. 60. National Council on Radiation Protection and Measurements, Bethesda, MD.

Newton, D., 2003. Human biokinetics of inhaled terbium oxide. Radiat. Prot. Dosim. 106, 53–61.

Pairon, J. C., Roos. F., Iwatsubo, Y., et al., 1994. Lung retention of cerium in humans. Occup. Environ. Med. 51, 195–199.

Palmer, H. E., Nelson, I. C., Crook, G. H., 1970. The uptake, distribution and excretion of promethium in humans and the effect of DTPA on these parameters. Health Phys. 18, 53–61.

Pasquier, C. 1973. Etude de l'épuration pulmonaire précoce du lanthane 140. Centre d'Etudes Nucléaires de Fontenay-aux-Roses. CEA-R-4431.

Pearson, R.G., 1963. Hard and soft acids and bases. J. Am. Chem. Soc. 85, 3533–3539.

Pennick, M., Dennis, K., Damment, S. J. P., 2006. Absolute bioavailability and disposition of lanthanum in healthy human subjects administered lanthanum carbonate. J. Clin. Pharmacol. 46, 738–746.

Porru, S., Placidi, D., Quarta, C., et al., 2000. The potencial role of rare earths in the pathogenesis of interstitial lung disease: a case report of movie projectionist as investigated by neutron activation analysis. J. Trace Elem. Med. Biol. 14, 232–236.

Priest, N. D., 2007. Comparative biokinetics of trivalent radionuclides with similar ionic dimensions: promethium-147, curium-242 and americium-241. Radiat. Res. 168, 327–331.

Raabe, O. G., Al-Bayati, M. A., Teague, S. V., Rasolt, A., 1988. Regional deposition of inhaled monodisperse coarse and fine aerosol particles in small laboratory animals. In: Inhaled Particles VI, Proceedings of an International Symposium and Workshop on Lung Dosimetry organised by the British Occupational Hygiene Society in Co-operation with the Commission of the European Communities, Cambridge, 2–6 September 1985, (Eds. Dodgson, J., McCallum, R. I., Bailey, M. R., Fisher, D. R.), Pergamon Press, Oxford, United Kingdom, Ann. occup. Hyg., 32 (Suppl. 1), 53–63.

Ramounet, B., Moutairou, K., Renaud-Salis, V., Menetrier, F., Fritsch, P., 2000. Some modifying factors of the absorption and the gastrointestinal retention of ingested lanthanides and actinides. Proceedings IRPA 10, P-3a, 189.

Richmond, C. R., London, J. E., 1966. Long-term *in vivo* retention of cerium-144 by beagles. Nature 211, 1179.

Roth, P., Molho, N., Cantone, M. C., Taylor, D. M., McAughey, J. A., 1997. Assessment of internal dose from plutonium and other radionuclides using stable isotope techniques in man. Final Report EU Contract F13P-CT920048, EUR 16769DE/EN/FR, 605–649.

Sabbioni, E., Pietra, R., Gaglione, P., 1982. Long-term occupational risk of rare-earth pneumoconiosis. A case report as investigated by neutron activation analysis. Sci. Total Environ. 26, 19–34.

Shannon, R. 1976. Revised effective ionic-radii and systematic studies of interatomic distances in halides and chalcogenides. Acta Crystallogr., Sext A 32, 751–767.

Shipler, D. B., Ballou, J. E., Griffin, B. I., Nelson, I. C., 1976. Development of a diagnostic model for inhaled promethium-147 oxide. In: Diagnosis and treatment of incorporated radionuclides. IAEA, Vienna, IAEA-SR-6/28, 209–221.

Shutt, A. L., Etherington, G., 2002. Private communication.

Shutt, A. L., Youngman, M. J., Raine, C., et al., 2001. A study of the human biokinetics of inhaled gadolinium oxide. Ann. Occup. Hyg. 46, Suppl. 1, 320–322.

Shyr, L. J., Griffith, W. C., Boecker B. B., 1991. An optimization strategy for a biokinetic model of inhaled radionuclides. Fundam. Appl. Toxicol. 16, 423–434.

Smith, R.M., Martell, A.E., 1989. Critical stability constants. Plenum Press.

Snipes, M. B., Boecker, B. B., McClellan, R. O.,1983. Retention of monodisperse or polydisperse aluminosilicate particles inhaled by dogs, rats, and mice. Toxicol. Appl. Pharmacol., 69, 345–362.

Spencer, H., 1968. Metabolism and removal of some radioisotopes in man. In: Diagnosis and treatment of deposited radionuclides. Proceedings of a symposium held at Richland, WA, USA, 15-17 May, 1967. Edited by H. A. Kornberg and W. D. Norwood. Excerpta Medica Foundation. 489–520.

Stuart, B. O., 1964. Preliminary studies of inhaled ^{147}Pm perchlorate. Hanford Biologu Research Annual Report for 1963. HW-80500. UC-48, Biology and Medicine (TID-4500, 30th Ed.)

Stuart, B. O., 1967. Inhalation of promethium oxide by beagle dogs. Health Phys. 13, 929.

Stuart, B. O., Gavin, J. C., 1968. Inhalation studies with promethium oxide in beagle dogs. Pacific Northwest Annual Report for 1967, BNWL-714.

Sullivan, M. F., Miller, B. M., Goebel, J. C., 1984. Gastrointestinal absorption of metals (^{51}Cr, ^{65}Zn, ^{95m}Tc, ^{109}Cd, ^{113}Sn, ^{147}Pm, and ^{238}Pu) by rats and swine. Environ. Res. 35, 439–453.

Sulotto, F., Romano, C., Berra, A., et al., 1986. Rare earth pneumoconiosis: a new case. Am. J. Ind. Med. 9, 567–575.

Suzuki, K.T., Kobayashi, E., Ito, Y., Ozawa, H., Suzuki, E., 1992. Localization and health effects of lanthanum chloride instilled intratracheally into rats. Toxicology 76, 141–152.

Taylor, D. M., Leggett, R. W., 1998. A generic biokinetic model for the lanthanide elements. Radiat. Prot. Dosim. 79, 351–354.

Taylor, D. M., Leggett, R. W., 2003. A generic biokinetic model for predicting the behavior of the lanthanide elements in the human body. Radiat. Prot. Dosim. 105, 193–198.

Thomas, R. G., Durbin, P. W., McInroy, J. F., Healy, J. W., 1989. Estimation of human gonadal Pu and Ce concentrations from animal data. Health Phys. 57, Suppl. 1, 97–107.

Vidaud, C,. Bourgeois, D., Meyer, D., 2012. Bone as target organ for metals: the case of f-elements. Chem. Res. Tox. 25, 1161–1175.

Vocaturo, G., Colombo, F., Zanoni, M., et al., 1983. Human exposures to heavy metals: rare earth pneumoconiosis in occupational workers. Chest 83, 780–783.

1386 Waring, P.M., Watling, J., 1990. Rare earth deposits in a deceased movie projectionist. A new
1387 case of rare earth pneumoconiosis? Med. J. Australia 153, 726–730.
1388 Yoneda, S., Emi, N., Fujita, Y., et al., 1995. Effects of gadolinium chloride on the rat lung
1389 following intratracheal instillation. Fundam. Appl. Toxicol. 28, 65–70.
1390 Zalikin, G. A., 1974. Distribution of gadolinium-153 in the rat organism. In: Moskalev, Yu. I.;
1391 Kalistratova, V. S., eds. Biological Effects of Radiation from External and Internal
1392 Sources. AEC-tr-7457, 288–296.
1393 Zalikin, G. A., Tronova, I. N., 1971. Distribution of terbium-160,161 in the body of rats. In:
1394 Moskalev, Yu. I., ed. Radioactive isotopes and the body. AEC-tr-7195.
1395 Zhu, H., Wang, N., Zhang, Y., et al., 2010. Element contents in organs and tissues of Chinese
1396 adult men. Health Phys. 98, 61–71.
1397

3. LANTHANUM (Z = 57)

3.1. Chemical Forms in the Workplace

(82) Lanthanum is the first element of the lanthanide series which occurs mainly in oxidation state III. Lanthanum may be encountered in industry in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, sulphates, carbonates and citrates).

Table 3. 1. Isotopes of lanthanum addressed in this report.

Isotope	Physical half-life	Decay mode
La-129	11.6 m	EC, B+
La-131	59 m	EC, B+
La-132	4.8 h	EC, B+
La-132m	24.3 m	IT, EC, B+
La-133	3.912 h	EC, B+
La-135	19.5 h	EC, B+
La-137	6.0E+4 y	EC
La-138	1.02E+11 y	EC, B-
La-140[a]	1.678 d	B-
La-141	3.92 h	B-
La-142	91.1 m	B-
La-143	14.2 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

3.2. Routes of Intake

3.2.1. Inhalation

Absorption Types and parameter values

(83) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including lanthanum (La) (see general lanthanide section). Information on absorption from the respiratory tract is available from experimental studies of lanthanum, mainly as chloride. However, the behaviour of ionic (soluble) lanthanides following deposition in the respiratory tract is difficult to determine because ionic solutions (e.g. chloride) are unstable at neutral pH and in many biological media, resulting in colloid formation. The radiotracer studies reported were of short duration because they used ^{140}La, which has a half-life of only 1.7 d. Lanthanum-140 is usually encountered as the daughter of the important fission product barium-140 (half-life 12.8 d).

(84) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides.

(85) Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including lanthanum, are given in Table 2.4 of the general lanthanide section.

Lanthanum chloride ($LaCl_3$)

(86) Cuddihy and Boecker (1970) followed the biokinetics of ^{140}La up to 8 d in beagle dogs that inhaled ^{140}La as $^{140}LaCl_3$ in a $LaCl_3$-CsCl vector (6.3 mg $LaCl_3$ and 3.7 mg CsCl per ml, pH not reported). Further details are given by Cuddihy and Griffith (1970). Complementary studies were conducted of $^{140}LaCl_3$ administered by gavage and $^{140}LaCl_3$ or ^{140}La citrate administered by intravenous injection. Cuddihy et al. estimated from the results that fractional absorption from the alimentary tract was ~0.3%. It was observed that following inhalation ~50% of the initial body content of ^{144}La cleared during the first 2 d: this was attributed to clearance of the upper respiratory tract (URT) by mucociliary action and swallowing, suggesting that the rapid dissolution rate was comparatively slow. Nevertheless, Cuddihy and Boecker noted that in dogs killed immediately after exposure ^{140}La was already present in muscle, skeleton and kidney. Activity remaining in lungs over the period of observation (8 d) was retained with a biological half time of ~7 d, cleared mainly by absorption. It was observed that the ^{140}La concentration in the nasal turbinates was higher at all times than in other tissues, including lung. The authors noted that persistent high local concentrations of other radionuclides in the nasal turbinates had been observed following inhalation (see e.g. cerium section). While this suggests the presence of a bound fraction, the authors were not certain whether similar behaviour would occur in man because of differences in nasal structure. A biokinetic model for the retention of ^{140}La was developed (Cuddihy and Boecker, 1970; Cuddihy and Griffith, 1972). Analysis carried out here (i.e. by the Task Group) showed that most of the results could be fit well with absorption parameter values of $f_r = 0.07$, $s_r = 12\ d^{-1}$ and $s_s = 0.10\ d^{-1}$, which would give (by extrapolation) assignment to Type F. However, the relatively high values of s_r and s_s compared to that obtained for cerium inhaled as chloride (0.44 and 0.0015 d^{-1} respectively, see cerium section) could be due to the short duration of the ^{140}La measurements.

(87) Comparison made here with the behaviour of cerium deposited in the respiratory tract under similar conditions indicated that the two elements behaved similarly (see general lanthanide section). Application here of absorption parameter values $f_b = 0.07$; $s_b = 0.021\ d^{-1}$ and $s_s = 0.0015\ d^{-1}$, based on analysis of the cerium experiments, to the $LaCl_3$ data gave $s_r = 0.73\ d^{-1}$ and $f_r = 0.52$, similar to the values for ^{144}Ce in $CeCl_3$, and giving assignment to Type M.

(88) Cuddihy and Griffith (1972) followed the biokinetics of ^{140}La up to 64 d in beagle dogs that inhaled ^{140}Ba and ^{140}La as chlorides in a $BaCl_2$-$LaCl_3$ vector (6.3 mg $LaCl_3$ and 3.7 mg $BaCl_2$ per ml, pH not reported). Although at the time of administration the ^{140}La activity was equal to or greater than that of ^{140}Ba, because of the relatively short physical half-life of ^{140}La (1.7 d), the ^{140}La present was increasingly due to ingrowth from decay of ^{140}Ba. Barium is more readily absorbed from both the respiratory and alimentary tracts than lanthanum. Hence the authors estimated that ^{140}Ba and ^{140}La were essentially in equilibrium in all bone samples obtained at times greater than 4 d after exposure. Nevertheless, the results enabled them to improve the biokinetic model for inhaled lanthanum developed by Cuddihy and Boecker (1970).

(89) Ducousso and Pasquier (1974) investigated the rapid phase of absorption of ^{140}La inhaled by monkeys as $^{140}LaCl_3$ in a vector of NaCl in 0.1N HCl solution (pH 1). Alveolar deposition was maximised by inhaling small particles through an endotracheal tube. An external detector was positioned to measure activity predominantly in the alveolar region. The fraction absorbed (estimated by the decrease in lung activity, assuming that particle transport was negligible) in 1 hour decreased with increasing mass deposited, from ~6% ILD at 0.2 µg to ~3% ILD at 9 µg. (However, it was noted that the absolute mass absorbed increased.) Assuming a single absorption rate, 6% ILD absorbed in 1 hour suggests a value of ~1.5 d^{-1}. Alternatively, assuming this represents a rapid phase of absorption, it suggests values of f_r ~0.1 and s_r >10 d^{-1}. By 4 hours the amount absorbed at the highest mass increased to ~6% ILD. Measurements were also made under the same conditions with ^{144}Ce inhaled as $^{144}CeCl_3$ in a vector of NaCl in 0.1N HCl solution (see general lanthanide inhalation section). Broadly similar results were obtained for ^{144}Ce as for ^{140}La.

(90) Similar experiments (with ILD ~10 µg) had previously been carried by Pasquier (1973), but significant transfer from lungs to blood was observed in only 6 out of 40 experiments. Pasquier (1973) also conducted studies of the physico-chemical state of lanthanum in solution. *In vitro*, at biological pH (7.2-7.4), some hydrolysis and polymerization occurred but >50% of the lanthanum was filterable (presumably monomeric). *In vivo* it was found that lanthanum is rapidly fixed by alveolar lipo-proteins.

(91) Pasquier et al. (1969) studied the effectiveness of inhaled DTPA (diethylenetriamine-pentaacetic acid) on removal of ^{140}La from the lungs following its inhalation as chloride by monkeys.

(92) Suzuki et al. (1992) followed the biokinetics of lanthanum for 168 d following intratracheal instillation of stable lanthanum chloride (50 µg) into rats. The lanthanum was mainly retained in the lung with a biological half-time of 244 d. The clearance was considerably slower than observed in the radiotracer studies described above, and considerably slower than would be expected for insoluble particles in rats (ICRP, 2002), suggesting that there was considerable binding of lanthanum to lung structures. Similar observations were reported for stable yttrium and gadolinium compared to tracer level radionuclides (see general lanthanide section).

(93) Although specific parameter values for lanthanum chloride based on *in vivo* data could be derived, inhalation exposure to it is unlikely. Instead, lanthanum chloride is assigned to water-soluble forms of lanthanides (see general lanthanide section, Table 3).

^{140}La-labelled DTPA

(94) Pasquier et al. (1969) investigated the absorption from the lungs of ^{140}La inhaled by monkeys as ^{140}La-DTPA and measured a half-time of 44 minutes. In complementary experiments ^{140}La-DTPA was intravenously injected: 50% was excreted in urine in ~1 hour, and the rest within a few hours. These results are similar to conclusions from extensive measurements of ^{99m}Tc-DTPA inhaled by human subjects (see DTPA in technetium section in OIR Part 2). In healthy non-smokers, lung retention half-times of ^{99m}Tc were reported to be ~1 hour, and there is evidence that the ^{99m}Tc-DTPA did not dissociate during its movement from lungs to urine. A similar absorption rate was estimated for ^{14}C-DTPA inhaled by healthy volunteers (see carbon section). This suggests that the half-time of 44 minutes measured by Pasquier et al. (1969) is characteristic of DTPA, rather than lanthanum. Although specific parameter values for lanthanum-DTPA based on *in vivo* data could be derived, inhalation

exposure to it is unlikely. Based on its absorption from the lungs, it could be assigned to Type F. However, uptake from the alimentary tract, and systemic biokinetics, are also likely to be determined by DTPA, rather than lanthanum (see DTPA in carbon and technetium sections in OIR Part 2).

Lanthanum oxide

(95) Barnes (1971) studied the distribution within the lungs of ^{140}La oxide formed by heat treatment of chloride at 1150°C, inhaled by dogs. Measurements were only made immediately after inhalation, and therefore absorption parameters cannot be determined, but the material did not dissolve readily in the lungs.

Fused aluminosilicate particles (FAP)

(96) FAP or "fused clay" particles have been extensively used as relatively insoluble particles in inhalation studies, both of biokinetics and of radiation effects (see, e.g. cerium section). Barnes (1971) studied the distribution within the lungs of ^{140}La-labelled FAP, inhaled by dogs. Measurements were only made immediately after inhalation, and therefore absorption parameters cannot be determined, but the material did not dissolve readily in the lungs.

Kaolin

(97) Cohn et al. (1957) reported the tissue distribution of ^{140}La in mice up to 3 d after inhalation of $^{140}LaCl_3$ adsorbed onto kaolin, or administration of a suspension of the particles by gavage. There is insufficient information to estimate parameter values, but absorption from the respiratory tract seems to have been greater than from the alimentary tract.

3.2.2. Ingestion

(98) The fractional absorption of lanthanum in rats was reported to be less than 5×10^{-4} (Hamilton, 1948; Moskalev et al., 1972). However, in experiments on dogs the fractional absorption of lanthanum, ingested as the chloride, from the gastrointestinal tract was found to be about 2×10^{-3} (Cuddihy and Boecker, 1970).

(99) Damnent et al. (2003) and Pennick et al. (2006) have reported low values of the bioavailability of lanthanum administered as an oral dose of carbonate: in dogs the rate of absorption was estimated $< 7 \times 10^{-6}$ (Damnent et al., 2003) and in human around 10^{-5} (Pennick et al., 2006).

(100) In *Publication 30* (ICRP, 1979), an f_1 of 10^{-3} was recommended for all compounds of lanthanum. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

3.2.3. Systemic distribution, retention and excretion of lanthanum

3.2.3.1. Data

(101) After intravenous administration of $^{140}LaCl_3$ to human subjects, urinary excretion ranged from 0.5% to 2% of the dose in 24 h (Spencer, 1968). Faecal excretion accounted for approximately 0.5% of the dose during the first four days.

(102) Following intravenous administration of lanthanum chloride to healthy human subjects, renal clearance amounted to 1.7% of total plasma clearance over the first 7 d (Pennick et al., 2006). Following intravenous administration of lanthanum chloride to rats, 74% of the administered lanthanum was excreted in faeces in 42 days, and <2% was recovered in urine (Damment and Pennick, 2007).

(103) Cuddihy and Boecker (1970) studied the biokinetics of ^{140}La in beagle dogs following administration of $^{140}LaCl_3$ by inhalation, gavage, and intravenous injection. The division of ^{140}La between liver and skeleton depended on the route of administration, with lower relative uptake by liver for inhaled lanthanum than for injected lanthanum. The tissue distribution patterns were greatly influenced by the chemical form administered. The investigators concluded that injection studies involving ^{140}La are of limited value for interpreting the results or predicting the fate of inhaled lanthanum. They developed a biokinetic model for lanthanum as a fit to the inhalation data for dogs. The model assigns 45% of outflow from blood to liver, 32% to skeleton, 3.8% to kidneys, 0.0048% to spleen, 9.6% to urine, and 9.6% to the intestinal contents. The estimated rates of return from tissue compartments to blood are as follows: 0.002 h^{-1} from liver, 0.001 h^{-1} from skeleton, 0.01 h^{-1} from kidneys, and 0.05 h^{-1} from spleen.

(104) In rats, relatively larger concentrations were observed in the kidneys and bones and relatively lower concentrations in the liver after intramuscular or subcutaneous administration than after intravenous administration (Moskalev, 1961).

3.2.3.2. Biokinetic model

(105) The biokinetic model for systemic lanthanum applied in this report is described in Section 2.2.3.2.

3.2.3.3. Treatment of progeny

(106) The treatment of radioactive progeny of lanthanum produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in section 2.2.3.3.

3.3. Individual monitoring

^{140}La

(107) Measurements of ^{140}La concentrations in urine and faeces are performed to determine intakes of the radionuclide for routine monitoring. Measurements of ^{140}La may be performed by *in vivo* whole-body measurement technique. I*n vivo* lung measurement is used as an additional technique for special investigations. The main technique is gamma spectrometry.

Table 3. 2. Monitoring Techniques for ^{140}La.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{140}La	Urine Bioassay	γ-ray spectrometry	6 Bq/L
^{140}La	Faecal Bioassay	γ-ray spectrometry	6 Bq/24h
^{140}La	Lung Measurement[a]	γ-ray spectrometry	320 Bq

^{140}La	Whole-body Measurement[b]	γ-ray spectrometry	60 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) for counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

3.4. Dosimetric data for lanthanum

Dosimetric data will be provided in the final version of the document.

REFERENCES

Barnes, J. E., 1971. Distribution of inhaled radionuclides in the respiratory tract. Health Phys. 21, 227–232.

Cohn, S. H., Lane, W. B., Gong, J. K., Weisbecker, L., Milne, W. L., 1957. Studies on the metabolism of inhaled aerosols of strontium and lanthanum. Research and Development Technical Report USNRDL-TR-175. NM 006-015 and FCDA.

Cuddihy, R. G., Boecker, B. B., 1970. Kinetics of lanthanum retention and distribution in the beagle dog following administration of $^{140}LaCl_3$ by inhalation, gavage and injection. Health Phys. 19, 419–426.

Cuddihy, R. G., Gomez, S. R., Pfleger, R. C., 1975. Inhalation exposures of beagle dogs to cerium aerosols: Physical chemical and mathematical analysis. Health Phys. 29, 257–265.

Cuddihy, R.G., Griffith, W.C., 1970. Application of a biological model of the tissue distribution and retention of inhaled ^{140}La in Beagle dogs to an analysis of radiological hazards to humans inhaling various isotopes of lanthanum. In Fission Product Inhalation Program Annual Report 1969-1970, LF-43. 82–91. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Cuddihy, R.G., Griffith, W.C., 1972. A biological model describing tissue distribution and whole-body retention of barium and lanthanum in beagle dogs after inhalation and gavage. Health Phys. 23, 621–633.

Damment, S. J. P., Pennick, M., 2007. Systemic lanthanum is excreted in the bile of rats.

Damnent, S. J. P., Gill, M., 2003. The pharmacokinetics and tissue distribution of lanthanum carbonate (Fosrenol®), a new non-aluminium, non calcium phosphate binder. J. Am. Soc. Nephrol. 14, 204A.

Ducousso, R., Béréziat, G., Perrault, G., Pasquier, C., 1971. Influence de la charge pulmonaire en lanthane sur l'épuration précoce provoquée par un aerosol de DTPA. Health Phys. 21, 21–29.

Ducousso, R., Pasquier, C., 1974. Lung contamination by Ce and La evolution of the early spontaneous absorption as a function of the initial lung burden. Health Phys. 26, 519–524.

Hamilton, J. G., 1948. The metabolism of the fission products and the heaviest elements. Revs. Mod. Phys. 20, 718–728.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. Supporting Guidance 3. Ann. ICRP 32(1/2).

Moskalev, Yu. I., 1961. Distribution of lanthanum-140 in the animal organism. In: Raspredelenie. Biologischeskoe de&vie i migratsiia radioaktivnykh izotopoq pp. 40-53 (ads. Let&i&ii, A. V. and Moskalev, Yu. I.). Moscow. Translated in Distribution, biological effects and migration of radioactive isotopes, AEC-tr-7512, 45–59.

Moskalev, Yu. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: Biologicheskoye deystviye vneshnikh i vnutrennikh istochnikov r&&ii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

NCRP, 1978. Physical, chemical, and biological properties of radiocerium relevant to radiation protection guidelines. NCRP Report No. 60. National Council on Radiation Protection and Measurements, Bethesda, MD.

Pasquier, C., 1973. Etude de l'épuration pulmonaire précoce du lanthane 140. Centre d'Etudes Nucléaires de Fontenay-aux-Roses. CEA-R-4431.

Pasquier, C., Voisin, D., Thieblemont P., Perrault, G., Bayard, J.-P., 1969. Influence du DTPA en aerosol sur les contaminations pulmonaire au lanthane. Centre d'Etudes Nucléaires de Fontenay-aux-Roses. CEA-R-3735.

Pennick, M., Dennis, K., Damnent, S. J. P., 2006. Absolute bioavailability and disposition of lanthanum in healthy human subjects administered as lanthanum carbonate. J. Clin. Pharmacol. 46, 738–746.

Spencer, H., 1968. Metabolism and removal of some radioisotopes in man. In: Diagnosis and treatment of deposited radionuclides. Proceedings of a symposium held at Richland, WA, USA, 15-17 May, 1967. Edited by H. A. Kornberg and W. D. Norwood. Excerpta Medica Foundation.489–520.

Suzuki, K.T., Kobayashi, E., Ito, Y., Ozawa, H., Suzuki, E., 1992, Localization and health effects of lanthanum chloride instilled intratracheally into rats. Toxicology 76, 141–152.

4. CERIUM (Z = 58)

4.1. Chemical Forms in the Workplace

(108) Cerium is an element of the lanthanide series which occurs mainly in oxidation state III and IV.

(109) Cerium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, sulphates, carbonates and citrates). Cerium is most commonly obtained from bastnäsite and monazite. Cerium isotopes (e.g. ^{144}Ce) are fission products.

Table 4.1 Isotopes of cerium addressed in this report.

Isotope	Physical half-life	Decay mode
Ce-130	22.9 m	EC, B+
Ce-131	10.2 m	EC, B+
Ce-132	3.51 h	EC
Ce-133	97 m	EC, B+
Ce-133m	4.9 h	EC, B+
Ce-134	3.16 d	EC
Ce-135	17.7 h	EC, B+
Ce-137	9.0 h	EC, B+
Ce-137m	34.4 h	IT, EC
Ce-139 [a]	137.641 d	EC
Ce-141 [a]	32.508 d	B-
Ce-143	33.039 h	B-
Ce-144 [a]	284.91 d	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

4.2. Routes of Intake

4.2.1. Inhalation

Absorption Types and parameter values

(110) Studies have been reported of the behaviour of cerium (Ce) radioisotopes in man following accidental inhalation, and of lung retention in man following chronic inhalation exposure to the stable element (see general lanthanide section). Information on absorption from the respiratory tract is available from experimental studies of cerium in various chemical forms, including chloride, citrate, dioxide, irradiated fuel fragments, and in fused aluminosilicate particles (FAP). The behaviour of ionic (soluble) cerium following deposition in the respiratory tract is complex and difficult to quantify because ionic solutions (e.g. chloride) are unstable at neutral pH and in many biological media, resulting in colloid formation (see general lanthanide

section). For example, cerium hydroxide precipitates from nitrate solution at pH 8.1 (NCRP, 1978). Hence in some studies described below chloride was administered in dilute acid. The question of whether cerium deposited in the respiratory tract in relatively soluble forms is retained in particulate and/or bound form has been discussed for about 50 years, and remains unresolved (see section on bound state below). However, because absorption of cerium from the alimentary tract is low, most uptake to blood following intake by inhalation generally originates in the respiratory tract, which simplifies analysis.

(111) A report on the properties of radiocerium relevant to radiation protection, published by the National Council on Radiation Protection and Measurements (NCRP) includes a review of information available at that time on the retention of cerium deposited in the respiratory tract in various chemical forms (NCRP, 1978). The biological effects of irradiation from ^{144}Ce inhaled in both soluble and insoluble forms have been studied extensively: ^{144}Ce was chosen as an important fission product, representative of beta-emitters of intermediate (of order 1 year) half-life. Complementary studies of tissue distribution were conducted, but mainly to enable radiation doses to be determined in the studies of effects. Cerium-144 decays to ^{144}Pr which has a half-life of only 17 minutes. Thus, "^{144}Ce" generally refers to an equilibrium mixture of ^{144}Ce with ^{144}Pr.

(112) Absorption parameter values and Types, and associated f_A values for particulate forms of cerium are given in Table 4.2.

(113) Special consideration is given in this section to the lung clearance characteristics of cerium deposited in the respiratory tract because they are used as a model for other lanthanide elements. As discussed in the general lanthanide section there is relatively little relevant information for other lanthanides, but there are strong similarities in the chemical behaviour of this series of elements. Comparisons are made there between the lung clearance characteristics of different lanthanides deposited in the respiratory tract under similar conditions.

(114) As described below, the parameter values for the rapid dissolution rate and bound fraction assessed from studies in which dogs inhaled ^{144}Ce in a CsCl vector (s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}) were applied in the analysis of the results of other cerium studies. Unless specific data indicated otherwise, s_r, s_b and f_b were fixed at these 'default' values. Thus, in general, only values of f_r and s_s were determined.

Cerium chloride ($CeCl_3$)

(115) In the most comprehensive of several studies of ^{144}Ce inhaled as chloride, Boecker and Cuddihy (1974) followed for 512 d the biokinetics in beagle dogs of carrier-free1 ^{144}Ce inhaled in a caesium chloride (CsCl) vector aerosol, in 0.1N or 1N HCl, (to reduce colloid formation). The experiment was conducted to complement a life-span dose-effects study (Hahn et al., 1997), which also provides some measurements of tissue distribution at times up to 1600 d (Boecker et al., 1970a). Cuddihy et al. (1975, 1976) made additional measurements (including earlier times and more tissues) in dogs that inhaled similar aerosols. The results of these experiments are discussed here first because they were considered to provide the best available information on which to estimate the rapid dissolution rate and bound state parameter values for cerium. As well as being the most comprehensive studies in terms of duration: with both early

1 No stable cerium was added during the separation process.

and late measurements, and conducted in large animals, the use of carrier-free ^{144}Ce in a CsCl vector was considered to represent best the behaviour of soluble cerium at tracer level.

(116) It was observed that ~60% of the initial body content of ^{144}Ce cleared with a half-time less than 1 d: this was attributed to clearance of the upper respiratory tract (URT) by mucociliary action and swallowing, suggesting that the rapid dissolution rate was comparatively slow. There was rapid absorption of most of the initial lung deposit (ILD) during the first week, but about 10% was retained much longer. It was noted that the ^{144}Ce concentration in the nasal turbinates was much higher than in other samples of skeleton (from 32 to 512 d). A biokinetic model for the retention of ^{144}Ce was developed (Boecker and Cuddihy, 1974; Cuddihy et al., 1975; NCRP, 1978). It was assumed that there is relatively little absorption of cerium from the URT, based partly on the findings of Cuddihy and Ozog (1973) who observed low absorption following administration of cerium chloride directly onto the nasal membranes of hamsters (see below). The model included two compartments to represent relatively long-term lung retention, with 3.4% and 2.4% of the initial respiratory tract deposit being absorbed into blood at 0.02 d^{-1} and 0.0012 d^{-1} respectively.

(117) Cuddihy et al. (1975) followed the biokinetics of ^{144}Ce up to 32 d in beagle dogs that inhaled ^{144}Ce as $^{144}CeCl_3$ or as ^{144}Ce in a CsCl vector (both in 0.1N HCl). Following inhalation as $^{144}CeCl_3$, lung retention of ^{144}Ce was much greater than when inhaled in a CsCl vector: at 32 d, ~27% and ~4% respectively of the estimated ILD. Systemic uptake was correspondingly lower. They noted that Morrow et al. (1968, see below) observed even slower lung clearance, and had generated aerosols from solutions that had been treated to remove excess acid: this difference in aerosol preparation might have resulted in different biological behaviour.

(118) Analysis carried out here involved simultaneous fitting to the data from Boecker and Cuddihy (1974), and Cuddihy et al. (1975, 1976). Values of s_r, f_b, s_b, and s_s were assumed to be the same in each experiment, while f_r was allowed to vary. This was based on the assumption that similar materials were involved, but the extent of particle formation (and hence the value of f_r) varied with the mass concentration of cerium deposited. Most of the results could be fit well, with absorption parameter values of s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1} and s_s = 0.0015 d^{-1}. Values of f_r were 0.94 and 0.96 for carrier-free ^{144}Ce in a CsCl vector (Boecker and Cuddihy 1974; Cuddihy et al., 1975), giving assignment to Type F; 0.84 for ^{144}Ce in a solution containing 0.3 mg $CeCl_3$ and 9.7 mg CsCl per ml (Cuddihy et al., 1976); and 0.52 for ^{144}Ce in $CeCl_3$ (Cuddihy et al., 1975) both giving assignment to Type M. Fits that were less good (but with similar values of f_r) were obtained if it was assumed instead that the slowest component of lung clearance was due to the bound fraction and the intermediate component was due to particulate material, *i.e.*, s_b ~ 0.0015 d^{-1} (f_b = 0.03) and s_s ~ 0.02 d^{-1}.

(119) Measurements of activity in the trachea were reported by Boecker and Cuddihy (1974), and were underestimated by both models considered above (i.e. with parameter values s_b ~ 0.02 d^{-1} and s_s ~ 0.0015 d^{-1}, or with s_b ~ 0.0015 d^{-1} and s_s ~ 0.02 d^{-1}). The underestimation was less with the lower value of s_b, especially at later times.

(120) By definition, the particulate fraction is cleared by particle transport, whereas the bound fraction is not. Hence, clearance of a lung deposit in particulate form results in more activity in faeces and less in systemic tissues (liver and skeleton) than clearance of the same deposit in bound form. However, as particle transport from the alveolar region of the lung is so slow in dogs, it was not possible to distinguish clearly between the two models from these data.

(121) Alveolar particle transport in rodents is much faster than in dogs (see e.g. Fig. E.6 in ICRP, 1994a; Snipes et al., 1983), and so potentially differences can more easily be seen between particulate and bound fractions. In rodent studies with chloride and citrate in which

low values of f_r (<0.5) were assessed, suggesting that material retained in the lung was mainly in particulate form, values of s_s were estimated to be in the range 0.001 – 0.005 d^{-1} (see below: Cember and Watson, 1958; Morgan et al., 1970; Sturbaum, 1970; Lustgarten et al., 1974). It was therefore assumed here that the intermediate component of lung retention was due to the bound fraction *i.e.*, s_b = 0.021 d^{-1}, and the slowest component of lung clearance was due to particulate material.

(122) The parameter values for the rapid dissolution rate and bound fraction assessed from these dog studies (s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}) were applied in the analysis of the results of other cerium studies below. Thus, only values of f_r and s_s were determined.

(123) Cuddihy et al. (1975) also measured dissolution *in vitro* of ^{144}Ce from filter samples collected during inhalation exposures of the dogs. They found that for both chloride aerosol forms, retention of ^{144}Ce on filter samples in solvents that included sodium citrate (a complexing agent) most closely resembled lung retention. Dissolution was much slower in a saline solution, and negligible (up to ~16 d) in a serum simulant. They observed that cerium readily precipitates in very dilute mixtures with the serum simulant and attributed this to the formation of insoluble complexes with the phosphate present.

(124) Further studies with $^{144}CeCl_3$ inhaled by dogs investigated the effectiveness of lung lavage and DTPA (diethylenetriaminepentaacetic acid) at reducing lung content and radiation effects (Pfleger et al., 1972a, 1972b; Muggenburg et al., 1972).

(125) Cember and Watson (1958) followed for 56 d the biokinetics of ^{144}Ce after intratracheal instillation of $^{144}CeCl_3$ into rats. Lung clearance was slow, with ~50% ILD remaining at 56 d. There was little absorption into blood: the amounts in liver and skeleton combined being only ~2% ILD throughout the experiment. Analysis here assuming default parameter values for cerium (see above) gave f_r = 0.02 and s_s = 0.0015 d^{-1}, and assignment to Type M. (Note that the value of s_s is similar to that obtained in the dog inhalation experiments.) Cember and Stemmer (1964) studied the radiation effects following intratracheal instillation of $^{144}CeCl_3$ into rats, but biokinetic data were not reported. However, they noted that ^{144}Ce was cleared more slowly from the lungs of rats when administered in soluble form (chloride) than in an insoluble form (fluoride) (Cember and Watson, 1958), and discussed possible retention mechanisms (see below on extent of binding of cerium).

(126) Gensicke and Spode (1962) followed for 30 d the biokinetics of ^{144}Ce following inhalation of $^{141}CeCl_3$ (pH 3.5) by mice. Although there are measurements at eight times between 1 hour and 30 d, the results are difficult to interpret. At 1 d, the amounts in liver and skeleton combined amount to ~25% of that in the lungs. There was little further clearance from the lungs, but amounts in liver and skeleton continued to increase. (It may be partly due to variability in the data: the total activity in lungs plus systemic tissues does not show a clear decrease with time.) Even for insoluble particles, clearance from the lungs of mice would normally be readily observable over this period, suggesting that a considerable fraction is bound. Similar studies were carried out by this research group with chlorides of ^{143}Pr, ^{147}Pm, and ^{153}Sm, and the results are compared in the general lanthanide section. The other lanthanides administered behaved similarly to each other, and did not show the avid retention shown by ^{144}Ce.

(127) Morrow et al. (1968) followed for 40 d lung retention of ^{141}Ce following inhalation of $^{141}CeCl_3$ by dogs. Few details were given, but the authors reported that retention in the thorax could be described by a two-component exponential function, with ~40% of the initial amount in the thorax clearing with a half-time of 2.5 d, and the rest with a half-time more than 170 d, suggesting Type M behaviour.

(128) Sturbaum et al. (1970) followed for 260 d the biokinetics of ^{144}Ce inhaled by Chinese hamsters as $^{144}CeCl_3$. About 80% of the initial total body deposit cleared in the first week: this was attributed to clearance of the URT and excretion in faeces. There was rapid absorption from the lungs. By 64 d, the lung activity had decreased to 3.5% ILD, while liver and skeleton increased to ~5% and 1.7% ILD respectively. The authors noted that since these did not equal the decrease in lung activity, there was continuing particle transport from the lungs. This suggests that at least some of the ^{144}Ce retained in the lungs was in particulate form. Analysis here assuming default parameter values for cerium (see above) gave $f_r = 0.3$ and $s_s = 0.005$ d^{-1}, and assignment to Type M.

(129) Morgan et al. (1970) followed (up to 128 d) the biokinetics of ^{144}Ce inhaled by mice as $^{144}CeCl_3$, citrate or FAP. For the chloride, ~70% of the initial total body deposit cleared in the first week. There was substantial rapid uptake to blood, presumably from the lungs, so that about 10% of the remaining total body content ("sacrifice body burden", SBB) was in liver from a few days onwards. There was also considerable long-term lung retention, with the fraction of SBB in lung decreasing from about 25% initially, to 10% at 128 d. Analysis here assuming default parameter values for cerium (see above) gave $f_r = 0.6$ and $s_s = 0.003$ d^{-1}, and assignment to Type M.

(130) Cuddihy and Ozog (1973) deposited $^{144}CeCl_3$ directly onto the nasal membranes of Syrian hamsters and followed the biokinetics of the ^{144}Ce for 4 hours. They estimated that in this time ~2% of the initial deposit had been absorbed. This was much less than for caesium, strontium and barium chlorides which were also administered. It is noted in the inhalation sections of those elements that their absorption was slower than observed in other experiments, but that the results may have been affected by the experimental techniques used, including the anaesthetic. About 50% of the ^{144}Ce administered was retained in the head at 4 hours.

(131) Ducousso and Pasquier (1974) investigated the rapid phase of absorption of ^{144}Ce inhaled by monkeys as $^{144}CeCl_3$ in a vector of NaCl in 0.1N HCl solution. Alveolar deposition was maximised by inhaling small particles through an endotracheal tube. An external detector was positioned to measure activity predominantly in the alveolar region. The fraction absorbed (estimated by the decrease in lung activity, assuming that particle transport was negligible) in 1 hour decreased with increasing mass deposited, from ~15% ILD at 0.01 µg to ~3.4% ILD at 10 µg. (However, it was noted that the absolute mass absorbed increased.) Assuming a single absorption rate, 15% ILD absorbed in 1 hour suggests a value of ~4 d^{-1}. Alternatively, assuming this represents a rapid phase of absorption, it suggests values of f_r ~0.1 and s_r >10 d^{-1}. By 4 hours the amounts absorbed increased to ~19% at 0.01 µg and 4.3% ILD at 10 µg. (Broadly similar results were obtained for ^{140}La: see the general lanthanide section.) Although these experiments were of short duration, they give measurements of the initial absorption in a primate, and so were taken into account in assessing the rapid dissolution rate for cerium for radiation protection purposes (see below).

(132) Kanapilly and Sparling (1976) followed for 32 d the biokinetics in Syrian hamsters of ^{144}Ce inhaled as $^{144}CeCl_3$ at pH 1.0, 2.9 or 5.0. There were no clear differences between the three exposures. Lung retention was ~25% ILD at 32 d, by which time the liver content was also ~25% ILD. The relatively slow absorption was attributed to the presence of carrier cerium. Aerosol samples obtained during exposures to pH 1 and pH 2.9 aerosols were subject to *in vitro* dissolution tests using a static method at 37°C, in three solvents. Dissolution in a synthetic ultrafiltrate (SUF) was much lower than *in vivo*, while dissolution in SUF + 2 x10^{-4}M DTPA and in 0.15M NaCl at pH 4 was higher.

Water-soluble forms of cerium and Type F cerium

(133) Absorption parameter values for cerium chloride based on *in vivo* data are available from several studies. The absorption characteristics of cerium administered as cerium chloride appear to depend strongly on the methods of preparing and administering the material. In particular, the fraction dissolved rapidly seems to decrease with increasing mass administered and increasing pH. Although inhalation exposure to the chloride is unlikely, exposure to other water-soluble forms e.g. nitrate, is not. However, the only water-soluble forms of cerium studied *in vivo* were chloride and citrate. The behaviour of cerium following inhalation of citrate was similar to that of chloride (see below), which supports the application of the results obtained with chloride to other water-soluble forms.

(134) As described above, the most comprehensive studies of cerium chloride deposited in the lungs involved inhalation by dogs. Analysis was carried out here by simultaneously fitting data from experiments in which carrier-free ^{144}Ce was inhaled in a CsCl vector, in a mixture of CsCl and $CeCl_3$, or in $CeCl_3$ (Boecker and Cuddihy, 1974; Cuddihy et al., 1975, 1976). Values of s_r, f_b, s_b, and s_s were assumed to be the same in each experiment, while f_r was allowed to vary between them. The results could be fit well, with absorption parameter values of s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1} and s_s = 0.0015 d^{-1}. These results were used to select the rapid dissolution rate and bound state parameter values for cerium (see below). Most of the data were for ^{144}Ce inhaled in a CsCl vector, and thus these parameter values represent the behaviour of tracer-level cerium, as might arise as a result of slow dissolution of relatively insoluble materials in the lungs. For this material, the value of f_r obtained was ~0.95. It was, however, considered here that inhalation of water-soluble forms was better represented by inhalation of ^{144}Ce in $CeCl_3$, for which the value of f_r obtained was 0.52. (Results of studies above in which ^{144}Ce in $CeCl_3$ was inhaled by hamsters and mice gave f_r values of 0.3 and 0.6.) This value, with those for s_r and s_s above, were rounded to give specific parameter values of f_r = 0.5; s_r = 1 d^{-1}; and s_s = 0.0015 d^{-1}, which are used here for water-soluble forms of cerium.

(135) Default Type F cerium (with dissolution parameter values: f_r = 1, s_r = 1 d^{-1}) is nevertheless retained as an option.

Cerium citrate

(136) As noted above, Morgan et al. (1970) followed (up to 128 d) the biokinetics of ^{144}Ce inhaled by mice as $^{144}CeCl_3$, citrate (pH not reported) or FAP. Whole body retention of citrate as a fraction of the estimated total initial deposit was somewhat higher for citrate than for chloride, but there were no clear differences in tissue distribution or excretion. Analysis here assuming parameter values assessed above for cerium (s_r = 0.44 d^{-1}; f_b = 0.07; s_b = 0.021 d^{-1}) gave f_r = 0.8 and s_s = 0.001 d^{-1}, and assignment to Type M. (However, the excretion data and some early tissue data were not well fitted.) Values are broadly similar to those estimated for the complementary chloride experiment (f_r = 0.6 and s_s = 0.003 d^{-1}).

(137) Lustgarten et al. (1974, 1975) followed the biokinetics of ^{144}Ce inhaled by rats and Syrian hamsters as citrate in a CsCl vector aerosol (pH not reported). A biokinetic model for the retention of ^{144}Ce was developed (Lustgarten et al., 1976). At 128 d lung retention was ~10% ILD in both species: the main difference between them was that in the Syrian hamsters liver and skeleton both contained ~10% ILD, whereas in the rats, liver and skeleton contained ~1% and ~10% ILD, respectively. Analysis here assuming parameter values assessed above for cerium gave f_r = 0.3 and s_s = 0.001 d^{-1} in rats and similar results in hamsters f_r = 0.3 and s_s = 0.004 d^{-1}, (and assignment to Type M for both).

(138) Although absorption parameter values for cerium citrate based on *in vivo* data were derived, as for cerium chloride, a wide range of values of f_r (0.3 – 0.8) was obtained in different studies. Furthermore, inhalation exposure to it is unlikely. Therefore, specific parameter values for cerium citrate are not used here. Instead, it is assigned to water-soluble forms of cerium. However, the results contributed to selection of the rapid dissolution rate and bound state parameter values for cerium, and to justifying application of cerium chloride results to other water-soluble forms.

Cerium hydroxide

(139) Thomas et al. (1972) followed for 670 d the biokinetics of ^{144}Ce inhaled by rats as hydroxide, heat treated at 150°C. Although this was expected to be a relatively insoluble form of cerium, by the time of the first measurement of tissue distribution (47 d) the liver content was greater than that of the lungs. (Measurements of tissue distribution were made as animals in a high exposure level group died.) Analysis here assuming parameter values assessed above for cerium (s_r = 0.44 d^{-1}; f_b = 0.07; s_b = 0.021 d^{-1}) gave f_r = 0.8 and s_s = 0.0004 d^{-1} and assignment to Type M. The relatively high fraction absorbed rapidly suggests that hydroxide formation may not account for prolonged lung retention following deposition of cerium chloride or citrate.

(140) Although absorption parameter values for cerium hydroxide based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for cerium hydroxide are not used here. Instead, it is assigned to Type M.

Cerium fluoride (CeF_3)

(141) Cember and Watson (1958) followed for 180 d the biokinetics of ^{144}Ce after intratracheal instillation of $^{144}CeF_3$ into rats. About 25% ILD cleared from the lungs in the first few days, with little (~1% ILD) uptake into systemic organs. Lung clearance was faster than for $^{144}CeCl_3$ in a similar study (see above) with ~25% ILD remaining at 56 d and ~12% ILD at 180 d. The skeleton content increased to ~5% ILD by 180 d. Analysis here assuming parameter values assessed above for cerium (s_r = 0.44 d^{-1}; f_b = 0.07; s_b = 0.021 d^{-1}) gave f_r = 0.02 and s_s = 0.0014 d^{-1} and assignment to Type M. These values are very similar to those estimated for $^{144}CeCl_3$ studied by Cember and Watson (1958) (see above).

(142) Ivanov and Gorel'chik (1966) followed lung retention and distribution within lung (but not transfer to other tissues) of ^{144}Ce following intratracheal instillation of a colloidal suspension (25 nm) of $^{144}CeF_3$ into rabbits. Insufficient information was reported to derive parameter values, but at 240 d, ~15% ILD remained in the lungs, suggesting Type M or S behaviour.

(143) Although absorption parameter values for cerium fluoride based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for cerium fluoride are not used here. Instead, it is assigned to Type M.

Cerium dioxide (CeO_2)

(144) Stuart et al. (1964) followed for 480 d the biokinetics of ^{144}Ce inhaled by dogs as dioxide, prepared by addition of NaO_2 to $CeCl_3$ or by calcination of oxalate at 400°C. Tombropoulos et al. (1969) followed for 128 d the biokinetics of ^{144}Ce inhaled by dogs as dioxide, prepared by addition of NaO_2 to $CeCl_3$. For both studies insufficient information was

reported to derive parameter values, but at 128 d, and 8–16 months, the amounts retained in liver and skeleton were similar to or greater than in lungs, suggesting Type M behaviour.

(145) Boecker et al. (1969) measured the tissue distribution of ^{144}Ce at 8 and 260 d after inhalation by dogs as dioxide, heat treated at 1150°C. The results were very similar to those at these times in dogs that inhaled ^{144}Ce-FAP in complementary experiments, for which parameter values assessed here were f_r = 0.04 and s_s = 0.001 d^{-1} (see below). These give assignment to Type M, but are close to the criterion for Type S.

(146) Thomas and McClellan (1972) followed for 380 d the biokinetics of ^{144}Ce inhaled by Syrian hamsters as dioxide, heat treated at 1100°C. There was very little rapid absorption: at 32 d the lungs contained ~98% SBB, which decreased to ~90% SBB by 300 d, with corresponding increases in liver and skeleton. Analysis here assuming parameter values assessed above for cerium (s_r = 0.44 d^{-1}; f_b = 0.07; s_b = 0.021 d^{-1}) gave f_r = 0.0012 and s_s = 0.0002 d^{-1} and assignment to Type S.

(147) Hobbs et al. (1973, 1974, 1975) followed for 728 d the biokinetics of ^{144}Ce inhaled by Syrian hamsters as dioxide, heat treated at 850°C. The hamsters were 28, 84 or 340 d old at the time of exposure. (Tissue distribution data were only reported up to 128 d, the study being mainly concerned with toxicity.) There was very little rapid absorption: at 16 d the lungs contained ~97% SBB, which decreased to ~80% SBB by 228 d, with corresponding increases in liver and skeleton. Analysis here assuming parameter values assessed above for cerium gave f_r = 0.001 and s_s = 0.001 d^{-1} for immature Syrian hamsters and f_r = 0.001 and s_s = 0.002 d^{-1} for young adult Syrian hamsters (both giving assignment to Type M).

(148) Lundgren et al. (1974) followed for 431 d the biokinetics of ^{144}Ce inhaled by mice as dioxide, heat treated at 1100°C. Insufficient information was given to determine both f_r and s_s. Analysis here, assuming that f_r = 0.001 (and other parameter values assessed above for cerium), gave s_s = 0.001 d^{-1}, indicating assignment to Type M.

(149) Lundgren et al. (1980a, 1980b) followed for ~1 year the biokinetics of ^{144}Ce inhaled by mice as dioxide, heat treated at 850°C. The mice were 70, 260 or 450 d old at the time of exposure. The studies investigated the effects of age and repeated exposure on the retention and toxicity of $^{144}CeO_2$ in mice. Analysis here of results for single exposures (assuming parameter values assessed above for cerium) gave: f_r = 0.0003 and s_s = 0.002 d^{-1} (70-d age group); f_r = 0.004 and s_s = 0.005 d^{-1} (260-d age group); and f_r = 0.004 and s_s = 0.004 d^{-1} (450-d age group). There was no obvious effect of age on the value of either parameter and a single fit with all three datasets gave f_r = 0.002 and s_s = 0.003 d^{-1}. All these results give assignment to Type M. (Lundgren et al., 1980b, reported results for repeated exposures, which were not analysed here.)

(150) Shiao-Shan et al. (1988) followed for 126 d the biokinetics of ^{141}Ce inhaled by rats as irradiated cerium dioxide. Insufficient information was given to determine both f_r and s_s. Analysis here, assuming that f_r = 0.001 (and other parameter values assessed above for cerium), gave s_s = 0.005 d^{-1}, indicating assignment to Type M.

(151) Johnson (1989) followed for 146 d the biokinetics of ^{141}Ce after intratracheal instillation into rats of irradiated cerium dioxide (used as an "insoluble" material for comparison with dust containing ^{14}C). Insufficient information was given to determine absorption parameter values. However, only trace amounts of ^{141}Ce (<10^{-4} of lung content) were found in liver and carcass, indicating assignment to Type S.

(152) Lundgren et al. (1992) followed for 672 d the biokinetics of ^{144}Ce inhaled by rats as dioxide, heat treated at 850°C. The studies investigated the effects of age and repeated exposure on the retention and toxicity of $^{144}CeO_2$ in rats. Insufficient information was given to determine

both f_r and s_s. Analysis here, assuming that f_r = 0.001 (and other parameter values assessed above for cerium), gave s_s = 0.007 d^{-1}, indicating assignment to Type M.

(153) Lundgren et al. (1996) followed for 448 d the biokinetics of ^{144}Ce inhaled by rats as dioxide, heat treated at 1500°C. Analysis here, assuming that f_r = 0.001 (and other parameter values assessed above for cerium), gave s_s = 0.0005 d^{-1} indicating assignment to Type S. Mauderly et al. (1987) showed that exposure to cigarette smoke retarded lung clearance of ^{144}Ce in rats that had inhaled similar $^{144}CeO_2$ aerosols.

(154) Absorption parameter values for cerium dioxide based on *in vivo* data are available from several studies. The results are variable, apparently depending partly on the method of preparation. Some results give assignment to Type S, others to Type M, but close to the criterion for assignment to Type S. Generally the values are very different from the default values for either Type M or Type S. Values of f_r could only be estimated for a few experiments, and these were ~0.001, less than the default value for Type S (0.01), and much less than the default value for Type M (0.2). Estimated values of s_s range from 0.0002 to 0.007 d^{-1} (geometric mean 0.001 d^{-1}), all higher than the default value for Type S (0.0001 d^{-1}) and similar to the default value for Type M (0.005 d^{-1}). Inhalation exposure to cerium dioxide is not unlikely. Specific parameter values of f_r = 0.001 and s_s = 0.001 d^{-1} are used here for cerium dioxide.

Irradiated fuel and other contaminated dusts associated with nuclear facilities.

(155) Following an accidental release, cerium could be present in fragments of irradiated fuel, where the matrix is predominantly uranium oxide.

(156) Rundo (1965) reported a retention half-time of not less than 2800 d for ^{141}Ce and ^{144}Ce studied during 6–850 d after accidental inhalation of irradiated uranium; the measurements were of whole-body radioactivity, but no evidence was found of movement from the chest. This suggests Type S behaviour of the cerium present.

(157) Lang et al. (1994) followed the tissue distribution and retention of several radionuclides for 3 months after intratracheal instillation of irradiated UO_2 powder into rats. For ^{141}Ce, the amount in bone and liver together at 3 months was about 0.3% ILD, indicating assignment to Type S.

(158) Glenn et al. (1979) carried out measurements on a worker following accidental exposure to airborne fission products, including ^{144}Ce–Pr. External measurements of whole body and chest activity were made for 792 d, although the former fell below the detection limit by 290 d. Fecal and urine measurements were reported, but the latter could not be used in analysis because of repeated treatment with DTPA. *In vitro* dissolution tests on samples taken from clothing suggest that ~10% of the ^{144}Ce was soluble and the rest insoluble. The results of estimated lung retention are consistent with assignment to Type M.

(159) Mirell and Blahd (1989) made whole-body measurements of activity on seven people from about two weeks to several months after exposure to the initial Chernobyl reactor accident plume in Kiev, Ukraine. Biological retention half-times were similar for different radionuclides (17 d for $^{141/144}$Ce) and different from those expected for systemic retention, indicating that they were trapped in particles and metabolically inert, thus indicating Type M rather than Type F behaviour.

(160) Stradling et al. (1989a, 1989b), Stradling and Moody (1995) followed the biokinetics of ^{144}Ce (and other radionuclides) for 360 d after intratracheal instillation into rats of a suspension of residues from a nuclear power plant cooling pond. For the ^{144}Ce present, tissue

distributions at 28, 168 and 360 d were reported. At 28 d, the lung content had decreased to 44% ILD and liver and carcass each contained ~2% ILD. Analysis here (limited by the few data points) gave approximate values of f_r ~0.1 and s_s ~ 0.003 d^{-1}, consistent with assignment to Type M.

(161) Cuddihy et al. (1989) measured the *in vitro* dissolution of samples of particles released from the Chernobyl accident for up to 60 d. For all radionuclides measured, including ^{144}Ce, 10% dissolved in a few hours, and the rest with a half-time of 160 d. Hence f_r = 0.1, s_r ~10 d^{-1}, and s_s = 0.004 d^{-1}, giving assignment to Type M.

(162) Cerium associated with irradiated fuel fragments is assigned here to Type S, based on the studies by Rundo (1965) and Lang et al. (1994). With regard to cerium associated with other, unspecified, contaminated dusts from nuclear facilities, specific absorption parameter values were derived from the results of one *in vivo* study, but were only approximate, and based on the studies above it is assigned to Type M.

Fused aluminosilicate particles (FAP)

(163) FAP or “fused clay” particles have been extensively used as relatively insoluble particles in inhalation studies, both of biokinetics and of radiation effects. A natural clay mineral is labelled by ion exchange, and the labelled clay particles heated to about 1100˚C, to form aluminosilicate glass microspheres in which the label is incorporated. It has been demonstrated that when cerium is incorporated into FAP, only a small fraction may be rapidly absorbed, while the remainder is retained within the particles and absorbed slowly.

(164) Boecker et al. (1969, 1970b) followed for 512 d the biokinetics in beagle dogs of ^{144}Ce-FAP. The study was conducted to complement a life-span dose-effects study (Hahn et al., 1999, 2001), which also provides some measurements of tissue distribution at times up to 1300 d (Boecker et al., 1971). Biokinetic models for the retention of ^{144}Ce were developed (Cuddihy and Boecker, 1975; Shyr et al., 1991). Analysis here assuming parameter values assessed above for cerium (s_r = 0.44 d^{-1}; f_b = 0.07; s_b = 0.021 d^{-1}) gave f_r = 0.04 and s_s = 0.001 d^{-1}. These give assignment to Type M, but are close to the criterion for Type S.

(165) Further studies with dogs investigated the effects of age at exposure and multiple exposures (Boecker et al., 1973; Hahn et al., 1973; Boecker et al., 1974a). Results were not analysed here, but there did not appear to be a marked difference in absorption from lungs to blood between dogs exposed at 3 months old (immature) or at 18 months (young adult), although, as expected, there was greater deposition in the skeleton of the immature dogs. Other studies investigated the effectiveness of lung lavage at reducing lung content and radiation effects (Boecker et al., 1974b; Felicetti et al., 1975).

(166) Studies of the biokinetics of ^{144}Ce following inhalation of ^{144}Ce-FAP have also been conducted in mice. As noted above, Morgan et al. (1970) followed the biokinetics (up to 128 d) of ^{144}Ce inhaled by mice as $^{144}CeCl_3$, citrate or FAP. For the ^{144}Ce-FAP, there was little absorption from the lungs: the liver content reached about 1% of the remaining total body content ("sacrifice body burden", SBB) of ^{144}Ce within a few days, with little further change, while the lung content was still about 80% SBB at 128 d. Analysis here assuming parameter values assessed above for cerium gave f_r = 0.03 and s_s = 0.0002 d^{-1} and assignment to Type S.

(167) Thomas et al. (1973) measured the tissue distribution of ^{144}Ce at 32 and 64 d after inhalation by mice of ^{144}Ce-clay particles produced at different temperatures. For particles formed at 90, 200 or 500°C, the lung content was about 10% SBB at 64 d, and the liver ~30%, SBB. For particles formed at 900 or 1150°C, the lung content was about 85% SBB at 64 d, and

the liver ~7% SBB. Analysis here, assuming parameter values assessed above for cerium, gave values of f_r in the range 0.05–0.5 and of s_s ~0.1 d^{-1} for particles formed at 90–500°C; and values of f_r <0.05 and of s_s ~0.003 d^{-1} for particles formed at 900–1150°C. All these results give assignment to Type M.

(168) Although absorption parameter values for cerium-labelled FAP based on *in vivo* data were derived, they were variable, some giving assignment to Type M, others to Type S. Inhalation exposure to it is unlikely. Therefore specific parameter values for cerium- labelled FAP are not used here, nor is it assigned to a default Type.

Polystyrene (PSL)

(169) Radiolabelled polystyrene (PSL) particles have been used extensively as relatively insoluble particles in inhalation studies (see e.g. inhalation sections on cobalt and strontium in OIR Part 2). ^{141}Ce-labelled PSL has been used to study particle clearance from the lungs in rats and dogs (e.g. Snipes and Clem, 1981; Wolff et al., 1989; Oberdörster et al, 1992). Wolff et al. (1989) followed lung retention in dogs up to 36 d after administration and noted that there was little loss of the label: only trace levels were found in other tissues. Oberdörster et al. (1992) followed lung retention in rats up to 200 d and noted that fecal excretion almost exactly complemented lung clearance. The results indicate Type S behaviour.

Nuclear weapons fallout.

(170) During the early 1960s, measurements were made of radionuclides in human lungs due to fall-out from atmospheric nuclear weapons tests. For further information see the zirconium section in OIR Part 2, and the plutonium section in this report. Schönfeld et al. (1960) detected $^{141+144}$Ce (with ^{95}Zr-Nb and ^{103}Ru) in *post mortem* lung samples, but only found ^{137}Cs in liver and muscle. Liebscher et al. (1961) reported ^{144}Ce concentrations in lymph nodes between 10 and 60 times higher than in lungs. Wegst et al. (1964) showed that $^{141+144}$Ce was present in the lungs in particulate form. Irlweck et al. (1980) measured ^{144}Ce and ^{239}Pu activities in the lungs: they reported that the two radionuclides appeared to show similar lung deposition and clearance characteristics. Overall these results indicate Type M or S behaviour.

Unspecified compounds.

(171) Paul et al. (1998, 2000) investigated *in vitro* dissolution of several elements, including cerium, on samples of airborne dust collected from monazite and rare earth processing. They also made measurements on urine and blood samples from workers exposed to such dusts. However insufficient information was reported to enable dissolution characteristics to be assessed.

Rapid dissolution rate for cerium

(172) As described above, studies of the biokinetics following deposition of relatively soluble forms of cerium (chloride and citrate) in the respiratory tract generally indicate that there is little absorption from the URT, and hence that $s_r << 100$ d^{-1}. Studies of the biokinetics in beagle dogs of ^{144}Ce inhaled in a caesium chloride (CsCl) vector aerosol (to reduce colloid formation) or as $^{144}CeCl_3$, both in 0.1N or 1N HCl, give values of s_r of 0.44 d^{-1}. For ^{144}Ce inhaled by monkeys as $^{144}CeCl_3$ (in a vector of NaCl in 0.1N HCl solution) the initial lung clearance suggests a value for s_r of at least ~4 d^{-1}. A rounded value of 1 d^{-1} is applied here to all

Type F forms of cerium. Because it is lower than the general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S forms of cerium.

Extent of binding of cerium to the respiratory tract

(173) When relatively soluble forms of cerium (chloride, citrate) are deposited in the respiratory tract, absorption has in all cases been found to be incomplete. The question of whether the cerium is retained in particulate or bound form has been discussed for about 50 years, and remains unresolved. It is considered in detail here, because other lanthanides, for which there is little or no relevant information, might be expected to behave in a similar way to cerium, and so conclusions drawn for cerium are, by analogy, applied to them. Relevant comments from the literature are summarised here in chronological order. While most relate to retention of cerium in the lungs, some are specifically concerned with retention of cerium in conducting airways – the nasal passage and trachea. Particulate materials are rapidly cleared from these airways, and so retention in them indicates that binding may well be occurring.

(174) Cember and Stemmer (1964) discussed lung retention of cerium and other "...soluble materials that might form an insoluble precipitate in the biochemical milieu of the lung, or bind to the tissue protein in the lung...". They noted that earlier studies had shown slower clearance of soluble cerium chloride than of insoluble cerium fluoride. This suggests binding rather than, or in addition to, precipitate formation. They also reported that protein (human serum albumin) is capable of binding relatively large quantities of cerium.

(175) Kanapilly et al. (1973) noted that: "...materials that are soluble in water may undergo hydrolysis at the relatively constant pH of physiological fluids. Other properties of the physiological solvent which may be important in determining the solubility of a material are the concentrations of chelating agents, precipitate forming constituents such as phosphates and carbonates and non-reacting ionic materials." To examine the relationship between the lung retention of an inhaled polyvalent radionuclide and its *in vitro* dissolution and hydrolysis at neutral pH, the *in vitro* dissolution of ^{144}Ce from $CeCl_3$ + CsCl aerosol particles in saline solution (0.154 M NaCl at pH 7.2) was determined. The solvent flowed through a filter sandwich containing the particles at 3 ml min^{-1}. After 140 ml solvent had flowed through, ~50% of the ^{144}Ce remained. This was attributed to the "formation of hydrolytic products of ^{144}Ce which may be insoluble particles or capable of adsorbing on the membrane filters." They speculated that the lung retention observed by Boecker et al. (1970a) after inhalation of $^{144}CeCl_3$ by dogs might be attributed to the hydrolysis of ^{144}Ce.

(176) Ducousso and Pasquier (1974) investigated the rapid phase of absorption of ^{144}Ce inhaled by monkeys as $^{144}CeCl_3$ in a vector of NaCl in 0.1N HCl solution (see above). They observed that as the ILD (mass) increased, the relative absorption decreased. In discussing the results, the authors considered that there was competition between diffusion of ionic cerium into the blood; hydrolysis of ionic cerium; and uptake by proteins, especially albumin. They noted that the higher the concentration of cerium in the alveolar fluid, the more rapid would be the formation of hydroxide, reducing absorption.

(177) Boecker and Cuddihy (1974) reported measurements of ^{144}Ce in the trachea (+larynx) of ~0.2% SBB from 2 to 512 d after inhalation by dogs of $^{144}CeCl_3$ in a CsCl vector. Since particle transport of material deposited in these airways would be almost complete by 2 d, and this is more than expected from material in transit from distal airways, this suggests a bound fraction in the trachea and larynx, but no information on the location of the activity was given. While it is possible that it is located in the epithelium, it could be further from the

surface and the target cells. For example in the case of cobalt (see cobalt section in OIR Part 2), there is strong evidence for a bound fraction, which can be quantified, but autoradiography showed that it was mainly located in airway cartilage.

(178) As described above, Cuddihy et al. (1975) observed that lung retention of ^{144}Ce was greater following inhalation as $^{144}CeCl_3$, than as a tracer in a CsCl vector. They also measured dissolution *in vitro* of ^{144}Ce from filter samples collected during the inhalation exposures. As noted elsewhere, this "carrier effect" suggests the formation of insoluble particles. They observed that cerium readily precipitates in the serum simulant used, and attributed this to the formation of insoluble complexes with the phosphate present.

(179) Cuddihy et al. (1976) observed that following inhalation by dogs of ^{144}Ce as a tracer in a CsCl vector, the concentration in nasal turbinates was higher at all times (2 h to 32 d) than in any other tissue. However, no comment was made on the mechanism of retention.

(180) Kanapilly (1977) discussed possible mechanisms for the retention kinetics in the lung of inhaled, water-soluble trivalent materials, with special reference to lanthanum and cerium. He argued that the greater lung retention observed with increasing stable cerium carrier present suggested particulate formation (p 97): "Carrier effect, such as the larger fractional retention for longer periods with higher carrier concentration, may indicate particulate formation of the Ce(III) in the alveoli. If protein binding or adsorption onto cellular surfaces is the major mechanism of retention of Ce(III) in the alveoli, no differences in retention pattern with respect to carrier concentrations should be expected unless saturation of the binding sites occurs. If this saturation does occur, lower fractional retention may be expected with higher carrier concentrations. The observed higher retention with higher carrier concentration thus indicates precipitation of Ce(III) in the alveoli."

(181) Benjamin et al. (1979) discussed the large number of nasal carcinomas in dogs that inhaled $^{144}CeCl_3$ or $^{91}YCl_3$ but not $^{90}SrCl_2$. One difference in dosimetry noted was that cerium and yttrium are retained on bone surfaces whereas strontium goes to bone volume. However, there was also unusually high retention of ^{144}Ce and ^{91}Y in the nasal turbinate tissues. Some of this was related to radionuclide deposited on bone surfaces, but there also appeared to be radionuclide associated with turbinate epithelium. They observed that autoradiographs of nasal turbinate tissue sections from dogs killed 8 d after exposure to $^{144}CeCl_3$ suggested that the ^{144}Ce was associated with foci of nasal epithelium. Dogs exposed to ^{144}Ce or ^{91}Y also had long-term pulmonary retention of a small fraction of the ILD, which might be related to the long-term retention of these radionuclides being associated with the nasal cavity epithelium, which does not appear to be the case with ^{90}Sr. This long term retention of relatively soluble $^{144}CeCl_3$ and $^{91}YCl_3$ also contrasts with the rapid and more complete nasopharyngeal clearance observed for insoluble particles inhaled by dogs.

(182) Boecker et al. (1986) discussed further the induction of nasal tumours in dogs following inhalation of $^{144}CeCl_3$ or $^{91}YCl_3$, but noted that some also arose following inhalation of $^{90}SrCl_2$ and injection of ^{144}Ce or ^{90}Sr.

(183) Galle et al. (1992) examined lung sections from rats 3 hours after exposure to a submicron aerosol of a 1% solution of $CeCl_3$ (5 hrs per day for 5 weeks). They observed lysosomes in the alveolar macrophages containing dense deposits, in which both cerium and phosphorus were detected by microanalysis. The authors suggested that the cerium was precipitated as phosphate, as they had previously observed in renal lysosomes.

(184) Hahn et al. (1997) pointed out that a notable finding of the life-span study of the effects of irradiation by ^{144}Ce following inhalation of $^{144}CeCl_3$ by dogs was the relatively high incidence of tumours which appeared to arise in the mucosa lining the nasal turbinate bones.

However, it was not clear whether the high concentration of ^{144}Ce, presumably retained near the site of deposition, was located in the epithelium or in the underlying bone.

(185) Thus, there is evidence supporting both mechanisms of retention of cerium in the respiratory tract: formation of relatively insoluble particles, and retention in a bound state. Indeed, it seems quite possible that both are involved, perhaps with particle formation becoming increasingly important as the mass deposited increases, as suggested by Ducousso and Pasquier (1974) and Kanapilly (1977).

(186) As described above, the most comprehensive study of the biokinetics of cerium following its inhalation in a relatively soluble form: ^{144}Ce inhaled in a CsCl vector by dogs (Boecker and Cuddihy, 1974; Cuddihy et al.,1975, 1976) showed two long-term lung retention components of similar magnitude, with absorption rates of 0.02 d^{-1} and 0.0012 d^{-1}. Analysis carried out here showed that most of the results could be fit well, assuming that the faster component represented bound material and the slower component particulate material, with absorption parameter values: f_b = 0.07; s_b = 0.021 d^{-1} and s_s = 0.0015 d^{-1}. Fits that were less good were obtained if it was assumed instead that the slowest component of lung clearance was bound and the intermediate component was particulate: s_b ~0.0015 d^{-1} (f_b = 0.03) and s_s ~0.02 d^{-1}. Measurements of ^{144}Ce retained in the trachea were fit better by assuming the slower rate of uptake from the bound state. However, the results of rodent studies with chloride and citrate suggested that material retained in the lung in particulate form was absorbed at the slower rate. On that basis it was assessed here that bound state parameter values were f_b = 0.07 and s_b = 0.02 d^{-1} and these values were adopted here for cerium.

(187) As described above, there is evidence of retention of cerium deposited in relatively soluble form in both the ET and BB regions. There is evidence of some retention in the nasal epithelium, but there is no information on where it might be retained in the trachea. The bound fraction of 0.07 is therefore applied in the ET_2 region as well as in the AI region, but not in the BB and bb regions.

Table 4.2 Absorption parameter values for inhaled and ingested cerium.

	Absorption parameter values[a]			Absorption from the alimentary tract, f_A[b]
Inhaled particulate materials	f_r	s_r (d^{-1})	s_s (d^{-1})	
Specific parameter values[c]				
Water soluble forms, including chloride and citrate[d]	0.5	1	0.0015	3×10^{-4}
Dioxide	0.001	1	0.001	5×10^{-7}
Default parameter values[d,e]				
Absorption Type	Assigned forms			
F	— NB: Type F should not be assumed without evidence	1	1	–	5×10^{-4}
M[e]	Fluoride, hydroxide	0.2	1	0.005	1×10^{-4}
S	Irradiated fuel fragments	0.01	1	$1 \times 10^{-}$	5×10^{-6}

Ingested material[f]	
All compounds	5×10^{-4}

a It is assumed that for cerium a bound fraction $f_b = 0.07$ with an uptake rate $s_b = 0.02$ d^{-1} is applied to material in the ET and AI regions, and associated lymph nodes LN_{ET} and LN_{TH}. It is assumed that $f_b = 0.0$ for material deposited in the BB and bb regions. The values of s_r for Type F, M and S forms of cerium (1 d^{-1}) are element-specific.

b For inhaled material deposited in the respiratory tract and subsequent cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the (rounded) product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of cerium (5×10^{-4}).

c See text for summary of information on which parameter values are based, and on ranges of parameter values observed in different studies. For both water soluble forms of cerium, and cerium dioxide, specific parameter values are used for dissolution in the lungs, but a default value of f_A (footnote b).

d Materials (*e.g* cerium fluoride) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

e Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

f Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A ($=5 \times 10^{-4}$) for ingestion of the radionuclide.

4.2.2. Ingestion

(188) The fractional absorption of cerium in rats was reported to be less than 10^{-3} (Durbin et al., 1956). Similar low values of absorption have also been reported in pigs (McClellan et al., 1965), goats (Ekman and Åberg, 1962) and cattle (Miller et al., 1967). In man, data from a case of accidental inhalation also indicated that absorption from the gastrointestinal tract is very small (Sill et al., 1969).

(189) Taylor and Leggett (1998) reviewed the available information on the absorption of cerium, promethium and neodymium in humans and, noting that the reported values fell within the same range as those observed for the actinides thorium, neptunium, plutonium, americium and curium, proposed that the same absorption value should be applied.

(190) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of cerium. In *Publication 68* (ICRP, 1994b), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

4.2.3. Systemic distribution, retention and excretion of cerium

4.2.3.1. Data

(191) Ewaldsson and Magnusson (1964) performed an autoradiographic study of the distribution of ^{144}Ce and ^{147}Pm in pregnant and non-pregnant female mice following their intravenous injection as chlorides. Blood levels of both radionuclides declined rapidly, with promethium appearing to leave the blood more readily than cerium. There were similarities but

also noticeable differences in the tissue distributions of the two radionuclides. Shortly after injection, the liver contained much of the administered quantity of both radionuclides.

(192) Cerium was uniformly distributed in liver tissue, while promethium showed a somewhat irregular distribution. The skeletal distribution patterns were similar for the two radionuclides. As observed by Durbin (1962) in rats, activity accumulated in the periosteum and endosteum of bone but not in the cortex. The accumulation of both radionuclides was remarkably high in the dental pulp.

(193) Stuart (1964) studied the biokinetics and adverse effects of ^{147}Pm in dogs following inhalation or intravenous injection of ^{147}Pm perchlorate. Activity reaching the systemic circulation deposited primarily in the liver and skeleton. At 2 weeks after inhalation the mean liver and bone contents in two dogs were 40% and 35%, respectively, of the total body burden. At 2 wk after injection, the mean liver and bone contents in two dogs were 47% and 43%, respectively, of the total body burden. The distribution and retention of ^{147}Pm showed little change between the first and second months.

(194) Stuart and Gaven (1968) studied the behavior and adverse effects of ^{147}Pm following its acute inhalation as promethium oxide (Pm_2O_3). At 5 mo after inhalation the average liver and bone contents in two dogs represented about 50% and 40%, respectively, of the total systemic burden. At 12-15 mo the average liver and bone content in two dogs were each about 45% of the total systemic burden. The contents of soft tissues other than liver represented about 5-8% of the total systemic burden at 5-15 mo.

(195) McClellan et al. (1965) studied the biokinetics of ^{144}Ce in miniature swine following its oral or intravenous administration as chloride. At 10 d after oral administration, activity was detectable in the skeleton, liver, and kidneys but amounted to less than 0.01% of the administered amount due to low fractional absorption to blood. At 10 d after intravenous administration, the skeleton, liver, and kidneys contained on average about 40%, 35%, and 0.4%, respectively, of the administered amount.

(196) Richmond and London (1966) determined whole-body retention of ^{144}Ce in adult dogs over 1050 d following intravenous administration of $^{144}CeCl_3$. An exponential curve fit to whole-body retention data indicated a biological half-time of about 10 y (3283 – 3873 d).

(197) Cuddihy et al. (1975) developed a biokinetic model for systemic Ce as a fit to data for dogs exposed by inhalation to ^{144}Ce aerosols. The model describes the systemic behavior of cerium in terms of compartments named Blood, Urine, Intestinal Contents, Liver 1 (relatively fast removal), Liver 2 (relatively slow removal), Skeleton 1 (fast), Skeleton 2 (slow), Soft Tissue 1 (fast), and Soft Tissue 2 (slow). Absorbed cerium is removed from Blood with a half-time of about 25 min, with about 2% going to Urine, 12.5% to the Intestinal Contents, 35.5% to Liver 1, 27% to Skeleton 1, and 23% to Soft Tissue 1. Cerium moves from Liver 1 to Liver 2 at 0.1 d^{-1}, Liver 1 to Blood at 0.04 d^{-1}, Skeleton 1 to Skeleton 2 at 0.1 d^{-1}, Skeleton 1 to Blood at 0.04 d^{-1}, Soft Tissue 1 to Soft Tissue 2 at 0.2 d^{-1}, Soft Tissue 1 to Blood at 1 d^{-1}, and long-term compartments of tissues back to the corresponding short-term compartments at 0.0001 d^{-1}.

(198) Hahn et al. (1997) studied the biokinetics and adverse effects of ^{144}Ce in dogs following acute inhalation of $^{144}CeCl_3$. Absorbed ^{144}Ce accumulated largely in the liver and skeleton and was removed from these tissues with an effective half-time approaching the physical half-life of ^{144}Ce, indicating little net biological removal during the observation period.

(199) Thomas et al. (1989) reviewed published data on the Ce and Pu content of the gonads and total body for several animal species. They reduced collected data to fractional concentrations in gonads, i.e., to ratios of the concentration of Ce or Pu in gonads to its concentration in the total body. Logarithmic regression lines were used to relate fractional Pu or

Ce concentration in testes or ovaries to body weight of the animals and to predict fraction Pu or Ce concentrations in human gonads. The authors concluded that: (1) extrapolation of their regression lines to reference body weights of adult human males and females yields human values that agree reasonably well with the gonadal deposition fraction of 10^{-5} g^{-1} recommended in ICRP *Publication 30* (1979) and later ICRP documents, assuming permanent retention in gonads; (2) there is reasonably good agreement between the fractional concentrations of Ce and those of Pu in testes or ovaries; (3) fractional concentrations of gonadal Ce and Pu are reasonable substitutes for human gonadal concentrations of other elements with principal III and IV oxidation states.

4.2.3.2. Biokinetic model

(200) The biokinetic model for systemic cerium applied in this report is described in Section 2.2.3.2.

4.2.3.3. Treatment of progeny

(201) The treatment of radioactive progeny of cerium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

4.3. Individual monitoring

^{139}Ce

(202) Measurements of ^{139}Ce are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{139}Ce concentrations in urine and faeces may be used to determine intakes of the radionuclide. I*n vivo* whole body measurement is used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 4.3. Monitoring techniques for ^{139}Ce.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{139}Ce	Urine Bioassay	γ-ray spectrometry	2 Bq/L
^{139}Ce	Faecal Bioassay	γ-ray spectrometry	2 Bq/24h
^{139}Ce	Lung Measurement[a]	γ-ray spectrometry	5 Bq
^{139}Ce	Whole-body Measurement[b]	γ-ray spectrometry	70 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) for counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

^{141}Ce

(203) Measurements of ^{141}Ce are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{141}Ce concentrations in urine and faeces may be used to

determine intakes of the radionuclide. I*n vivo* whole body measurement is used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 4.4. Monitoring techniques for ^{141}Ce.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{141}Ce	Urine Bioassay	γ-ray spectrometry	9 Bq/L	
^{141}Ce	Faecal Bioassay	γ-ray spectrometry	9 Bq/24h	
^{141}Ce	Lung Measurement[a]	γ-ray spectrometry	8 Bq	4 Bq
^{141}Ce	Whole-body Measurement[b]	γ-ray spectrometry	150 Bq	100 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

^{144}Ce

(204) Measurements of ^{144}Ce are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{144}Ce concentrations in urine and faeces may be used to determine intakes of the radionuclide. I*n vivo* whole body measurement is used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 4.5. Monitoring techniques for ^{144}Ce.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{144}Ce	Urine Bioassay	γ-ray spectrometry	40 Bq/L	5 Bq/L
^{144}Ce	Faecal Bioassay	γ-ray spectrometry	40 Bq/24h	
^{144}Ce	Lung Measurement[a]	γ-ray spectrometry	20 Bq	10 Bq
^{144}Ce	Whole-body Measurement[b]	γ-ray spectrometry	600 Bq	250 Bq

[a] Measurement system comprised of two Broad Energy Germanium detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium detectors (BEGe) and counting time of 15 minutes.

4.4. Dosimetric data for cerium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Benjamin S. A., Boecker B. B., Cuddihy R. G., McClellan R. O., 1979, Nasal carcinomas in beagles after inhalation of relatively soluble forms of beta emitting radionuclides. J. Natl. Cancer Inst. 63, 133–139.

Boecker, B. B., Cuddihy, R. G. 1974. Toxicity of ^{144}Ce inhaled as $^{144}CeCl_3$ by the Beagle: Metabolism and dosimetry. Radiat. Res. 60, 133–154.

Boecker, B. B., Benjamin, S. A., Chiffelle, T. L., et al., 1970a, Toxicity of inhaled $^{144}CeCl_3$ in Beagle dogs. IV. Fission Product Inhalation Program Annual Report 1969–1970, LF-43. pp. 128–136. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Boecker, B. B., Chiffelle, T. L., Clapper, W. E., et al., 1969. Toxicity of inhaled ^{144}Ce fused clay in beagle dogs. II. Fission Product Inhalation Program Annual Report 1968–1969, LF-41, 19–35. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Boecker, B. B., Chiffelle, T. L., Hobbs, C. H., et all, 1970b. Toxicity of inhaled ^{144}Ce fused clay in beagle dogs. III. Fission Product Inhalation Program Annual Report 1969–1970, LF-43. 183–187. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Boecker, B. B., Hahn, F. F., Hobbs, C. H., et al., 1971. Toxicity of inhaled ^{144}Ce fused clay in beagle dogs. IV. Fission Product Inhalation Program Annual Report 1970–1971, LF-44. 164–180. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Boecker, B. B., Lustgarten, C. S., McClellan, R. O., Thomas, R. L., 1974a. Biological effects of repeated inhalation exposure of Beagle dogs to aerosols of ^{144}Ce in fused clay particles I. Inhalation Toxicology Research Institute Annual Report 1973–1974, LF-49. 314–317. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Boecker, B. B., McClellan, R. O., Hahn, F. F., Hobbs, C. H., Mauderly, J. L., 1973. Toxicity of ^{144}Ce fused clay inhaled by immature Beagle dogs. II. Inhalation Toxicology Research Institute Annual Report 1972–1973. LF-46. 117–121. Albuquerque, NM: Lovelace Biomedical and Environmental Research Institute. Available from National Technical Information Service, Springfield, Virginia.

Boecker, B. B., Muggenburg, B. A., McClellan, R. O., et al., 1974b, Removal of ^{144}Ce in fused clay particles from the Beagle dog lung by bronchopulmonary lavage. Health Phys. 26, 505–517.

Boecker, B.B., Hahn, F. F., Cuddihy, R. G., Snipes, M. B., McClellan, R. O., 1986. Is the human nasal cavity at risk from inhaled radionuclides? Life-Span Radiation Effects Studies in Animals: What Can They Tell Us? USDOE, CONF-830951, Eds. Thompson, R. C., Mahaffey, J. A. 564–577.

Cember, H., Stemmer, K., 1964. Lung cancers from radioactive cerium chloride. Health Phys. 10, 43–48.

Cember, H., Watson, J. A., 1958. Lung hazards from inhaled radioactive particulate matter. Progress Report, U.S.A.E.C. Contract AT(30–1), 912.

Cuddihy, R. G., Boecker, B. B., 1975, Application of the GASP IV simulation language to modeling of biological retention patterns for inhaled ^{144}Ce. Inhalation Toxicology Research Institute Annual Report 1974–1975. LF-52. 96–100. Albuquerque, NM: Lovelace Biomedical and Environmental Research Institute. Available from National Technical Information Service, Springfield, Virginia.

Cuddihy, R. G., Boecker, B. B., McClellan, R. O., Kanapilly, G. M., 1976. ^{144}Ce in tissues of beagle dogs after inhalation of $CeCl_3$ with special emphasis on endocrine glands and reproductive organs. Health Phys. 30, 53–59.

Cuddihy, R. G., Finch, G. L., Newton, G. J., et al., 1989. Characteristics of radioactive particles released from the Chernobyl nuclear reactor. Environ. Sci. Technol. 23, 89–95.

Cuddihy, R. G., Gomez, S. R., Pfleger, R. C., 1975. Inhalation exposures of beagle dogs to cerium aerosols: Physical chemical and mathematical analysis. Health Phys. 29, 257–265.

Cuddihy, R.G., Ozog, J.A., 1973. Nasal absorption of CsCl, $SrCl_2$, $BaCl_2$, and $CeCl_3$ in Syrian Hamsters. Health Phys., 25, 219–224.

Ducousso, R., Pasquier, C., 1974. Lung contamination by Ce and La evolution of the early spontaneous absorption as a function of the initial lung burden. Health Phys. 26, 519–524.

Durbin, P. W., 1962. Distribution of the Transuranic Elements in Mammals. Health. Phys. 8, 665-671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

Ekman, L., Åberg, B., 1961. Excretion of Niobium-95, Yttrium-91, and Promethium-147 in Goats. Res. Vet. Sci. 2, 100–105 .

Ewaldsson, B., Magnusson, G., 1964. Distribution of radiocerium and radiopromethium in mice. Acta Radiol. Ther. Phys. Biol. 2, 65-72.

Felicetti, S. A., Silbaugh, S. A., Muggenburg, B. A., Hahn, F. F., 1975. Effect of time post-exposure on the effectiveness of bronchopulmonary lavage in removing inhaled ^{144}Ce in fused clay from beagle dogs. Health Phys. 29, 89–96.

Galle, P., Berry, J. P., Galle, C., 1992. Role of alveolar macrophages in precipitation of mineral elements inhaled as soluble elements. Env. Health Perspect. 97, 145–147.

Gensicke, F., Spode E., 1962. Zur Frage des Stoffwechsels von inhaliertem Radiocer (Ce144 bis Pr144) Radiobiologia radiotherapia 3, 147–151.

Glenn, R. D., Heid, K. R., Houston J. R., 1979. Assessments of a cerium–praseodymium-144 inhalation case. Health Phys. 36, 117–125.

Hahn, F. F., Boecker, B. B., Griffith, W. C., Muggenburg, B. A., 1997. Biological effects of inhaled $^{144}CeCl_3$ in beagle dogs. Radiat. Res. 147, 92–108.

Hahn, F. F., Muggenburg, B. A., Guilmette, R. A., Boecker, B. B., 1999. Comparative stochastic effects of inhaled alpha- and beta-particle-emitting radionuclides in beagle dogs. Radiat. Res. 152, 6 Suppl. 19–22.

Hahn, F. F., Muggenburg, B. A., Snipes, M. B., Boecker, B. B., 2001. The toxicity of insoluble cerium-144 inhaled by beagle dogs: non-neoplastic effects. Radiat. Res. 155, 95–112.

Hahn, F. F., Boecker, B. B., Griffith, W. C., Muggenburg, B. A., 1997. Biological effects of inhaled $^{144}CeCl_3$ in beagle dogs. Radiat. Res. 147, 92–108.

Harrison, J.D., 1995. Ingested radionuclides. In: Radiation and Gut. Eds Potten, C.S. and Hendry J.H. (Oxford, Elsevier). 253-289.

Hobbs, C. H., McClellan, R. O., Benjamin, S. A., 1972. Toxicity of inhaled $^{144}CeO_2$ in immature, young adult and aged Syrian Hamsters I. Inhalation Toxicology Research Institute Annual Report 1972–1973, LF-46. 141–145. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Hobbs, C. H., McClellan, R. O., Benjamin, S. A., 1973. Toxicity of inhaled $^{144}CeO_2$ in immature, young adult and aged Syrian Hamsters II. Inhalation Toxicology Research Institute Annual Report 1973–1974, LF-49. 130–135. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Hobbs, C. H., McClellan, R. O., Benjamin, S. A., 1974. Toxicity of inhaled $^{144}CeO_2$ in immature, young adult and aged Syrian Hamsters III. Inhalation Toxicology Research Institute Annual Report 1974–1975, LF-52. 178–181. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

ICRP, 1979. Limits for intakes of radionuclides by workers. ICRP Publication 30 (Part 1). Ann. ICRP 2(3/4).

ICRP, 1994a. Human respiratory tract model for radiological protection. ICRP Publication 66. Ann. ICRP 24(1–3).

ICRP, 1994b. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Irlweck, K., Friedmann C., Schonfield, T., 1980. Plutonium in the lungs of Austrian residents. Health Phys. 39, 99–103.

Ivanov, A. E., Gorel'chik, K. I., 1966. Radiometric studies of the lungs in the process of the development of cancer induced by intratracheal administration of ^{144}Ce fluoride. Distribution and Biological Effects of Radioactive Isotopes. AEC-TR-6944.

Johnson, J. R., 1989. Lung retention and clearance classification of a 14C-containing aerosol produced during re-tubing of a nuclear reactor. Health Phys. 57, 645–657.

Kanapilly, G. M., 1977. Alveolar microenvironment and its relationship to the retention and transport into blood of aerosols deposited in the alveoli. Health Phys. 32, 89–100.

Kanapilly, G. M., Raabe, O. G., Goh, C. H. T. and Chimenti, R. A., 1973. Measurement of *in vitro* dissolution of aerosol particles. Health Phys. 24, 497–507.

Kanapilly, G. M., Sparling, L. C., 1976. Effect of acidity on the retention and distribution of inhaled $^{144}CeCl_3$. Inhalation Toxicology Research Institute Annual Report 1975–1976, LF-56. 88–92. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Lang, S., Kosma, V. M., Kumlin, T., et al., 1994. Distribution and short-term effects of intratracheally instilled neutron-irradiated UO_2 particles in rat. Environ. Res. 15, 119–131.

Liebscher, K., Schönfeld, T., Schaller, A., 1961. Concentration of inhaled cerium-144 in pulmonary lymph nodes of human beings. Nature 192, 1308.

Lundgren, D. L., Hahn, F. F., McClellan, R. O., 1980a. Influence of age at the time of inhalation exposure to aerosols of $^{144}CeO_2$ on the ^{144}Ce retention, dosimetry and toxicity in mice. Health Phys. 38, 643–655.

Lundgren, D. L., Hahn, F. F., Diel, J. H., Snipes, M. B., 1992. Repeated inhalation exposure of rats to aerosols of $^{144}CeO_2$. I. Lung, liver, and skeletal dosimetry. Radiat. Res. 132, 312–324.

Lundgren, D. L., Hahn, F. F., Griffith, W. C., et al., 1996. Pulmonary carcinogenicity of relatively low doses of beta-particle radiation from inhaled $^{144}CeO_2$ in rats. Radiat. Res. 146, 525–535.

Lundgren, D. L., McClellan, R. O., Hahn, F. F., Newton G. J., Diel J. H., 1980b. Repeated inhalation exposure of mice to $^{144}CeO_2$. I. Retention and dosimetry. Radiat. Res. 82, 106–122.

Lundgren. D. L., McClellan, R. O., Thomas, R. L., Hahn, F. F., Sanchez, A., 1974, Toxicity of inhaled $^{144}CeO_2$ in mice. Radiat. Res. 58, 448–461.

Lustgarten, C. S., Boecker, B. B., Cuddihy, R. G., Kanapilly, G. M., 1975. Biliary excretion of ^{144}Ce following inhalation of ^{144}Ce citrate in rats and Syrian hamsters II. Inhalation Toxicology Research Institute Annual Report 1974–1975, LF-52. 84–87. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Lustgarten, C. S., Boecker, B. B., Cuddihy, R. G., Kanapilly, G. M., 1976. Biliary excretion of ^{144}Ce following inhalation of ^{144}Ce citrate in rats and Syrian hamsters III. Inhalation Toxicology Research Institute Annual Report 1975–1976, LF-56. 84–87. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Lustgarten, C. S., Cuddihy, R. G., Boecker, B. B., Huber, N., 1974. Biliary excretion of ^{144}Ce following inhalation of ^{144}Ce citrate by rats. Inhalation Toxicology Research Institute Annual Report 1973–1974, LF-49, 57–61. Lovelace Foundation.

Mauderly, J. L., Lundgren, D. L., Nameny, J., Chen, T.B., 1987. The effects of cigarette smoke and pulmonary emphysema on long-term pulmonary retention of 144cerium oxide. Inhalation Toxicology Research Institute Annual Report 1986–1987, LMF-120 430–435. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

McClellan, R.O., Bustad, L. K., Keough, R. F., 1965. Metabolism of some SNAP Radionuclides in Miniature Swine. Aerospace Med. 36, 16–20.

Miller, J. K., Perry, S. C., Chandler, P. T., Craig R. G., 1967. Evaluation of radiocerium as a non-absorbed reference material for determining gastrointestinal nutrient absorption in cattle. J. Dairy Sci. 50, 355.

Mirell, S. G., Blahd, W. H., 1989. Biological retention of fission products from the Chernobyl plume. Health Phys. 57, 649–652.

Morrow, P.E., Gibb, F.R., Davies, H., Fisher, M., 1968. Dust removal from the lung parenchyma: an investigation of clearance stimulants. Toxicol. Appl. Pharmacol. 12, 372–396.

Muggenburg, B. A., Pfleger, R. C., Cuddihy, R. G., McClellan, R. O., 1972. The removal of inhaled $^{144}CeCl_3$ from Beagle dogs. III. Bilateral bronchopulmonary lavage with a DTPA solution. Health Phys. 23, 611–619.

NCRP, 1978. Physical, chemical, and biological properties of radiocerium relevant to radiation protection guidelines. NCRP Report No. 60. National Council on Radiation Protection and Measurements, Bethesda, MD.

Oberdörster, G., Ferin, J., Morrow, P. E., 1992. Volumetric loading of alveolar macrophages (AM): a possible basis for diminished AM-mediated particle clearance. Expl. Lung Res. 18, 87–104.

Paul, A. C., Pillai, P. M. B., Maniyan, C. G., et al., 2000. Characterisation of airborne Ce, Th and Cd in workplace and their correlation with their concentrations in body fluids and excreta of occupational workers using NAA, ICP-AES and XRF. Research co-ordination meeting on assessment of levels and health-effects of airborne particulate matter in mining, metal refining and metal working industries using nuclear and related analytical techniques. Belo Horizonte (Brazil) 17–20 May 1999.

Paul, A. C., Pillai, P. M. B., Radhakrishnan, S., et al., 1998. Characterisation of airborne Ce, Th and Cd in workplace and their co-relation with their concentrations in body fluids and excreta of occupational workers using NAA, ICP - AES and XRF. Research co-ordination meeting on co-ordinated research project on assessment of levels and health-effects of airborne particulate matter in mining, metal refining and metal working industries using nuclear and related analytical techniques. Vienna 20–24 Oct 1997.

Pfleger, R. C., Muggenburg, B. A., Cuddihy, R. G., McClellan, R. O., 1972b. The removal of inhaled $^{144}CeCl_3$ from Beagle dogs. II. Intravenous administration of a DTPA solution. Health Phys. 23, 605–609.

Pfleger, R. C., Muggenburg, B. A., Sesline, D. H., et al., 1972a. The removal of inhaled $^{144}CeCl_3$ from Beagle dogs. I. Unilateral bronchopulmonary lavage with a DTPA solution. Health Phys. 23, 605–609.

Richmond, C. R., London, J. E., 1966. Long-term *in vivo* retention of cerium-144 by beagles. Nature 211, 1179.

Rundo, J., 1965. A case of accidental inhalation of irradiated uranium. Brit. J. Radiol. 38, 39–50.

Schönfeld, T., Liebscher, K., Karl, F., Friedman, C., 1960. Radioactive fission products in lungs. Nature 185, 192–193.

Shyr, L. J., Griffith, W. C., Boecker B. B., 1991. An optimization strategy for a biokinetic model of inhaled radionuclides. Fundam. Appl. Toxicol. 16, 423–434.

Sill, C., Voelz, G., Olson, D., Anderson, J., 1969. Two studies of acute internal exposure to man involving cerium and tantalum radioisotopes. Health Phys. 16, 325–332.

Snipes, M. B., Boecker, B. B., McClellan, R. O., 1983. Retention of monodisperse or polydisperse aluminosilicate particles inhaled by dogs, rats, and mice. Toxicol. Appl. Pharmacol. 69, 345–362.

Snipes, M.B., Clem, M.F., 1981. Retention of microspheres in the rat lung after intratracheal instillation. Environ. Res. 24, 33–41.

Stradling, G. N., Moody, J. C., 1995. Use of animal studies for assessing intakes of inhaled actinide-bearing dusts. J. Radioanal. Nucl. Chem. 197, 309–329.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1989a. The metabolic behaviour in rats of actinide bearing residues formed during the storage of irradiated Magnox fuels: An experimental basis for interpreting in-vivo monitoring data to assess intakes of plutonium by workers. NRPB-M162. Chilton, National Radiological Protection Board.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1989b. Assessment of intake of an actinide-bearing dust formed from pond storage of spent Magnox fuel. Radiat. Prot. Dosim. 26, 201–206.

Stuart, B. O., 1964. Preliminary studies of inhaled ^{147}Pm perchlorate. Hanford Biologu Research Annual Report for 1963. HW-80500. UC-48, Biology and Medicine (TID-4500, 30th Ed.).

Stuart, B. O., Casey, H. W., Bair, W. J., 1964. Acute and chronic effects of inhaled $^{144}CeO_2$ in dogs. Health Phys. 10, 1203–1209.

Stuart, B. O., Gaven, J. C., 1968. Inhalation Studies with Promethium Oxide in Beagle Dogs. Pacific Northwest Annual Report for 1967, BNWL-714.

Sturbaum, D., Brooks, A. L., McClellan, R. O., 1970. Tissue distribution and dosimetry of ^{144}Ce in Chinese Hamster. Radiat. Res. 44, 459–367.

Taylor, D. M., Leggett, R. W., 1998. A generic biokinetic model for the lanthanide elements. Radiat. Prot. Dosim. 79, 351-354.

Thomas, R. G., Durbin, P. W., McInroy, J. F., Healy, J. W., 1989. Estimation of human gonadal Pu and Ce concentrations from animal data. Health Phys. 57, Suppl. 1, 97–107.

Thomas, R. L., McClellan, R. O., 1972. Retention and tissue distribution of ^{144}Ce following inhalation of $^{144}CeO_2$ in Syrian hamsters. Fission Product Inhalation Program Annual Report, 1971–1972, LF–45, 74–76. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Thomas, R. L., Kanapilly, G. M., McClellan, R. O., 1973. Influence of aerosol production temperature on retention of inhaled and injected 144Ce-clay particles in mice. Inhalation Toxicology Research Institute Annual Report 1972–1973, LF-46. 55–66. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Thomas, R. L., Scott, J, K., Chiffelle, T. L., 1972. Metabolism and toxicity of inhaled ^{144}Ce in rats. Radiat. Res. 49, 589–610.

Tombropoulos, E. G., Bair, W. J., Park, J. F., 1969. Removal of inhaled ^{144}Ce-^{144}Pr oxide by diethylenetriaminepentacetic acid (DTPA) treatment. I. ^{144}Ce-^{144}Pr oxide prepared by peroxide oxidation. Health Phys. 16, 333–338.

Wegst, A.V., Pelletier, C. A., Whipple, G. H., 1964. Detection and quantitation of fallout particles in a human lung. Science 143, 957–959.

Wolff, R.K., Tillquist, H., Muggenburg, B.A., Harkema, J.R., Mauderley, J.L., 1989. Deposition and clearance of radiolabelled particles from small ciliated airways in beagle dogs. J. Aerosol Med. 2, 261–270.

Yan, S., Shan, Y., Lu, H., et al., 1988. Deposition and clearance of $^{141}CeO_2$ in rats. IN: Inhaled Particles VI, Proceedings of an International Symposium and Workshop on Lung Dosimetry Organised by the British Occupational Hygiene Society in Co-operation with the Commission of the European Communities, Cambridge, 2–6 September 1985, (Eds. Dodgson, J., McCallum, R. I., Bailey, M. R. Fisher, D. R). Ann. Occup. Hyg. 32, Suppl. 1, 957–962.

5. PRASEODYMIUM (Z = 59)

5.1. Chemical Forms in the Workplace

(205) Praseodymium is an element of the lanthanide series which occurs mainly in oxidation states III and IV.

(206) Praseodymium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides, carbonates and citrates), but also tellurides, selenides and nitrides. Praseodymium is most commonly obtained from bastnäsite and monazite.

(207) Praseodymium isotopes (e.g. ^{143}Pr) are fission products.

Table 5. 1. Isotopes of praseodymium addressed in this report.

Isotope	Physical half-life	Decay mode
Pr-134	11 m	EC, B+
Pr-134m	17 m	EC, B+
Pr-135	24 m	EC, B+
Pr-136	13.1 m	EC, B+
Pr-137	1.28 h	EC, B+
Pr-138m	2.12 h	EC, B+
Pr-139	4.41 h	EC, B+
Pr-142	19.12 h	EC, B-
Pr-142m	14.6 m	IT
Pr-143[a]	13.57 d	B-
Pr-144	17.28 m	B-
Pr-145	5.98 h	B-
Pr-146	24.15 m	B-
Pr-147	13.4 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

5.2. Routes of Intake

5.2.1. Inhalation

Absorption Types and parameter values

(208) No information was found on the behaviour of inhaled praseodymium (Pr) in man, except for ^{144}Pr as the short-lived (half-life 17 minutes) progeny of the important fission product cerium-144 (half-life 284 d), which is covered in the cerium inhalation section. Information on absorption from the respiratory tract is available from experimental studies of praseodymium chloride. The studies reported were of short duration because they used ^{143}Pr, which has a half-life of only 13.7 d.

(209) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including praseodymium, are given in Table 2.4 of the general lanthanide section.

Water-soluble forms of praseodymium

(210) Moskalev et al. (1972) followed the biokinetics of ^{143}Pr (and other lanthanides, see general lanthanide section) for 32 d after deposition in the lungs of rats. However, few details are given. Fig. 135 of Moskalev et al. (1972) shows retention (presumably in the lungs) of praseodymium falling to ~10% "of given dose" by 32 d. Analysis was carried out here (i.e. by the Task Group) assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with f_r ~0.7 (which would give assignment to Type M), in broad agreement with the value of 0.5 chosen for water-soluble forms of lanthanides.

Praseodymium chloride ($PrCl_3$)

(211) Gensicke and Nitschke (1964) followed the biokinetics of ^{143}Pr up to 14 d in mice that inhaled ^{143}Pr chloride (pH 3.5). There was moderate transfer from lungs to blood and systemic tissues. Lung content dropped to ~60% of the initial lung deposit (ILD) at 1 d and ~40% ILD at 14 d. The contents of liver and skeleton each increased to ~7% ILD at 1 d and ~10% ILD at 14 d. Analysis was carried out here assuming that s_r = 0.44 d^{-1}, f_b = 0.07, s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1} (see above). The results fit well with f_r = 0.4, (which would give assignment to Type M) in broad agreement with the value of 0.5 chosen for water-soluble forms of lanthanides. Similar studies were carried out by this research group with chlorides of ^{144}Ce, ^{147}Pm, and ^{153}Sm (see general lanthanide section).

(212) Although specific parameter values for praseodymium chloride based on *in vivo* data could be derived, inhalation exposure to it is unlikely. Instead, it is assigned to water-soluble forms of lanthanides (see general lanthanide section, Table 3).

5.2.2. Ingestion

(213) The fractional absorption of praseodymium in rats was reported to be less than 5 x 10^{-4} (Hamilton, 1948; Moskalev et al., 1972).

(214) In *Publication 30* (ICRP, 1979), an f_1 of 3 x 10^{-4} was recommended for all compounds of praseodymium. In *Publication 68* (ICRP, 1994), a value of 5 x 10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

5.2.3. Systemic distribution, retention and excretion of praseodymium

5.2.3.1. Data

(215) The absorption and distribution of inhaled liquid ^{143}Pr aerosols were investigated in mice. Absorbed activity was stored mainly in the liver and skeleton, with low activity concentrations in the other investigated organs. The systemic biokinetics of ^{143}Pr was broadly

similar to that observed in similar studies involving ^{144}Ce, but excretion was faster for ^{143}Pr than for ^{144}Ce (Gensicke and Henneberger, 1964).

5.2.3.2. Biokinetic model

(216) The biokinetic model for systemic praseodymium applied in this report is described in Section 2.2.3.2.

5.2.3.3. Treatment of progeny

(217) The treatment of radioactive progeny of praseodymium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in section 2.2.3.3.

5.3. Individual monitoring

(218) Information of detection limit for individual measurement techniques is not available.

5.4. Dosimetric data for praseodymium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Gensicke, F., Nitschke, H.W., 1964. On the problem of radiopraseodymium metabolism after inhalation. [Zur Frage des Stoffwechsels von Radiopraseodym (^{143}Pr) nach Inhalation von Flüssigkeitaerosolen bei der weissen Maus.] Strahlentherapie 123, 259–266.

Hamilton, J. G., 1948. The metabolism of the fission products and the heaviest elements. Revs. Mod. Phys. 20, 718–728.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Supplement to Part 1). Ann. ICRP 3 (1-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements In: *Biologicheskoye deystviye vneshnikh* i *vnutrennikh istochnikov* r&&ii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

6. NEODYMIUM (Z = 60)

6.1. Chemical Forms in the Workplace

(219) Neodymium is an element of the lanthanide series which occurs mainly in oxidation state III.

(220) Neodymium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates), but also carbides, phosphides and nitrides. Neodymium is most commonly obtained from bastnäsite and monazite.

(221) Neodymium glass solid-state lasers are used in extremely high energy multiple beam systems for inertial confinement fusion.

(222) Neodynium isotopes (e.g. ^{147}Nd) are fission products.

Table 6. 1. Isotopes of neodymium addressed in this report.

Isotope	Physical half-life	Decay mode
Nd-135	12.4 m	EC, B+
Nd-136	50.65 m	EC, B+
Nd-137	38.5 m	EC, B+
Nd-138	5.04 h	EC
Nd-139	29.7 m	EC, B+
Nd-139m	5.50 h	EC, B+, IT
Nd-140	3.37 d	EC
Nd-141	2.49 h	EC, B+
Nd-144	2.29E+15 y	A
Nd-147[a]	10.98 d	B-
Nd-149	1.728 h	B-
Nd-151	12.44 m	B-
Nd-152	11.4 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

6.2. Routes of Intake

6.2.1. Inhalation

Absorption Types and parameter values

(223) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including neodymium (see general lanthanide section). No reports of experimental studies of neodymium were found. As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including neodymium, are given in Table 2.4.

Absorption parameter values for inhaled and ingested lanthanidesof the general lanthanide section.

6.2.2. Ingestion

(224) McAughey (1996) using a dual stable isotope technique, measured the absorption of Nd in eight adults (four males and four females): the observed f_1 values ranged between < 1.4 x 10^{-4} and 3.6 x 10^{-3}, with a medium value of 5 x 10^{-4}.

(225) In *Publication 30* (ICRP, 1979), an f_1 of 3 x 10^{-4} was recommended for all compounds of neodymium. In *Publication 68* (ICRP, 1994), a value of 5 x 10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

6.2.3. Systemic distribution, retention and excretion of neodymium

6.2.3.1. Data

(226) In rats (Durbin, 1960, 1962), neodymium had somewhat lower liver uptake and higher urinary excretion than its neighbours in the periodic chart and thus did not closely fit the trend indicated by the collective data for the lanthanides, i.e., a gradual, continuous change with ionic radius in deposition fractions in major repositories. However, the rate of urinary excretion of neodymium during the first week after injection into human subjects (Roth et al., 1995) was similar to that observed in human subjects injected with promethium (Palmer et al., 1970) and was much lower than that measured in rats (Durbin, 1960, 1962). The mean faecal to urinary excretion ratio over the first 7 d (~0.11) and mean whole-body retention of absorbed neodymium after 7 d (94 ± 3%) in the human subjects were also similar to values determined for promethium in human subjects.

6.2.3.2. Biokinetic model

(227) The biokinetic model for systemic neodymium applied in this report is described in Section 2.2.3.2.

6.2.3.3. Treatment of progeny

(228) The treatment of radioactive progeny of neodymium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

6.3. Individual monitoring

^{147}Nd

(229) Measurements of ^{147}Nd are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{147}Nd concentrations in urine may be used to determine intakes of the radionuclide. The main technique is gamma spectrometry.

Table 6. 2. Monitoring techniques for ^{147}Nd.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{147}Nd	Urine Bioassay	γ-ray spectrometry	15 Bq/L
^{147}Nd	Lung Measurement[a]	γ-ray spectrometry	10 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

6.4. Dosimetric data for neodymium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Durbin, P. W., 1960. Metabolic Characteristics within a Chemical Family Health Phys. 2, 225–238.

Durbin, P. W., 1962. Distribution of the Transuranic Elements in Mammals. Health. Phys. 8, 665–671.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

McAughey, J.A., 1996. Assessment of internal dose from plutonium and other radionuclides using stable isotope tracers techniques in man. Contract report N° BI3P-CT920048, Commission of the European communities radiation protection programme 1992–1994.

Palmer, H. E., Nelson, I. C., Crook, G. H., 1970. The uptake, distribution and excretion of promethium in humans and the effect of DTPA on these parameters. Health Phys. 18, 53–61.

Roth, P., Molho, N., Cantone, M. C., Taylor, D. M., McAughey, J. A., 1995. Assessment of internal dose from plutonium and other radionuclides using stable isotope techniques in man. CEC Radiation Protection Programme 1992–1994, Report on EU Contract F13P-CT920048, September, 33–45.

7. PROMETHIUM (Z = 61)

7.1. Chemical Forms in the Workplace

(230) Promethium is an element of the lanthanide series which occurs mainly in oxidation state III. All of its isotopes are radioactive.

(231) Promethium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, sulphates, sulphides and carbonates). Promethium is used in luminous paint and atomic batteries. Promethium is most commonly obtained from bastnäsite and monazite.

(232) Promethium isotopes (e.g. ^{147}Pm) are fission products.

Table 7. 1. Isotopes of promethium addressed in this report.

Isotope	Physical half-life	Decay mode
Pm-141	20.9 m	EC, B+
Pm-143	265 d	EC
Pm-144	363 d	EC
Pm-145	17.7 y	EC, A
Pm-146	5.53 y	EC, B-
Pm-147[a]	2.623 y	B-
Pm-148	5.368 d	B-
Pm-148m	41.29 d	B-, IT
Pm-149	53.08 h	B-
Pm-150	2.68 h	B-
Pm-151	28.40 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

7.2. Routes of Intake

7.2.1. Inhalation

Absorption Types and parameter values

(233) No information was found on the behaviour of inhaled promethium (Pm) in man. Information on absorption from the respiratory tract is available from experimental studies of promethium as chloride and oxide.

(234) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including promethium, are given in Table 2.4. Absorption parameter values for inhaled and ingested lanthanidesof the general lanthanide section.

Promethium perchlorate

(235) Stuart (1964) measured the tissue distribution of ^{147}Pm at 28 and 56 d in two dogs that inhaled ^{147}Pm perchlorate. In both dogs, the amounts of ^{147}Pm in the lungs at 20 d were ~30–40% of that at 2 d, and amounts in lung, liver and skeleton when sacrificed were ~10%, 40%, 35% of the total in the body (Sacrifice Body Burden, SBB), respectively. There is insufficient information to assess parameter values, and there was tissue damage that might have affected the biokinetics, but the results indicate Type M behaviour.

Promethium chloride ($PmCl_3$)

(236) Gensicke and Nitschke (1965) followed the biokinetics of ^{147}Pm up to 30 d in mice that inhaled $^{147}PmCl_3$ (pH 3.5). There was moderate transfer from lungs to blood and systemic tissues. Lung content dropped to ~70% of the initial lung deposit (ILD) at 1 d and ~20% ILD at 14 d. The contents of liver and skeleton increased to ~15% and ~5% ILD respectively at 1 d, after which the liver content fell and the skeleton content remained fairly constant. In a complementary study, Hölzer and Gensicke (1965) studied the distribution of ^{147}Pm within organs by autoradiography, up to 120 d after inhalation.

(237) Gensicke et al. (1973) investigated the effect of hexametaphosphate (used as decorporation agent) on retention of ^{147}Pm in mice that inhaled $^{147}PmCl_3$ administered as described by Gensicke and Nitschke (1965). Data on the control group provide information on the biokinetics of ^{147}Pm. Up to 30 d results were similar to those in the earlier study. At 200 d, there was ~2% ILD remaining in the lungs, ~2% ILD in liver and ~10% ILD in the skeleton.

(238) Analysis was carried out here (i.e. by the Task Group) to the combined results of both studies, assuming that $s_r = 0.44$ d^{-1}, $f_b = 0.07$; $s_b = 0.021$ d^{-1}, and $s_s = 0.0015$ d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with $f_r = 0.3$ (which would give assignment to Type M), in broad agreement with the value of 0.5 chosen for water-soluble forms of lanthanides.

(239) Similar studies were carried out by this research group with chlorides of ^{144}Ce, ^{143}Pr, and ^{153}Sm (see general lanthanide section).

(240) Although specific parameter values for promethium chloride based on *in vivo* data could be derived, inhalation exposure to it is unlikely. Instead, promethium chloride is assigned to water-soluble forms of lanthanides (see general lanthanide section, Table 2.4).

Promethium oxide (Pm_2O_3)

(241) Stuart (1966, 1968) followed the biokinetics of ^{147}Pm and ^{148m}Pm up to at least 50 d in dogs that inhaled calcined $^{147}Pm_2O_3$ that had been neutron-irradiated to produce ^{148m}Pm: a hard gamma-emitter, as a tracer for whole body counting. Forty to 50% of the total initial deposit was cleared in the first week, mainly to faeces. Whole body counts beyond 5 or 6 d reflected only radioactive decay. Urinary excretion was higher than expected for an 'insoluble' compound, and it was inferred that the neutron irradiation led to more rapid dissolution than expected. The observed pulmonary retention half-time of 4–5 months is much less than expected for an 'insoluble' material in dogs.

(242) Stuart (1967, 1968) followed the biokinetics of ^{147}Pm and ^{148m}Pm up to 12 months in dogs that inhaled calcined $^{147}Pm_2O_3$ that had been re-calcined after neutron irradiation to produce ^{148m}Pm. The urinary excretion was typical of relatively insoluble materials and for the first few days it was about one order of magnitude lower than for the calcined material. The

lung measurements at five and ten months indicated a retention half-time of the order of about one year or longer. There is insufficient information to estimate absorption parameter values: the results suggest Type M or S behaviour.

Samarium oxide (Sm_2O_3)

(243) Shipler et al. (1976) followed the biokinetics of ^{145}Sm and ^{143}Pm up to 30 d in rats and beagle dogs that inhaled stable Sm_2O_3 labelled with $^{145}Sm_2O_3$ and $^{143}Pm_2O_3$. The particles were formed by thermal degradation of the oxalates at 750°C for rats and 1170°C for dogs. (The authors considered that some material may have been converted to hydroxide.) The objective was to provide information to develop guidance on bioassay for $^{147}Pm_2O_3$. Promethium-143 was used as the tracer because, unlike ^{147}Pm, it has photon emissions suitable for external counting. Because of the low mass of ^{143}Pm and the absence of a stable isotope of promethium, Sm_2O_3 was used as a carrier. Ratios of ^{145}Sm to ^{143}Pm were similar in most tissue and excreta samples to those in the aerosol suspension, indicating that absorption from lungs to blood and systemic biokinetics of the two elements were similar. In both species a large fraction of the initial deposit cleared in faeces in the first few days, attributed to clearance from the upper respiratory tract. Subsequent lung clearance was slow, but the ^{143}Pm content of liver averaged ~18% of the initial lung deposit (ILD) in dogs and ~4% ILD in rats. Analysis carried out here (i.e. by the Task Group), showed that the results for both dogs and rats could be fit well with absorption parameter values of f_r =0.04, s_r = 1.1 d^{-1}, and s_s = 0.004 d^{-1}. Assuming (based on cerium, see general lanthanide section) that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, most results fit well with f_r = 0.05, and s_s = 0.005 d^{-1}. Both sets of values give assignment to Type M.

Fused aluminosilicate particles (FAP)

(244) FAP or “fused clay” particles have been extensively used as relatively insoluble particles in inhalation studies, both of biokinetics and of radiation effects (see, e.g. cerium section). Snipes et al. (1975, 1977) studied the effect of lung lavage on the distribution within the lungs of FAP labelled with ^{147}Pm and ^{169}Yb, at times up to 56 d after inhalation by dogs. No biokinetic data were reported, but the ability to measure the effectiveness of lung lavage, and particle distributions in lung sections by autoradiography, demonstrated that the material did not dissolve readily in the lungs. Herbert et al. (1987, 1988) investigated effects of lung irradiation in rats for 18 months after inhalation of FAP labelled with ^{147}Pm and ^{169}Yb (the latter as a tracer for *in vivo* measurements). Little biokinetic information was reported. However, effective lung retention half-times were ~5 d for 58% ILD and 150 d for 42% ILD, showing that the material was relatively insoluble.

7.2.2. Ingestion

(245) Early studies by Hamilton (1948) and Moskalev (1959) showed total retention of $<5x10^{-4}$ for adult rats. Studies performed by Sullivan et al. (1984) with ^{147}Pm administered as chloride to rats suggested values of 7 x 10^{-5} for adult rats.

(246) Palmer et al. (1970) studied the oral absorption of $^{143}PmCl_3$ in two adult males and the f_1 has been estimated to 10^{-5}.

(247) In *Publication 30* (ICRP, 1979), an f_1 of 3 x 10^{-4} was recommended for all compounds of promethium. In *Publication 68* (ICRP, 1994), a value of 5 x 10^{-4} was adopted by

analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

7.2.3. Systemic distribution, retention and excretion of promethium

7.2.3.1. Data

(248) Palmer et al. (1970) studied the biokinetics of ^{143}Pm in six human volunteers following its intravenous administration as chloride. Approximately 25% of the injected amount remained in blood after 30 min, 15% after 1 h, and 2–3% after 5 h. About half of the injected activity accumulated in the liver within a few minutes. Most of the remaining activity deposited in bone within the next 5 h. Measurements of whole-body retention and urinary and faecal excretion are summarised in Figs. 7.1 to 7.3. More than 10% of the injected amount was excreted within the first 20 d. The retention half-time of the amount remaining in the body after the first 1-2 mo could not be determined due to the relatively short observation period but was estimated to be substantially greater than 1000 d. The urinary excretion rate was greater than the faecal excretion rate until about the seventh day, at which time the rates were about equal. Daily faecal samples were stopped after the seventh day, but measurements on the 15th day suggested that the faecal excretion rate was greater than the urinary excretion rate at that time. The excretion rates observed in the human subjects were similar to those observed by the investigators in experiments involving pigs and dogs, except that the urinary excretion rate was noticeably greater in the human subjects than in the laboratory animals on the first day. The pattern of decline in the urinary excretion rate of Pm over the first several weeks in the human subjects and large laboratory animals suggests a slow return to blood from tissues. A relatively high rate of faecal excretion in the human subjects during the first two weeks but only slow loss from the body thereafter suggests an initially high rate of secretion into the gastrointestinal tract but substantially slower secretion thereafter.

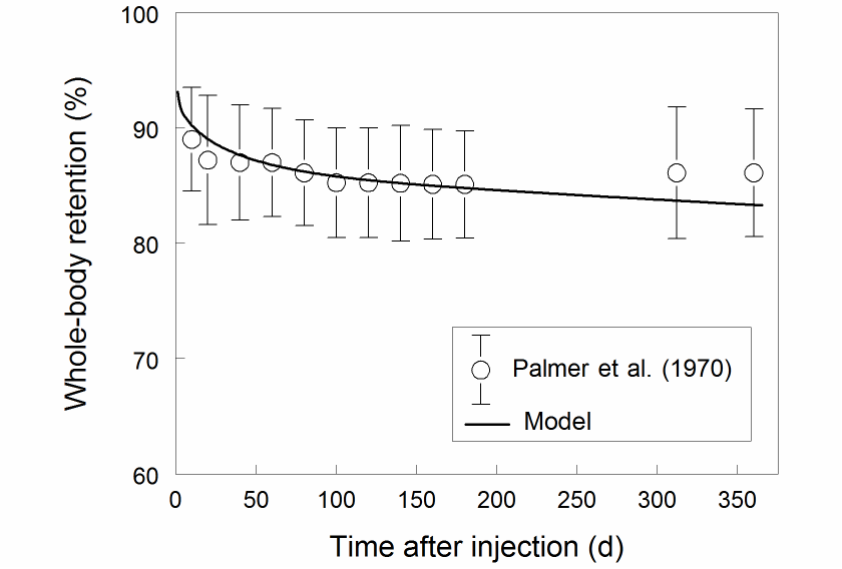


Fig. 7.1. Whole-body retention of intravenously injected ^{143}Pm as observed in six human subjects (Palmer et al., 1970) and derived from the model used in this report.

The vertical lines represent observed ranges of values.

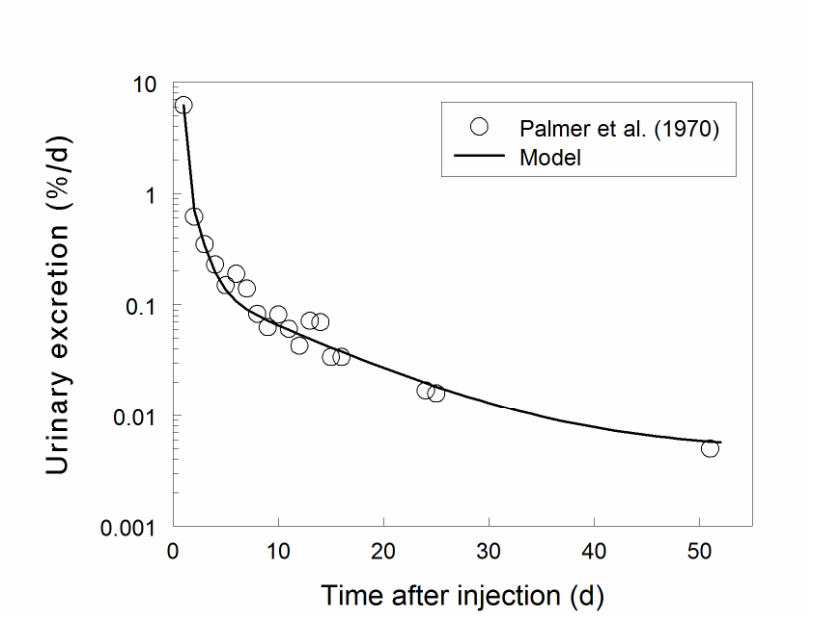


Fig. 7.2.Urinary excretion of intravenously injected ^{143}Pm as observed in six human subjects (Palmer et al., 1970) and derived from the model used in this report.

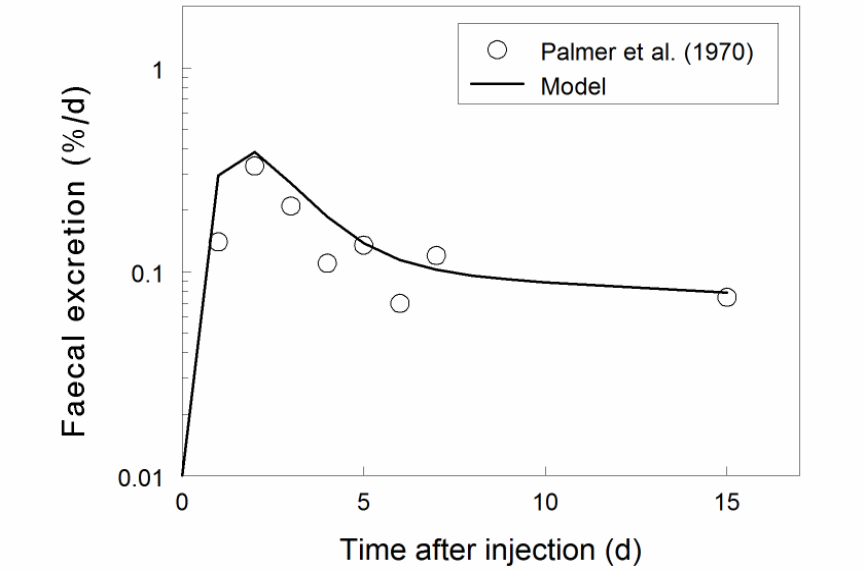


Fig. 7.3. Faecal excretion of intravenously injected ^{143}Pm as observed in six human subjects (Palmer et al., 1970) and derived from the model used in this report.

(249) McConnon and Cole (1971) compared the behavior of intravenously injected $PmCl_3$ in swine and normal human subjects. No major differences were seen the systemic biokinetics of Pm in the two species.

(250) In beagle dogs exposed to $^{147}Pm_2O_3$ by inhalation, about 40–50% of the total body burden was in the lungs, 3% in TB lymph nodes, 25% in liver, and 20% in bone at five months after exposure (Stuart, 1967).

(251) McClellan et al. (1965) studied the biokinetics of ^{147}Pm in miniature swine following its oral and intravenous administration as chloride. At 10 d after oral administration, activity was detectable in the skeleton, liver, kidneys, and spleen but amounted to less than 0.001% of the administered amount due to low fractional absorption to blood. At 10 d after intravenous administration the skeleton, liver, kidneys, and spleen contained on average about 40%, 40%, 0.3%, and 0.1%, respectively, of the administered amount.

(252) The distribution of ^{147}Pm was investigated in mice following inhalation of $^{147}PmCl_3$ liquid aerosols (Gensicke and Nitschke, 1965; Hölzer and Gensicke, 1965). Activity was quickly absorbed to blood or transferred to the gastrointestinal contents. Absorbed activity accumulated primarily in the liver and skeleton. Activity was distributed homogeneously in the liver. In the femur, activity was found mainly in the osteoblastic tissue of the perichondrium and on the surfaces of the primary spongiosa.

(253) Priest (2007) compared the distributions of three trivalent elements with a similar ionic radius following their intravenous administration to rats. Activity concentrations were determined in the liver, kidneys, femur, spleen, and gastrointestinal tract at 1, 4, 14, and 32 d. The distributions of the two ions with the same crystal ionic radius (111 pm), promethium and curium, were indistinguishable. The distribution of americium, which has a slightly larger cystal ionic radius (111.5 pm), was similar to, but distinguishable from, the distributions of promethium and curium.

7.2.3.2. Biokinetic model

(254) The biokinetic model for systemic promethium applied in this report is described in Section 2.2.3.2.

7.2.3.3. Treatment of progeny

(255) The treatment of radioactive progeny of promethium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in section 2.2.3.3.

7.3. Individual monitoring

^{147}Pm

(256) Measurements of ^{147}Pm concentrations in urine and faeces are used to determine intakes of the radionuclide.

Table 7. 2. Monitoring techniques for ^{147}Pm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit

^{147}Pm	Urine Bioassay	Liquid scintillation	5 Bq/L
^{147}Pm	Faecal Bioassay	γ-ray spectrometry	15 Bq/24h

7.4. Dosimetric data for promethium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Gensicke, F., Hölzer, F., Nitschke, H.W., 1973. The behaviour of inhaled radiopromethium in the organism and the effect of hexametaphosphate on the excretion of the nuclide. [Das Verhalten von inhaliertem Radiopromethium im Organismus und die Wirkung von hexametaphosphat auf die Ausscheidung des Nuklids.] Radiobiologia radiotherapia. 14, 199–211.

Gensicke, F., Nitschke, H.W., 1965. Metabolism of radiopromethium (^{147}Pm) following inhalation of liquid aerosols in mice [Der Stoffwechsel von Radiopromethium (^{147}Pm) nach Inhalation von Flüssigkeitsaerosolen bei Mäusen.] Strahlentherapie, 128, 288–295.

Hamilton, J.G., 1948. The metabolic properties of the fission products and actinide elements; Rev. Mod. Phys. 20, 718–728.

Herbert, R. A., Scott, B. R., Hahn, F. F., et al., 1987. The prevalence and morphology of primary pulmonary neoplasms in rats 18 months after inhalation of ^{147}Pm in fused aluminosilicate particles. Inhalation Toxicology Research Institute Annual Report 1986–1987, LMF-120, 331–335. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Herbert, R. A., Scott, B. R., Hahn, F. F., et al., 1988. The occurrence of primary pulmonary neoplasms in rats 18 months after inhalation of ^{147}Pm in fused aluminosilicate particles. Inhalation Toxicology Research Institute Annual Report 1987–1988, LMF-121, 234–240. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Hölzer, F., Gensicke, F., 1965. Studies on the microdistribution of inhaled radiopromethium (^{147}Pm). Strahlentherapie 128, 396–405.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

McClellan, R. O., Bustad, L. K., Keough, R. F., 1965. Metabolism of some SNAP Radionuclides in Miniature Swine. Aerospace Med. 36, 16–20.

McConnon, D., Cole, C. R., 1971. The comparative metabolism of intravenously injected promethium in swine and humans. Health Phys. 21, 61.

Moskalev, I., 1959. Data on the distribution of 147Pm [translated in US atomic energy commission document, AEC Tr 3938]. Med. Radiol. 4, 73–75.

Nelson, I.C., Ballou, J.E., Shipler, D.B., Craig, D.K., Thompson, R.C., 1975. Quantification of inhaled promethium. Technical report BNWL-1950 (Pt.1), 130.

Palmer, H.E., Nelson IC., Crook GH., 1970. The uptake, distribution and excretion of promethium in humans and and the effect of DTPA on these parameters. Health Phys. 18, 53–61.

Priest, N. D., 2007. Comparative biokinetics of trivalent radionuclides with similar ionic dimensions: promethium-147, curium-242 and americium-241. Radiat. Res. 168, 327–331.

Shipler, D.B., Ballou, J.E., Griffin, B.I., Nelson, I.C., 1976. Development of a diagnostic model for inhaled promethium-147 oxide. Diagnosis and Treatment of Incorporated Radionuclides, 209–221. (Vienna: IAEA) IAEA-SR-6/28.

Snipes, M. B., Runkle, G. E., Muggenburg, B. A., 1977. Influence of lavage therapy on the distribution patterns of inhaled relatively insoluble particles in the lung. Inhalation Toxicology Research Institute Annual Report 1976–1977, LF-58, 200–204. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Snipes, M. B., Runkle, G. E., Muggenburg, B. A., Hulbert, A. J., 1975. Distribution patterns of inhaled polydisperse ^{147}Pm fused clay particles in the beagle dog thorax with and without lavage therapy. II. Inhalation Toxicology Research Institute Annual Report 1974–1975, LF-52, 91–95. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Stuart, B. O., 1964. Preliminary studies of inhaled Pm^{147} perchlorate. In USAEC Report HW-80500, 59–63.

Stuart, B. O., 1967. Inhalation of promethium oxide by beagle dogs. Health Phys. 13, 929.

Stuart, B.O., 1966. Promethium oxide inhalation studies. Pacific Northwest Laboratory Annual Report for 1965 to the USAEC Division of Biology and Medicine. 56–59. U. S. Atomic Energy Commission.

Stuart, B.O., 1968, Inhalation studies with promethium oxide in beagle dogs. Pacific Northwest Laboratory Annual Report for 1967 to the USAEC Division of Biology and Medicine. BNWL-714. 3.29–3.33. U. S. Atomic Energy Commission

Sullivan, M.F., Miller, B.M., Goebel, J.C., 1984. Gastrointestinal absorption of metals (51Cr, 65Zn, 95mTc, 109Cd, 113Sn, 147Pm, and 238Pu) by rats and swine. Environ. Res. 35, 439–453.

8. SAMARIUM (Z=62)

8.1. Chemical Forms in the Workplace

(257) Samarium is an element of the lanthanide series which occurs mainly in oxidation states II and III.

(258) Samarium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates) but also tellurides, selenides and organometallic compounds. Samarium is most commonly obtained from bastnäsite and monazite.

^{149}Sm is a strong neutron absorber added to the control rods of nuclear reactors and ^{153}Sm is commonly used in the treatment of cancer.

(259) Samarium isotopes (e.g. ^{151}Sm, ^{153}Sm) are fission products.

Table 8. 1. Isotopes of samarium addressed in this report.

Isotope	Physical half-life	Decay mode
Sm-140	14.82 m	EC, B+
Sm-141	10.2 m	EC, B+
Sm-141m	22.6 m	EC, B+, IT
Sm-142	72.49 m	EC, B+
Sm-145	340 d	EC
Sm-146	1.03E+8 y	A
Sm-147	1.06E+11 y	A
Sm-148	7E+15 y	A
Sm-151	90 y	B-
Sm-153[a]	46.50 h	B-
Sm-155	22.3 m	B-
Sm-156	9.4 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

8.2. Routes of Intake

8.2.1. Inhalation

Absorption Types and parameter values

(260) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including samarium (Sm) (see general lanthanide section). Information on absorption from the respiratory tract is available from experimental studies of samarium as chloride and oxide.

(261) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and

Types, and associated f_A values for particulate forms of lanthanides, including samarium, are given in Table 2.4 of the general lanthanide section.

Samarium chloride ($SmCl_3$)

(262) Gensicke and Nitschke (1970) followed the biokinetics of ^{153}Sm up to 7 d in mice that inhaled $^{153}SmCl_3$ (2 x 10^{-6} mg/kBq at pH 3.5). Because of the short half-life of ^{153}Sm (2.0 d) measurements were restricted to 7 d. Over this period lung retention followed a single exponential function with a half-time of about 11 d. The contents of liver and skeleton increased to ~3% and ~6% ILD respectively at 7 d.

(263) Analysis was carried out here (i.e. by the Task Group), assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with f_r = 0.4 (which would give assignment to Type M), in broad agreement with the value of 0.5 chosen for water-soluble forms of lanthanides.

(264) Similar studies were carried out by this research group with chlorides of ^{144}Ce, ^{143}Pr, and ^{147}Pm (see general lanthanide section).

(265) Although specific parameter values for samarium chloride based on *in vivo* data could be derived, inhalation exposure to it is unlikely. Instead, samarium chloride is assigned to water-soluble forms of lanthanides (see general lanthanide section, Table 2.4).

Samarium oxide (Sm_2O_3)

(266) Shipler et al. (1976) followed the biokinetics of ^{145}Sm and ^{143}Pm up to 30 d in rats and beagle dogs that inhaled stable Sm_2O_3 labelled with $^{145}Sm_2O_3$ and $^{143}Pm_2O_3$. The particles were formed by thermal degradation of the oxalates at 750°C for rats and 1170°C for dogs. (The authors considered that some material may have been converted to hydroxide.) The objective was to provide information to develop guidance on bioassay for $^{147}Pm_2O_3$. Promethium-143 was used as the tracer because, unlike ^{147}Pm, it has photon emissions suitable for external counting. Because of the low mass of ^{143}Pm and the absence of a stable isotope of promethium, Sm_2O_3 was used as a carrier. Ratios of ^{145}Sm to ^{143}Pm were similar in most tissue and excreta samples to those in the aerosol suspension, indicating that absorption from lungs to blood and systemic biokinetics of the two elements were similar. In both species a large fraction of the initial deposit cleared in faeces in the first few days, attributed to clearance from the upper respiratory tract. Subsequent lung clearance was slow, but the ^{145}Sm content of liver averaged ~15% of the initial lung deposit (ILD) in dogs and ~3% ILD in rats.

Analysis carried out here (i.e. by the Task Group), showed that the results for both dogs and rats could be fit well with absorption parameter values of f_r =0.04, s_r = 1.1 d^{-1}, and s_s = 0.004 d^{-1} (f_b = 0.07 and s_b = 0.021 d^{-1}). Assuming (based on cerium - see general lanthanide section) that s_r = 0.44 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1}, most results fit well with f_r = 0.05, and s_s = 0.005 d^{-1}. Both sets of values give assignment to Type M.

(267) Shinohara et al. (2009) measured the distribution of samarium in mice at 1 and 28 d after protracted inhalation of stable Sm_2O_3 (7 hours per day, 5 days per week) for one or four weeks. In both groups the highest concentration at 1 d after the end of exposure was in the lungs; between 1 and 28 d concentrations in lungs, liver, kidney and spleen fell, while the concentration in bone increased. Analysis carried out here, assuming (based on cerium) that s_r = 0.44 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1} showed that most of the results could be fit well with absorption parameter values of f_r ~0.1, and s_s = 0.02 d^{-1}, giving assignment to Type M.

(268) Shinohara et al. (2010) carried out similar experiments with cerium oxide, and compared the results with those for samarium reported by Shinohara et al. (2009). The authors noted that there was relatively little deposition of cerium in systemic organs (liver, bone, etc.) compared to samarium, and concluded that the behaviour of inhaled cerium was different from that of samarium, although their chemical properties are similar. However, no information was given on the method of preparation of either material, and so it is not clear to what extent that might account for the differences observed.

8.2.2. Ingestion

(269) Experiments on the acute toxicity of samarium nitrate and oxide to the rat (Bruce et al., 1963) and studies on absorption of $SmCl_3$ in man as a non-absorbable faecal marker of iron (Fairweather et al., 1997) indicate that the fractional absorption of samarium from the gastrointestinal tract is very small.

(270) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of samarium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

8.2.3. Systemic distribution, retention and excretion of samarium

8.2.3.1. Data

(271) Shipler et al. (1976) compared the kinetics of ^{145}Sm and ^{143}Pm in rats and dogs exposed by inhalation to an aerosol containing $^{145}Sm_2O_3$ and $^{143}Pm_2O_3$. The animals were sacrificed at 0, 14, and 30 days after exposure. Quantitative analysis for several tissues and excreta indicate that the two radionuclides behaved virtually identically in each of these animal species.

8.2.3.2. Biokinetic model

(272) The biokinetic model for systemic samarium applied in this report is described in Section 2.2.3.2.

8.2.3.3. Treatment of progeny

(273) The treatment of radioactive progeny of samarium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

8.3. Individual monitoring

^{153}Sm

(274) Measurements of ^{153}Sm are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{153}Sm concentrations in urine may be used to determine intakes of the radionuclide. I*n vivo* whole body measurement is used as an additional technique for special investigations. The main technique is gamma spectrometry.

Table 8. 2. Monitoring Techniques for ^{153}Sm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
153Sm	Urine Bioassay	γ-ray spectrometry	20 Bq/L
153Sm	Lung Measurementa	γ-ray spectrometry	8 Bq
153Sm	Whole-body Measurementb	γ-ray spectrometry	170 Bq

[a] Measurement system comprised of two Broad Energy Germanium detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium detectors (BEGe) and counting time of 15 minutes.

8.4. Dosimetric data for samarium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Bruce, D. W., Hietbrink, B.E., Dubois, K.P., 1963. The acute mammalian toxicity of rare earth nitrates and oxides; toxicol. Appl. Pharmacol. 5, 750–759.

Fairweather, S.J., Minihane, A-M., Eagles, J., Owen, L., Crews, H.M., 1997. Rare earth elements as nonabsorbable fecal markers in studies of iron absorption. Am; J. Clin. Nutr; 65, 970–976.

Gensicke, F., Nitschke, H. W., 1970. Der Stoffwechsel von inhaliertem Radiosamarium bei Mausen. Radiobiol. Radiother. 11, 57–61.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Shinohara A., Matsukawa T., Chiba M., et al., 2010. Comparative study of behavior of inhaled samarium and cerium in mice. J. Rare Earths 28, Suppl. 1, 507–509.

Shinohara, A., Chiba, M., Kumasaka, T., 2009. Behavior of samarium inhaled by mice: Exposure length and time-dependent change. J. Radioanal. Nucl. Chem. 281, 119–122

Shipler, D.B., Ballou, J.E., Griffin, B.I., Nelson, I.C., 1976. Development of a diagnostic model for inhaled promethium-147 oxide. Diagnosis and Treatment of Incorporated Radionuclides, 209–221. (Vienna: IAEA) IAEA-SR-6/28.

9. EUROPIUM (Z = 63)

9.1. Chemical Forms in the Workplace

(275) Europium is an element of the lanthanide series which occurs mainly in oxidation states II and III.

(276) Europium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Europium is most commonly obtained from bastnäsite and monazite.

(277) Europium is used in nuclear reactor control rods. Europium isotopes (e.g. ^{155}Eu) are fission products.

Table 9. 1. Isotopes of europium addressed in this report.

Isotope	Physical half-life	Decay mode
Eu-145	5.93 d	EC, B+
Eu-146	4.61 d	EC, B+
Eu-147	24.1 d	EC, B+, A
Eu-148	54.5 d	EC, B+, A
Eu-149	93.1 d	EC
Eu-150	36.9 y	EC, B+
Eu-150m	12.8 h	B-, EC, B+
Eu-152[a]	13.537 y	EC, B+, B-
Eu-152m	9.312 h	B-, EC, B+
Eu-152n	96 m	IT
Eu-154[a]	8.593 y	B-, EC
Eu-154m	46.0 m	IT
Eu-155[a]	4.761 y	B-
Eu-156	15.19 d	B-
Eu-157	15.18 h	B-
Eu-158	45.9 m	B-
Eu-159	18.1 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

9.2. Routes of Intake

9.2.1. Inhalation

Absorption Types and parameter values

(278) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including europium (Eu) (see general

lanthanide section). One study was found on the behaviour of europium radioisotopes in man following accidental inhalation. Information on absorption from the respiratory tract is available from experimental studies of europium as chloride, nitrate and oxide.

(279) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including europium, are given in Table 2.4 of the general lanthanide section.

Water-soluble forms of europium

(280) Moskalev et al. (1972) followed the biokinetics of ^{152}Eu (and other lanthanides, see general lanthanide section) for at least 32 d after deposition in the lungs of rats. However, few details are given. Fig. 135 of Moskalev et al. (1972) shows retention (presumably in the lungs) of europium falling to ~3% "of given dose" by 32 d. Analysis was carried out here (i.e. by the Task Group) assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with f_r >0.95, (which would give assignment to Type F), higher than the value of 0.5 chosen for water-soluble forms of lanthanides.

Europium chloride ($EuCl_3$)

(281) Berke and Vorwald (1964) administered $^{152\text{-}154}$Eu chloride by inhalation to rats and mice in single or repetitive short (30-minute) exposures. However, no results were reported, except that it was noted that clearance of $^{152\text{-}154}$Eu from the lung and whole body was similar for chloride and oxide (see below). It was also noted that the information was published in a Masters Degree thesis (Willard, 1963). The biological behavior of Eu152 as the nitrate and oxide (following inhalation and after intraperitoneal and subcutaneous injections) M.S. thesis, Wayne State Univ., Detroit, Michigan.) Unfortunately, the Task Group was unable to obtain a copy.

(282) Results were given for three groups of rats that repeatedly inhaled $^{152\text{-}154}$Eu chloride (7 hours/d and 5 d/week) for six months. In one group, retention in lungs and other major organs was followed for an additional six months after exposure. Analysis was carried out here on the results of two exposures simultaneously, assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1} (see above). The results fit well with f_r = 0.9, which would give assignment to Type F. Further information on the third group was given by Berke et al. (1968) and was analysed here with other results reported in that paper.

(283) Berke et al. (1968) followed whole body and lung retention of $^{152\text{-}154}$Eu for 700 d after inhalation by rats of $^{152\text{-}154}$Eu chloride (5 d/week for 6 months) at two exposure levels. Analysis was carried out here on the results of both exposures simultaneously, assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1} (see above). The results fit well with f_r = 0.8, which would give assignment to Type M.

(284) Berke (1970) measured tissue distributions of $^{152\text{-}154}$Eu at times up to 365 d after intratracheal instillation of $^{152\text{-}154}$Eu chloride into dogs. No details are given, but it was noted that: "One of the most surprising observations was the very long retention time in lung tissue, only 10-15% of the activity being cleared in a one year period while absorption into soft tissue and bone was minimal." This is considerably greater retention than observed following inhalation by rats.

(285) Although absorption parameter values for europium chloride based on *in vivo* data were derived, the results from different studies varied considerably. Furthermore, inhalation exposure to it is unlikely. Therefore specific parameter values for europium chloride are not used here. Instead, it is assigned to water-soluble forms of lanthanides (see general lanthanide section, Table 2.4).

Europium nitrate ($Eu(NO_3)_3$)

(286) Suzuki et al. (1969) followed the biokinetics of $^{152\text{-}154}$Eu for 55 d after inhalation by rats of $^{152\text{-}154}$Eu nitrate. There was very little clearance from the lungs after the first few days and very little absorption to blood, ~0.5% initial lung deposit (ILD) in both liver and skeleton. The authors concluded that inhaled europium nitrate was absorbed very little (~1%) from the lung and gut, even though europium nitrate is a soluble compound. Analysis carried out here, assuming (based on cerium, see above) that s_r = 0.44 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1}, gave f_r = 0.005, and s_s = 0.0012 d^{-1}, and assignment to Type M. This absorption is much lower than generally found for water-soluble forms of lanthanides, including europium (see above), but it is not unique. As described in the cerium section, absorption is very variable, tending to decrease with increasing mass administered and increasing pH, but it is not clear why it should be so low in this case.

(287) Although absorption parameter values for europium nitrate based on *in vivo* data were derived, the results differed greatly from those generally found for water-soluble forms of lanthanides. Furthermore, inhalation exposure to it is unlikely. Therefore specific parameter values for europium nitrate are not used here. Instead, it is assigned to water-soluble forms of lanthanides (see general lanthanide section, Table 2.4).

Europium oxide (Eu_2O_3)

(288) Berke and Vorwald (1964) administered $^{152\text{-}154}$Eu oxide by inhalation to rats and mice in single or repetitive short (30-minute) exposures. Results were reported for mice up to ~50 d after a single exposure: lung retention fell to ~50% ILD by 50 d; the amount in liver was ~10% of that in the lungs over most of the period. Results are reported for rats during ~65 d of repeated exposure. Activities in all organs measured increased steadily at similar rates, with the total activity in skeleton, liver and kidneys reaching ~45% of that in the lungs. Analysis carried out here, assuming (based on cerium, including Type M default values for s_r and s_s) that s_r = 1 d^{-1}, f_b = 0.07, and s_b = 0.021 d^{-1} and s_s = 0.005 d^{-1}, gave f_r = 0.4, consistent with assignment to Type M.

(289) Ziemer et al. (1968) followed whole-body retention and excretion of $^{152\text{-}154}$Eu for 200 d after accidental inhalation by two men of europium oxide labelled with $^{152\text{-}154}$Eu (and other isotopes) by neutron irradiation. About 80-90% of the initial respiratory tract deposits were cleared within 48 hr via the alimentary tract. Subsequently urine to fecal ratios of europium activity were close to one. Analysis carried out here, assuming (based on cerium) that s_r = 1 d^{-1}, f_b = 0.07, s_b = 0.021 d^{-1} and s_s = 0.005 d^{-1}, gave f_r = 0.3, suggesting Type M behaviour. Johnson and Ziemer (1971) followed whole-body retention and excretion of $^{152\text{-}154}$Eu for 30 d after inhalation by rats of europium oxide labelled with $^{152\text{-}154}$Eu by neutron irradiation. They measured the tissue distribution of $^{152\text{-}154}$Eu at 30 d, but found only traces (not quantified) in tissues measured other than lungs. Analysis carried out here, assuming (based on cerium) that s_r = 1 d^{-1}, f_b = 0.07, s_b = 0.021 d^{-1} and s_s = 0.005 d^{-1}, gave f_r ~0.2, suggesting Type M behaviour.

(290) Although absorption parameter values for europium oxide based on *in vivo* data were derived, the results from different studies varied considerably. Furthermore, inhalation exposure to it is unlikely. Therefore specific parameter values for europium oxide are not used here. Instead, it is assigned to Type M.

Fly ash

(291) Griffis et al. (1981) measured whole body retention and tissue distribution in rats of several radionuclides, including ^{152}Eu, at times up to 127 d after inhalation by rats of neutron-activated fly ash. The activities of ^{152}Eu, ^{134}Cs, ^{54}Mn and ^{60}Co in the lungs decreased significantly with time relative to ^{46}Sc and ^{59}Fe indicating that some elements, including europium, may be preferentially dissolved from the fly ash particles *in vivo*, and indicating assignment to Type M.

9.2.2. Ingestion

(292) The fractional absorption of europium, administered as $EuCl_3$ from the gastrointestinal tract of the rat was reported in the range 2×10^{-4} to 3×10^{-3} (Berke, 1970). Other experiments on rats (Durbin et al., 1956; Moskalev et al., 1972) also indicate that the gastrointestinal absorption of various compounds of europium were in this order of magnitude.

(293) The urinary excretion of europium, administered as $EuCl_3$ in a wide range of mass from 10^2 µg to 40 g from the gastrointestinal tract of rats, was reported in the range 7.8×10^{-5} to 1.6×10^{-2} with an average value of 3×10^{-3} (Ohnishi et al., 2011).

(294) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of europium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

9.2.3. Systemic distribution, retention and excretion of europium

9.2.3.1. Data

(295) Berke (1968) studied the systemic behavior of $^{152\text{-}154}$Eu in rats following its intravenous administration as chloride. Activity cleared quickly from the circulation and accumulated primarily in the skeleton, with elevated concentration also seen in the liver and kidneys. Skeletal tissues contained about 85% of the body burden at 252 d and virtually the entire body burden at 445 d. After the first few days excretion was primarily via the gastrointestinal tract. Whole-body retention could be described as a sum of two exponential terms indicating biological half-times of 4.4 d and 3.5 y.

9.2.3.2. Biokinetic model

(296) The biokinetic model for systemic europium applied in this report is described in Section 2.2.3.2.

9.2.3.3. Treatment of progeny

(297) The treatment of radioactive progeny of europium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

9.3. Individual monitoring

^{152}Eu

(298) Measurements of ^{152}Eu are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{152}Eu concentrations in urine and faeces may be used to determine intakes of the radionuclide. I*n vivo* skeleton measurement (knee geometry) and whole body measurement may be used as additional bioassay techniques. The main technique is gamma spectrometry.

Table 9. 2. Monitoring Techniques for ^{152}Eu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{152}Eu	Urine Bioassay	γ-ray spectrometry	16 Bq/L
^{152}Eu	Faecal Bioassay	γ-ray spectrometry	16 Bq/24h
^{152}Eu	Lung Measurement[a]	γ-ray spectrometry	10 Bq
^{152}Eu	Whole-body Measurement[b]	γ-ray spectrometry	200 Bq
^{152}Eu	Skeleton Measurement (knee)[c]	γ-ray spectrometry	4 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.
[c] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes.

^{154}Eu

(299) Measurements of ^{154}Eu are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{154}Eu concentrations in urine and faeces may be used to determine intakes of the radionuclide. I*n vivo* skeleton measurement (knee geometry) and whole body measurement may be used as additional bioassay technique. The main technique is gamma spectrometry.

Table 9. 3. Monitoring Techniques for ^{154}Eu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{154}Eu	Urine Bioassay	γ-ray spectrometry	10 Bq/L
^{154}Eu	Faecal Bioassay	γ-ray spectrometry	16 Bq/24h
^{154}Eu	Lung Measurement[a]	γ-ray spectrometry	7 Bq
^{154}Eu	Whole-body	γ-ray spectrometry	150 Bq

	Measurement[b]		
^{154}Eu	Skeleton Measurement (knee)[c]	γ-ray spectrometry	3 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.
[c] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes.

^{155}Eu

(300) Measurements of ^{155}Eu are performed by *in vivo* lung measurement technique for routine monitoring. Measurements of ^{155}Eu concentrations in urine and faeces may be used to determine intakes of the radionuclide. I*n vivo* skeleton measurement (knee geometry) and whole body measurement may be used as additional bioassay technique. The main technique is gamma spectrometry.

Table 9. 4. Monitoring Techniques for ^{155}Eu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{155}Eu	Urine Bioassay	γ-ray spectrometry	10 Bq/L
^{155}Eu	Faecal Bioassay	γ-ray spectrometry	16 Bq/24h
^{155}Eu	Lung Measurement[a]	γ-ray spectrometry	10 Bq
^{155}Eu	Whole-body Measurement[b]	γ-ray spectrometry	210 Bq
^{155}Eu	Skeleton Measurement (knee)[c]	γ-ray spectrometry	6 Bq

[a] Measurement system comprised of 2 Broad Energy Germanium detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of 2 Broad Energy Germanium detectors (BEGe) and counting time of 15 minutes.
[c] Measurement system comprised of 2 Broad Energy Germanium detectors (BEGe), counting time of 36 minutes.

9.4. Dosimetric data for europium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Berke, H. L., 1968. The metabolism of the rare earths. 1. The distribution and excretion of intravenous $^{152\text{-}154}$Europium in the rat. Health Phys. 15, 301–312.

Berke, H. L., 1970. The metabolism of rare earths following inhalation: pathologic and biochemical response in the lung and other organs, Technical Progress Report, COO-1630-22, Wayne State Univ., Detroit, Michigan, USA.

Berke, H. L., Vorwald, H. A., 1964. The response of the respiratory tract and lung to inhaled stable and radioactive isotopes of certain elements. Annual Technical Report, March 1, 1963 – February 28, 1964, COO-1181-1 Wayne State Univ., Detroit, Michigan.

Berke, H. L., Wilson, G. H., Berke, E. S., 1968. Changes in size distribution of blood lymphocytes following inhalation of radio-europium. Int. J. Radiat. Biol. 14, 561–565.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

Griffis, L.C., Snipes, M.B., Brooks, A.L., 1981. Clearance by the rat of inhaled fly ash from fluidized-bed coal combustion. J. Toxicol. Environ. Health, 7, 117–124.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Johnson Jr., R. F., Ziemer, P. L., 1971. The deposition and retention of inhaled $^{152-154}$europium oxide in the rat. Health Phys. 20, 187–193.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements In: *Biologicheskoye deystviye vneshnikh* i *vnutrennikh istochnikov* radiastsii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

Onishi, K., Usuda, K., Nakayama, S., et al., 2011. Distribution, elimination and renal effects of single oral doses of europium in rats. Biol. Trace; Elem. Res. 143, 1054–1063.

Suzuki, M., Ohno, S., Okabayashi, H., Hongo, S., Oohata, T., 1969. Distribution and excretion of inhaled Eu by rats as applied for and activable tracer. Proc. 9th Japanese Conference on Radioisotopes, Tokyo, 442–444 (in Japanese).

Ziemer, P. L., George, R. E., Kessler, W. V., 1968. The uptake, retention, and excretion of inhaled europium oxide in two healthy adult males. In: Proc. 1st International Congress of the International Radiation Protection Assn, Rome, CONF-660920, 1199–1203 of Radiation Protection. Part 2. Snyder, W. S., Abee, H. H., Burton, L. K., Maushart, R., Benco, A., Duhamel, F., Wheatley, B. M. (eds.). New York, Pergamon Press Inc.

10. GADOLINIUM (Z = 64)

10.1. Chemical Forms in the Workplace

(301) Gadolinium is an element of the lanthanide which occurs mainly in oxidation state III.

(302) Gadolinium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Gadolinium is most commonly obtained from bastnäsite and monazite.

(303) Gadolinium as a metal or salt has exceptionally high absorption of neutrons and therefore is used for shielding in neutron radiography and in nuclear reactors. Chelated organic gadolinium complexes are commonly used as intravenously administered contrast agents in medical magnetic resonance imaging.

(304) Gadolinium isotopes (e.g. ^{153}Gd) are fission products.

Table 10.1. Isotopes of gadolinium addressed in this report.

Isotope	Physical half-life	Decay mode
Gd-145	23.0 m	EC, B+
Gd-146	48.27 d	EC
Gd-147	38.1 h	EC, B+
Gd-148	74.6 y	A
Gd-149	9.28 d	EC, B+
Gd-150	1.79E+6 y	A
Gd-151	124 d	EC, A
Gd-152	1.08E+14 y	A
Gd-153[a]	240.4 d	EC
Gd-159	18.479 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

10.2. Routes of Intake

10.2.1. Inhalation

Absorption Types and parameter values

(305) Information on absorption from the respiratory tract is available from experimental studies of gadolinium (Gd) as chloride, citrate and oxide, including one volunteer experiment.

(306) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including gadolinium, are given in Table 2.4 of the general lanthanide section.

Water-soluble forms of gadolinium

(307) Moskalev et al. (1972) followed the biokinetics of ^{153}Gd (and other lanthanides, see general lanthanide section) for at least 32 d after deposition in the lungs of rats. However, few details are given. Fig. 135 of Moskalev et al. (1972) shows retention (presumably in the lungs) of gadolinium falling to ~10% "of given dose" at 1 hour, which was much lower than that of the other lanthanides administered (~75%). Retention fell to ~1% by 32 d. Analysis was carried out here (i.e. by the Task Group) assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with f_r ~0.9 (assuming that there was much greater deposition in the bronchial tree, and hence more rapid clearance to the alimentary tract than for the other lanthanides). This would give assignment to Type F, and is higher than the value of 0.5 chosen for water-soluble forms of lanthanides.

Gadolinium chloride ($GdCl_3$)

(308) Zalikin (1972) followed the biokinetics of ^{153}Gd for 128 d after intratracheal instillation into rats of ^{153}Gd-labelled $GdCl_3$ ($^{153}GdCl_3$) at pH 3.0–4.5 (and citrate, see below), described as "unweighable" – presumably carrier-free. (This might be the same work as summarised by Moskalev et al. (1972) see above, but it is not certain.) Lung clearance was rapid: the lung content falling to ~20% of the initial lung deposit (ILD) at 1 d, but with some long-term retention, giving ~3% ILD at 16 d, and ~0.5% at 128 d. Much of the clearance was by absorption to blood: with liver and skeleton containing ~15% ILD and 25% ILD respectively at 1 d. Retention of activity in the trachea was also reported (but not its location within the trachea). It fell from ~3% ILD at the first measurement (30 minutes) to ~0.3% ILD at 1 d, and remained at ~0.3–0.5% ILD throughout the rest of the experiment.

(309) Analysis was carried out here, assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1} (see above). The results fit reasonably well with f_r = 1, but the amount transferred to systemic tissues at t = 1 d is underestimated. As there are data available at early times (30 minutes, 1, 6 and 24 hours) analysis was also carried out with all absorption parameter values allowed to vary. (The chloride and citrate data were fit simultaneously, with only the value of f_r allowed to differ.) A better fit was obtained with f_r = 0.96, s_r = 3.5 d^{-1}, f_b = 0.08; s_b = 0.24 d^{-1}, and s_s = 0.0015 d^{-1}. Both sets of parameter values would give assignment to Type F.

(310) Yoneda et al. (1995) followed the biokinetics of gadolinium for 174 d following intratracheal instillation of stable gadolinium chloride (10 – 100 µg) into rats. The gadolinium was mainly retained in the lung with a biological half-time of 136 d (determined with an ILD of 50 µg). Clearance from the lungs was much slower than observed in the radiotracer studies described above. The authors inferred that the gadolinium was retained in the lung in an insoluble form. However, the clearance was also slower than would be expected for insoluble particles in rats (ICRP, 2002), suggesting that there was considerable binding of gadolinium to lung structures. Similar observations were reported for stable yttrium and lanthanum compared to tracer level radionuclides (see general lanthanide section).

Gadolinium citrate

(311) Zalikin (1972) followed the biokinetics of ^{153}Gd for 256 d after intratracheal instillation into rats of ^{153}Gd-labelled gadolinium citrate at pH 4.5–6.0, described as

"unweighable" – presumably carrier-free. Lung clearance was faster than for the chloride (see above): the lung content falling to ~10% ILD at 1 d, but with some long-term retention, giving ~2% ILD at 16 d, and ~0.2% at 128 d. Much of the clearance was by absorption to blood: with liver and skeleton both containing ~40% ILD at 1 d. Retention of activity in the trachea was also reported (but not its location within the trachea). It was in the range ~0.3–0.5% ILD from the first measurement (1 d) to the last (128 d).

(312) Analysis was carried out here assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1} (see above). The results fit reasonably well with f_r = 1, but the amount transferred to systemic tissues at early times (t <1 d) is underestimated. As there are data available at early times for citrate (30 minutes, 1, 6 and 24 hours) analysis was also carried out with all absorption parameter values allowed to vary. (The chloride and citrate data were fit simultaneously, with only the value of f_r allowed to differ.) A better fit was obtained with f_r = 1, s_r = 3.5 d^{-1}, f_b = 0.08; s_b = 0.24 d^{-1}, with s_s fixed at 0.0015 d^{-1}. Both sets of parameter values would give assignment to Type F.

Gadolinium oxide (Gd_2O_3)

(313) Stradling et al. (2000, 2002) gave interim summaries of the results of an interspecies comparison of the lung clearance of ^{153}Gd-labelled gadolinium oxide ($^{153}Gd_2O_3$) particles. More detailed reports on some of the experiments have been published (Hodgson et al., 2003; Pellow et al., 2016; Shutt et al., 2016). Monodisperse particles were prepared from ^{153}Gd-labelled gadolinium nitrate droplets which were dried and heated at 800°C to produce the oxide. This method was chosen to produce a porous material with a moderate dissolution rate in the lungs to facilitate its measurement and hence comparisons of rates between species, and determination of the effects of other factors (particle size, method of administration). It was not intended to represent any specific material to which workers might be exposed.

(314) In some of the earlier reports provisional estimates of the dissolution parameters f_r, s_r and s_s were made by the authors assuming f_b = 0.0. Analyses were carried out here on the full data sets (Pellow et al., 2016; Shutt et al., 2016) assuming that f_b = 0.07 and s_b = 0.021 d^{-1} (see above), and results are given in Table 10.2. It was confirmed that assuming that f_b = 0.0 instead of assuming f_b = 0.07 and s_b = 0.021 d^{-1} had little effect on the estimated values of f_r, s_r and s_s. There were five experiments with rats: inhalation and intratracheal instillation of 2.2-µm MMAD (mass median aerodynamic diameter) particles and instillation of three other sizes. To facilitate investigation of the effects of particle size and/or method of administration on dissolution, a simultaneous fit was carried out here of the five rat data sets, in which s_r and s_s were estimated as optimised parameters shared across the data sets, while f_r was estimated individually for each data set.

Table 10.2. Dissolution parameter values for Gd in $^{153}Gd_2O_3$ particles derived here assuming that f_b = 0.07 and s_b = 0.021 d^{-1}.

Study	Species	Administration	MMAD, µm	f_r	s_r, d^{-1}	s_s, d^{-1}	Reference
Preliminary	Rat[a]	Instillation	1.14	0.18	0.34	0.007	Stradling et al. 2000
	Rat[a]	Instillation	1.86	0.06	0.34	0.007	Stradling et al. 2000

Inter-species	Man	Inhalation	2.2	0.5	0.3	<0.002	Shutt et al. 2015
Comparison	Dog	Inhalation	2.2	0.36	0.13	0.005	Hodgson et al. 2003
(Main study)	Rat[a]	Inhalation	2.2	0.2	0.34	0.007	Pellow et al. 2015
	Rat[a]	Instillation	2.2	0.13	0.34	0.007	Pellow et al. 2015
Surface area	Rat[a]	Instillation	0.65	0.35	0.34	0.007	Pellow et al. 2005
	Rat[a]	Instillation	2.37	0.06	0.34	0.007	Pellow et al. 2005

a The fast and slow dissolution rates were estimated to be s_r = 0.34 d^{-1} and s_s = 0.007 d^{-1} as optimised shared parameters in a simultaneous fit using data from all five experiments with rats. Note that rats used by Pellow et al. (2005) were Sprague Dawley, while those used in the other experiments were HMT strain.

(315) A preliminary study was carried out in which the biokinetics of ^{153}Gd was followed for 180 d after intratracheal instillation into rats of $^{153}Gd_2O_3$ particles with MMAD 1.14 and 1.86 μm. A graphical summary of data for the 1.14 μm MMAD particles (Stradling et al., 2000) shows that ~30% ILD cleared during the first day, mainly to feces. By 60 d, lung retention had fallen to ~15% ILD and the amount in the "carcass" (all tissues except lung and alimentary tract) had increased to ~15% ILD. The results confirmed that the material was moderately soluble and therefore suitable for the main intercomparison study. About 10% ILD dissolved rapidly and the rest at a rate of ~0.01 d^{-1} (Table 10.2).

(316) The main study was carried out with a separate batch of $^{153}Gd_2O_3$ (MMAD 2.2 μm). The particles were administered by inhalation to two human volunteers and 36 rats, by intubation (inhalation via an endotracheal tube) to four dogs, and by intratracheal instillation to 45 rats: the biokinetics of ^{153}Gd was followed for about 6 months. For all species studied, complementary experiments were carried out in which the biokinetics of ^{153}Gd was followed after intravenous injection of ^{153}Gd citrate (Bailey et al., 1997, 1999; Stradling et al., 2000; Taylor and Leggett, 2003). In-vitro dissolution tests were carried out using canine alveolar macrophages and a solvent.

(317) The two volunteers inhaled the $^{153}Gd_2O_3$ with ^{51}Cr-labelled polystyrene latex (PSL) particles with the same aerodynamic diameter (Shutt et al., 2002, 2016). Measurements of ^{51}Cr-PSL enabled particle deposition and particle transport rates from the lung to be determined and thus allow more precise determination of the absorption of ^{153}Gd. Measurements of ^{153}Gd in whole body, chest, liver, skull and excreta were made at times up to 180 d.

(318) To study intracellular particle dissolution, canine alveolar macrophages were cultured with the $^{153}Gd_2O_3$: the dissolution rate was 0.011 d^{-1} of the initially phagocytised particle mass. In-vitro dissolution using Gamble's solution was very slow, with less than 0.1% dissolved in 30 d (Bailey et al., 1999).

(319) In a later study, Pellow et al. (2005) followed the biokinetics of ^{153}Gd for 180 d after intratracheal instillation into rats of $^{153}Gd_2O_3$ particles (prepared in the same way) with median geometric diameters of 0.36 μm and 1.52 μm (MMAD 0.65 μm and 2.37 μm respectively), to investigate the effect of specific surface area on particle dissolution in the lungs. For both particle sizes ~50% ILD cleared during the first day, mainly to feces; with ~1% and ~0.4% ILD

deposited in liver, for the 0.36 μm and 1.52 μm particles respectively. By 84 d, lung retention had fallen to ~2% and 5% ILD respectively.

(320) The estimated parameter values given in Table 10.2 are all consistent with assignment to Type M.

(321) Ball and van Gelder (1966) and Abel and Talbot (1967) investigated the toxicity, in mice and guinea pigs respectively, of stable gadolinium oxide following chronic inhalation. No useful biokinetic data were reported, but the text indicates that the material was relatively insoluble.

Polystyrene (PSL)

(322) Radiolabelled polystyrene (PSL) particles have been used extensively as relatively insoluble particles in inhalation studies (see e.g. inhalation section on cerium in this report). Oberdörster et al. (1997) followed lung retention of 10-μm diameter ^{153}Gd-labelled PSL for 180 d following intratracheal instillation into mice. The estimated alveolar retention half time of 103 d was longer than observed for 3-μm diameter ^{85}Sr-labelled PSL in a complementary experiment (33 d), and indicates Type S behaviour.

10.2.2. Ingestion

(323) The fractional absorption of gadolinium, administered as $^{153}GdCl_3$ in a wide range of mass from 2×10^{-2} μg to 4×10^{-2} g from the gastrointestinal tract of rats, was reported in the range 7.6×10^{-5} to 2×10^{-4} (Ramounet et al., 2000).

(324) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of gadolinium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides. An f_A value of 5×10^{-4} is applied here.

10.2.3. Systemic distribution, retention and excretion of gadolinium

10.2.3.1. Data

(325) The systemic behavior of ^{153}Gd was studied in human subjects after injection and inhalation (Shutt et al., 2001; Shutt and Etherington, 2002). The findings regarding the early distribution, retention, and excretion are reasonably consistent with data for rats (Durbin, 1960; Ando et al., 1989). For example, the human data indicate relatively low uptake by the liver (~15% of the injected amount), relatively high urinary excretion, and relatively low faecal excretion. Estimates of cumulative urinary and faecal excretion suggest that urinary excretion may account for 80-90% of total losses of absorbed Gd. External measurements indicate that about one-fourth of the injected amount was excreted over the first 3 weeks, but only 5-10% was excreted during the next 7-8 months. Measurements of whole-body retention following intravenous administration of ^{153}Gd to the human subjects are summarised in Fig. 10.1.

(326) Zalikin (1974) investigated the biokinetics of ^{153}Gd in female rats following its intravenous or intratracheal administration. For intravenously injected activity they estimated that about 16% of the administered activity remained in blood at 30 min, 4.5% at 1 h, and 0.4% at one day. Most of the injected activity accumulated in the liver (~42%) and skeleton (~32%). Activity was removed from the liver over a period of days or weeks, with only 15% remaining after 8 d and 1.5% remaining after 64 d. The skeleton accumulated activity more slowly than

the liver and also released the activity much more slowly than the liver. The maximum skeletal content was about 47% of the injected amount at 4 d. The skeletal content declined to about 41% at 64 d and 35% at 256 d. The kidneys contained about 6.5% of the injected amount at 6 h, 4.8% at 1 d, 2.5% at 8 d, 1.6% at 16 d, and 0.5% at 256 d.

10.2.3.2. Biokinetic model

(327) The biokinetic model for systemic gadolinium applied in this report is described in Section 2.2.3.2.

10.2.3.3. Treatment of progeny

(328) The treatment of radioactive progeny of gadolinium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

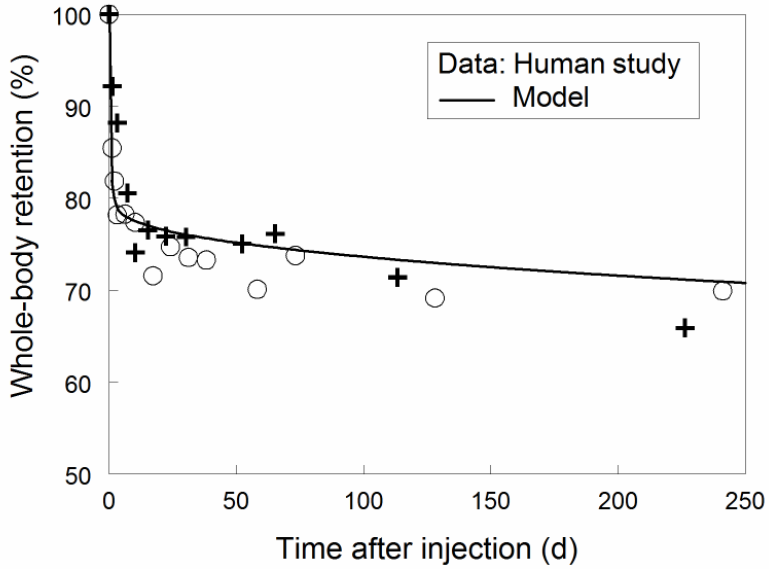


Fig. 10.1. Whole-body retention of intravenously injected ^{153}Gd as observed in two human subjects (Shutt and Etherington, 2002) and derived from the model used in this report.

10.3. Individual monitoring

^{153}Gd

(329) *In vivo* lung measurements of ^{153}Gd are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{153}Gd concentrations in urine and faeces may be used to determine intakes of the radionuclide. *In vivo* whole body measurement may be used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 10.3. Monitoring techniques for ^{153}Gd.

Isotope	Monitoring	Method of	Typical

	Technique	Measurement	Detection Limit
^{153}Gd	Urine Bioassay	γ-ray spectrometry	14 Bq/L
^{153}Gd	Faecal Bioassay	γ-ray spectrometry	14 Bq/24h
^{153}Gd	Lung Measurement[a]	γ-ray spectrometry	10 Bq
^{153}Gd	Whole-body Measurement[b]	γ-ray spectrometry	180 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

10.4. Dosimetric data for gadolinium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Abel, M., Talbot, R.B., 1967. Gadolinium oxide inhalation by guinea pigs: A correlative functional and histopathologic study. J. Pharmacol. Exper. Thera. 157, 207–213.

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Bailey, M. R., Etherington, G., Stradling, G. N., et al., 1997. Inhalation of radionuclides. Mid-term Report January 1996 – December 1997 of Contract F14PCT950026. NRPB-M909, Chilton, National Radiological Protection Board.

Bailey, M. R., Etherington, G., Stradling, G. N., et al, 1999. Inhalation of Radionuclides. Final Report January 1996 – June 1999 of Contract F14PCT950026. NRPB-M1103, Chilton, National Radiological Protection Board.

Ball, R.A., Van Gelder, G., 1966. Chronic toxicity of gadolinium oxide for mice following exposure by inhalation. Arch. Environ. Health 13, 601–608.

Durbin, P. W., 1960. Metabolic Characteristics within a Chemical Family Health Phys. 2, 225–238.

Harrison, J.D., 1995. Ingested radionuclides In: Radiation and Gut. Eds Potten, C.S. and Hendry J.H. (Oxford, Elsevier), 253–289.

Hodgson, A., Shutt, A.L., Etherington, G., et al., 2003. Comparison of predicted with observed biokinetics of inhaled plutonium nitrate and gadolinium oxide in humans. Radiat. Prot. Dosim. 105, 91–94.

ICRP, 2002. Guide for the practical application of the ICRP human respiratory tract model. Supporting Guidance 3. Ann. ICRP 32(1/2).

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: Biologicheskoye

deystviye vneshnikh i vnutrennikh istochnikov radiastsii, 183–190 (eds. Moskalev, Yu. I., and Kalistratova, V. S.). Moscow. Translated in Biological effects of radiation from external and internal sources. AEC-tr-7457, 278–287.

Oberdörster, G., Ferin, J., Baggs, R., Pinkerton, K., Morrow, P. E., 1997. Alveolar macrophage cluster formation: a clearance mechanism for large particles in mouse lungs? In: Inhaled Particles VIII, Proceedings of the Eighth International Symposium on Inhaled Particles, Cambridge, United Kingdom, August 26–30 1996. (Eds. Cherry, N., Ogden, T.) Ann. Occup. Hyg. 41 (Suppp. 1), 554-560.

Pellow, P. G. D., Hodgson, S. A., Gregoratto, D., Hodgson, A., 2016. Biokinetics of gadolinium-153 oxide after inhalation or instillation. PHE-CRCE-XXX Report.

Pellow, P. G. D., Hodgson, S. A., Hodgson, A., et al., 2005. Comparison of absorption after instillation of gadolinium oxide particles with different surface areas. RPD-DA-02-2005, Health Protection Agency, Centre for Radiation, Chemical and Environmental Hazards, Radiation Protection Division, Chilton, Didcot, Oxfordshire OX11 0RQ.

Ramounet, B., Moutairou, K., Renaud-Salis, V., Menetrier, F., Fritsch, P., 2000. Some modifying factors of the absorption and the gastrointestinal retention of ingested lanthanides and actinides. Proceedings IRPA 10, P-3a, 189.

Shutt, A. L., Etherington, G., 2002. Private communication.

Shutt, A. L., Youngman, M. J., Raine, C., et al., 2001. A study of the human biokinetics of inhaled gadolinium oxide. Ann. Occup. Hyg. 46 (Suppl. 1), 320–322.

Shutt, A.L., Youngman, M.J., Raine, C., et al., 2016. A human volunteer study of the biokinetics of inhaled gadolinium oxide. To be submitted to Radiat. Prot. Dosim.

Shutt, A.L., Youngman, M.J., Raine, C., et al., 2002. A study of the human biokinetics of inhaled gadolinium oxide. Proc. Inhaled Particles IX, Cambridge, September 2001, (Oxford: Oxford University Press) Ann. occup. Hyg., 46, Suppl. 1, 320–322.

Stradling, G. N., Bailey, M. R., Birchall, A. et al., 2000. Clearance of radioactivity deposited in the respiratory tract to blood: Progress in a multinational interspecies comparison project. J. Radioanal. Nucl. Chem. 243, 323–337.

Stradling, N., Etherington, G., Hodgson, A., et al., 2002. Comparison between biokinetics of inhaled plutonium nitrate and gadolinium oxide in humans and animals. J. Radioanal. Nucl. Chem. 252, 315–325.

Taylor, D.M., Leggett, R.W., 2003. A generic biokinetic model for predicting the behaviour of the lanthanide elements in the human body. Radiat. Prot. Dosim. 105, 193–198.

Yoneda, S., Emi, N., Fujita, Y., et al., 1995. Effects of gadolinium chloride on the rat lung following intratracheal instillation. Fundam. Appl. Toxicol. 28, 65–70.

Zalikin, G. A., 1972. Distribution of gadolinium 153 in the rat organism. In: Biologicheskoye deystviye vneshnikh I vnutrennikh istochnikov radiatsii, 190–197 (eds. Moskalev, Yu. I. and Kalistratova, V. S.). Moscow. Translated in “Biological effects of radiation from external and internal sources”, AEC-tr-7457, 288–296.

Zalikin, G. A., 1974. Distribution of gadolinium-153 in the rat organism. In: Moskalev, Yu. I.; Kalistratova, V. S., eds. Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457; 288–296.

11. TERBIUM (Z = 65)

11.1. Chemical Forms in the Workplace

(330) Terbium is an element of the lanthanide series which occurs mainly in oxidation states III and IV.

(331) Terbium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Terbium is most commonly obtained from bastnäsite and monazite.

(332) ^{161}Tb is a fission product.

Table 11. 1. Isotopes of terbium addressed in this report.

Isotope	Physical half-life	Decay mode
Tb-147	1.64 h	EC, B+
Tb-148	60 m	EC, B+
Tb-149	4.118 h	EC, B+, A
Tb-150	3.48 h	EC, B+, A
Tb-151	17.609 h	EC, B+, A
Tb-152	17.5 h	EC, B+
Tb-153	2.34 d	EC, B+
Tb-154	21.5 h	EC, B+
Tb-155	5.32 d	EC
Tb-156	5.35 d	EC
Tb-156m	24.4 h	IT
Tb-156n	5.3 h	IT
Tb-157	71 y	EC
Tb-158	180 y	EC, B-
Tb-160[a]	72.3 d	B-
Tb-161	6.906 d	B-
Tb-163	19.5 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

11.2. Routes of Intake

11.2.1. Inhalation

Absorption Types and parameter values

(333) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including terbium (Tb) (see general

lanthanide section). Information on absorption from the respiratory tract is available from experimental studies of terbium as oxide, including one volunteer experiment.

(334) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including terbium, are given in Table 2.4 of the general lanthanide section.

Water-soluble forms of terbium

(335) Moskalev et al. (1972) followed the biokinetics of ^{160}Tb (and other lanthanides, see general lanthanide section) for at least 32 d after deposition in the lungs of rats. However, few details are given. Fig. 135 of Moskalev et al. (1972) shows retention (presumably in the lungs) of terbium falling to ~3% "of given dose" by 32 d. Analysis was carried out here (i.e. by the Task Group) assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with f_r >0.95, (which would give assignment to Type F), higher than the value of 0.5 chosen for water-soluble forms of lanthanides.

Terbium oxide (Tb_4O_7)

(336) An interspecies comparison was conducted of the lung clearance of ^{160}Tb-labelled terbium oxide ($^{160}Tb_4O_7$) particles (Kreyling et al., 1998; Hodgson et al., 2003). Monodisperse particles were prepared from stable terbium nitrate droplets which were dried and heated at 800°C to produce the oxide. This method was chosen to produce a porous material with a moderate dissolution rate in the lungs to facilitate its measurement and hence comparisons of rates between species, and determination of the effects of other factors (method of administration). It was not intended to represent any specific material to which workers might be exposed, but it was noted that the results might be relevant to other lanthanide oxides. After characterisation, the oxide particles were neutron-irradiated to produce the ^{160}Tb label.

(337) A preliminary study was carried out in which the biokinetics of ^{160}Tb were followed for 84 d after intratracheal instillation into rats of $^{160}Tb_4O_7$ particles (produced as described above, but heat treated at 1000°C) with mass median aerodynamic diameters (MMAD) of 1.2 and 1.8 μm (Hodgson et al., 1994). For both particle sizes, during the first day ~10–20% of the initial lung deposit (ILD) cleared, mainly to faeces, with ~2% ILD transferred to the "carcass" (all tissues except lung and alimentary tract). By 84 d, ~20% ILD remained in the lung and the content of the carcass had increased to ~20% ILD. The results confirmed that the material was moderately soluble and therefore suitable for the main intercomparison study.

(338) The main study was carried out with a separate batch of $^{160}Tb_4O_7$ (MMAD 1.28 μm). The particles were administered by inhalation to four human volunteers, seven rhesus monkeys, three dogs and 45 rats, and by intratracheal instillation to 45 rats: brief descriptions are given in the following paragraphs. Complementary experiments were carried out in which the biokinetics of ^{160}Tb were followed after intravenous injection of ^{160}Tb citrate or nitrate in one monkey, two dogs and 32 rats.

(339) Guilmette et al. (1996) reported results of measurements of retention in the lungs, liver and skeleton of rhesus monkeys up to 180 d after inhalation of the $^{160}Tb_4O_7$. Lung retention accounted for ~60% of the initial body burden (IBB), indicating that up to ~40% IBB cleared rapidly from the upper respiratory tract (URT) to faeces. By 14 d, ~40% IBB remained in the lungs, falling to ~10% IBB at 180 d. (Assuming that the ILD was 60% IBB, these values

correspond to ~70% ILD and 15% ILD, respectively.) Amounts in liver and skeleton increased to ~6% and 36% IBB (10% and 60% ILD) by 14 d, with little change thereafter. It was assessed that clearance from the alveolar region was mainly by absorption to blood, with 36% IBB clearing with a half time of 9 d and 24% with a half time of 136 d.

(340) It was assessed here (assuming that $f_b = 0.07$ and $s_b = 0.021$ d^{-1}, based on cerium, see general lanthanide section) that $f_r = 0.58$, $s_r = 2$ d^{-1} and $s_s = 0.0063$ d^{-1}.

(341) In the human study (Newton, 2003), measurements of ^{160}Tb in the chest and lower legs (as a measure of skeletal deposit) were made with external detectors at times up to 112–177 d in the four subjects. Further details were given by Hodgson et al. (2003). Whole-body retention was measured at times up to 338–420 d. Urine and faeces were collected for the first 3 days and occasionally thereafter. From the results, estimates were made of lung retention, which were subject to considerable uncertainty because of interference in the chest measurements from systemic ^{160}Tb, especially at later times. During the first 2–3 d, between ~3% and 30% ILD cleared to faeces, presumably representing activity deposited in the URT. Activity was detected in the skeleton immediately after the inhalation exposure and increased steadily throughout the period of measurements. By 120 d, an estimated ~15% ILD remained in the lungs, while whole body retention was in the range 50–80% ILD. It was assessed that most of the systemic activity was in the skeleton, which would therefore have contained ~35–60% ILD. It was also assessed by the authors that clearance from the alveolar region was mainly by absorption to blood at an average rate of ~0.006 d^{-1}.

(342) It was assessed here (simultaneous fit to the data for the four subjects, assuming that $f_b = 0.07$ and $s_b = 0.021$ d^{-1}) that $f_r = 0.32$, $s_r = 0.12$ d^{-1}, and s_s=0.006 d^{-1}.

(343) Hodgson et al. (2003) reported details of the experiments in dogs and rats. The biokinetics of ^{160}Tb were followed for 240 d after inhalation (intubation via an endotracheal tube) by three dogs. Tissue distributions were obtained at 3 d and 240 d. Measurements of ^{160}Tb in the lungs, liver and pelvis were made with external detectors throughout the experiment, as were measurements of excreta. There was considerable rapid absorption: by 3 d, lung, liver and skeleton contained ~45%, 10% and 30% ILD respectively. Absorption continued at a lower rate, so that by 240 d the amounts were ~10%, 10% and 50% ILD respectively. Absorption parameter values fit by the authors (assuming $f_b = 0.0$) to results for the two dogs sacrificed at 240 d were similar:

Dog 347: $f_r = 0.49$, $s_r = 1.8$ d^{-1} and $s_s = 0.0074$ d^{-1}
Dog 349: $f_r = 0.51$, $s_r = 1.1$ d^{-1} and $s_s = 0.0063$ d^{-1}

(344) It was assessed here (simultaneous fit to the data for the two dogs, assuming that $f_b = 0.07$ and $s_b = 0.021$ d^{-1}) that $f_r = 0.54$, $s_r = 1.0$ d^{-1}, s_s=0.0067 d^{-1}. It was noted that the assumption of $f_b = 0.07$ and $s_b = 0.021$ d^{-1}, rather than $f_b = 0$ made little difference to the values determined for f_r, s_r and s_s.

(345) The biokinetics of ^{160}Tb in rats was followed for 200 d after inhalation and intratracheal instillation of $^{160}Tb_4O_7$. (A complementary experiment was carried out in which the biokinetics of ^{160}Tb in rats was followed for 7 d after instillation of a suspension of the particles into the stomach. Results were variable, but indicated that fractional absorption was low, of the order of 0.1%.) The biokinetics following administration to the respiratory tract was broadly similar to those observed in the other species, although the rapid phase seemed slower than in the dogs. Absorption parameter values fit by the authors (assuming $f_b = 0.0$) to the results were similar for the two methods of administration:

Rat inhalation: $f_r = 0.61$, $s_r = 0.15$ d^{-1} and $s_s = 0.0068$ d^{-1}
Rat instillation: $f_r = 0.43$, $s_r = 0.14$ d^{-1} and $s_s = 0.0060$ d^{-1}

(346) In analysis carried out here (assuming that $f_b = 0.07$ and $s_b = 0.021$ d^{-1}) independent estimates were made for inhalation and instillation administration:

Rat inhalation: $f_r = 0.71$, $s_r = 0.12$ d^{-1} and $s_s = 0.007$ d^{-1}
Rat instillation: $f_r = 0.42$, $s_r = 0.16$ d^{-1} and $s_s = 0.006$ d^{-1}

Independent estimates of the value of the parameter f_r, for inhalation and instillation, with optimised shared values $s_r = 0.12$ d^{-1} and $s_s = 0.0054$ d^{-1}, gave 0.74 and 0.49 respectively.

(347) All these parameter values are consistent with assignment to Type M. Although absorption parameter values for terbium oxide based on *in vivo* data were derived, the material was designed to be moderately soluble. Therefore specific parameter values for terbium oxide are not used here. Instead, it is assigned to Type M.

11.2.2. Ingestion

(348) The fractional absorption of terbium from the gastrointestinal tract of rats has been variously reported to be less than 10^{-3} (Durbin et al., 1956) and less than 5×10^{-4} (Moskalev et al., 1972).

(349) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of terbium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

11.2.3. Systemic distribution, retention and excretion of terbium

11.2.3.1. Data

(350) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu, all showed similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Compared with Gd, which neighbors Tb in the period table, these seven elements showed higher deposition in the skeleton (roughly 60%), lower deposition in the liver (roughly 10%), and similar cumulative loss in urine (15-28%) through day 4.

(351) Newton (2003) studied the whole-body retention, distribution, and urinary and faecal excretion of ^{160}Tb in four healthy men following acute inhalation of ^{160}Tb-labelled terbium oxide particles. Within a year after exposure most of the retained activity had become systemic, with the principal deposit in bone. Measurements of total-body retention after 1 y suggested a clearance half-time on the order of 5 y.

(352) Zalikin and Tronova (1971) investigated the biokinetics of terbium in rats following intravenous injection of ^{160}Tb in chloride or citrate solutions and ^{161}Tb in a chloride solution. Up to 15% of the administered amount remained in blood at 30 min, 6% at 1 h, and 0.26% at 1 d. Activity accumulated rapidly in the liver and more slowly in the skeleton. The maximum liver content was 26% of the administered amount at 6 h. Thereafter the liver content gradually declined to about 0.3% at 64 d. The skeletal content gradually increased to a maximum of about 40% by the second day and remained at that level throughout the 64-d period of observation. A relatively high activity concentration was also observed in the kidneys, which contained about 5.0% of the administered amount at 6 h, 2.7% at 1 d, 1.8% at 8 d, and 0.5% at 64 d.

11.2.3.2. Biokinetic model

(353) The biokinetic model for systemic terbium applied in this report is described in Section 2.2.3.2.

11.2.3.3. Treatment of progeny

(354) The treatment of radioactive progeny of terbium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

11.3. Individual monitoring

Information of detection limit for individual measurement techniques is not available.

11.4. Dosimetric data for terbium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Durbin, P. W., 1960. Metabolic Characteristics within a Chemical Family Health Phys. 2, 225–238.

Durbin, P. W., 1962. Distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

Guilmette, R. A., Snipes, M. B., Barr, E. B., Muggenburg, B. A., 1996. Biokinetics of inhaled terbium oxide ($^{160}Tb_4O_7$) in nonhuman primates. Inhalation Toxicology Research Institute Annual Report 1995–1996, ITRI-148, 36–38. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Hodgson, A., Kreyling, W.G., Newton, D., Stradling, G.N., 2003. Interspecies Comparison of Lung Clearance of ^{160}Terbium Oxide. Report NRPB-DA/4/2003 (Chilton: National Radiological Protection Board).

Hodgson, A., Stradling, G. N., Foster, P. P., Kreyling, W. G., Pearce, M. J., 1994. The biokinetics of ^{160}terbium oxide: studies to determine its solubility for an interspecies comparison of lung clearance. In: Proc. 17th IRPA Regional Conference on Radiological Protection, Portsmouth, June 1994, 193–196.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Kreyling, W.G., Hodgson, A., Guilmette, R.A., et al., 1998. Interspecies comparison of lung clearance using monodisperse terbium oxide particles. Radiat. Prot. Dosim. 79, 241–243.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: Biologicheskoye deystviye vneshnikh i vnutrennikh istochnikov radiastsii, 183–190 (eds. Moskalev, Y. I., and Kalistratova, V. S.). Moscow. Translated in Biological effects of radiation from external and internal sources. AEC-tr-7457, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

Newton, D. 2003. Human biokinetics of inhaled terbium oxide Radiat. Prot. Dosim. 106, 53–61.

Newton, D. 2003. Human biokinetics of inhaled terbium oxide. Radiat. Prot. Dosim. 106, 53–61.

Zalikin, G. A., Tronova, I. N., 1971. Distribution of terbium-160,161 in the body of rats. In: Moskalev, Y. I., ed. Radioactive isotopes and the body. AEC-tr-7195.

12. DYSPROSIUM (Z = 66)

12.1. Chemical Forms in the Workplace

(355) Dysprosium is an element of the lanthanide series which occurs mainly in oxidation states III and IV.

(356) Dysprosium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Dysprosium is most commonly obtained from bastnäsite and monazite.

(357) Dysprosium is used for its high thermal neutron absorption cross-section in making control rods in nuclear reactors. ^{165}Dy is a fission product.

Table 12.1. Isotopes of dysprosium addressed in this report.

Isotope	Physical half-life	Decay mode
Dy-151	17.9 m	EC, B+, A
Dy-152	2.38 h	EC, A
Dy-153	6.4 h	EC, B+, A
Dy-154	3.0E+6 y	A
Dy-155	9.9 h	EC, B+
Dy-157	8.14 h	EC
Dy-159[a]	144.4 d	EC
Dy-165	2.334 h	B-
Dy-166	81.6 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

12.2. Routes of Intake

12.2.1. Inhalation

Absorption Types and parameter values

(358) No reports were found of experimental studies on the behaviour of dysprosium (Dy) following deposition in the respiratory tract, nor of its retention in the lung following accidental intake. As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides, including dysprosium. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including dysprosium, are given in Table 2.4. of the general lanthanide section.

12.2.2. Ingestion

(359) There is no relevant data available concerning ingestion of dysprosium, but the fractional absorption from the gastrointestinal tract of rats for several similar lanthanides has

been variously reported to be less than 10^{-3} (Durbin et al., 1956) and less than 5×10^{-4} (Moskalev et al., 1972).

(360) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of dysprosium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

12.2.3. Systemic distribution, retention and excretion of dysprosium

12.2.3.1. Data

(361) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu showed broadly similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Roughly 60% of the activity entering blood deposited in the skeleton and roughly 10% deposited in the liver. Cumulative loss in urine through day 4 amounted to about 15-28% of the amount reaching blood.

12.2.3.2. Biokinetic model

(362) The biokinetic model for systemic dysprosium applied in this report is described in Section 2.2.3.2.

12.2.3.3. Treatment of progeny

(363) The treatment of radioactive progeny of dysprosium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

12.3. Individual monitoring

^{159}Dy

(364) *In vivo* lung measurements of ^{159}Dy are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{159}Dy concentrations in urine and faeces may be used to determine intakes of the radionuclide. *In vivo* whole body measurement may be used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 12.2. Monitoring Techniques for ^{159}Dy.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{159}Dy	Urine Bioassay	γ-ray spectrometry	6 Bq/L
^{159}Dy	Faecal Bioassay	γ-ray spectrometry	8 Bq/24h
^{159}Dy	Lung Measurement[a]	γ-ray spectrometry	4 Bq
^{159}Dy	Whole-body Measurement[b]	γ-ray spectrometry	70 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

12.4. Dosimetric data for dysprosium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Durbin, P. W., 1960. Metabolic Characteristics within a Chemical Family. Health Phys. 2, 225–238.

Durbin, P. W., 1962. Distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Dose coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: *Biologicheskoye deystviye vneshnikh* i *vnutrennikh istochnikov* r&&ii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

13. HOLMIUM (Z = 67)

13.1. Chemical Forms in the Workplace

(365) Holmium is an element of the lanthanide which occurs mainly in oxidation state III.

(366) Holmium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Holmium is most commonly obtained from gadolinite and monazite.

(367) Holmium is used in solid-state YAG lasers and for its high thermal neutron absorption cross-section in making control rods in nuclear reactors.

Table 13. 1. Isotopes of holmium addressed in this report.

Isotope	Physical half-life	Decay mode
Ho-154	11.76 m	EC, B+, A
Ho-155	48 m	EC, B+
Ho-156	56 m	EC, B+
Ho-157	12.6 m	EC, B+
Ho-159	33.05 m	EC, B+
Ho-160	25.6 m	EC, B+
Ho-161	2.48 h	EC
Ho-162	15.0 m	EC, B+
Ho-162m	67.0 m	IT, EC, B+
Ho-163	4570 y	EC
Ho-164	29 m	EC, B-
Ho-164m	38.0 m	IT
Ho-166[a]	26.80 h	B-
Ho-166m	1.20E+3 y	B-
Ho-167	3.1 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

13.2. Routes of Intake

13.2.1. Inhalation

Absorption Types and parameter values

(368) No reports were found of experimental studies on the behaviour of holmium (Ho) following deposition in the respiratory tract, nor of its retention in the lung following accidental intake. As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides, including holmium. Absorption

parameter values and Types, and associated f_A values for particulate forms of lanthanides, including holmium, are given in Table 2.4 Table 2.4of the general lanthanide section.

13.2.2. Ingestion

(369) There is no relevant data available concerning ingestion of holmium, but the fractional absorption from the gastrointestinal tract of rats for several similar lanthanides has been variously reported to be less than 10^{-3} (Durbin et al., 1956) and less than 5×10^{-4} (Moskalev et al., 1972).

(370) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of holmium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

13.2.3. Systemic distribution, retention and excretion of holmium

13.2.3.1. Data

(371) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu showed broadly similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Roughly 60% of the activity entering blood deposited in the skeleton and roughly 10% deposited in the liver. Cumulative loss in urine through day 4 amounted to about 15-28% of the amount reaching blood.

13.2.3.2. Biokinetic model

(372) The biokinetic model for systemic holmium applied in this report is described in Section 2.2.3.2.

13.2.3.3. Treatment of progeny

(373) The treatment of radioactive progeny of holmium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

13.3. Individual monitoring

^{166}Ho

(374) *In vivo* lung measurements of ^{166}Ho are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{166}Ho concentrations in urine and faeces may be used to determine intakes of the radionuclide. *In vivo* whole body measurement may be used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 13. 2. Monitoring techniques for ^{166}Ho.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit

^{166}Ho	Urine Bioassay	γ-ray spectrometry	4 Bq/L
^{166}Ho	Faecal Bioassay	γ-ray spectrometry	14 Bq/24h
^{166}Ho	Lung Measurement[a]	γ-ray spectrometry	5 Bq
^{166}Ho	Whole-body Measurement[b]	γ-ray spectrometry	100 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

13.4. Dosimetric data for holmium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225–238.

Durbin, P. W., 1962. Distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Dose coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: *Biologicheskoye deystviye vneshnikh* i *vnutrennikh istochnikov* r&&ii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

14. ERBIUM (Z = 68)

14.1. Chemical Forms in the Workplace

(375) Erbium is an element of the lanthanide series which occurs mainly in oxidation state III.

(376) Erbium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Erbium is most commonly obtained from gadolinite and monazite.

(377) Erbium is used in solid-state YAG lasers and for its high thermal neutron absorption cross-section in making control rods in nuclear reactors.

Table 14. 1. Isotopes of erbium addressed in this report.

Isotope	Physical half-life	Decay mode
Er-156	19.5 m	EC
Er-159	36 m	EC, B+
Er-161	3.21 h	EC, B+
Er-163	75.0 m	EC, B+
Er-165	10.36 h	EC
Er-169[a]	9.40 d	B-
Er-171	7.516 d	B-
Er-172	49.3 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

14.2. Routes of Intake

14.2.1. Inhalation

Absorption Types and parameter values

(378) No reports were found of experimental studies on the behaviour of erbium (Er) following deposition in the respiratory tract, nor of its retention in the lung following accidental intake. As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides, including erbium. Absorption parameter values and Types, and associated f_A values for particulate forms of erbium are given in Table 2.4 of the general lanthanide section.

14.2.2. Ingestion

(379) There is no relevant data available concerning ingestion of erbium, but the fractional absorption from the gastrointestinal tract of rats for several similar lanthanides has been variously reported to be less than 10^{-3} (Durbin et al., 1956) and less than 5×10^{-4} (Moskalev et al., 1972).

(380) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of erbium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

14.2.3. Systemic distribution, retention and excretion of erbium

14.2.3.1. Data

(381) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu showed broadly similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Roughly 60% of the activity entering blood deposited in the skeleton and roughly 10% deposited in the liver. Cumulative loss in urine through day 4 amounted to about 15-28% of the amount reaching blood.

14.2.3.2. Biokinetic model

(382) The biokinetic model for systemic erbium applied in this report is described in Section 2.2.3.2.

14.2.3.3. Treatment of progeny

(383) The treatment of radioactive progeny of erbium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

14.3. Individual monitoring

Information of detection limit for individual measurement techniques is not available.

14.4. Dosimetric data for erbium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69 .

Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225–238.

Durbin, P. W., 1962. Distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: *Biologicheskoye deystviye vneshnikh* i *vnutrennikh istochnikov* r&&ii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

15. THULIUM (Z = 69)

15.1. Chemical Forms in the Workplace

(384) Thulium is an element of the lanthanide series which occurs mainly in oxidation state III.

(385) Thulium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Thulium is most commonly obtained from monazite.

(386) Thulium is used as the radiation source in portable x-ray devices and in solid-state YAG lasers.

Table 15. 1. Isotopes of thulium addressed in this report.

Isotope	Physical half-life	Decay mode
Tm-161	30.2 m	EC, B+
Tm-162	21.70 m	EC, B+
Tm-163	1.810 h	EC, B+
Tm-165	30.06 h	EC, B+
Tm-166	7.70 h	EC, B+
Tm-167	9.25 d	EC
Tm-168	93.1 d	EC, B+, B-
Tm-170	128.6 d	B-, EC
Tm-171[a]	1.92 y	B-
Tm-172	63.6 h	B-
Tm-173	8.24 h	B-
Tm-175	15.2 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

15.2. Routes of Intake

15.2.1. Inhalation

Absorption Types and parameter values

(387) Studies were found on the behaviour of thulium radioisotopes (Tm) in man following accidental inhalation. Information on absorption from the respiratory tract is available from experimental studies of thulium as oxide. As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including thulium, are given in Table 2.4. of the general lanthanide section.

Thulium oxide (Tm_2O_3)

(388) Eakins and Morgan (1964) reported measurements (external and excreta) made on a worker up to ~50 d after accidental inhalation of $^{170}Tm_2O_3$. The exposure occurred during cleaning a handling cell in which there were aluminium cans containing ^{170}Tm oxide. The amount excreted in faeces during the first week was many times the single estimate of activity in lungs (at 4 d), but ^{170}Tm was not detected in urine. Analysis carried out here (*i.e.*, by the Task Group), assuming (based on cerium - see general lanthanide section) that s_r = 1 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1}, gave f_r = 0.0 and s_s = 0.001 d^{-1}, exactly equal to the criterion for assignment to Type S rather than Type M.

(389) Strambi and Testa (1966) reported measurements made on a worker up to ~50 d after accidental inhalation of dust containing ^{170}Tm oxide during decontamination operations at an experimental reactor. Activity in nasal swabs was identified as ^{170}Tm. No ^{170}Tm was detected in the urine the first day, nor in a whole body measurement after 7 d. Faecal samples were measured from 3 d to 10 months. The activity excreted on the fifth day was ~1% of that on the third day. The time pattern of faecal excretion was very similar to that reported by Eakins and Morgan (1964). The results suggest Type S behaviour.

(390) Thomas and Kingsley (1970) followed the biokinetics of ^{171}Tm for 128 d after inhalation by dogs of ^{171}Tm-labelled thulium oxide ($^{171}Tm_2O_3$) prepared by thermal degradation of the hydroxide at 1100°C (Boyd and Thomas 1970). On average ~60% of the initial body burden (IBB) was cleared rapidly, and this was attributed to deposition in the upper respiratory tract (URT). There was moderate absorption: the content of the skeleton increased from ~5% of the sacrifice body burden (SBB) at 2 d, to ~60% SBB at 128 d, exceeding that in the lungs by ~40 d. Analysis carried out here, assuming (see above) that s_r = 1 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1}, gave f_r = 0.1–0.2, and s_s = 0.02 d^{-1}, giving assignment to Type M. The wide range of values for f_r is mainly due to the uncertainty on the time of the first measurement, reported only as "on the day of exposure".

(391) Yabe et al. (1973) measured ^{170}Tm in the chest and in excreta of a man at times between 4 and ~450 d after accidental inhalation of $^{170}Tm_2O_3$. The exposure was detected following arc welding to seal a neutron-activated thulium oxide pellet in a titanium metal capsule. Thulium-170 was detected in the majority of urine samples collected: initially it accounted for less than 10% of daily excretion, but fecal excretion decreased faster than urinary excretion and by 130 d the fecal: urine ratio was about 2:1. Analysis carried out here, assuming (see above) that s_r = 1 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1}, gave f_r ~ 0.2, and s_s = 0.003 d^{-1}, giving assignment to Type M.

(392) Lambert et al. (1981) measured the tissue distribution of ^{170}Tm at times up to 44 d after inhalation by mice of $^{170}Tm_2O_3$. Commercially available thulium oxide was ground, the small particle fraction separated and neutron activated to produce ^{170}Tm. During the experiment, the ^{170}Tm concentration in the lungs decreased with a half-time of ~30 d; the amount in the kidneys remained at ~0.2% of the initial lung deposit (ILD); and the amount in tibia increased to ~0.1% ILD. Analysis carried out here, assuming (see above) that s_r = 1 d^{-1}, f_b = 0.07 and s_b = 0.021 d^{-1}, gave $f_r \leq 0.01$, and s_s = 0.002 d^{-1}, giving assignment to Type M.

15.2.2. Ingestion

(393) The fractional absorption of thulium from the gastrointestinal tract of rats has been variously reported to be less than 10^{-3} (Durbin et al., 1956) and less than 5 x 10^{-4} (Moskalev et al., 1972).

(394) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of thulium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

15.2.3. Systemic distribution, retention and excretion of thulium

15.2.3.1. Data

(395) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu showed broadly similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Roughly 60% of the activity entering blood deposited in the skeleton and roughly 10% deposited in the liver. Cumulative loss in urine through day 4 amounted to about 15-28% of the amount reaching blood.

15.2.3.2. Biokinetic model

(396) The biokinetic model for systemic thulium applied in this report is described in Section 2.2.3.2.

15.2.3.3. Treatment of progeny

(397) The treatment of radioactive progeny of thulium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

15.3. Individual monitoring

Information of detection limit for individual measurement techniques is not available.

15.4. Dosimetric data for thulium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Boyd, H.A., Thomas, R. L., 1970. Preparation of aerosols of thulium and americium by thermal degradation. In Fission Product Inhalation Program Annual Report 1969–1970, LF-43, 25–30. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225-238.

Durbin, P. W., 1962. Distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

Eakins J.D., Morgan A. 1964. The role of fecal analysis in a bioassay programme. In Assessment of Radioactivity in Man. I, 231–244, International Atomic Energy Agency, Vienna.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by Workers. ICRP Publication 68. Ann. ICRP 24(4).

Lambert, B.E., Hansen, L.S., Black, A., Phipps, M.L., 1981. A short term effect of homogeneous internal irradiation of the mouse lung with $^{170}Tm_2O_3$ particles. Radiat. Environ. Biophys. 20, 11–20.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: Biologicheskoye deystviye vneshnikh i vnutrennikh istochnikov r&&ii, 183–190 (ed. Moskalev, Yu. I.). MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

Strambi, E., Testa, C., 1966. On a case of internal contamination with thulium-170 [Su un caso di contaminazione interna da tulio-170] G. Fis. Sanit. Prot. Radiaz. 10, 199–202 (July–Sept. 1966). RT/PROT-(67)4.

Thomas, R. L., Kingsley, B. L., 1970. Retention of ^{171}Tm following inhalation of oxide by Beagle dogs. In Fission Product Inhalation Program Annual Report 1969–1970, LF-43, 71–78. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Yabe, A., Yamagishi, H., Fukuda, H., et al., 1973. A case study of human contamination due to inhaled thulium-170 oxide. Proc. 3rd Int. Cong. IRPA (ed. Snyder, W.), CONF-730907, 2, 1390–95.

16. YTTERBIUM (Z = 70)

16.1. Chemical Forms in the Workplace

(398) Ytterbium is an element of the lanthanide series which occurs mainly in oxidation states II and III.

(399) Ytterbium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides and carbonates). Ytterbium is most commonly obtained from xenotime and monazite.Ytterbium is used as a doping material in solid-state lasers.

Table 16. 1. Isotopes of ytterbium addressed in this report.

Isotope	Physical half-life	Decay mode
Yb-162	18.87 m	EC, B+
Yb-163	11.05 m	EC, B+
Yb-164	75.8 m	EC
Yb-166	56.7 h	EC
Yb-167	17.5 m	EC, B+
Yb-169[a]	32.026 d	EC
Yb-175	4.185 d	B-
Yb-177	1.911 h	B-
Yb-178	74 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

16.2. Routes of Intake

16.2.1. Inhalation

Absorption Types and parameter values

(400) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including ytterbium (Yb) (see general lanthanide section). Information on absorption from the respiratory tract is available from experimental studies of ytterbium, in water-soluble form and as oxide. Ytterbium-169 (half-life 32 d) has often been used as a gamma-emitting label for relatively insoluble particles (plutonium oxide, fused aluminosilicate) in inhalation experiments.

(401) As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including ytterbium, are given in Table 2.4. of the general lanthanide section.

Water-soluble forms of ytterbium

(402) Moskalev et al (1972) followed the biokinetics of ^{169}Yb (and other lanthanides, see general lanthanide section) for at least 32 d after deposition in the lungs of rats. However, few details are given. Fig. 135 of Moskalev et al (1972) shows retention (presumably in the lungs) of ytterbium falling to ~1% "of given dose" by 32 d. Analysis was carried out here (*i.e.*, by the Task Group) assuming that s_r = 0.44 d^{-1}, f_b = 0.07; s_b = 0.021 d^{-1}, and s_s = 0.0015 d^{-1}, based on analysis of the results of studies of cerium chloride inhaled by dogs – see general lanthanide section. The results fit well with f_r >0.95, (which would give assignment to Type F), higher than the value of 0.5 chosen for water-soluble forms of lanthanides.

Ytterbium oxide (Yb_2O_3)

(403) Rhoads and Sanders (1985) followed the biokinetics of ^{169}Yb in rats for 30 d after intratracheal instillation of ^{169}Yb-labelled oxide ($^{169}Yb_2O_3$), prepared from chloride solution calcined at 750°C. Lung retention was represented by a single exponential function with a half-time of 21 d. The authors stated that there was minimal transfer of ytterbium to other tissues because of the low solubility of the oxide in the lung. However, the amount in the skeleton varied between 0.3 and 7% of the initial lung deposit (ILD) in measurements made at times ranging from immediately after administration to 30 d, but with no clear trend with time, indicating Type M or S behaviour.

(404) Lundgren and McClellan (1975, 1976) administered stable Yb_2O_3 or $^{169}Yb_2O_3$ by inhalation to Syrian hamsters and mice as controls in studies of the biological effects of repeated inhalation exposure to $^{239}PuO_2$. The particles were prepared by thermal degradation of the hydroxide at 1100°C. (The $^{239}PuO_2$ was also labelled with ^{169}Yb to provide a gamma-emitting label to enable the $^{239}PuO_2$ deposits to be estimated by external counting, see below). The tissue distribution of ^{169}Yb was determined at times up to 364 d in hamsters (Lundgren et al., 1977), but results were not reported.

Plutonium oxide (PuO_2)

(405) Ytterbium-169 has been used as a gamma-emitting label for $^{239}PuO_2$ in inhalation studies, to enable the $^{239}PuO_2$ deposits to be estimated by external counting (Diel et al., 1981). For example, Lundgren and McClellan (1975, 1976) administered $^{239}PuO_2$ labelled with ^{169}Yb by inhalation to Syrian hamsters and mice in studies of the biological effects of repeated inhalation exposure to $^{239}PuO_2$. The particles were prepared by thermal degradation at 1100°C of plutonium hydroxide to which ^{169}Yb and stable ytterbium had been added. Lundgren et al. (1977) reported that the ratio Yb/Pu in the lungs of hamsters remained constant up to 128 d, indicating that the ^{169}Yb label was firmly retained.

Fused aluminosilicate particles (FAP)

(406) FAP or “fused clay” particles have been extensively used as relatively insoluble particles in inhalation studies, both of biokinetics and of radiation effects (see, e.g. cerium section).

(407) Snipes et al (1975, 1977) studied the effect of lung lavage on the distribution within the lungs of FAP labelled with ^{147}Pm and ^{169}Yb, at times up to 56 d after inhalation by dogs. No biokinetic data were reported, but the ability to measure the effectiveness of lung lavage, and particle distributions in lung sections by autoradiography, demonstrated that the material did not dissolve readily in the lungs. Herbert et al. (1987, 1988) investigated effects of lung irradiation

in rats for 18 months after inhalation of FAP labelled with ^{147}Pm and ^{169}Yb (the latter as a tracer for *in vivo* measurements). Little biokinetic information was reported. However, effective lung retention half-times were ~5 d for 58% of the initial lung deposit (ILD) and 150 d for 42% ILD, showing that the material was relatively insoluble.

(408) Raabe et al. (1988) used monodisperse ^{169}Yb-FAP to measure regional deposition of particles as a function of size in mice, Syrian hamsters, rats, guinea pigs and rabbits. Tissue distributions of ^{169}Yb were measured immediately after exposure and at 20 h. The authors noted that apart from the respiratory and alimentary tracts, internal organs were essentially free of ^{169}Yb, verifying the inherent insolubility of the aerosol particles and the label (but did not report the measurements themselves). The results thus indicate Type M or S behaviour.

16.2.2. Ingestion

(409) The fractional absorption of ytterbium from the gastrointestinal tract of rats has been reported to be less than 5×10^{-4} (Moskalev et al., 1972).

(410) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of ytterbium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

16.2.3. Systemic distribution, retention and excretion of ytterbium

16.2.3.1. Data

(411) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu showed broadly similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Roughly 60% of the activity entering blood deposited in the skeleton and roughly 10% deposited in the liver. Cumulative loss in urine through day 4 amounted to about 15-28% of the amount reaching blood.

16.2.3.2. Biokinetic model

(412) The biokinetic model for systemic ytterbium applied in this report is described in Section 2.2.3.2.

16.2.3.3. Treatment of progeny

(413) The treatment of radioactive progeny of ytterbium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

16.3. Individual monitoring

^{169}Yb

(414) *In vivo* lung measurements of ^{169}Yb are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{169}Yb concentrations in faeces may be used to determine intakes of the radionuclide. *In vivo* whole body measurement may be used as an additional technique for special investigation. The main technique is gamma spectrometry.

Table 16. 2. Monitoring techniques for ^{169}Yb.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{169}Yb	Faecal Bioassay	γ-ray spectrometry	10 Bq/24h
^{169}Yb	Lung Measurement[a]	γ-ray spectrometry	6 Bq
^{169}Yb	Whole-body Measurement[b]	γ-ray spectrometry	140 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

16.4. Dosimetric data for ytterbium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Diel, J. H., Guilmette, R. A., Kanapilly, G. M.,et al., 1981. Calibration of initial pulmonary burden measurement using ^{169}Yb whole body counting. Inhalation Toxicology Research Institute Annual Report 1980–1981. LMF-91. 53–57. Albuquerque, NM: Lovelace Biomedical and Environmental Research Institute. Available from National Technical Information Service, Springfield, Virginia.

Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225–238.

Durbin, P. W., 1962. distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Herbert, R. A., Scott, B. R., Hahn, F. F., et al., 1987. The prevalence and morphology of primary pulmonary neoplasms in rats 18 months after inhalation of ^{147}Pm in fused aluminosilicate particles. Inhalation Toxicology Research Institute Annual Report 1986–1987, LMF-120, 331–335. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Herbert, R. A., Scott, B. R., Hahn, F. F., et al., 1988. The occurrence of primary pulmonary neoplasms in rats 18 months after inhalation of ^{147}Pm in fused aluminosilicate particles. Inhalation Toxicology Research Institute Annual Report 1987–1988, LMF-121, 234–240. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Lundgren D.L., McClellan R.O., 1975. Biological effects of repeated inhalation exposure of Syrian hamsters to aerosols of $^{239}PuO_2$. Inhalation Toxicology Research Institute Annual Report 1974–1975, LF-52. 236–238. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Lundgren D.L., McClellan R.O., 1976. Biological effects of repeated inhalation exposure of Syrian hamsters and mice to polydisperse aerosols of $^{239}PuO_2$. Inhalation Toxicology Research Institute Annual Report 1975–1976, LF-56. 297–300. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Lundgren D.L., Rebar A. H., McClellan R.O., 1977. Biological effects of repeated inhalation exposure of Syrian hamsters to aerosols of $^{239}PuO_2$ III. Inhalation Toxicology Research Institute Annual Report 1976–1977, LF-58. 176–181. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Moskalev, Yu. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: Biologicheskoye deystviye vneshnikh i vnutrennikh istochnikov radiastsii, 183–190 eds. Moskalev, Yu. I., and Kalistratova, V. S.. Moscow. Translated in Biological effects of radiation from external and internal sources. AEC-tr-745, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

Raabe, O. G., Al-Bayati, M. A., Teague, S. V., Rasolt, A., 1988. Regional deposition of inhaled monodisperse coarse and fine aerosol particles in small laboratory animals. IN: Inhaled Particles VI, Proceedings of an International Symposium and Workshop on Lung Dosimetry Organised by the British Occupational Hygiene Society in Co-operation with the Commission of the European Communities, Cambridge, 2–6 September 1985, Eds. Dodgson, J., McCallum, R.I., Bailey, M.R., and Fisher, D.R, 53–63. Pergamon Press, Oxford, United Kingdom. Ann. Occup. Hyg 32 Suppl 1.

Rhoads, K., Sanders, C.L., 1985. Lung clearance, translocation, and acute toxicity of arsenic, beryllium, cadmium, cobalt, lead, selenium, vanadium, and ytterbium oxides following deposition in rat lung. Environ. Res. 36, 359–378.

Snipes, M. B., Runkle, G. E., Muggenburg, B. A., 1977. Influence of lavage therapy on the distribution patterns of inhaled relatively insoluble particles in the lung. Inhalation Toxicology Research Institute Annual Report 1976–1977, LF-58, 200–204. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Snipes, M. B., Runkle, G. E., Muggenburg, B. A., Hulbert, A. J., 1975. Distribution patterns of inhaled polydisperse ^{147}Pm fused clay particles in the beagle dog thorax with and without lavage therapy. II. Inhalation Toxicology Research Institute Annual Report 1974–1975, LF-52, 91–95. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

17. LUTETIUM (Z = 71)

17.1. Chemical Forms in the Workplace

(415) Lutetium is an element of the lanthanide series which occurs mainly in oxidation state III.

(416) Lutetium may be encountered in a variety of chemical and physical forms, including oxides, hydroxides, and inorganic salts (chlorides, fluorides, iodides, sulphates, sulphides, oxalates and carbonates). Lutetium is most commonly obtained from monazite. Lutetium-177 is used for radionuclide therapy on neuroendocrine tumours.

Table 17. 1. Isotopes of lutetium addressed in this report.

Isotope	Physical half-life	Decay mode
Lu-165	10.74 m	EC, B+
Lu-167	51.5 m	EC, B+
Lu-169	34.06 h	EC, B+
Lu-170	2.012 d	EC, B+
Lu-171	8.24 d	EC, B+
Lu-172	6.70 d	EC, B+
Lu-173	1.37 y	EC
Lu-174	3.31 y	EC, B+
Lu-174m	142 d	IT, EC
Lu-176	3.85E+10 y	B-
Lu-176m	3.635 h	B-, EC
Lu-177[a]	6.647 d	B-
Lu-177m	160.4 d	B-, IT
Lu-178	28.4 m	B-
Lu-178m	23.1 m	B-
Lu-179	4.59 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

17.2. Routes of Intake

17.2.1. Inhalation

Absorption Types and parameter values

(417) Studies have been reported of lung retention in man following chronic inhalation exposure to stable 'rare earth' (lanthanide) elements, including lutetium (see general lanthanide section). No reports of experimental studies of lutetium were found. As described in the general lanthanide section, absorption parameter values based on cerium are applied in this document to

the other lanthanides. Absorption parameter values and Types, and associated f_A values for particulate forms of lanthanides, including lutetium, are given in Table 2.4. of the general lanthanide section.

17.2.2. Ingestion

(418) There is no relevant data available concerning ingestion of lutetium, but the fractional absorption from the gastrointestinal tract of rats for several similar lanthanides has been variously reported to be less than 10^{-3} (Durbin et al., 1956) and less than 5×10^{-4} (Moskalev et al., 1972).

(419) In *Publication 30* (ICRP, 1979), an f_1 of 3×10^{-4} was recommended for all compounds of lutetium. In *Publication 68* (ICRP, 1994), a value of 5×10^{-4} was adopted by analogy with trivalent actinides and this f_A value is adopted in this report for every element of the lanthanide family.

17.2.3. Systemic distribution, retention and excretion of lutetium

17.2.3.1. Data

(420) The lanthanides, Tb, Dy, Ho, Er, Tm, Yb, and Lu showed broadly similar biokinetics in rats (Durbin, 1960, 1962; Moskalev et al., 1974; Ando et al., 1989). Roughly 60% of the activity entering blood deposited in the skeleton and roughly 10% deposited in the liver. Cumulative loss in urine through day 4 amounted to about 15-28% of the amount reaching blood.

17.2.3.2. Biokinetic model

(421) The biokinetic model for systemic lutetium applied in this report is described in Section 2.2.3.2.

17.2.3.3. Treatment of progeny

(422) The treatment of radioactive progeny of lutetium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 2.2.3.3.

17.3. Individual monitoring

^{177}Lu

(423) *In vivo* lung measurements of ^{177}Lu are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{177}Lu concentrations in urine and faeces may be used to determine intakes of the radionuclide. *In vivo* whole body measurement may be used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 17. 2. Monitoring techniques for ^{177}Lu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{177}Lu	Urine Bioassay	γ-ray spectrometry	9 Bq/L
^{177}Lu	Faecal Bioassay	γ-ray spectrometry	9 Bq/24h
^{177}Lu	Lung Measurement[a]	γ-ray spectrometry	5 Bq
^{177}Lu	Whole-body Measurement[b]	γ-ray spectrometry	120 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

17.4. Dosimetric data for lutetium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ando, A., Ando, I., Hiraki, T., Hisada, K., 1989. Relation between the location of elements in the periodic table and various organ-uptake rates. Nucl. Med. Biol. 16, 57–69.

Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225–238.

Durbin, P. W., 1962. distribution of the transuranic elements in mammals. Health. Phys. 8, 665–671.

Durbin, P.W., Williams, M.H., Gee, M., Newman, R.H., Hamilton, J.G., 1956. Metabolism of the lanthanons in the rat. Proc. Soc. Exp. Biol. Med. 91, 78–85.

ICRP, 1979. Limits for Intakes of Radionuclides by Workers. ICRP Publication 30 (Part 1). Ann. ICRP 2 (3-4).

ICRP, 1994. Doses coefficients for intake of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1972. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In: *Biologicheskoye deystviye vneshnikh* i *vnutrennikh istochnikov* r&&ii, 183–190 ed. Moskalev, Yu. I. MOSCOW. Translated in Biological effects of radiation from external and internal sources, AEC-tr-7457, 278–287.

Moskalev, Y. I., Zalikin, G. A., Stepanov, V. S., 1974. Distinctions of distribution in the organism of radioactive isotopes of lanthanide elements. In:Biological Effects of Radiation from External and Internal Sources. AEC-tr-7457.

18. A GENERIC BIOKINETIC MODELING SCHEME FOR THE ACTINIDES

(424) As is the case for the lanthanides, the initial distribution and rate of excretion of intravenously injected or absorbed activity varies across the actinide family. For the lanthanide elements, all of which are expected to be present in body fluids as trivalent ions, results of animal studies indicate a strong relation between the ionic radius and the early systemic distribution and excretion rate of an element. The biokinetics of the actinide family as a whole appears to be much less regular than that of the lanthanides and more difficult to describe in terms of physical or chemical properties. Presumably this is due in part to the different primary oxidation states of different actinides, ranging from trivalent to pentavalent. However, a relation between the ionic radius and the early systemic distribution broadly similar to that for the lanthanides is suggested by data for the heaviest actinides, Am through Es, which are expected to be present in body fluids as trivalent ions. As with the lanthanides, this relation can be used to assign element-specific parameter values to these elements in lieu of specific information. More generally, results of animal studies indicate sufficient overall biokinetic similarities within certain subgroups of the actinide family (e.g. Pa and Th; or Ac, Am, and Cm) that it is reasonable to assign parameter values for a frequently studied actinide to a less frequently studied actinide within its subgroup in the absence of specific information.

(425) For these reasons, a generic biokinetic modeling scheme is applied in this report series to the actinide elements Ac, Pa, Np, Pu, Am, Cm, Bk, Cf, Es, and Fm. The same modeling scheme was applied in Part 3 of this series to the actinide Th. This section describes the basis for the generic modeling scheme, the common model structure applied (with additional blood and liver compartments for Pu), and the generic and element-specific parameter values assigned to each of the actinide elements addressed here. Subsequent element sections expand on specific data or assumptions for each of these elements.

18.1. Actinides physico-chemistry

(426) The actinides (An) comprise 15 elements with atomic numbers 89 through 103: actinium (Ac), thorium (Th), protactinium (Pa), uranium (U), neptunium (Np), plutonium (Pu), americium (Am), curium (Cm), berkelium (Bk), californium (Cf), einsteinium (Es), fermium (Fm), mendelevium (Md), nobelium (No) and lawrencium (Lr). IUPAC prefers the term actinoid to actinide (IUPAC, 2005) but this terminology is not adopted in this document. Uranium and thorium are included in OIR Part 3 (ICRP, 2016b). The last three elements Md, No and Lr are not considered in the OIR series.

Sources and production

(427) Actinides may be encountered in the front end and the back end of the nuclear fuel cycle industry in a variety of chemical and physical forms, including oxides, hydroxides, inorganic salts (nitrates, chlorides, fluorides, sulphates, carbonates and phosphates) and in some specific cases in organic forms such as tributyl-phosphate (TBP).

(428) Of these actinides, only thorium and uranium, also called major actinides, occur naturally in substantial quantities as ores. Other actinides, also called minor actinides, are produced from transmutation reactions in nuclear reactors.

Uses

(429) Actinides have no stable isotopes and are mostly used as fuel in nuclear reactors. Some of these actinides (e.g. uranium, plutonium, and americium) are used as mixed oxide reactor fuel (MOX). Major actinides are also used in nuclear weapons. Nuclear reprocessing was developed to chemically separate and recover actinides of interest from irradiated nuclear fuel.

Physico-Chemistry

(430) The actinides (An) are also called f-transition metals or 5f elements in the periodic table of elements, because their general electronic structure is mostly $[Rn]7s^2 5f^n$ except for Ac and Th which are only in 6d and 7s orbitals. Consequently, actinides are strong electron acceptors and can be considered as hard acids as defined by HSAB theory of Pearson (Pearson, 1963). They tend to interact with strong electron donors such as oxygen, being present in aqueous systems of interest such as biological and environmental media.

(431) A comparative evolution of the ionic radii (Shanon, 1976) for a given coordination number of VI (Fig. 18.1) shows a significant and regular decrease in the series for the main valence state (from III to VI), and underlines the specificity of "yle" cations (AnO_2^{2+} with An(VI) and An= U, Np, Pu, Am) which are larger due to the oxygen binding.

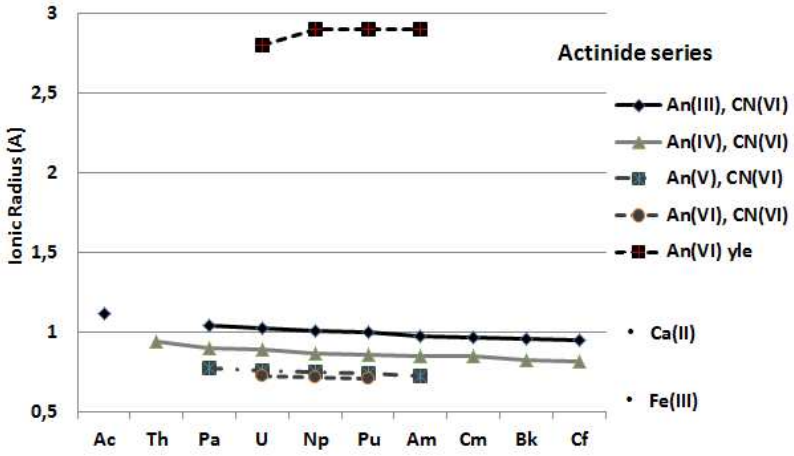


Fig. 18.1. Ionic radii of actinide series for different oxidation states (III to VI) for a coordination number (CN = VI).

(432) Actinides in aqueous solution can occur as solids, colloids or solvated species. The presence of these species is regulated by thermodynamic and kinetic laws and is sensitive to parameters such as cation/anion concentration, ionic strength, temperature, gas-liquid-solid phase equilibria and oxidation-reduction potential.

(433) In aqueous media, actinides exhibit a range of oxidation state from +II to +VIII, with the more stable oxidation states detailed in Table 18.1. This table shows the various number of oxidation states in some early elements of the series (mainly U, Np, Pu, Am) and a predominant oxidation state of III for the heaviest actinides (Am, Cm, Bk, Cf…).

(434) For the +III and +IV oxidation state (An^{3+}, An^{4+}), the coordination numbers of the cation range from 6 to 12. Oxidation states +V and +VI possess a particular molecular shape: this group, also called the actinyl group, is a linear trans-dioxo cation ($An(V)O_2^+$, $An(VI)O_2^{2+}$),

with strong covalent interactions between the actinides (An) and the oxygen (O), a large effective charge of the central actinides ion (e.g. 3.3 and 2.3, respectively), and coordination numbers of II to VIII. This actinyl geometry is ubiquitous and both An(V) and An(VI) aquo ions have five water molecules in their equatorial plane, whereas both An(III) and An(IV) exist as simple hydrated (or aquo) ions $An(H_2O)_n^{p+}$, where n=8 and p=3 or 4.

Table 18.1.Oxidation states for the actinide elements[a].

Element	Oxidation state
Ac	**III**
Th	**IV**
Pa	IV, **V**
U	III, IV, V, **VI**,
Np	III, IV, V, **VI**,VII
Pu	III, **IV**, V, VI,VII, *VIII*
Am	**III**, IV, V, VI,*VII*
Cm	**III**, IV
Bk	**III**, IV
Cf	**III**, IV
Es	II,**III**
Fm	II,**III**

[a] In bold font are the most stable oxidation states under aqueous conditions.

A noteworthy aspect of actinide solution chemistry is the importance of hydrolysis reactions (Eq. 18.1) (Allard et al., 1980; Altmaier et al., 2013; Knope et al., 2013), which may be significant even in acidic media.

$$An^{n+} + m\ H_2O \leftrightarrow An(OH)_m^{(n-m)+} + m\ H^+ \quad \text{(Eq. 18.1)}$$

(435) The strength of hydrolysis follows the order $An^{4+} > AnO_2^{2+} > An^{3+} > AnO_2^{+}$. The An^{4+} and AnO_2^{2+} species are reported also to form very stable hydroxide oligomers (i.e. $[An(OH)_i]_n$), depending on the actinide concentration.

(436) A second important aspect of actinides solution chemistry is disproportionation reactions, leading to several oxidation states simultaneously in aqueous media: the redox reactions of actinide species have been divided into 2 groups, namely those involving only electron transfer (An^{4+}/An^{3+} and AnO_2^{2+}/AnO_2^{+} pairs), for which reactions of simple electron exchange are fast, and those also requiring formation and/or rupture of metal/oxygen bonds (e.g. An^{4+}/AnO_2^{+} pairs), which tend to be kinetically slow.

(437) The “hard acid” properties of actinide cations (Pearson, 1963) involve a stronger preference for oxygen donor atoms and preferential interactions with ligands containing such groups rather than nitrogen, sulphur or phosphorous donors. Their ability to form complexes with inorganic ligands diminishes as follows: $PO_4^{3-} > CO_3^{2-} > OH^- > SO_4^{2-} > Cl^-$. At the same oxidation state, it is well known that the relative stability of the complexes with hard acids increases with the atomic number, due to the contraction of the actinide ionic radii.

Behaviour within biological media

(438) Considering the complexity of actinide chemistry (e.g. Seaborg, 1993; Neck et al., 2001; Gorden et al., 2003; Choppin et al., 2006; Knope et al., 2013, Altmaier et al., 2013), numerous studies have been conducted in order to better understand their biological behaviour

(Durbin, 1960, 1962, 2006; Duffield and Taylor, 1987; Maher et al., 2013). Moreover, recent reviews focusing on developments of speciation tools (e.g. Paquet et al., 2003; Ansoborlo at al., 2006; Bresson at al., 2011; Vidaud et al., 2005, 2007, 2012; Maher et al., 2012) and on recent methodologies such as transcriptomics and proteomics (Hood et al., 2012; Aryal et al., 2011), have shown significant progress made in speciation of actinides (mainly uranium and plutonium) with specific biological ligands such as proteins involved in transportation (e.g. Prat et al, 2005; Vidaud et al., 2007; Jensen et al., 2011; Basset et al., 2013).

(439) Most studies on actinide binding with biological ligands either in blood (Taylor, 1998; Duffield, 1991; Yule , 1991; Durbin, 2006) or in tissue/organ target deposition sites such as liver, bone and kidney, have shown that proteins such as transferrin and albumin are mainly in charge of the distribution from blood to organs, and that some other proteins were more or less organ-specific such as calmodulin, ferritin and lipofuscin for the liver (Taylor et al., 1987; Paquet et al., 2003; Duffield and Taylor, 1991), sialoproteins, chondroitin sulphate-protein complexes and glycoproteins for the bone (Duffield and Taylor, 1991).

(440) Recent studies using methodologies such as proteomics and transcriptomics, and mainly focused on uranium and plutonium, carried out either *in vitro* by acute exposure of various cell line (Prat et al., 2005) or *in vivo* by studying organ response to acute or chronic exposure (Taulan et al., 2004, 2006), have generally shown that mechanisms such as oxidative stress, apoptosis, signal transduction, inflammation and catabolism might contribute to actinide toxicity. These studies provided a set of new interesting proteins involved in gene expression, such as fetuin-A (Basset et al., 2013), actin D, tubulin A, heat shock protein 90 (HSP 90) (Prat et al., 2005, 2012; Malard et al., 2009), glucose regulated protein (GRP78) and Nucleoside diphosphate kinase B (Aryal et al., 2011), osteopontin (Taulan et al., 2004, 2006; Qi et al., 2014; Safi et al., 2013; Vidaud et al., 2012). Some of these proteins might be good biomarker candidates such as osteopontin (Prat et al., 2011).

18.2. Routes of intake

18.2.1. Inhalation

(441) As for the lanthanides (Section 2.2.1) the behaviour of many ionic (water-soluble) forms of actinides (e.g. nitrate) following deposition in the respiratory tract is complex and difficult to determine because their solutions are unstable at neutral pH and in many biological media, resulting in hydrolysis (see above and ICRP, 1986).

(442) Another similarity with the lanthanides is the very wide range between elements in the amount of information on their behaviour following deposition in the respiratory tract. For two elements, uranium and plutonium, there is extensive information covering a wide range of chemical forms: more than for any other elements. For thorium, neptunium, americium and curium there is as much information as there is for most other elements in this document series. However, for actinium, protactinium, berkelium, californium, einsteinium and fermium there are few, if any, relevant experimental studies.

(443) The similarities in chemical properties of the actinides also noted above raise the possibility of the application of model parameter values derived for well-informed elements to those elements for which information is lacking. However, there appears to be much greater variation in behaviour across the actinides than across the lanthanides. For example, Table 18.1 shows marked differences in the range of oxidation states for each element, and differences in the most stable oxidation state in aqueous media for each element.

(444) ICRP (1986) noted that the competing phenomena of hydrolysis and complex formation play important roles in determining the biological behaviour of the actinides. The tetravalent actinides, thorium and plutonium, show a strong tendency to hydrolysis, leading to the formation of polymers or particles at pH values greater than about 2. The trivalent transplutonium elements, americium to fermium, hydrolyse to a much lesser degree but do show decreasing solubility in the pH range 6.5 to 9, forming insoluble hydroxides or other hydroxy species. The Np(V) ion shows virtually no tendency to undergo hydrolysis below a pH of about 7.

(445) For actinium (Section 19.2.1.), no experimental studies were found that give information on its absorption, and chemical analogy is applied here. Following the approach taken with the systemic model for actinium, HRTM absorption parameter values chosen for americium are applied in this document to actinium.

(446) For protactinium (Section 20.2.1.), the only experimental study found that gives information on its absorption from the respiratory tract involved administration of the citrate to rats by intratracheal instillation. As there is so little relevant information available, absorption parameter values for protactinium are based on chemical analogy. Following the approach taken with the systemic model for protactinium, HRTM absorption parameter values chosen for thorium (OIR Part 3, ICRP, 2016) are applied in this document to protactinium.

(447) For neptunium (Section 21.2.1.), as noted above, there is as much information as there is for most other elements in this document series, and it is treated as an individual element, as are thorium and uranium.

(448) For the four higher actinides (berkelium to fermium) there were only three studies (or fewer) on each element, and therefore consideration was given to use of chemical analogy. As noted above, there are greater similarities across the trivalent transplutonium elements, americium to fermium, than across the other actinides and there is a reasonable amount of information relating to americium and curium; there is far more information relating to plutonium, but this might be offset by differences in behaviour.

(449) To provide guidance on, and justification for, the approach taken, the following three sections review and summarise relevant information on the actinides from plutonium to einsteinium (more details are given in the individual element sections; there was no such information on fermium):

- comparisons which could be made between the clearance characteristics of soluble forms of different elements deposited in the respiratory tract under similar conditions;
- estimates of rapid dissolution rates;
- estimates of bound fraction parameter values.

Comparisons of respiratory tract clearance of higher actinides

(450) Comparisons that could be made between the clearance characteristics of soluble forms of the "higher" actinides (from plutonium to einsteinium) deposited in the respiratory tract under similar conditions are described in the next paragraphs. Ideally, comparisons would be made between elements administered simultaneously e.g. 'dual-isotope' experiments (provided the radionuclides behave independently), or at least as part of the same study. However, to provide a more comprehensive review, comparisons are also made here between studies carried out by the same research group under apparently similar conditions.

Nitrates and citrates: instillation into respiratory tract of rats

(451) Crawley and Goddard (1976) studied the biokinetics of ^{241}Am and ^{242}Cm following their deposition in the respiratory system of rats: nitrate or citrate solutions were administered by instillation into the nasopharyngeal (N-P), tracheobronchial (T-B) and pulmonary (P) regions. No differences were observed in the tissue distribution and excretion of ^{241}Am and ^{242}Cm at 1 or 7 d after administration. Translocation from the P region to extrapulmonary (systemic) tissues was higher than from the other regions. Administration of the nitrates gave higher lung retention and lower translocation to extrapulmonary tissues than the corresponding citrates. The authors compared their results with those from a similar study involving ^{239}Pu (Stather and Howden, 1975). Retention in the lungs after instillation into the P region was similar, but after deposition in the T-B region significantly more of both ^{241}Am and ^{242}Cm nitrates and citrates were retained compared with the ^{239}Pu compounds. The authors considered that this may be due to a lower binding capacity of americium and curium to the proteins in the mucus lining the epithelium, resulting in a lower clearance up the ciliary escalator.

(452) Stather and Priest (1977) compared tissue distributions of ^{238}Pu, ^{239}Pu and ^{241}Am at 1, 7, 30 and 120 d following simultaneous instillation of the nitrates into the P region of rats. All results for ^{238}Pu and ^{239}Pu were similar. Lung retention of Pu and ^{241}Am was also similar, but with some indication of greater clearance of Pu at 1 d. In a similar experiment, they compared tissue distributions of ^{241}Am and ^{242}Cm at 7, 30 and 150 d after administration of the nitrates. All results for ^{241}Am and ^{242}Cm were similar, as found by Crawley and Goddard (1976). However, lung retention of ^{241}Am (33%, 13% and 1.6% ILD, respectively) was less than in the first experiment (45%, 20% and 6% ILD, at 7, 30 and 120 d, respectively). The authors noted that the similarity in behaviour between ^{241}Am and ^{242}Cm could be due to similar behaviour of their hydroxides, or to the formation of mixed Am-Cm hydroxide polymers in the lungs, which clear at a rate determined by the properties of the mixed hydroxide. The latter explanation may account for the slower clearance of ^{241}Am when mixed with ^{239}Pu.

(453) Stradling et al. (1980) measured tissue distributions of ^{239}Pu, ^{241}Am and ^{244}Cm at 1, 6 and 21 d after intratracheal instillation of the citrates into the lungs (P region) of rats (for comparison with their behaviour following administration of sized fractions of the dioxides). Further details (including measurements of the radionuclides in other tissues and excreta) for ^{239}Pu, ^{241}Am and ^{244}Cm are given in Stradling et al. (1978a), Stradling et al. (1978b) and Stradling et al. (1979), respectively. Results for lungs, liver and carcass are given in Table 18.2. The radionuclides appear to have been administered in separate experiments. In a similar study by the same group, Smith et al. (1977) measured tissue distributions of ^{239}Pu at 18 hours, 6 and 17 d after intratracheal instillation of the citrate into the lungs of rats (Table 18.2). Tissue distributions of ^{241}Am and ^{244}Cm were similar. Lung retention of ^{239}Pu was greater than that of ^{241}Am and ^{244}Cm up to about 1 d after administration, but was similar at later times (6 and 21 d). This suggests that the rapid dissolution rate s_r is lower for ^{239}Pu than for ^{241}Am or ^{244}Cm, but the rapidly dissolved fractions f_r are similar.

Table 18.2. Distribution of radionuclides (percentage of administered activity, Mean ±SEM) following intratracheal instillation of the citrate into the lungs of rats.

	Lungs			Liver			Carcass		
Time, d	^{239}Pu	^{241}Am	^{244}Cm	^{239}Pu	^{241}Am	^{244}Cm	^{239}Pu	^{241}Am	^{244}Cm
0.75[a]	26.8±0.7			5.12±0.23			53.7±1.1		
1[b]	28.2±1.7	11.5±0.6	10.7±0.6	11.0±1.0	42.6±1.4	41.7±1.9	51.7±2.7	32.9±0.8	37.1±1.3

6[a]	10.3±1.0			7.57±0.14			67.3±0.5		
6[b]	7.4±0.45	7.1±0.6	8.45±0.46	12.4±0.4	32.6±1.0	34.7±1.0	64.2±2.6	36.1±0.9	37.9±1.0
17[a]	7.43±0.60			6.38±1.32			67.2±0.4		
21[b]	5.4±0.38	4.2±0.6	3.74±0.17	9.79±0.33	14.1±0.8	17.2±0.7	64.7±2.7	37.9±0.5	37.7±0.8
60			1.35±0.05			5.54±0.30			35.7±0.9
106		0.68±0.05			3.19±0.24			34.9±0.5	

[a] ^{239}Pu: Smith et al (1977);
[b] ^{239}Pu: Stradling et al (1978a);
[c] Separate measurements reported of Spleen, Blood, and "Other tissues" (kidneys, testes, adrenals, thymus, gastro-intestinal tract)

(454) Davies et al. (1992, 1993) measured the distribution of ^{238}Pu and ^{241}Am at times from 1 hour to 28 d following instillation of a solution containing ^{238}Pu and ^{241}Am nitrates into the nasal passages of rats. They investigated the effect of site of deposition (6, 12 or 18 mm depth from the nostril) and the effect of duration of halothane anaesthesia. The main results are given in Table 18.3. Davies et al. (1993) also reported carcass, gastro-intestinal tract and feces measurements. The authors noted that rates of transfer from the nose were greater for ^{238}Pu than for ^{241}Am, but the difference was significant ($p < 0.01$) only for the 12 mm site.

(455) Davies et al. (1992, 1993) also measured the distribution of ^{238}Pu and ^{241}Am at times up to 28 d following intratracheal instillation of a solution containing ^{238}Pu and ^{241}Am nitrates into the lungs (P region) of rats, for comparison with uptake from the nose. The main results are given in Table 18.4. (Davies et al. also reported liver, carcass, and urine measurements). The authors noted that rates of transfer from the lung were greater for ^{241}Am than for ^{238}Pu, in contrast to the rates from the nose, but the difference was not significant.

Table 18.3. Distribution of ^{238}Pu and ^{241}Am (percentage of administered activity, Mean ±SEM) following simultaneous instillation of the nitrates into the nasal passages of rats.

Instillation depth		Nose		Total to blood	
		^{238}Pu	^{241}Am	^{238}Pu	^{241}Am
6 mm	1 h	6.0±2.1	11.7±2.2	1.1±0.2	0.7±0.1
	6 h	2.2±0.6	2.8±0.5	0.6±0.2	0.5±0.1
	24 h	1.8±0.5	3.0±0.8	1.4±0.4	0.7±0.2
	3 d	1.9±0.5	2.5±0.6	2.4±0.3	1.9±0.2
12 mm	1 h	52.2±15.3	34.6±7.9	1.5±0.4	1.0±0.1
	6 h	8.2±2.7	10.4±2.9	2.4±0.4	0.6±0.1
	24 h	3.1±1.1	4.0±1.3	2.4±0.3	0.8±0.2
	4 d	1.4±0.1	2.0±0.5	2.1±0.2	0.7±0.2
18 mm	1 h	55.6±7.6	59.2±6.6	2.4±0.7	1.2±0.1
	6 h	15.5±4.1	20.5±5.9	4.1±1.5	1.6±1.0
	24 h	17.3±3.2	16.5±2.8	3.8±0.5	2.3±0.3
	3 d	6.3±0.8	9.9±1.3	3.9±0.7	3.0±0.7

7 d	3.0±1.2	9.7±1.9	2.5±0.7	3.6±0.6
28 d	4.0±1.1	5.2±1.3	3.0±0.3	6.7±2.5

Table 18.4. Distribution of ^{238}Pu and ^{241}Am (percentage of administered activity, Mean ±SEM) following simultaneous instillation of the nitrates into the lungs of rats.

	Lung		Total to blood	
	^{238}Pu	^{241}Am	^{238}Pu	^{241}Am
Day				
1	47.1±6.3	45.5±4.7	25.8±2.1	31.6±2.4
3	39.0±2.2	34.2±4.7	43.6±2.3	49.0±2.4
7	32.3±2.2	30.1±2.1	46.4±1.7	54.7±1.2
28	20.2±1.3	13.5±0.9	45.8±3.9	58.7±2.7

Nitrates: inhalation by rats

(456) Nénot et al. (1971) compared the biokinetics of ^{239}Pu, ^{241}Am and ^{242}Cm following inhalation of Pu nitrate, Am nitrate and Cm chloride by rats. At 45 d after intake they observed significantly higher lung retention for ^{239}Pu than for ^{241}Am or ^{242}Cm: respectively ~30%, 4% and 8% "IAD" (initial alveolar deposit: estimated total inhaled activity, IA, minus fecal activity in the first 3 d); with correspondingly lower systemic retention (~8%, 20% and 10% "IAD" in bone plus liver for ^{239}Pu, ^{241}Am and ^{242}Cm respectively) and excretion (~61%, 72% and 79% "IAD" in urine plus feces respectively). After 2 months, 4% IA of ^{239}Pu was still retained in lung while 0.8% IA was retained in systemic organs. At the same time, 1.3% and 1.6% IA of ^{241}Am and ^{242}Cm respectively was retained in lung, with 8% and 3% IA respectively retained in systemic organs.

(457) Nénot et al. (1972) compared lung retention of ^{238}Pu, ^{239}Pu, ^{241}Am and ^{242}Cm following inhalation of the nitrates by rats up to ~50 d after inhalation (^{239}Pu and ^{241}Am up to ~100 d). Lung retention of ^{238}Pu and ^{239}Pu was similar (~40% of the initial lung deposit, ILD, at 50 d) and much greater than that of ^{241}Am and ^{242}Cm, which were also similar (~7% ILD, at 50 d). No details of the inhalation exposure were given. However, authors noted that some differences in retention could have been due to differences in mucociliary clearance and/or to the greater mass of ^{239}Pu than that of the other radionuclides, which suggests that the radionuclides were administered separately.

(458) Stradling et al. (1987) compared tissue distributions (lungs, liver and carcass) of $^{239(+240)}$Pu and ^{241}Am at 7, 28, 70, 168 and 252 d after simultaneous inhalation of the nitrates by rats. (Results were reported in relation to "initial lung deposit", but this was based on amounts measured in rats at 2 d after exposure, to allow for clearance from the upper airways, and so probably underestimates even the initial alveolar deposit, since there would have been some absorption to blood by 2 d.) Americium-241 was absorbed from lungs to blood somewhat faster than ^{239}Pu. At 7 d after exposure, lung retention of ^{239}Pu (64% "ILD") was somewhat greater than that of ^{241}Am (57% "ILD"). The Pu:Am ratio in lungs (normalised to that in the aerosol inhaled) increased steadily from 1.1 at 7 d, to 2.3 at 252 d. The estimated amount absorbed to blood was ~15% "ILD" for ^{239}Pu, and ~18% "ILD" for ^{241}Am at 7 d, and remained between 2 and 5% "ILD" higher for ^{241}Am than for ^{239}Pu throughout, suggesting that the greater absorption of ^{241}Am occurred mainly within the first 7 d.

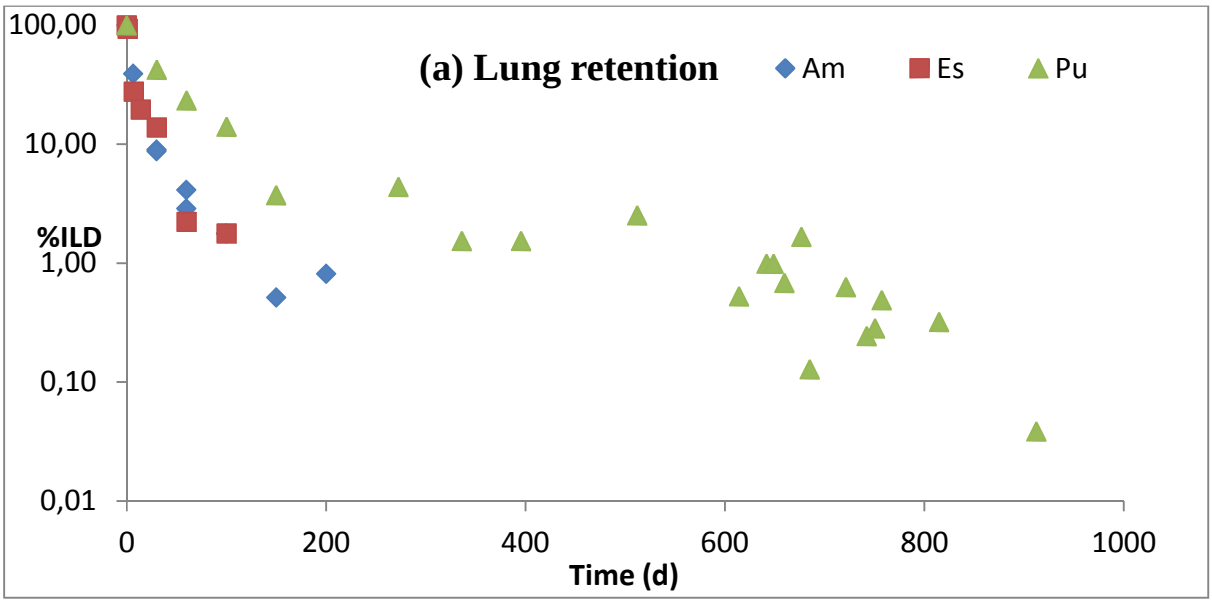
(459) In separate studies, a research group at the Biology Department, Pacific Northwest Laboratory followed the biokinetics of ^{239}Pu, ^{241}Am, and ^{253}Es after inhalation of the nitrates (in 0.27N nitric acid) by rats for 1000 d, 200 d and 100 d respectively, (Ballou et al., 1977; Ballou and Gies, 1978; Ballou et al.,. 1979; Fig. 18.2). In all three studies, the ILD was based on the estimated deposit in the lungs immediately after exposure.

(460) Ballou et al. (1977) followed the distribution of ^{239}Pu between lung, liver and skeleton after inhalation of the nitrate. They studied the effect of DTPA treatment and the long-term health effects. Lung retention decreased to 42% ILD at 30 d after inhalation, 14% ILD at 100 d and 0.04% ILD at 900 d. It was fit by a three-component exponential function with biological half-times (T_b) = 5 d (5% ILD), 35 d (30% ILD) and 155 d (10% ILD). At 30 d after inhalation by non-DTPA treated animals, 9% ILD had translocated to liver and skeleton. The retention in liver and skeleton then slowly decreased to 6% after 100 d and 0.7% at 900 d.

(461) Ballou and Gies (1978) followed the clearance of ^{241}Am from lung to liver, kidney and skeleton after inhalation of the nitrate. At 30 d post-inhalation 9% ILD was retained in lungs and 29% ILD had been transferred to skeleton and liver. After 100 d, 1.8% ILD was retained in lungs and 21% ILD was in skeleton and liver.

(462) Ballou et al. (1979) studied the tissue distribution of ^{253}Es after inhalation as the nitrate. Lung retention could be described by a two-component exponential function with T_b = 1.1 d (65% ILD) and 19.5 d (35% ILD). At 30 d post-inhalation, 14% ILD was retained in lungs while 47% had translocated to liver and skeleton. After 100 d, 1.8% ILD was retained in lungs and 38% ILD was in liver and skeleton.

(463) The kinetics of lung retention over the first 100 d appears broadly similar for Es and Am nitrates while Pu nitrate is more strongly retained (Fig. 18.2a). The differences in clearance to blood appear clearly from the observation of systemic retention after inhalation of the nitrate: more than 20% ILD of Es or Am is retained in skeleton and liver after a month, while less than 10% ILD of Pu is translocated to those systemic tissues (**Erreur ! Source du renvoi introuvable.**b). Although the time-dependent distribution of the three elements is consistent with Type M behaviour, Pu is significantly less absorbed to blood than Am and Es. The transfer from lung to blood of Es appears somewhat higher than that of Am. Unfortunately, the lack of data after 100 - 200 d for Es and Am nitrates prevents comparison of the long term kinetics.



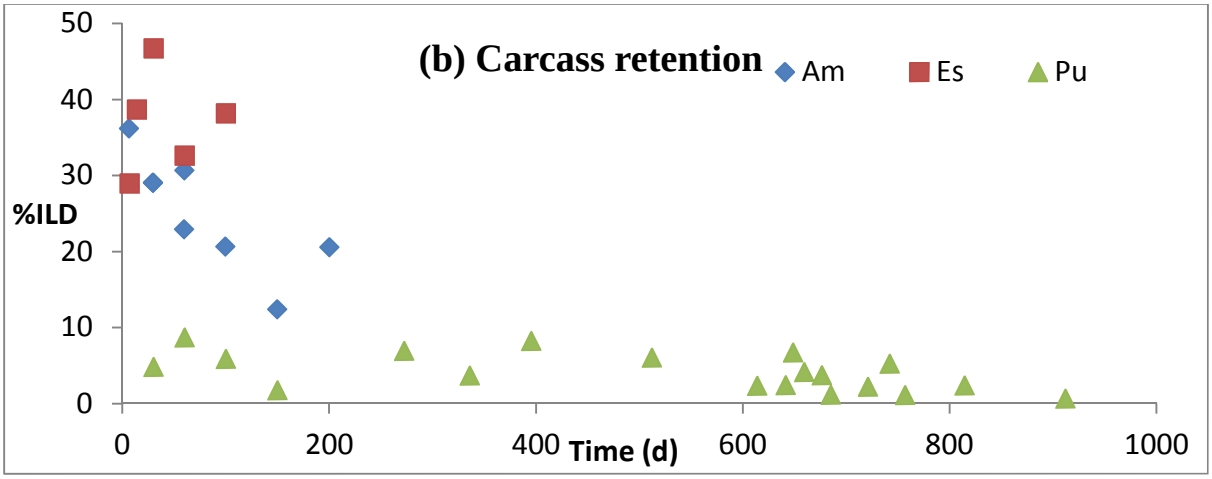


Fig. 18.2. Comparison of biokinetics of actinides inhaled by rats as nitrates. Data (decay-corrected) normalised to estimated initial lung deposit (ILD) (a) Lung retention (b) Carcass retention: (Δ) ^{239}Pu – Ballou et al (1977); (♦) ^{241}Am – Ballou and Gies (1978); (■) ^{253}Es – Ballou et al (1979).

(464) Ishigure et al. (2001) compared lung retention of plutonium ($^{238/239/240}$Pu) and ^{241}Am up to ~170 d following inhalation of plutonium nitrate containing ^{241}Am by rats. The activity ratio of ^{241}Am to plutonium in lungs, 0.024 ± 0.0004) : 1 at the exposure, slowly decreased to 0.021 (± 0.0005) : 1 at 4 weeks, and 0.020 (± 0.0004) : 1 at 24 weeks. Thus lung retention of ^{241}Am was broadly similar to that of plutonium, although clearance of ^{241}Am (presumably by absorption) was initially faster.

Nitrates: inhalation by dogs

(465) Buldakov et al. (1972) compared the tissue distributions of ^{241}Am and ^{239}Pu at times up to about 400 d after inhalation by dogs of "$^{241}Am(NO_3)_3$ and polymeric $^{239}Pu(NO_3)_4$, pH 1.5-2.0". Presumably the two radionuclides were inhaled by different dogs in order to study their effects. Lung retention of ^{239}Pu was much greater than that of ^{241}Am, e.g. ~80% and ~30% respectively of "initial deposit" at ~100 d after exposure. The authors noted that "The differences in the distribution of these alpha-emitters appear to be due to their physico-chemical properties". They consistently referred to the $^{239}Pu(NO_3)_4$ as "polymeric".

Conclusions

(466) The conclusions from most studies in which radionuclides were administered separately are that americium, curium and einsteinium behave similarly, but plutonium is absorbed from the lungs more slowly than the transplutonium elements. In most studies in which plutonium and americium were administered together, their behaviour was similar, but, as suggested by the authors of some such studies, this might be a "carrier" effect of the americium following the greater mass of plutonium administered.

Estimates of rapid dissolution rates of higher actinides

(467) Estimates of rapid dissolution rate were made for plutonium, americium, curium, californium and einsteinium. The information on which each was based and the estimated values are summarised here.

Plutonium

(468) In seventeen *in vivo* studies of the biokinetics of inhaled soluble plutonium compounds (citrate and nitrate), sufficient early retention data were available to allow estimates of s_r to be made here.

(469) Two human volunteers inhaled a mixed ^{237}Pu/^{244}Pu nitrate aerosol (Etherington et al., 2003). Measurements were made of ^{237}Pu lung and liver retention by external counting up to about 4 months; and of ^{237}Pu and/or ^{244}Pu in blood and excreta for several years. A combined analysis for the two volunteers (Puncher and Etherington, 2016) gave $s_r = 0.4$ d^{-1}.

(470) Brooks et al. (1992) followed the biokinetics of ^{239}Pu for 8 years after inhalation of ^{239}Pu nitrate by 20 cynomolgus monkeys. Tissue distributions of ^{239}Pu were measured at 4 d, 1, 3, 6, 12, 24, 40, and 99 months. Analysis of the results here gave $s_r > 0.1$ d^{-1}.

(471) Ballou et al. (1972) followed the biokinetics of ^{239}Pu for 100 d after inhalation of ^{239}Pu citrate by dogs. Tissue distributions were measured at 1, 3, 7, 14, 30, 62 and 100 d. Analysis of the results here gave $s_r = 0.5$ d^{-1}.

(472) Bair (1970) followed the biokinetics of ^{239}Pu for 300 d after inhalation of ^{239}Pu nitrate by 15 dogs. Analysis here gave $s_r = 0.2$ d^{-1}. Dagle et al. (1983) followed the biokinetics of ^{238}Pu or ^{239}Pu for 1 year after inhalation of plutonium nitrate by dogs: 12 inhaled each isotope. Tissue distributions were measured at 3 d, 1, 3 and 12 months. Analysis of the results here gave $s_r = 0.3$ d^{-1} for ^{238}Pu, and $s_r = 0.14$ d^{-1} for ^{239}Pu.

(473) Estimates of s_r made here from twelve inhalation studies in rats (Table 22.7) gave a wide range of values: from 0.2 to 12 d^{-1}. Some instillation studies, also included in Table 22.7, gave even higher values. Those with the earliest data show more than one phase of absorption over the first day or so, and that the rate decreases from ~100 d^{-1} to <1 d^{-1}. The values derived from analysis assuming a constant rate and so fitting a single value of s_r therefore depend on the time pattern of measurements and their weighting.

(474) The results of analyses performed here are summarised in Table 22.7. A default value of $s_r = 0.4$ d^{-1}, based principally on the human volunteer experiment, is adopted here for the default rapid dissolution rate of relatively soluble forms of plutonium.

Americium

(475) In 15 studies of inhaled soluble compounds sufficient early retention data were available to allow estimates of s_r.

(476) Breitenstein and Palmer (1989) and McInroy et al. (1995) reported the 11-year follow-up and autopsy measurements on a worker who received a combination of wound and inhalation exposures to ^{241}Am in nitric acid. Interpretation of these data is further complicated by DTPA decorporation therapy. Analysis of the results here gave $s_r = 0.2$ d^{-1}.

(477) Buldakov et al. (1972) followed the biokinetics of ^{241}Am in dogs for two years after inhalation of the nitrate. Buldakov and Kalmykova (1979) studied the biokinetics of ^{241}Am in dogs up to seven years after inhalation of the nitrate. Analysis here gave $s_r = 2.9$ and 0.2 d^{-1}, respectively.

(478) The other 12 studies were carried out in rats, involving inhalation of the chloride, citrate or nitrate.

(479) The results of analysis performed here are summarised in Table 23.4: Values of s_r were obtained ranging from 0.2 to 7.5 d^{-1} with a median of 1.3 d^{-1}.

Curium

(480) In 14 relevant studies sufficient early retention data were available to allow estimates of s_r.

(481) Bernard and Poston (1976) followed four workers who accidently inhaled ^{244}Cm, by urine, feces and chest measurements for one or two weeks after intake. From the chest retention in one worker a value of s_r = 0.3 d^{-1} was estimated here. Parkinson et al. (1976) reported measurement on two workers up to one year after accidental inhalation of ^{244}Cm. Analysis here of the early data from one case suggested s_r = 0.15 d^{-1}.

(482) McClellan et al. (1972) followed the biokinetics of ^{244}Cm in dogs for 256 d after inhalation of $^{244}CmO_{1.73}$ or $^{244}CmCl_3$ in a CsCl vector. Most of the curium was rapidly absorbed. Analysis here of both the oxide and chloride data gave s_r = 0.4 d^{-1}.

(483) Guilmette and Kanapilly (1988) studied the tissue distribution of ^{244}Cm in dogs for 2 years after inhalation of $^{244}Cm_2O_3$ and $^{244}Cm(NO_3)_3$ and observed broadly similar kinetics. Analysis here of the oxide and nitrate data gave s_r = 0.1 and 0.5 d^{-1}, respectively.

(484) Seven studies were carried out in rats, involving inhalation of the citrate, nitrate or oxide: estimated values of s_r ranged from 0.15 to 10 d^{-1}.

(485) The results of analyses here are summarised in Table 24.6: values of s_r range from 0.1 to 10 d^{-1} with a median of 0.4 d^{-1}.

Californium

(486) In one study sufficient early retention data were available to allow an estimate of s_r. Graham et al. (1978) followed the tissue distribution of ^{252}Cf in rats for 32 d after intratracheal instillation of the chloride. Analysis here gave s_r = 1 d^{-1}.

Einsteinium

(487) In one study sufficient early retention data were available to allow an estimate of s_r. Ballou et al (1975) measured the tissue distribution of ^{253}Es in rats for 42 d after intratracheal instillation of the chloride. Analysis here gave s_r = 3 d^{-1}.

Conclusions

(488) For plutonium, the s_r value of 0.4 d^{-1} is based mainly on one high quality human volunteer experiment, and analysis gives a small uncertainty on the value. It is supported by the results on inhalation studies in primates and dogs, which give estimates of >0.1 d^{-1}, and 0.2, 0.3 and 0.5 d^{-1}, respectively. Results from twelve inhalation studies in rats (Table 22.7) gave a wide range of values: from 0.2 to 12 d^{-1}.

(489) For the transplutonium elements, there is broad consistency in values around 1 d^{-1}, although considerable variation in the estimates based on rat studies. For both americium and curium the relevant data are reasonably consistent and comprehensive: there is at least one study in dogs and at least one accidental human intake, as well as several rat studies. There is as much information for each as for most other elements except plutonium and uranium. For

5382 americium and curium, median s_r values are 1.0 d^{-1} and 0.4 d^{-1}, respectively. For californium
5383 and einsteinium there is only one rat study for each, but the results 1 d^{-1} and 3 d^{-1}, respectively,
5384 are consistent with those for americium and curium.
5385 (490) Calculations were carried out here to provide information to guide the choice
5386 between a value of s_r of 0.4 d^{-1}, based mainly on the plutonium human volunteer study, and a
5387 'rounded' value of 1.0 d^{-1} reflecting the results for the transplutonium elements. They showed
5388 that for inhalation of ^{239}Pu nitrate, values of 0.4 d^{-1} and 1.0 d^{-1} gave very similar dose
5389 coefficients. However, a value of 0.4 d^{-1} gives a dose per Bq measured in urine on the first day
5390 after intake about twice that given by a value of 1 d^{-1}. Although this is offset by lower doses per
5391 Bq in urine at later times (Fig 22.1), because of the importance of the first day's urine sample in
5392 individual monitoring, the more precise value of 0.4 d^{-1} and is adopted here and applied to
5393 plutonium and the transplutonium elements.
5394
5395 ***Estimates of bound state parameter values for higher actinides***

5396 (491) Estimates of bound state parameter values: bound fraction (f_b) and associated uptake
5397 rate to blood (s_b) were made for plutonium, americium and curium. The information on which
5398 each was based, and the estimated values, are summarised here.
5399
5400 ***Plutonium***

5401 (492) Early applications of the HRTM to plutonium nitrate made use of a short-term bound
5402 state (e.g. ICRP, 2002) which enabled good fits to be made to the early experimental data (see
5403 comments above on observations in rat studies of plutonium dissolution rates decreasing with
5404 time). However, including this short-term bound state had little effect on lung doses. More
5405 recent studies indicate the presence of a small, but very long-term, bound state, which could
5406 potentially increase equivalent doses to the lungs significantly, particularly if it occurs in the
5407 bronchial (BB) and bronchiolar (bb) regions. Three studies investigated a long-term bound state
5408 for inhaled plutonium.
5409 (493) Pellow et al. (2016b) and Puncher et al. (2016a) analysed lung retention data from a
5410 15-year study in which dogs inhaled ^{239}Pu nitrate (Dagle et al., 1993). The central estimate of
5411 the bound fraction f_b was 0.0023 (95% confidence interval (CI) = 6 x 10^{-4} to 0.007). The
5412 associated uptake rate to blood (s_b) was $<10^{-5}$ d^{-1} and was assigned a value of 0 d^{-1}. This study
5413 is considered to provide strong evidence for the existence of a long-term retained component in
5414 the respiratory tract, for which the bound state provides the simplest explanation.
5415 (494) Puncher et al. (2016b) analysed the autopsy and bioassay data of United States
5416 Transuranium and Uranium Registries (USTUR) donor 269, who received a high acute intake
5417 of plutonium nitrate by inhalation. They used the results of recent measurements (Tolmachev et
5418 al., 2016) on plutonium in the extra-thoracic (ET_2), BB, bb and alveolar-interstitial regions and
5419 in the thoracic lymph nodes. The results indicate that a small bound fraction is required, mainly
5420 to account for plutonium present in the ET_2, BB and bb regions at autopsy. However, it is not
5421 known whether the plutonium present in these tissues was associated with the epithelium, as
5422 assumed in the dosimetric model for the bound fraction, or in underlying tissues, such as
5423 lymphatic channels. The conservative assumption is made here that the plutonium is retained in
5424 the epithelium. The value of f_b was determined as 0.0037 (95% CI = 0.0037 to 0.0039). There
5425 was no evidence for an s_b value other than 0 d^{-1}.
5426 (495) Puncher et al. (2016c) analysed autopsy data from 20 former workers of the Mayak
5427 Production Association (MPA) exposed only to plutonium nitrates. Given the evidence for a

long-term bound state provided by the two studies above, these analyses assumed that a bound state is present. The value of f_b was determined as 0.0014 (95% CI = 1.1 x 10^{-4} to 0.003). There was no evidence for an s_b value other than 0 d^{-1}.

(496) The information provided by the three studies therefore indicates a value for f_b for plutonium of about 0.002, with s_b = 0 d^{-1}. The autopsy measurements of plutonium for USTUR donor 269 indicate that the bound fraction should apply in all respiratory tract regions except ET_1. This small long-term bound state results in an additional contribution to the committed equivalent dose coefficient for the lungs from inhaled ^{239}Pu nitrate of about 20%.

Americium

(497) Mewhinney et al. (1978, 1982) and Mewhinney and Griffith (1983) studied the tissue distribution of ^{241}Am in dogs for six years after inhalation of monodisperse (3.0 µm, 1.5 µm and 0.75 µm AMAD) and polydisperse (1.8 µm AMAD) $^{241}AmO_2$ aerosols. They noted the long-term pulmonary retention of ~1% of the initial lung deposit (ILD). The effective retention half-time (~5000 d) for this fraction was longer than expected for clearance of insoluble particles. Autoradiography showed that as time progressed, fewer particles, but more single tracks, were found in the lungs as the AmO_2 dissolved. Particles could no longer be found when the activity retained in lung stabilised. Only single tracks, which were primarily associated with parenchymal interstitium, then remained. The value of f_b was estimated here to be 0.015 with s_b ~10^{-4} d^{-1}.

(498) Taya et al. (1994) observed that americium retained for a long time in the dog lung after inhalation of americium nitrate was associated with connective tissues.

(499) Thomas et al. (1972) followed the biokinetics of ^{241}Am in dogs for two years after inhalation of an aerosol formed by passing droplets of ^{241}Am in hydrochloric and oxalic acids through a heating column at 600°C. They observed long-term retention of about 1.5% ILD.

(500) Jeanmaire and Ballada (1970) measured ^{241}Am in lungs and excreta of two persons for more than 200 d following accidental inhalation of a soluble salt of americium. Analysis of results here gave f_b = 0.02 and 0.03 for the two cases.

(501) Lyubchanskiy and Nifatov (1972) measured the tissue distribution of ^{241}Am in rats at times up to 650 d after inhalation of ^{241}Am citrate or nitrate. Analysis of results here gave f_b = 0.006, somewhat lower than for the dog and human studies above.

(502) Thus there is good evidence, from both biokinetics and autoradiography, for a bound fraction for americium, with parameter values assessed to be f_b = 0.01 and s_b = 10^{-4} d^{-1}. Information was not found that might give evidence for a fraction similar to that for plutonium, with much slower uptake. There is no evidence of long-term retention of americium deposited in relatively soluble form in the ET, BB or bb regions. This small long-term bound state results in an additional contribution to the committed equivalent dose coefficient for the lungs from inhaled ^{241}Am nitrate of about 25%.

Curium

(503) Studies of curium deposited in the respiratory tract in most chemical forms showed rapid or moderately rapid absorption of most of the ILD. However, the studies of longer duration (>250 d) all show lung retention of small amounts: 0.3 – 4% ILD.

(504) McClellan et al. (1972) followed the biokinetics of ^{244}Cm in dogs for 256 d after inhalation of $^{244}CmO_{1.73}$ or $^{244}CmCl_3$ in a CsCl vector. Most of the curium was rapidly

absorbed, but ~3% ILD was retained in lungs at 256 d. Analysis here of both the oxide and chloride data gave $f_b = 0.025$.

(505) Similarly, Guilmette and Kanapilly (1988) followed the tissue distribution of ^{244}Cm in dogs for 2 years after inhalation of $^{244}Cm_2O_3$ and $^{244}Cm(NO_3)_3$ and observed broadly similar kinetics, with ~2% ILD present after 2 years.

(506) Sanders and Mahaffey (1978) followed the tissue distribution of ^{244}Cm in 5 groups of rats for 900 d after inhalation of ^{244}Cm oxide. While most of the ^{244}Cm cleared from the lung rapidly, ~2% was retained with a half-life of about 1 year. Analysis here of the data for four groups gave values of f_b between 0.01 and 0.06.

(507) Lundgren et al. (1997) followed the tissue distribution of ^{244}Cm in rats for 1200 d after inhalation of ^{244}Cm oxide. They observed that ~0.3% ILD was retained with a half-time >1000 d (rate $<2 \times 10^{-4}$ d^{-1}), and considered that it was probably dissolved curium bound to connective tissue in the lungs. Analysis here of the data gave $f_b = 0.1$.

(508) Lafuma et al. (1974) concluded from autoradiographic studies that Cm nitrate was widely dispersed in the rat lung at 20 d post-exposure, generating mostly single α tracks and very few particle-like clusters. Sanders and Mahaffey (1978) came to the same conclusion from autoradiographs of rat lung taken immediately after inhalation exposure, and up to 2 years later.

(509) Based on these considerations, the bound fraction for curium is assessed to be f_b = 0.02. There is no information to determine a non-zero clearance rate of the bound fraction. There is no evidence of long-term retention of curium deposited in relatively soluble form in the ET, BB or bb regions. This small long-term bound state nearly doubles the committed equivalent dose coefficient for the lungs from inhaled ^{244}Cm nitrate.

Conclusions

(510) For plutonium, three very different studies of long-term lung retention following inhalation of plutonium nitrate gave similar estimates of bound state parameter values: a life-time dose-response study in dogs; an autopsy study on a large group of workers with multiple exposures and few bioassay data; and a more detailed autopsy study on a single worker with extensive bioassay data. The information provided by the three studies indicates a value for f_b of ~0.002. The associated uptake rate to blood (s_b) was estimated to be $<10^{-5}$ d^{-1} and consistent with a value of 0 d^{-1}. Autopsy measurements on a single USTUR donor indicate that the bound fraction should apply in all respiratory tract regions except ET_1.

(511) For americium there is strong evidence for a bound fraction, from both biokinetics and autoradiography. Parameter values were assessed here to be $f_b = 0.01$ and $s_b = 10^{-4}$ d^{-1}, with reasonably consistent estimates from studies on man, dogs, and rats, and following inhalation of different chemical forms. There is no evidence of long-term retention of americium deposited in relatively soluble form in the ET, BB or bb regions. The information is probably as good as that on which bound state parameter values were estimated for any other element. The values of both f_b and s_b are higher than those estimated for plutonium.

(512) For curium there is also good evidence for a bound fraction, from both biokinetics and autoradiography: not as comprehensive as for americium, but from a similar range of studies. The bound fraction was assessed here to be $f_b = 0.02$, similar to that for americium. The uptake rate s_b was not well defined: one study giving a value of $\sim 10^{-3}$ d^{-1}, and another $<10^{-4}$ d^{-1}. There is no evidence of long-term retention of curium deposited in relatively soluble form in the ET, BB or bb regions.

(513) There is experimental evidence on americium and curium for a higher bound fraction, f_b, and higher rate of uptake from bound state to blood, s_b, than for plutonium (but no evidence to exclude another bound fraction with parameter values similar to those of plutonium). There is evidence for plutonium that the bound fraction should apply in the BB and bb regions, but no evidence for americium and curium to confirm or exclude application of the bound fraction in these regions. It has been calculated here that for ^{239}Pu nitrate application of the plutonium bound state parameter values increases the equivalent dose to the lungs by ~20%, for ^{241}Am nitrate application of the americium bound state parameter values also increases the equivalent dose to the lungs by ~20%, and for ^{244}Cm nitrate application of the curium bound state parameter values nearly doubles the equivalent dose to the lungs.

(514) As for the rapid dissolution rate, the plutonium bound state parameter values are applied here to the transplutonium elements, because they are based more on human data than those derived for americium and curium. Thus it assumed here that for plutonium and the transplutonium elements a bound fraction $f_b = 0.002$ and a rate of uptake $s_b = 0$ d^{-1}, are applied throughout the respiratory tract except in the ET_1 region.

18.2.2. Ingestion

(515) Data on human gastrointestinal absorption of uranium, neptunium, plutonium, americium and curium are now available from volunteer experiments. These data are complemented by extensive information from studies in laboratory animals.

(516) Data for various studies on absorption of plutonium and heavier elements in nine different animal studies have been reviewed in ICRP Publication 48 (ICRP, 1986). Additional data were then reported and analysed by Harrison (Harrison, 1991) and in ICRP *Publications 68* (ICRP, 1994) and *100* (ICRP, 2006).

(517) All these studies have shown that the absorption of actinides can be markedly influenced by fasting, diet, mass, chemical formof the ingested element and by drugs and diseases (NEA, 1988). These studies have also shown that quite large variations from individual to individual may occur for some elements.

(518) The difficulties of assessing very low levels of absorption from the gastrointestinal tract and the need for very careful control of the experimental conditions used has been emphasised by several authors (Larsen et al., 1981; Harrison et al., 1982). Wide variations in the absorption of plutonium after ingestion of the same compound have been reported, indicating that the actual chemical and/or physiological conditions in the alimentary tract at the time of absorption probably varied considerably. These large variations may be due to differences in the true chemical composition of the solutions administered. For example, the actinide concentration, the pH and the presence of inorganic or organic complexing anions would have influenced the proportions of soluble and colloidal or particulate species, especially in solutions of plutonium in dilute nitric acid. The presence of food residue in the alimentary tract may also influence absorption and it is not always stated whether the values reported were measured in fed or fasting animals.

(519) Table 18.5. reports the range of measured values for the fractional absorption of the actinides. It shows that, depending on the chemical form, the species and the experimental conditions, and apart for uranium, the absorption ranges from about 10^{-8} for insoluble forms of plutonium to about 10^{-2} for soluble, inorganic forms of neptunium and protactinium. The human data included in this table show a close similarity in the absorption of thorium, neptunium, plutonium, americium and curium, despite the differences in the chemical form

ingested, with mean f_A values of 1 x 10^{-4} to 2 x 10^{-4} (Harrison, 1991). These elements also show a remarkable similarity in their reactions with constituents of body fluids and cells, despite differences in solution chemistry (See Section 18.1).

(520) The gastrointestinal absorption of uranium is substantially greater than that of the other actinides, with f_A values ranging from 5 x 10^{-3} to 6 x 10^{-2} (Table 18.5). This is consistent with its different solution chemistry, the oxycation UO_2^{2+} being more resistant to hydrolysis at neutral pH than the predominant oxidation states of the other actinides.

(521) On the basis of results showing similar low levels of absorption in man for five actinide elements and taking account of animal data showing variations in f_A values resulting from differences in chemical forms, it is considered here that an appropriate general f_A value for all chemical forms of actinides except uranium is 5 x 10^{-4}. This value is adopted in this report.

Table 18.5. Range of fractional absorption f_A reported for the actinides[a].

Actinides	f_A [b]	ICRP recommendations
Actinium	$1x10^{-3}$	$5x10^{-4}$
Thorium[c]	$2x10^{-4}$ to $6x10^{-4}$	
Protactinium	$3x10^{-4}$ to $4x10^{-2}$	
Uranium[c]	$5x10^{-3}$ to $6x10^{-2}$	0.02 (F) to 0.002 (M and S)
Neptunium	$1x10^{-4}$ to $1x10^{-2}$	$5x10^{-4}$
Plutonium	$3x10^{-8}$ to $1x10^{-3}$	
Americium	$3x10^{-6}$ to $1x10^{-3}$	
Curium	$1x10^{-4}$ to $1.2x10^{-3}$	
Berkelium to Fermium	$1x10^{-4}$ to $1.2x10^{-3}$	

[a]Data reported for *in vivo* experiments performed on adult animals or humans, given the radionuclide in an inorganic form.
[b]For details, see the individual element sections in the current report.
[c] This element is described in OIR Part 3.

18.2.3. Systemic distribution, retention and excretion of actinide elements

General features of systemic behavior

(522) The systemic behaviors of all elements in the actinide sequence Ac-Es (atomic numbers 89-99) have been studied in mammalian species, and biokinetic data for several actinides have been derived from controlled human studies or follow-up of occupational intakes. With the exception of uranium (addressed in Part 3 of this report series), the systemic behaviors of the studied actinides follow the same general pattern as described earlier for the lanthanide family. The main sites of deposition of absorbed or injected activity are bone surfaces and liver, and the bone surface deposit is tenaciously retained until removed by bone restructuring processes. Activity removed from bone surfaces may be buried in bone volume or may transfer to blood after deposition and retention in bone marrow or, to some extent, may transfer directly to blood without uptake and retention in bone marrow. The behavior of actinide elements deposited in the liver is species dependent. For example, the residence time of Pu in

liver is at most a few months in rats, monkeys, and baboons but is measured in years or decades in hamsters, dogs, pigs, and humans (Taylor, 1984). The residence time in the human liver varies across the actinide family. For example, it is considerable longer for Pu than for Am.

(523) Burial of the skeletal deposition of actinides in bone volume may result by different mechanisms associated with the bone remodeling process. Activity depositing at bone remodelling units, either in the formation period or in the transitional period between resorption and formation, may be buried relatively quickly. Much slower burial of surface activity may result from a process referred to as local recycling, in which a portion of the surface activity removed by osteoclasts during bone remodelling is redeposited at closely adjacent sites of new bone formation without reentering the general circulation. Burial of surface deposits may also occur as a result of bone drift, a phenomenon in which new bone is deposited on previously formed bone without any prior resorption process. Bone drift occurs on a larger scale in immature bone than in mature bone, but drift within bones and expansion of bone volume via periostial-endosteal drift continues throughout life in humans (Epker and Frost, 1965a,b; Frost 1986; Priest et al., 1992). Drifting osteons are observed at all ages within human cortical bone.

(524) Activity buried in bone volume is gradually transferred back to blood, either directly or after deposition and retention in bone marrow. Activity is lost from bone marrow to blood over a period of months and presumably is subsequently redistributed in the same pattern as the original input to blood. The rates of transfer from cortical and trabecular bone compartments to all destinations are expected to reflect the turnover rate of cortical and trabecular bone.

(525) The initial distribution of activity on bone surfaces varies across the actinide family. Results of early autoradiographic studies on rodents (Hamilton, 1948) indicated that the sites of deposition on bone surfaces are similar for Am, Cm, and Ac but that the surface distribution of these elements differed from that of Pu. Later studies involving refined techniques and various animal species yielded relatively detailed descriptions of the distribution of some actinide elements, particularly Pu and Am, on bone surfaces (Herring, 1962; Lloyd et al., 1972; Durbin, 1973; Priest et al., 1983). Pu deposits mainly on endosteal surfaces, especially the surfaces of the trabeculae of spongy bone near the sinusoidal circulation of active marrow (Durbin, 2011). Deposition of Am on bone surfaces is much more uniform than that of Pu, although there are also gradations in the intensity of the Am label. Americium deposits to a much greater extent than Pu on cortical vascular channels. Pu and Am depositions are similar in that the initial concentrations are greater on resorbing and resting surfaces than on actively growing surfaces. There is no initial diffuse distribution of either Pu or Am in bone volume (Durbin, 2011).

(526) As is the case for the lanthanides, the initial division of injected or absorbed activity between bone and liver varies across the actinide family. For the lanthanide elements, all of which are expected to be present in body fluids as trivalent ions, results of animal studies indicate a strong relation between the ionic radius and the ratio bone deposit : liver deposit. The systemic behaviour of the actinides is much less regular than that of the lanthanides and not easily described in terms of physical or chemical properties. This is due in part to the different primary oxidation states of different actinides, ranging from trivalent to pentavalent. However, a relation between ionic radius and bone deposit : liver deposit similar to that for the lanthanides is suggested by data for the heaviest actinides, Am through Es, which are expected to be present in body fluids as trivalent ions.

Model structures for the actinides

(527) The structure of the systemic models for actinides other than Pu is shown in Fig. 18.3. All indicated paths of transfer are assigned non-zero transfers for each element, except that: the transfer from Liver 1 to Blood is non-zero only for Th (addressed in an earlier part of this report series) and Pa; and the transfer from Cortical marrow to Cortical surface is non-zero only for Am and Cm.

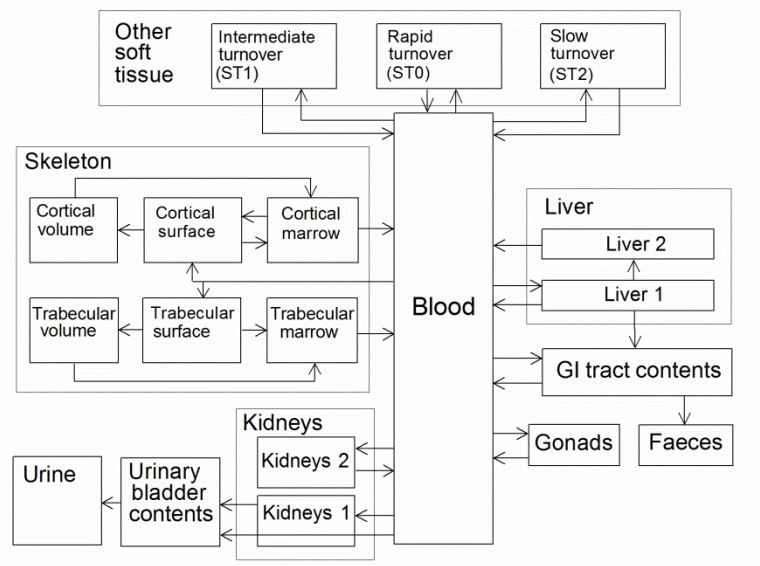


Fig. 18.3. Model structure for the actinide elements addressed in this report other than Pu.

(528) The structure of the systemic model for Pu is shown in Fig. 18.4.

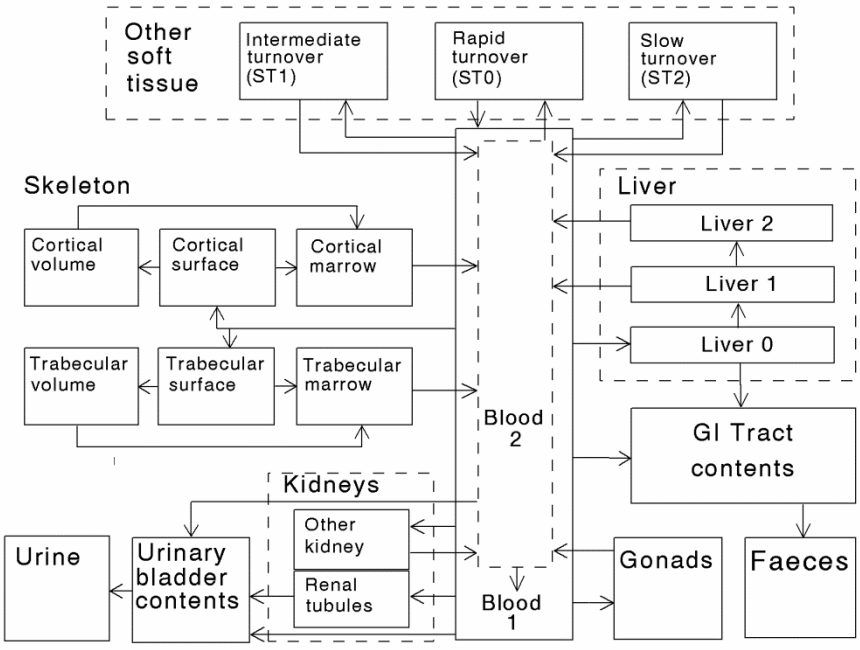


Fig. 18.4. Structure of the model for systemic Pu used in this report.

Primary considerations for modelling the behaviour of individual actinides

(529) Biokinetic data for each actinide element addressed in this report are reviewed in the sections 19.2.3 (Actinium) to 28.2.3 (Fermium). The following paragraphs summarise the main considerations in selection or construction of a systemic model for each element in view of the quantity and quality of available data.

Actinium

(530) The biokinetics of Ac has been studied in rats and accidentally exposed workers. The data are too sparse to allow development of transfer coefficients for most pathways in the generic model structure but suggest that the systemic behaviour of Ac is similar to that of Am. The systemic model applied in this report to Ac is a slightly modified version of the model applied here to Am. The only difference in the models for Ac and Am is that a non-zero transfer from cortical marrow to cortical bone surface in the Am model is not applied to Ac. Rather, Ac depositing in cortical marrow is assumed to transfer to blood with a half-time of 0.25 y, consistent with the generic model for bone-surface-seeking radionuclides.

Thorium

(531) Thorium is addressed in an earlier part of this report series. It is discussed briefly in this section for completeness in that its systemic behaviour fits the same pattern as the elements addressed here, and the systemic model developed for Th is applied to its infrequently studied periodic neighbour, protactinium.

(532) The systemic model for Th used in ICRP *Publication 69* (1995) is also applied in this report series (Part 3). The model was based largely on experimental, occupational, and environmental data on the behaviour of Th in the human body. Data for laboratory animals, primarily beagle dogs, were used to fill gaps in the information for humans. Parameter values describing the initial distribution and early excretion of Th were set for consistency with data on early retention, excretion, and blood clearance of Th derived in a controlled study involving healthy human subjects. The early systemic distribution of Th was based mainly on data for beagles, in the absence of such information for humans. Parameter values controlling predictions of the long-term distribution and retention of Th were developed mainly on the basis of autopsy measurements of the distribution of Th in human subjects, together with consideration of bone restructuring rates in humans.

Protactinium

(533) The systemic behaviour of Pa has been studied mainly in rats and baboons, and limited information is available from follow-up of an occupational exposure. The Pa-specific information is too sparse to allow development of most transfer coefficients within the generic model structure for actinides but suggest that the systemic behaviour of Pa is similar to that of Th. In this report the systemic model for Th described in an earlier part of this report series is applied to Pa.

Neptunium

(534) The systemic model for Np used in ICRP *Publication 67* (1993) is applied in the present report. The model is based on data on the distribution and excretion of Np in non-human primates, swine, and rodents; urinary excretion rates for intravenously administered Np

in healthy human subjects; and analogy with other actinides. Long-term retention of Np in the liver is based on animal data together with comparative autopsy data on ^{237}Np and ^{239}Pu in environmentally exposed humans.

Plutonium

(535) The ICRP's model for systemic Pu was last updated in ICRP *Publication 67* (1993). That model was based on several different data sources including: bioassay data and autopsy measurements for occupational exposed subjects; extensive measurements on 18 unhealthy subjects who were injected with tracer amounts of ^{239}Pu in biokinetic studies conducted in the mid-1940s; a more limited set of data from a controlled Pu injection study started a few years before the completion of *Publication 67*; and results of many studies of Pu kinetics in a variety of laboratory animals.

(536) The Pu model of *Publication 67* was updated several years later (Leggett et al., 2005) to reflect a substantially expanded database, particularly data from two Pu injection studies involving healthy human subjects and considerably expanded sets of bioassay and autopsy data for Pu workers. The most important change from the model of Publication 67 concerns the initial distribution of absorbed or injected Pu: Publication 67 assigns deposition fractions of 0.5 and 0.3 to bone and liver, respectively, while the updated model assigns fractions 0.3 and 0.6, respectively, based on the later human injection studies together with central tendencies indicated by autopsy data for Pu workers whose body burdens represented a wide range of times since exposure.

(537) A systemic model for Pu proposed by Leggett et al. (2005) is used in this report. The following paragraphs summarise the Pu model used here and indicate similarities and differences from the model of *Publication 67*.

Circulation:

(538) As in *Publication 67*, circulating Pu is defined as Pu in blood plus rapid-turnover soft tissues (ST0 in Fig. 2). Blood consists of two compartments, Blood 1 and Blood 2. Blood 2 receives recycled Pu and feeds ST0, Blood 1, and the urinary bladder contents. This provides a physically meaningful way of implementing the assumption, based on results of human injection studies, that fractional clearance from blood to urine increases for some time after the initial entry of Pu into blood. Specifically, it is assumed that:

- The initial input to blood distributes rapidly (half-time of 1 min) between a blood compartment called Blood 1 (70%) and a soft tissue compartment called ST0 (30%)Pu leaves Blood 1 with a half-time of 0.9 d.Soft tissue compartment ST0 empties into Blood 1 with a half-time of 7 dAll other feeds from tissues back to blood are to Blood 2.Pu is removed from Blood 2 at the rate 100 d^{-1} ($T_{1/2}$ ~ 10 min), with 3.5% going to the urinary bladder contents, 0.3 x (100-3.5)% = 28.95% going to ST0, and 0.7 x (100-3.5)% = 67.55% going to Blood 1In effect, the portion of activity leaving Blood 2 that does not go directly to the urinary bladder contents is assumed to distribute in the same way as the original input to blood.

Liver and fecal excretion:

(539) Rapid, intermediate, and slow phases of removal from the liver are depicted. Plutonium moves from Blood 1 to the rapid-turnover compartment Liver 0. Some Pu entering Liver 0 is lost in bile, but most moves to a compartment within the hepatocytes with

intermediate-term retention (Liver 1). Most of the activity lost from Liver 1 goes to Blood 2, but a portion enters reticuloendothelial cells (Liver 2), from which it is slowly lost to Blood 2. It is assumed that:

- 60% of activity leaving the circulation goes to Liver 0.
- The removal half-time from Liver 0 is 15 d; 2% goes to the contents of the small intestine and 98% to Liver 1.
- The removal half-time from Liver 1 is 1 year; 80% goes to Blood 2 and 20% to Liver 2.
- The removal half-time from Liver 2 to Blood 2 is 15 years.
- 1.5% of Pu leaving the circulation goes to the contents of the upper large intestine.

Bone:

It is assumed that:

- 30% of Pu leaving circulation deposits in bone; 18% goes to trabecular bone and 12% to cortical bone.
- 90% of the trabecular deposit and 95% of the cortical deposit is on bone surface, with the remainder entering bone volume by depositing in bone-forming sites.
- Transfer from cortical bone surface or volume to cortical marrow is 3% per year. Transfer from trabecular bone surface or volume to red marrow is 18% per year.
- The burial rate of surface Pu is 0.75% per year for cortical bone surface and 4.5% for trabecular bone surface (one-fourth the rate of bone remodeling).
- The removal half-time from bone marrow to Blood 2 is 0.25 y.

Kidneys and urinary excretion:

(540) The model of *Publication 67* includes a transfer from the intermediate-term soft-tissue compartment, ST1, to the urinary path. This transfer was used to model an increase with time in daily urinary clearance of circulating Pu, as observed in human injection studies. In the present model a blood compartment called Blood 2 is used to model a change with time in urinary clearance of circulating Pu. Plutonium that returns to blood from all systemic compartments except the rapid-turnover soft-tissue compartment ST0 is assumed to be cleared to the urinary bladder content at a higher rate than was the initial input of Pu to blood. It is assumed that:

- 2% of Pu leaving Blood 1 goes directly to the urinary bladder contents.
- 1% of Pu leaving Blood 1 goes to kidneys (Renal tubules in Fig. 18.4) and is removed to the bladder contents with $T_{1/2}$ = 40 d.
- 0.05% of Pu leaving Blood 1 goes to a long-term kidney compartment (Other kidney) from which it is removed to Blood 2 with a half-time of 15 y.

(541) As described earlier, 3.5% of Pu leaving Blood 2 (recycled Pu) goes directly to urinary bladder contents. Blood 2 also feeds the urinary bladder contents indirectly, since most of the activity leaving Blood 2 goes to Blood 1.

Gonads:

(542) Deposition fractions for the testes and ovaries are the same as used in the Pu model of *Publication 67*, but the removal half-time from gonads is reduced from 10 y to 5 y based on

comparisons of model predictions with updated information for workers and laboratory animals:

- 0.035% of Pu leaving the circulation deposits in the testes.
- 0.011% of Pu leaving the circulation deposits in the ovaries.
- The removal half-time from gonads to Blood 2 is 5 years.

Other soft tissues:

(543) Parameter values for ST0 were given earlier. For ST1 and ST2 it is assumed that:

- 3% of Pu leaving the circulation goes to ST2.
- The removal half-time from ST2 to Blood 2 is 15 y.
- The balance of Pu leaving the circulation (2.404%, after assignment of all other deposition fractions) goes to ST1.
- The removal half-time from ST1 to Blood 2 is 500 d.

Transfer coefficients for Pu derived from the assumed deposition fractions and removal half-times are listed in Table 18.6.

Table 18.6. Transfer coefficients in the model for systemic Pu.[a]

Source	*Destination*	*Transfer coefficient (d^{-1})*
Blood	ST0	3.0000×10^{2}
Blood	Blood 1	7.0000×10^{2}
Blood 1	Liver 0	4.6200×10^{-1}
Blood 1	Cortical surface	8.7780×10^{-2}
Blood 1	Cortical volume	4.6200×10^{-3}
Blood 1	Trabecular surface	1.2474×10^{-1}
Blood 1	Trabecular volume	1.3860×10^{-2}
Blood 1	Urinary bladder contents	1.5400×10^{-2}
Blood 1	Renal tubules	7.7000×10^{-3}
Blood 1	Other kidney	3.8500×10^{-4}
Blood 1	Right colon contents	1.1550×10^{-2}
Blood 1	Testes	2.6950×10^{-4}
Blood 1	Ovaries	0.8470×10^{-4}
Blood 1	ST1	1.8511×10^{-2}
Blood 1	ST2	2.3100×10^{-2}
ST0	Blood 1	9.9000×10^{-2}
Blood 2	Urinary bladder contents	3.5000×10^{0}
Blood 2	Blood 1	6.7550×10^{1}
Blood 2	ST0	2.8950×10^{1}
Renal tubules	Urinary bladder contents	1.7329×10^{-2}
Other kidney	Blood 2	1.2660×10^{-4}
ST1	Blood 2	1.3860×10^{-3}
ST2	Blood 2	1.2660×10^{-4}
Liver 0	Small intestine contents	9.2420×10^{-4}
Liver 0	Liver 1	4.5286×10^{-2}
Liver 1	Blood 2	1.5200×10^{-3}
Liver 1	Liver 2	3.8000×10^{-4}

Liver 2	Blood 2	1.2660×10^{-4}
Testes	Blood 2	3.8000×10^{-4}
Ovaries	Blood 2	3.8000×10^{-4}
Cortical surface	Cortical marrow	8.2100×10^{-5}
Cortical surface	Cortical volume	2.0500×10^{-5}
Cortical volume	Cortical surface	8.2100×10^{-5}
Trabecular surface	Trabecular marrow	4.9300×10^{-4}
Trabecular surface	Trabecular volume	1.2300×10^{-4}
Trabecular volume	Trabecular marrow	4.9300×10^{-4}
Cortical marrow	Blood 2	7.6000×10^{-3}
Trabecular marrow	Blood 2	7.6000×10^{-3}

[a]The initial input to blood via absorption or injection is assumed to enter the compartment named Blood and then distribute rapidly (half-time of 1 min) between Blood 1 (70%) and ST0 (30%).

Americium

(544) The biokinetic model for systemic Am is a modification of the model for Am in adults adopted in *Publication 67* (ICRP, 1993). That model was based on follow-up of workers acutely or chronically exposed to Am and experimental data for a variety of animal types including baboons, monkeys, dogs, sheep, cows, goats, and rodents.

(545) The following changes are made to the Am model used in *Publication 67*:

- For consistency with models for other actinide elements, liver is divided into compartments with relatively fast and relatively slow turnover. The biological half-time assigned to the fast-turnover compartment is the generic value of 30 d (Liver 1). A removal half-time of 1 y, the half-time applied in Publication 67 to the single-compartment liver, is applied to the compartment with slow turnover (Liver 2).
- The removal half-time from gonads is reduced from 10 y to 5 y, a generic value applied in this report to the actinides and lanthanides.
- The generic bone model is modified for application to Am (and its close physiological analogue Cm) in view of data indicating that the model of Publication 67 overestimates the rate of excretion of systemic ^{241}Am when expressed as a fraction of the total bone content. A simple resolution of this discrepancy between model predictions and observations that has some experimental basis is to depict explicitly local recycling of a sizable portion of Am resorbed from cortical bone. This requires a modification of the generic bone model for bone-surface seekers. In the generic model, activity removed from bone is assumed to transfer to bone marrow and subsequently from bone marrow to blood. For application to Am and Cm, the generic bone model is modified by assuming that a fraction F of the amount entering cortical marrow subsequently transfers to cortical surface (local recycling), and the fraction 1-F transfers to blood. The removal half-time from cortical marrow to all destinations remains at the generic value of 0.25 y. A local recycling fraction F = 2/3 is selected for reasonable consistency with reported data on the long-term relation of ^{241}Am in bone and urinary ^{241}Am, taking account of uncertainties in the reported data.

Curium

(546) The systemic behaviour of Cm is reasonably well characterised from biokinetic studies on a variety of laboratory animals including dogs, non-human primates, and rodents; measurements of urinary excretion of intravenously administered Cm in healthy human subjects; and follow-up of a few workers following accidental exposure to Cm. Comparative biokinetic data for Am and Cm in laboratory animals indicate that these chemically similar elements are also close physiological analogues. In this report, the systemic biokinetic model adopted for Am is also applied to Cm.

Berkelium, Californium, Einsteinium, Fermium

(547) Information on the systemic biokinetics of Bk, Cf, and Es comes mainly from studies on rodents and dogs. Comparisons of systemic data for these elements and Am suggests a relation between ionic radius and the relative amounts transferred to bone, liver, and urine similar to the relation observed for the lanthanides. That is, initial deposition in bone tends to increase, deposition in liver tends to decrease, and the early urinary excretion rate tends to increase with decreasing ionic radius. This apparent pattern is used together with available element-specific data to develop transfer coefficients describing the expected distribution and excretion of these three elements following uptake to blood, with the parameter values for Am used as a point of departure. The systemic model for Es is assigned to fermium, for which no biokinetic data were found.

Summary of parameter values for actinides addressed in this report, other than Pu

Generic parameter values

(548) The follow generic parameter values are applied to Ac, Pa, Np, Am, Cm, Bk, Cf, Es, and Fm:

- Percentage of outflow from blood going to rapid-turnover soft tissue (ST0): 30%
- Deposition fractions (% of activity leaving the circulation, defined as blood plus ST0):
    j. ST2 (soft tissues with tenacious retention): 2%
    k. Testes: 0.035%
    l. Ovaries: 0.011%
- Removal half-time from:
    a. Liver 1 (to SI content + Liver 2): 30 d (excluding Pa)
    b. Bone marrow compartments: 0.25 y
    c. Gonads to blood: 5 y
- Fractional transfer from:
    a. Trabecular surface to trabecular volume, 0.09 y^{-1}
    b. Cortical surface to cortical volume, 0.015 y^{-1}
    c. Trabecular surface to trabecular marrow, 0.18 y^{-1}
    d. Cortical surface to cortical marrow, 0.03 y^{-1}
    e. Trabecular volume to trabecular marrow, 0.18 y^{-1}
    f. Cortical volume to cortical marrow, 0.03 y^{-1}
    g. Trabecular or cortical marrow to blood, 2.77 y^{-1}

(549) Non-generic deposition fractions and removal half-times for the actinides elements other than Pu addressed in this report are listed in

(550) Table 18.7. and Table 18.8., respectively. Transfer coefficients derived from these values and the generic parameter values are listed in Table 18.9.

5893 Table 18.7. Non-generic deposition fractions for actinide elements.
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Destination	Ac	Pa, Th[a]	Np	Am, Cm	Bk	Cf	Es, Fm
UB contents	0.07	0.055	0.32	0.07	0.09	0.11	0.13
Right colon	0.013	0.005	0.007	0.013	0.06	0.06	0.06
Bone surface	0.3	0.7	0.45	0.3	0.4	0.5	0.55
Liver 1	0.5	0.05	0.1	0.5	0.3	0.2	0.15
Kidneys 1	0.02	0.035	0.015	0.02	0.02	0.02	0.01
Kidneys 2	0.005	0.01	0.005	0.005	0.01	0.01	0.005
ST1[b]	0.071	0.125	0.083	0.071	0.10	0.08	0.075
ST2	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Testes	0.00035	0.00035	0.00035	0.00035	0.00035	0.00035	0.00035
Ovaries	0.00011	0.00011	0.00011	0.00011	0.00011	0.00011	0.00011

[a]Thorium is addressed in an earlier part of this report series.

[b]Derived as 100% minus the sum of all other deposition fractions (rounded to three decimal places).

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Table 18.8. Non-generic values describing biological removal of actinide elements from compartments.

Parameter	Ac	Pa, Th[a]	Np	Am, Cm	Bk	Cf	Es, Fm
Removal half-time, Blood	30 min	6 h	6 h	30 min	18 h	1 h	1 h
Removal half-time, ST0	0.5 d	1.5 d	1 d	0.5 d	0.5 d	0.5 d	0.5 d
Removal half-time, ST1	50 d	2 y	100 d	50 d	100 d	100 d	100 d
Removal half-time, Kidneys1	7 d	15 d	14 d	7 d	7 d	7 d	7 d
Removal half-time, Kidneys2	500 d	5 y	500 d	500 d	5 y	5 y	5 y
Fraction, Liver 1 to Blood	0.974	0.25	0.0	0.974	0.974	0.974	0.974
Fraction, Liver 1 to SI cont	0.026	0.25	0.07	0.026	0.026	.026	0.026
Fraction, Liver 1 to Liver 2	0.0	0.5	0.93	0.0	0.0	0.0	0.0
Removal half-time, Liver 2	NA	9 y	1 y	NA	NA	NA	NA
Fraction of bone deposit assigned to trab bone	0.5	0.5	0.55	0.5	0.5	0.5	0.5
Fraction of bone deposit assigned to cort bone	0.5	0.5	0.45	0.5	0.5	0.5	0.5

[a]Thorium is addressed in an earlier part of this report series.

5904 Table 18.9. Transfer coefficients for the actinide elements addressed in this report (other than Pu).

Path[a]		Transfer coefficient (d^{-1})						
From	To	Ac	Pa, Th[b]	Np	Am, Cm	Bk	Cf	Es,Fm
Blood	Liver 1	11.6	0.097	0.194	11.6	0.194	2.33	1.75
Blood	Trab surf	3.49	0.679	0.480	3.49	0.129	2.91	3.20
Blood	Cort surf	3.49	0.679	0.393	3.49	0.129	2.91	3.20
Blood	Kidneys 1	0.466	0.0679	0.0291	0.466	0.0129	0.233	0.116
Blood	Kidneys 2	0.116	0.0194	0.0097	0.116	0.00647	0.116	0.0582
Blood	UB cont	1.63	0.107	0.621	1.63	0.0582	1.28	1.51
Blood	RC cont	0.303	0.0097	0.0136	0.303	0.0388	0.699	0.699
Blood	Testes	0.0082	0.00068	0.00068	0.0082	0.00023	0.00408	0.00408
Blood	Ovaries	0.0026	0.00021	0.00021	0.0026	0.00007	0.00128	0.00128
Blood	ST0	10.0	0.832	0.832	10.0	0.277	4.99	4.99
Blood	ST1	1.67	0.243	0.161	1.67	0.0647	0.926	0.868
Blood	ST2	0.466	0.0388	0.0388	0.466	0.0129	0.233	0.233
Liver 1	SI cont	0.0006	0.000475	0.000133	0.0006	0.0006	0.0006	0.0006
Liver 1	Liver 2	0.0225	0.00095	0.00177	0.0225	0.0225	0.0225	0.0225
Liver 1	Blood	0	0.000475	0	0	0	0	0
Liver 2	Blood	0.0019	0.000211	0.0019	0.0019	0.0019	0.0019	0.0019
Trab surf	Trab mar	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$
Trab surf	Trab vol	$2.47\cdot10^{-4}$	$2.47\cdot10^{-4}$	$2.47\cdot10^{-4}$	$2.47\cdot10^{-4}$	$2.47\cdot10^{-4}$	$2.47\cdot10^{-4}$	$2.47\cdot10^{-4}$
Trab vol	Trab mar	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$	$4.93\cdot10^{-4}$
Trab mar	Blood	0.0076	0.0076	0.0076	0.0076	0.0076	0.0076	0.0076
Cort surf	Cort mar	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$
Cort surf	Cort vol	$4.11\cdot10^{-5}$	$4.11\cdot10^{-5}$	$4.11\cdot10^{-5}$	$4.11\cdot10^{-5}$	$4.11\cdot10^{-5}$	$4.11\cdot10^{-5}$	$4.11\cdot10^{-5}$
Cort vol	Cort mar	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$	$8.21\cdot10^{-5}$
Cort mar	Blood	0.0076	0.0076	0.0076	0.00253	0.0076	0.0076	0.0076
Cort mar	Cort surf	0	0	0	0.00507	0	0	0
Kidneys 1	UB cont	0.099	0.0462	0.0495	0.099	0.099	0.099	0.099
Kidneys 2	Blood	0.00139	0.00038	0.00139	0.00139	0.00038	0.00038	0.00038
Testes	Blood	0.00038	0.00038	0.00038	0.00038	0.00038	0.00038	0.00038
Ovaries	Blood	0.00038	0.00038	0.00038	0.00038	0.00038	0.00038	0.00038
ST0	Blood	1.39	0.462	0.693	1.39	1.39	1.39	1.39
ST1	Blood	0.0139	0.00095	0.00693	0.0139	0.00693	0.00693	0.00693
ST2	Blood	$1.9\cdot10^{-5}$	$1.9\cdot10^{-5}$	$1.9\cdot10^{-5}$	$1.9\cdot10^{-5}$	$1.9\cdot10^{-5}$	$1.9\cdot10^{-5}$	$1.9\cdot10^{-5}$

[a]Trab = trabecular; Cort = cortical; surf = surface; vol = volume; mar = marrow; UB = urinary bladder; RC = right colon; cont = content; ST0, ST1, ST2 are compartments of Other soft tissues with fast, intermediate, and slow turnover, respectively.

[b]Thorium is addressed in an earlier part of this report series.

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5907 **18.2.4. Treatment of radioactive progeny**

5908 (551) Chain members addressed in the derivation of dose coefficients for the actinides
5909 addressed in this document include isotopes of thallium, lead, bismuth, polonium, astatine,
5910 radon, francium, radium, actinium, thorium, protactinium, uranium, neptunium, plutonium,
5911 americium, curium, berkelium, californium, einsteinium, and fermium.

5912 (552) The models applied here to thallium, lead, bismuth, polonium, and radium as actinide
5913 progeny are the models applied to these elements as progeny of radium (described in Part 3 of
5914 this report series). The model applied here to uranium as an actinide progeny is the model
5915 applied to uranium as a progeny of thorium (also described in Part 3).

(553) The model applied here to radon as an actinide progeny is a generic model applied in this report series to radon produced by radioactive decay in a systemic compartment. Radon produced in a compartment identified as non-exchangeable bone volume, exchangeable bone volume, or bone surface transfers to blood at the rate 0.36 d^{-1}, 1.5 d^{-1}, or 100 d^{-1}, respectively; radon produced in a compartment identified simply as bone volume transfers to blood at 0.36 d^{-1}; radon produced in a soft-tissue compartment transfers to blood at 33.3 d^{-1}; and radon produced in blood or entering blood is removed from the body (exhaled) at 1000 d^{-1}.

(554) Radioisotopes of francium and astatine appearing in actinide chains considered in this report have short half-lives and are assumed to decay at their site of production in systemic tissues or blood.

(555) The model applied here to thorium as an actinide progeny is the model applied in Part 3 of this report series to thorium as a progeny of radium. Briefly, two compartments, one representing spleen and the other representing skin, are added to the explicitly identified source regions in the characteristic model for thorium described in Part 3. Spleen and Skin are assumed to receive 0.5% and 2%, respectively, of thorium leaving the circulation and to return thorium to blood with a biological half-time of 2 y. Thorium produced in a compartment that is not identifiable with a compartment in the thorium model is assumed to transfer to blood at the following rates: 1000 d^{-1} if produced in blood; 0.462 d^{-1} if produced in soft tissue; and at the rate of bone turnover if produced in a bone volume compartment.

(556) The models applied here to actinium, protactinium, neptunium, plutonium, americium, curium, berkelium, californium, einsteinium, and fermium as actinide progeny are modifications of their characteristic models described earlier in this section. For a given element in this group, two compartments representing skin and spleen are added to the explicitly identified source regions in the element's characteristic model. These compartments are taken from the intermediate soft-tissue compartment, ST1; that is, the deposition fraction for ST1 is reduced by the deposition fractions assigned to Spleen and Skin, and the removal half-time from ST1 is assigned to these added compartments. Deposition of the element in Skin is calculated as its mass fraction of Other soft tissue times its deposition fraction in Other soft tissue excluding the rapid-turnover compartment, ST0. The deposition fraction for Spleen is set at one-third of the deposition fraction for Skin, considering the relative masses of these tissues and the typically higher concentrations of actinides in spleen than skin observed in laboratory animals and human subjects. If the element is produced in a compartment that is not identifiable with a compartment in its characteristic model, it is assumed to transfer to the element's blood compartment (Blood 1 in the case of plutonium, which has multiple blood compartments – see Table 18.6) at the rate 1000 d^{-1} if produced in a blood compartment, at the rate of transfer from the fast-turnover soft-tissue compartment ST0 to Blood if produced in a soft-tissue compartment, and at the rate of bone turnover if produced in a bone volume compartment.

(557) The model for plutonium as a progeny is further modified by removing the transfers from Blood to ST0 and from Blood to Blood 1 (Table 18.6) and adding a transfer of 0.33 d^{-1} from Blood 1 to ST0. This simplifies the model for plutonium as a progeny by eliminating a blood compartment (Blood in Table 18.6). The added transfer coefficient of 0.33 d^{-1} from Blood 1 to ST0 implies that ST0 receives 30% of plutonium leaving Blood 1. Total deposition in ST0 is virtually the same as in the model for plutonium as a parent, but the rate of accumulation of plutonium in ST0 is substantially lower in this simplified version of the model.

REFERENCES

Allard, B., Kipatsi, H., Liljenzin J.O., 1980. Expected species of uranium, neptunium and plutonium in neutral aqueous solutions, J. Inorg. Nucl. 42,1015–1027.

Altmaier, M., Gaona, X., Fanghanel, T., 2013. Recent advances in aqueous actinide chemistry and thermodynamics. Chem. Rev. 113, 901–943.

Ansoborlo, E., Prat, O., Moisy, P., et al., 2006. Actinide speciation in relation to biological processes. Biochimie 88, 1605−1618.

Aryal, B.P., Paunesku, T., Woloschak, G.E., He, C., Jensen, M.P., 2012. A proteomic approach to identification of plutonium-binding protein in mammalian cells. J. Prot. 75, 1505–1514.

Ballou, J. E., Dagle, G. E., Gies, R. A., Smith, L. G., 1979. Late effects of inhaled 253Es(NO3)3 in rats. Health Phys. 37, 301–310.

Ballou, J. E., Dagle, G. E., McDonald, K. E., Bushbom, R. L., 1977. Influence of inhaled Ca-DTPA on the long-term effects of inhaled Pu nitrate. Health Phys. 37, 479–487.

Ballou, J.E., Gies, R.A., 1978. Inhalation toxicology of 241Am(NO3)3. Pacific Northwest Laboratory Annual Report for 1977 to the DOE Assistant Secretary for Environment, PNL–2500 Part 1, Biomedical Sciences, 3.36–3.37. Richland, Washington. Available from National Technical Information Service, Springfield, Virginia.

Basset C., Averseng O., Ferron P-J., et al., 2013. Revision of the biodistribution of uranyl in serum: is Fetuin-A the major protein target. Chem. Res. Tox. 26, 645–653.

Bresson, C., Ansoborlo, E., Vidaud, C., 2011. Radionuclide speciation: a key point in the field of nuclear toxicology studies. J. Anal. At. Spectrom. 26, 593–601.

Buldakov, L.A., Kalmykova, Z.I., Nifatov, A.P., et al., 1972, Metabolism and biological effects of inhaled 241Am and 239Pu in dogs. Health Phys., 22, 873–874.

Choppin, G.R., Jensen, M.P., 2006. Actinides in Solution: complexation and kinetics, The Chemistry of the Actinide and Transactinide Elements (Morss, L. R.,Edelstein, and N. M., Fuger, J., Eds.) 4th ed., Chapter 23, 2524–2621, Springer,New York.

Crawley, F. E. H., Goddard, E. A., 1976. The translocation of 241-americium and 242-curium from the respiratory system of the rat. Health Phys. 30, 191–197.

Davies, C .P., Hodgson, A., Stradling, G. N., et al., 1993. Studies on the nasal clearance of 238Pu and 241Am nitrates in the rat. NRPB-M417, National Radiological Protection Board, Chilton.

Davies, C. P., Hodgson, A., Stradling, G. N., et al., 1992. Studies on the nasal clearance of 238Pu and 241Am nitrates in the rat. J. Aerosol Sci. 23, Suppl. 1, S511–S514.

Duffield, J., Taylor, D.M., 1991. The biochemistry of the actinides, Handbook on the Physics and Chemistry of the Actinides. Freeman, A. J. and Keller, C, Elsevier Science.

Duffield, J., Taylor, D.M., 1987. A spectroscopic study on the binding of plutonium (IV) and its chemical analogues to transferrin, Inorg. Chim. Acta 140, 365–367.

Durbin, P. W., 1960. Metabolic characteristics within a chemical family. Health Phys. 2, 225−238.

Durbin, P. W., 1962. Distribution of the transuranic elements in mammmals. Health Phys. 8, 665−671.

Durbin, P.W., 2006. Actinides in animals and man, The Chemistry of the Actinide and Transactinide Elements (Morss, L. R.,Edelstein, and N. M., Fuger, J., Eds.) 4th ed., Chapter 31, 3339−3440, Springer,New York.

6006 Durbin, P.W., 1973. Metabolism and biological effects of the transplutonium elements. In:
6007 Handbook of Experimental Pharmacology (Ed. by H.C.Hodge, J.N.Stannard &
6008 J.B.Hursh), 739-883. Berlin, Springer Verlag.
6009 Durbin, P.W., 2011. Actinides in animals and man. Chapter 31 in: The chemistry of the
6010 actinide and transactinide elements, 4th edition, Vol. 5, Morss, L. R., Edelstein, N. M.,
6011 Fuger, J., Katz, J. J. (Eds.) Springer, 3339-3474.
6012 Epker, B.N., Frost, H.M., 1965a. Correlation of bone resorption and formation with the
6013 physical behaviour of loaded bone. J. Dental Res. 44, 33–41.
6014 Epker, B.N., Frost, H.M., 1965b. The direction of transverse drift of actively forming osteons
6015 in human rib cortex. J. Bone Joint Surg. 47, 1211–1215.
6016 Frost, H. M., 1986. Intermediary organization of the skeleton, Volumes I & II. CRC Press,
6017 Boca Raton, FL, USA.
6018 Gorden, A.E.V., Xu, J., Raymond, K.N., Durbin P., 2003. Rational design of sequestering
6019 agents for plutonium and other actinides, Chem. Rev. 103, 4207–4282.
6020 Hamilton, J. G., 1948. The metabolic properties of the fission products and actinide elements.
6021 Rev. Mod. Phys. 20, 718–728.
6022 Herring, G. M., Vaughan, J., Williamson, M., 1962. Preliminary report on the site of
6023 localization and possible binding agent for yttrium, americium and plutonium in cortical
6024 bone. Health Phys. 8:717-724.
6025 Hood, L.E., Omenn, G.S., Moritz, R.L., et al., 2012. New and improved proteomics
6026 technologies for understanding complex biological systems: addressing a grand challenge
6027 in the life sciences. Proteomics 12, 2773–2783.
6028 ICRP, 1995 . Age dependent doses to members of the public from intake of radionuclides: part 3
6029 ingestion dose coefficients. ICRP Publication 69. Ann. ICRP 25(1).
6030 ICRP. 1991. 1990 Recommendations of the International Commission on Radiological Protection.
6031 ICRP Publication 60. Ann. ICRP 21(1/3).
6032 ICRP. 1993. Age dependent doses to members of the public from intake of radionuclides: part
6033 2 ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).
6034 Ishigure, N., Nakano, T., Enomoto, H., 2001. 241Am as a metabolic tracer for inhaled
6035 plutonium nitrate in external chest counting. Radiat. Prot. Dosim. 97, 271–273.
6036 IUPAC, 2005. International Union of Pure and applied Chemistry. Nomenclature of inorganic
6037 chemistry. IRSC Publishing. 51.
6038 Jensen, M. P., Gorman-Lewis, D., Aryal, B., et al., 2011. An iron-dependent and transferrin-
6039 mediated cellular uptake pathway for plutonium. Nature Chem. Biol. 7, 560−565.
6040 Knope, K.E., Soderholm. I., 2013. Solution and solid-state structural chemistry of actinide
6041 hydrates and their hydrolysis and condensation products. Chem. Rev. 113, 944–994.
6042 Leggett, R. W., Eckerman, K. F., Khokhryakov, V. F., et al., 2005. Mayak worker study: An
6043 improved biokinetic model for reconstructing doses from internally deposited plutonium.
6044 Radiat. Res. 164, 111–122.
6045 Lloyd, E., Marshall, J. H., 1972. Toxicity of 239Pu relative to 226Ra in man and dog, in
6046 Radiobiology of Plutonium (eds. B. J. Stover and W. S. S. Jee), The J. W. Press,
6047 University of Utah, 377–384.
6048 Maher, K., Bargar, J.R., Brown, G.E, 2013. Environmental speciation. Inorg. Chem. 52, 3510-
6049 3532.
6050 Malard, V., Gaillard, J.C., Berenguer, F., Sage, N., Quemeneur, E., 2009. Urine proteomic
6051 profiling of uranium nephrotoxicity. Biochim. Biophys. Acta. 1794, 882–891.

6052 Malátová, I., Foltánová, Š, Becková, V., et al., 2003. Assessment of occupational doses from
6053 internal contamination with 241Am. Radiat. Prot. Dosim. 105, 325–328.
6054 Malátová, I., Vrba, T., Becková, V., Pospíšilová, H., 2010. Twelve years of follow up of cases
6055 with old 241Am internal contamination. Health Phys. 99, 495–502.
6056 Neck, V., Kim, J.I, 2001. Solubility and hydrolysis of tetravalent actinides. Radiochim. Acta.
6057 89, 1–16.
6058 Nénot, J.C., Masse, R., Morin, M., Lafuma, J., 1972. An experimental comparative study of
6059 the behaviour of 237Np, 238Pu, 239Pu, 241Am and 242Cm in bone. Health Phys. 22,
6060 657–665.
6061 Nénot, J.C., Morin, M., Lafuma, J., 1971. Etude métabolique et thérapeutique des
6062 contaminations respiratoires par certains actinides en solutions [Metabolic and
6063 therapeutic study of respiratory contaminations by some actinides solutions]. Health
6064 Phys. 20, 167–177.
6065 Paquet, F., Frelon, S., Cote, G., Madic, C., 2003. The contribution of chemical speciation to
6066 internal dosimetry, Radiat. Prot. Dosim. 105, 179–185.
6067 Pearson, R. G., 1963. Hard and soft acids and bases. J. Am.Chem. Soc. 85, 3533−3539.
6068 Prat, O., Berenguer, F., Malard, V., et al., 2005. Transcriptomic and proteomic responses of
6069 human renal HEK293 cells to uranium toxicity, Proteomics 5, 297–306.
6070 Prat, O., Berenguer, F., Steinmetz, G., et al., 2012. Alterations in gene expression in cultured
6071 human cells after acute exposure to uranium salt: involvement of a mineralization
6072 regulator, Toxicol. *In vitro*, 24, 160–168.
6073 Prat, O., Ansoborlo, E., Sage, N., et al., 2011. From cell to man: evaluation of osteopontin as
6074 a possible biomarker of uranium exposure. Env. Int. 37, 657–662.
6075 Priest, N.D., Haines, J.W., Humphreys, J.A.M., et al., 1992. The bone volume effect on the
6076 dosimetry of plutonium-239 and americium-241 in the skeleton of man and baboon. J.
6077 Radioanal. Nucl. Chem. 156, 33–53.
6078 Qi L., Basset C., Averseng O., et al., 2014. Characterization of UO_2^{2+} binding to osteopontin,
6079 a highly phosphorylated protein : insights into potential mechanisms of uranyl
6080 accumulation in bones" Metallomics. 6, 166–176
6081 Safi, S., Creff, G., Jeanson, A., et al., 2013. Osteopontin: A Uranium Phosphorylated Binding-
6082 Site Characterization, Chemistry 19, 11261–11269.
6083 Seaborg, G. T., 1993. Overview of the actinide and lanthanide (the F) elements. Radiochim.
6084 Acta 61, 115−122.
6085 Shannon, R. D., 1976. Revised effective ionic-radii and systematic studies of interatomic
6086 distances in halides and chalcogenides. Acta Crystallogr., Sect. A 32, 751−767.
6087 Smith, H., Stradling, G. N., Loveless, B. W., Ham, G. J.,1977. The in-vivo solubility of
6088 plutonium-239 in the rat lung. Health Phys. 33, 539–551.
6089 Stather, J.W., Howden, S., 1975. The effect of chemical form on the clearance of plutonium-
6090 239 from the from the respiratory system of the rat. Health Phys. 28, 29–39.
6091 Stather, J.W., Priest, N.D., 1977. The pulmonary clearance and the comparative metabolism
6092 of plutonium-238, plutonium-239, americium-241 and curium-242 in the rat. NRPB
6093 Annual Research and Development Report for 1976. NRPB R&D 1. 46–48. (Chilton,
6094 HMSO).
6095 Stradling, G. N., Cooper, J. R., Smith, H., Ham, S. E., 1979. The mobility of curium-244
6096 dioxide in the bronchially intubated rat. Int. J. Radiat. Biol. 36, 19–32.
6097 Stradling, G. N., Ham, G. J., Smith, H., Breadmore, S. E., 1978b. The mobility of americium
6098 dioxide in the rat. Radiat. Res. 76, 549–560.

6099 Stradling, G. N., Loveless, B. W., Ham, G. J., Smith, H., 1978a. The biological solubility in
6100 the rat of plutonium present in mixed plutonium sodium aerosols. Health Phys. 35, 229–
6101 235.
6102 Stradling, G. N., Smith, H., Cooper, J. R., 1980. Factors affecting the mobility of actinide
6103 oxides and their influence on radiological protection. In: Proc. 19th Annual Hanford Life
6104 Sciences Symposium, Oct 22-24 1979, Richland, Washington. DOE Symposium Series
6105 53. Springfield, VA: National Technical Information Service. 209–223.
6106 Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1987. Studies on the metabolic behaviour
6107 of industrial actinide-bearing aerosols after deposition in the rat lung: an experimental
6108 basis for interpreting chest monitoring data and assessing ALIs for workers. Human
6109 Toxicol. 6, 365–375.
6110 Taulan, M., Paquet, F., Maubert, C., et al., 2004. Renal toxicogenomic response to chronic
6111 uranyl nitrate insult in mice. Environ. Health Perspect. 112, 1628–1635.
6112 Taulan, M., Paquet, F., Argiles, A., Demaille, J., Romey, M.C., 2006. Comprehensive
6113 analysis of the renal transcriptional response to acute uranyl nitrate exposure. BMC
6114 Genomics 7, 1–14.
6115 Taylor, D. M., 1998. The bioinorganic chemistry of actinides in blood. J. Alloys Compd. 271,
6116 6−10.
6117 Taylor, D. M., 1984. The retention of plutonium and americium in liver: an interspecies
6118 comparison. Radiation Risk Protection. 1, 431–434. 6th International Radiation Protection
6119 Association Congress, Berlin.
6120 Taylor, D.M., Seidel A., Planas-Bohne, F., et al., 1987. Biochemical studies of the interactions
6121 of plutonium, neptunium and protactinium with blood and liver cell proteins. Inorg.
6122 Chim. Acta, 140, 361–363.
6123 Vidaud, C., Bourgeois D., Meyer, D., 2012. Bone as Target Organ for Metals: The Case of f-
6124 Elements, Chem. Res. Toxicol. 25, 1161–1175.
6125 Vidaud, C., Dedieu, A., Basset, C., et al., 2005. Screening of human serum proteins for
6126 uranium binding, Chem. Res. Toxicol. 18, 946–953.
6127 Vidaud, C., Gourion-Arsiquaud, S., Rollin-Genetet, F., et al., 2007. Structural consequences
6128 of binding of UO22+ to apotransferrin:Can this protein account for entry of uranium into
6129 human cells? Biochemistry 46, 2215−2226.
6130 Yule, L.A., 1991. A comparison of the binding of plutonium and iron to transferrin and citrate,
6131 Thesis: University of Wales - Cardiff (U.K.).
6132

19. ACTINIUM (Z=89)

19.1. Chemical Forms in the Workplace

(558) Actinium is the first element of the actinide series which mainly occurs in oxidation state III. Lanthanides such as Eu(III) or Gd(III), and Am(III) are good chemical analogues of Ac(III). Actinium has no significant industrial use and may be encountered in industry in a variety of chemical and physical forms, including oxides (Ac_2O_3), chlorides and nitrates.

(559) Traces of actinium-227 are present in uranium ores and it can be obtained by the neutron irradiation of ^{226}Ra in a nuclear reactor.

Table 19.1. Isotopes of actinium addressed in this report.

Isotope	Physical half-life	Decay mode
Ac-224	2.78 h	EC, A
Ac-225	10.0 d	A
Ac-226	29.37 h	B-, EC, A
Ac-227	21.772 y	B-, A
Ac-228[a]	6.15 h	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

19.2. Routes of Intake

19.2.1. Inhalation

Absorption Types and parameter values

(560) Two studies were found in the literature relating to lung retention of actinium (Ac) in man following accidental intakes. No experimental studies were found that give information on absorption of actinium from the respiratory tract.

(561) As noted in the general actinide section, in the absence of relevant information, absorption parameter values for actinium are based on chemical analogy: values chosen for americium are applied in this document to actinium.

(562) Absorption parameter values and Types, and associated f_A values for particulate forms of actinium are given in Table 19.2.

Protactinium oxide.

(563) Newton (1968) followed lung retention of ^{231}Pa and its progeny radionuclide ^{227}Ac after accidental inhalation by a research student, by external measurement of X- and gamma-rays from ^{231}Pa and the radioactive progeny of ^{227}Ac: ^{227}Th and ^{223}Ra. For the decay scheme see Fig. A.7. in OIR Part 1 (ICRP, 2015) or Fig. 15-2 in OIR Part 3 (ICRP, 2016b). The contamination consisted of recently separated ^{231}Pa, probably in the form of Pa_2O_5 or $KPaO_3$. Analysis of air and surface contamination showed that the ^{231}Pa was accompanied by large amounts of its progeny; the ^{227}Ac: ^{231}Pa ratio was ~0.08. Autoradiography of an air filter indicated that the largest particle sizes involved were in the range 3 – 5 μm. Whole-body and/or

chest measurements were made from 7 to 883 d after intake. Over the period 7 to 427 d, lung retention could be fit by a single exponential function with a biological half-life for ^{231}Pa of 1000 ± 300 d. After correction for ingrowth from decay of ^{231}Pa, the biological half-life of ^{227}Ac was estimated to be in the range 300 – 400 d. Several 24-hour collections of urine and faeces voided during the first few weeks (but not before day 7) were analysed: no ^{231}Pa, or radioactive progeny attributable to the intake were detected. Insufficient information is available to assess absorption parameter values. However, the activity was concentrated in the chest, from which little clearance was observed, indicating Type S behaviour.

Unspecified compounds.

(564) A worker was referred for body radioactivity measurements following discovery of high levels of airborne ^{227}Ac as well as surface activity in his laboratory and on his work clothes (Newton, 1966). Nothing was known of the chemical form of the contaminant, nor of its size distribution. Retention of ^{227}Ac in his body was studied over more than 800 d after intake by external measurement (scintillation gamma-ray spectrometry) of x- and gamma-rays from ^{227}Ac progeny radionuclides ^{227}Th and ^{223}Ra. Whole-body and/or chest measurements were made from 5 to 838 d after intake. Insufficient information is available to assess absorption parameter values. However, the activity remained largely confined to the chest region and was estimated to have cleared from the thorax with a biological half-time of at least 10 y, indicating Type S behaviour.

Actinium progeny formed in the respiratory tract

(565) The general approach to treatment of progeny radionuclides formed in the respiratory tract is described in OIR Part 1, Section 3.2.3 and Annex A (ICRP, 2015). In summary, it is expected that generally the rate at which a particle dissociates is determined by its matrix, and hence the physico-chemical form of the inhaled material. It is recognised that nuclei formed by alpha decay within a particle matrix may be expelled from it into the surrounding medium by recoil, but to implement this routinely would add greatly to the complexity of calculations. It is expected that the behaviour of soluble (e.g. Type F) material in the respiratory tract would depend on its elemental form, *i.e.* that of the progeny radionuclides. Nevertheless, for simplicity, in this series of documents the absorption parameter values of the parent are, by default, applied to all members of the decay chain formed in the respiratory tract. Exceptions are made for noble gases formed as progeny radionuclides, which are assumed to escape from the body directly, in addition to other routes of removal. For calculation purposes it is assumed that radon formed as a progeny radionuclide within the respiratory tract escapes from the body at a rate of 100 d^{-1}, in addition to other routes of removal. [For further information see the section on thorium progeny formed in the respiratory tract in OIR Part 3, (ICRP, 2016)].

(566) Studies specifically relevant to comparing the behaviour of actinium with that of its radioactive progeny (actinium, thorium and radium isotopes) are summarised here. For further information, see the thorium and radium inhalation sections in OIR Part 3 (ICRP, 2016).

(567) As described above, Newton (1968) followed lung retention of ^{231}Pa (and ^{227}Ac) after accidental inhalation in a relatively insoluble form, by external measurement of X- and gamma-rays from ^{231}Pa and the decay products of ^{227}Ac: ^{227}Th and ^{223}Ra. However, much of the ^{227}Ac was inhaled with the ^{231}Pa, rather than formed as a progeny radionuclide within the lungs, and the ^{227}Ac was not observed directly: it was assumed to be in equilibrium with its radioactive progeny. The estimated biological half-life of ^{227}Ac in the lungs was shorter than that of ^{231}Pa,

suggesting that it was cleared more rapidly. In contrast, no significant difference was found between the levels of ^{227}Th and ^{223}Ra in the chest, indicating that they were in equilibrium, with no significant preferential clearance of the ^{223}Ra progeny.

Rapid dissolution rate for actinium

(568) By analogy with americium, a value of 0.4 d^{-1} is applied here to all Type F forms of actinium. Because it is lower than the general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S forms of actinium.

Extent of binding of actinium to the respiratory tract

(569) By analogy with americium, a bound fraction with f_b = 0.002 and a rate of uptake s_b = 0 d^{-1}, applied throughout the respiratory tract except in the ET_1 region (where no absorption occurs), is adopted here for actinium. (These are the generic bound fraction parameter values, based on plutonium, applied in this document to all transplutonium elements.)

Table 19.2. Absorption parameter values for inhaled and ingested actinium.

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A[b]
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Citrate	1	0.4	–	5×10^{-4}
M[d]	Chloride, oxide	0.2	0.4	0.005	1×10^{-4}
S	Actinium associated with plutonium oxide compounds	0.01	0.4	1×10^{-4}	5×10^{-6}
Ingested material[e]					
All compounds					5×10^{-4}

a It is assumed that for actinium a bound fraction f_b = 0.002 with an uptake rate s_b = 0 d^{-1} is applied throughout the respiratory tract, except in the ET_1 region. The values of s_r for Type F, M and S forms of actinium (1 d^{-1}) are element-specific.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of actinium (5×10^{-4}).

c Materials (e.g. chloride) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

d Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

e Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A (=5×10^{-4}) for ingestion of the radionuclide.

19.2.2. Ingestion

(570) Early studies by Hamilton (1948) and by Campbell et al. (1950) indicated that fractional absorption of actinium in rats is considerably less than 0.01.

(571) In *Publication 30* Part 3 (ICRP, 1981) and *Publication 48* (1986) an absorption value of 1×10^{-3} for actinium was used. However, in this report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all actinides other than U.

(572) An f_A value of 5×10^{-4} is adopted here for all chemical forms of actinium.

19.2.3. Systemic distribution, retention and excretion of actinium

19.2.3.1. Data

(573) A worker was referred for body radioactivity measurement following discovery of high levels of airborne ^{227}Ac as well as surface activity in his laboratory and on his work clothes (Newton, 1966). Retention of ^{227}Ac in his body was studied over more than 800 d after intake by scintillation gamma-ray spectrometry. The activity remained largely confined to the chest region and was estimated to have cleared from the thorax with a biological half-time of at least 10 y.

(574) Newton and co-workers (Newton, 1968; Newton and Brown, 1974) reported a case of internal exposure to ^{227}Ac and ^{231}Pa through a puncture wound. An estimated 90% of ^{227}Ac reaching the systemic circulation was retained indefinitely. Three years after the accident, activity appeared to be deposited primarily in bone with some involvement of liver. After 9 y most of the liver content apparently had transferred to the skeleton. For example, during the period 1570-2330 d after the incident, daily urinary excretion of the ^{231}Pa/^{227}Ac chain member ^{223}Ra was approximately 60 times greater than that of ^{231}Pa and 150 times greater than that of ^{227}Ac. Daily faecal excretion of ^{223}Ra during that period was about 1300 times that of ^{231}Pa and 2100 times that of ^{227}Ac.

(575) Taylor (1970) studied the biokinetics of ^{227}Ac in rats following its intravenous administration in various chemical forms. Similar tissue distributions were observed when ^{227}Ac was administered as a complex with serum proteins, as nitrate, or as citrate. At 4 d ^{227}Ac was found mainly in the liver and skeleton, and the kidneys contained about 1.5% of the administered amount. By 189 d the liver content was less than 1% of the content at 4 d. There was little if any net loss from bone during the period 4-189 d. Over the first week, cumulative urinary and faecal excretion amount to about 1% and 20%, respectively, of the administered activity.

(576) Campbell et al. (1956) investigated the behavior of ^{227}Ac and its progeny ^{227}Th and ^{223}Ra in young adult male rats following administration of ^{227}Ac alone or in equilibrium with its progeny by intravenous, intramuscular, and subcutaneous injection; orally via a stomach tube; or by absorption through the skin. The skeleton accumulated roughly half of intravenously administered ^{227}Ac. It appeared that activity deposited in the skeleton was not removed. Rats injected with ^{227}Ac in equilibrium with its progeny excreted about half of the administered ^{227}Ac in three months. The remaining 50% was tenaciously retained in the body. Actinium-227 deposited in the skeleton was not removed, but ^{227}Ac deposited in soft tissues was readily excreted. Actinium-227 deposited in the skeleton remained in equilibrium with its progeny, but ^{227}Ac deposited in soft tissues was stripped of its progeny. Normal skin was found to be an

effective barrier to ^{227}Ac and its progeny, but abraded skin allowed some passage of ^{227}Ac and its progeny.

(577) The plasma disappearance pattern of ^{227}Ac following intravenous administration to rats is similar to Am and Cm in the same animals. Clearance was about 90% complete in 50 min and 99% complete in 400 min (Durbin, 2001). At 4 d after intramuscular administration of ^{227}Ac to rats, the contents of liver, skeleton, other tissues, cumulative urine, and cumulative faeces accounted for 27%, 56%, 4%, 5%, and 8%, respectively, of the administered activity. This is broadly similar to the distributions of Am and Cm in the same animals.

(578) Biokinetic studies of actinium in rats indicate that its systemic behavior is generally consistent with the pattern found for most other actinide elements. That is, actinium deposits mainly in the skeleton and liver, is a bone surface seeker with tenacious retention in the skeleton, and is only slowly removed from the body. Its systemic biokinetics appears to be broadly similar to that of americium.

19.2.3.2. Biokinetic model

(579) The biokinetic model for systemic actinium applied in this report is described in Section 18.2.3.

19.2.3.3. Treatment of progeny

(580) The treatment of radioactive progeny of actinium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in section 18.2.4.

19.3. Individual monitoring

^{228}Ac

(581) *In vivo* lung measurements of ^{228}Ac are used to determine intakes of the radionuclide for routine monitoring. *In vivo* whole body measurement may be used as additional technique for special investigation. The main technique is gamma spectrometry.

Table 19.3. Monitoring techniques for ^{228}Ac.

Isotope		Method of Measurement	Typical Detection Limit
^{228}Ac	Lung Measurement[a]	γ-ray spectrometry	50 Bq
^{228}Ac	Whole Body Measurement[b]	γ-ray spectrometry	100 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

19.4. Dosimetric data for actinium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Campbell, J. E., Robajdek, E. S., Anthony, D. S., 1956. The metabolism of ^{227}Ac and its daughters ^{227}Th and ^{223}Ra by rats. Rad. Res. 4, 294–302.

Durbin, P. W., 2011. Actinides in animals and man. Chapter 31 in: The chemistry of the actinide and transactinide elements, 4th edition, Vol. 5, Morss, L. R., Edelstein, N. M., Fuger, J., Katz, J. J. (Eds.) Springer, 3339–3474.

Hamilton, J. G., 1948. The metabolic properties of the fission products and actinide elements. Rev. Mod. Phys. 20, 718–728.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1986. Transfer of environmental plutonium and americium across the human gut. Sci. Total Environ. 53, 89–109.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1989. Transfer of environmental plutonium and americium across the human gut. Radiol. Prot. Bull. 106, 7–11.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B. 1990. Transfer of environmental plutonium and americium across the human gut: A second study. Sci. Total Environ. 90, 273–282.

ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6 (2/3).

ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).

ICRP, 2015. Occupational intakes of radionuclides: Part 1. ICRP Publication 130. Ann. ICRP 44(2).

ICRP, 2016. Occupational intakes of radionuclides: Part 3. Ann. ICRP...

Newton, D., 1966. A case of accidental inhalation of actinium-227. Health Phys. 12, 1129–1138.

Newton, D., 1968. A case of accidental inhalation of protactinium-231 and actinium-227. Health Phys. 15, 11–17.

Newton, D., Brown, D. A., 1974, The long-term retention of systemic protactinium-231 and actinium-227, Health Phys. 27, 459–467.

Newton. D., 1966. A case of accidental inhalation of actinium-227. Health Phys. 12, 1129–1138.

Popplewell, D. S., Ham, G. J., 1989. Distribution of plutonium and americium in tissues from a human autopsy case. J. Radiol. Prot. 9, 159–164.

Popplewell, D. S., Harrison, J. D., Ham, G. J., 1991. The gastrointestinal absorption of neptunium and curium in humans. Health Phys. 60, 797–805.

Taylor, D. M., 1970. The metabolism of actinium in the rat, Health Phys. 19, 411–418.

20. PROTACTINIUM (Z=91)

20.1. Chemical Forms in the Workplace

(582) Protactinium is a rare actinide element which mainly occurs in oxidation state V and IV. Protactinium may be encountered in industry in a variety of chemical and physical forms, including oxides (Pa_2O_5, PaO_2), chlorides, citrates and nitrates.

(583) Protactinium-231 is present as traces in uranium ores. Protactinium-231 and ^{234}Pa are produced from thorium in nuclear reactors.

Table 20.1. Isotopes of protactinium addressed in this report.

Isotope	Physical half-life	Decay mode
Pa-227	38.3 m	EC, A
Pa-228	22 h	EC, B+, A
Pa-229	1.50 d	EC, A
Pa-230	17.4 d	EC, B-, A
Pa-231[a]	3.276E+4 y	A
Pa-232	1.31 d	B-, EC
Pa-233[a]	26.967 d	B-
Pa-234	6.70 h	B-
Pa-235	24.5 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

20.2. Routes of Intake

20.2.1. Inhalation

Absorption Types and parameter values

(584) One study was found in the literature relating to lung retention of protactinium (Pa) in man following accidental intake. One experimental study was found that gives information on absorption of protactinium from the respiratory tract.

(585) As there is so little relevant information available, absorption parameter values for protactinium are based on chemical analogy. As noted in the general actinide section, absorption parameter values chosen for thorium are applied in this document to protactinium.

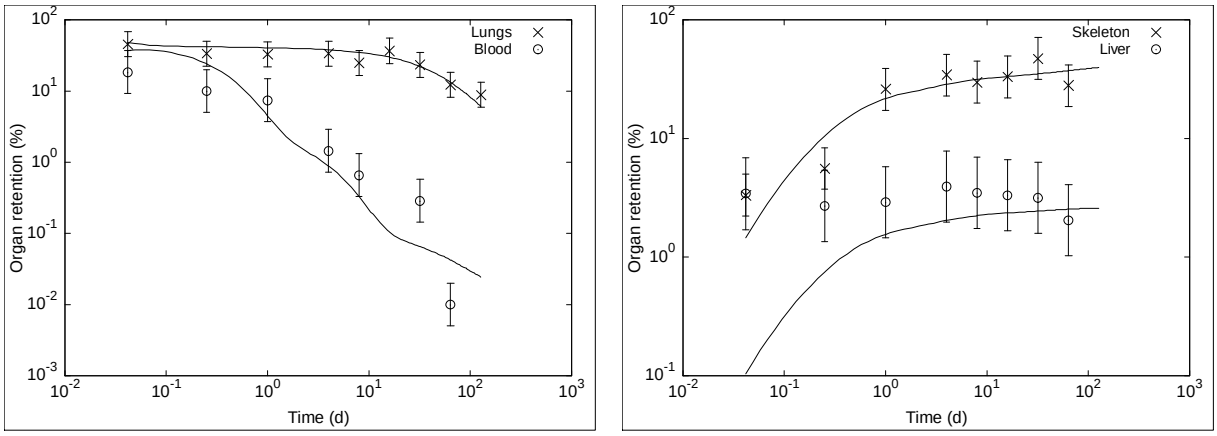
(586) Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values: the revised Human Respiratory Tract Model (ICRP, 2015) and the rat model for particle transport in the respiratory tract of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002); the Human Alimentary Tract Model (ICRP, 2006); and the human systemic model for thorium (ICRP, 2016).

(587) Absorption parameter values and Types, and associated f_A values for particulate forms of protactinium are given in Table 20.2.

Protactinium citrate

(588) Zalikin (1966) followed the tissue distribution of ^{233}Pa for 128 d after administration of protactinium citrate (pH 3) to rats by intratracheal instillation. Complementary experiments were conducted in which the tissue distribution of ^{233}Pa was measured after subcutaneous and oral administration. Absorption from the alimentary tract was low, in the range 0.006 – 0.02%. About 30% of the initial lung deposit (ILD) was absorbed by the time of the first measurement (1 hour). Long term lung retention was also observed: 34% ILD at 6 hours and 9.6% ILD at 128 d. It was noted that ^{233}Pa absorbed from the lungs behaved similarly to ^{233}Pa administered by subcutaneous injection.

(589) As described in the section below on Systemic Distribution, Retention and Excretion, there are strong similarities between the systemic biokinetics of protactinium and that of thorium, and the systemic model for thorium is applied in this document to protactinium. To test whether thorium might also be a suitable analogue for protactinium with regard to absorption from the respiratory tract, analysis was carried out here in which thorium biokinetic models were fit to the data from Zalikin (1966): i.e., the thorium systemic model (see above) and thorium respiratory tract absorption parameter values s_r = 50 d^{-1}, s_s =0.005 d^{-1}, and f_b =0 (no bound fraction) (see thorium section in OIR Part 3, ICRP, 2016). The rapidly-dissolved fraction, f_r, was allowed to vary. A good fit to the data was obtained (Fig. 20.1) with f_r = 0.5. For water soluble forms of thorium, a central value for f_r of 0.1 was adopted. However, following administration by intratracheal instillation into rats of ^{224}Th citrate (Thomas et al, 1963), ~50% ILD was absorbed rapidly from the lungs when administered at "tracer level", and ~10% when administered with carrier (^{228}Th). Zalikin (1966) did not report the mass administered nor whether any carrier was added. However, the longest-lived isotope of protactinium (^{231}Pa) has a half-life of only 3.3 x 10^4 years, and so even if any were added, it seems likely that the total mass would still be at tracer level. Thus the only experimental data are consistent with the assumption that absorption from the respiratory tract is similar to that of thorium.



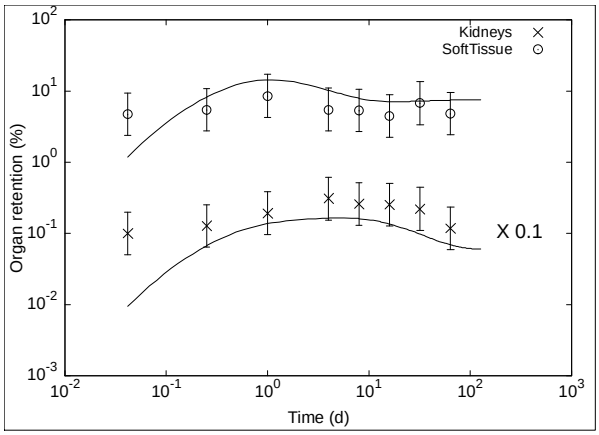


Fig. 20.1 Tissue distribution of ^{233}Pa in rats following intratracheal instillation of ^{233}Pa citrate (Zalikin, 1966b, mean with lognormal errors), and derived from the models described here. (Data and curve for kidneys have been rescaled by 0.1 to make the figure more readable.)

Protactinium oxide

(590) Newton (1968) followed lung retention of ^{231}Pa (and its progeny radionuclide ^{227}Ac) after accidental inhalation by a research student, by external measurement of X- and gamma-rays from ^{231}Pa (and the radioactive progeny of ^{227}Ac: ^{227}Th and ^{223}Ra). For the decay scheme see Fig. A.7. in OIR Part 1 (ICRP, 2015) or Fig. 15-2 in the uranium section of OIR Part 3 (ICRP, 2016). The contamination consisted of recently separated ^{231}Pa, probably in the form of Pa_2O_5 or $KPaO_3$. Analysis of air and surface contamination showed that the ^{231}Pa was accompanied by large amounts of its progeny; the ^{227}Ac: ^{231}Pa ratio was ~0.08. Autoradiography of an air filter indicated that the largest particle sizes involved were in the range 3–5 µm. Whole-body and/or chest measurements were made from 7 to 883 d after intake. The activity was concentrated in the chest, from which little clearance was observed. Over the period 7 to 427 days, lung retention could be fit by a single exponential function with a biological half-life for ^{231}Pa of 1000 ± 300 d. (The biological half-life of ^{227}Ac was estimated to be ~350 d). Several 24-hour collections of urine and faeces voided during the first few weeks (but not before day 7) were analysed: no ^{231}Pa, or its progeny attributable to the intake were detected. Analysis here showed that the experimental data are consistent with the assumption that absorption from the respiratory tract is similar to that of Type S forms of thorium. However, the very slow clearance from the chest indicates a lower particle transport rate from the alveolar to the bronchiolar region than the central value assumed in the HRTM (ICRP 2015): 8 x 10^{-4} d^{-1}, consistent with a chest biological half-time for ^{231}Pa of 1000 ± 300 d.

Protactinium progeny formed in the respiratory tract

(591) The general approach to treatment of radioactive progeny formed in the respiratory tract is described in OIR Part 1, Section 3.2.3 and Annex A (ICRP, 2015). In summary, it is expected that generally the rate at which a particle dissociates is determined by its matrix, and hence the physico-chemical form of the inhaled material. It is recognised that nuclei formed by alpha decay within a particle matrix may be expelled from it into the surrounding medium by recoil, but to implement this routinely would add greatly to the complexity of calculations. It is expected that the behaviour of soluble (e.g. Type F) material in the respiratory tract would

depend on its elemental form, i.e. that of the progeny radionuclide. Nevertheless, for simplicity, in this series of documents the absorption parameter values of the parent are, by default, applied to all members of the decay chain formed in the respiratory tract. Exceptions are made for noble gases formed as progeny radionuclides, which are assumed to escape from the body directly, in addition to other routes of removal. For calculation purposes it is assumed that radon formed as a progeny radionuclidewithin the respiratory tract escapes from the body at a rate of 100 d^{-1}, in addition to other routes of removal. [For further information see OIR Part 1, Section 3.2.3 and Annex A (ICRP, 2015), and the section on thorium progeny formed in the respiratory tract in OIR Part 3 (ICRP, 2016)].

(592) Studies specifically comparing the behaviour of protactinium with that of its radioactive progeny (actinium, thorium and radium isotopes) are summarised here. For further information, see the thorium and radium inhalation sections in OIR Part 3 (ICRP, 2016).

(593) As described above, Newton (1968) followed lung retention of ^{231}Pa (and ^{227}Ac) after accidental inhalation in a relatively insoluble form, by external measurement of X- and gamma-rays from ^{231}Pa and the radioactive progeny of ^{227}Ac: ^{227}Th and ^{223}Ra. However, much of the ^{227}Ac was inhaled with the ^{231}Pa, rather than formed as a progeny radionuclide within the lungs. The estimated biological half-life of ^{227}Ac in the lungs was shorter than that of ^{231}Pa, suggesting that it cleared more rapidly. In contrast, no significant difference was found between the levels of ^{227}Th and ^{223}Ra in the chest, indicating that they were in equilibrium, with no significant preferential clearance of the ^{223}Ra progeny.

Rapid dissolution rate for protactinium

(594) By analogy with thorium, a value of 50 d^{-1} is applied here to all Type F forms of protactinium. However, as noted in the thorium inhalation section (ICRP, 2016), the results of studies of water-soluble forms of thorium (chloride, citrate, nitrate, sulphate) deposited in the lungs, indicate that there are no commonly encountered Type F forms of thorium.

Extent of binding of protactinium to the respiratory tract

(595) By analogy with thorium, it is assumed that for protactinium the bound state can be neglected, i.e. $f_b = 0.0$.

Table 20.2. Absorption parameter values for inhaled and ingested protactinium (based on thorium, ICRP, 2015).

	Absorption parameter values[a]			Absorption from the alimentary tract, f_A[b]
Inhaled particulate materials	f_r	s_r (d^{-1})	s_s (d^{-1})	
Specific parameter values[c]				
Water soluble forms, including chloride, citrate, fluoride, nitrate and sulphate[d]	0.1	50	0.005	5×10^{-5}
Default parameter values[e]				
Absorption Type / Assigned forms				
F — NB: Type F should not be assumed without	1	50	-	5×10^{-4}

	evidence				
M[f]	Hydroxide	0.2	3	0.005	1×10^{-4}
S[f,g]	Oxide	0.01	3	1×10^{-4}	5×10^{-6}
Ingested material[h]					
All forms					5×10^{-4}

[a] It is assumed that for protactinium the bound state can be neglected, i.e. $f_b = 0.0$. The value of s_r for Type F forms of protactinium (50 d^{-1}) is element-specific. The values for Types M and S (3 d^{-1}) are the general default values.

[b] For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: i.e. the (rounded) product of f_A for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of protactinium (5×10^{-4}).

[c] See text (above and for thorium in ICRP, 2016) for summary of information on which parameter values are based, and on ranges of parameter values observed for individual materials. For water soluble forms of protactinium specific parameter values are used for dissolution in the lungs, but the default value of f_A.

[d] Decay products assigned to Type F.

[e] Materials (e.g. hydroxide) are listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

[f] Decay products assigned to Type M.

[g] Default Type S is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

[h] Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A ($=5 \times 10^{-4}$) for ingestion of the radionuclide.

20.2.2. Ingestion

(596) Early studies by Hamilton (1948) and by Zalikin (1966a,b, 1969) indicated that fractional absorption of citrate and other unspecified forms of protactinium in rats is about 1×10^{-3} or less. Later studies by Harrison and Stather (1981) estimated intestinal absorption of protactinium after intragastric administration and intravenous injection in adult hamsters. The values obtained were 0.039 and 2.2×10^{-3} for ^{231}Pa-citrate and ^{231}Pa-fluoride, respectively. Sullivan (1983) reported absorption of 3×10^{-4} for nitrate forms in adult males and females rats.

(597) In *Publication 30* Part 3 (ICRP, 1981) and *Publication 48* (1986) an absorption value of 1×10^{-3} for protactinium was used. However, in this report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all actinides other than U.

(598) An f_A value of 5×10^{-4} is adopted here for all chemical forms of protactinium.

20.2.3. Systemic distribution, retention and excretion of protactinium

20.2.3.1. Data

(599) Newton and Brown (1974) studied the behavior of ^{231}Pa and ^{227}Ac in an adult male over a 9-y period following their internal deposition via a puncture wound. The investigators estimated on the basis of external measurements and analysis of activity in excreta that 70-80% of the ^{231}Pa that reached blood was retained with a half-life in the range 70-125 y. After 3 y total-body activity was contained mainly in bone, with lower accumulation in the liver. After 9 y the body burden was almost completely contained in the skeleton.

(600) At 24 h after intravenous administration of ^{233}Pa in citrate buffer to baboons, the skeleton contained about half of the injected amount (Ralston et al., 1986). About 6% of the injected activity was excreted in urine during the first 24 h. By 21 days, when the slowly clearing plasma activity had been reduced to about 2% of the injected, the skeleton and soft tissues contained about 65% and 13%, respectively, of the injected amount. Cumulative urinary and faecal excretion of ^{233}Pa during the first 21 d amount to about 15% and 3%, respectively, of the injected amount.

(601) Following intravenous administration of protactinium to rats, ~99% of injected activity was removed from plasma compartment in 3 d. Plasma clearance was comparable to that of plutonium and much slower than that of neptunium, americium, or curium. At 1-7 d the skeleton contained70-80% and the liver contained 2-3% of the injected amount. The high deposition in the skeleton and low uptake by liver following systemic uptake in rats closely resembled the distribution of thorium (Lanz et al., 1946; Schuppler et al., 1988; Durbin, 2011).

(602) Zalikin (1969) investigated the accumulation of ^{233}Pa in tissues of rats during its chronic oral administration. The absorbed activity accumulated primarily in the skeleton. After 150 d of chronic intake the skeleton contained about 10 times as much activity as the liver and about 16 times as much activity as the kidneys.

20.2.3.2. Biokinetic model

(603) The biokinetic model for systemic protactinium applied in this report is described in Section 18.2.3.

20.2.3.3. Treatment of progeny

(604) The treatment of radioactive progeny of protactinium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in section 18.2.4.

20.3. Individual monitoring

^{231}Pa

(605) *In vivo* lung measurements of ^{231}Pa are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{231}Pa concentrations in urine and faeces may be used to determine intakes of the radionuclide. *In vivo* whole body measurement may be used as an additional technique for special investigations. The main technique is gamma spectrometry.

Table 20.2. Monitoring techniques for ^{231}Pa.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{231}Pa	Urine Bioassay	γ-ray spectrometry	34 Bq/L
^{231}Pa	Faecal Bioassay	γ-ray spectrometry	34 Bq/24h
^{231}Pa	Lung Measurement[a]	γ-ray spectrometry	46 Bq
^{231}Pa	Whole-body Measurement[b]	γ-ray spectrometry	600 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

^{233}Pa

(606) *In vivo* lung measurements of ^{233}Pa are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{231}Pa concentrations in urine and faeces may be used to determine intakes of the radionuclide. I*n vivo* skeleton measurement (knee geometry) and whole body measurement may be used as additional bioassay techniques for special investigations. The main technique is gamma spectrometry.

Table 20.3. Monitoring techniques for ^{233}Pa.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{233}Pa	Urine Bioassay	γ-ray spectrometry	7 Bq/L
^{233}Pa	Faecal Bioassay	γ-ray spectrometry	7 Bq/24h
^{233}Pa	Lung Measurement[a]	γ-ray spectrometry	20 Bq
^{233}Pa	Whole Body Measurement	γ-ray spectrometry	160 Bq
^{233}Pa	Skeleton Measurement (knee)[c]	γ-ray spectrometry	1 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.
c Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes.

20.4. Dosimetric data for protactinium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Durbin, P. W., 2011. Actinides in animals and man. Chapter 31 in: The chemistry of the actinide and transactinide elements, 4th edition, Vol. 5, Morss, L. R., Edelstein, N. M., Fuger, J., Katz, J. J. (Eds.) Springer, 3339–3474.

Hamilton, J. G., 1948. The metabolic properties of the fission products and actinide elements. Rev. Mod. Phys. 20, 718–728.

Harrison, J.D., Stather J.W., 1981. The gastrointestinal absorption of protactinium, uranium and neptunium in the hamster. Radiat. Res. 88, 47–55.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1986. Transfer of environmental plutonium and americium across the human gut. Sci. Total Environ. 53, 89–109.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1989. Transfer of environmental plutonium and

americium across the human gut. Radiol. Prot. Bull. 106, 7-11.
Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1990. Transfer of environmental plutonium and americium across the human gut: A second study. Sci. Total Environ. 90, 273–282.
ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6(2/3).
ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).
ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).
ICRP 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. ICRP Supporting Guidance 3. Ann. ICRP 32(1/2). Pergamon Press, Oxford.
ICRP, 2006. Human alimentary tract model for radiological protection. ICRP Publication 100. Ann. ICRP 36(1-2).
ICRP 2015. Occupational intakes of radionuclides: Part 1. ICRP Publication 130. Ann. ICRP 44(2).
ICRP 2016. Occupational intakes of radionuclides: Part 3. Ann. ICRP...
Lanz, H., Scott, K. G., Crowley, J., Hamilton, J. G., 1946. The metabolism of thorium, protactinium, and neptunium in the Rat, USAEC MDDC-648 (CH-3606).
Newton, D., 1968. A case of accidental inhalation of protactinium-231 and actinium-227. Health Phys. 15, 11–17.
Newton, D., Brown, D. A., 1974, The long term retention of systemic protactinium 231 and actinium 227, Health Phys. 27, 459–467.
Popplewell, D. S., Ham, G. J., 1989. Distribution of plutonium and americium in tissues from a human autopsy case. J. Radiol. Prot. 9, 159–164.
Popplewell, D. S., Harrison, J. D., Ham, G. J., 1991. The gastrointestinal absorption of neptunium and curium in humans. Health Phys. 60, 797–805.
Ralston, L. G., Cohen, N., Bhattacharyya, M. H., et al., 1986. The metabolism and gastrointestinal absorption of neptunium and protactinium in adult baboons. In: Bulman, R. A.; Cooper, J. R., eds. Speciation of fission and activation products in the environment. London: Elsevier Applied Science Publishers.
Schuppler, U., Planas-Bohne, F., Taylor, D. M., 1988. Biochemical binding and distribution of protactinium-233 in the rat. Int. J. Radiat. Biol. 53, 457–66.
Thomas, R.G., Lie, R., Scott, J.K., 1963. Thorium distribution and excretion studies I. Patterns following parenteral administration. Health Phys. 9, 153–163.
Zalikin, G. A., 1966a. Distribution of ^{233}Pa in the organism of the rat. In: Raspredelenie i biologicheskoe deistvie radioaktivnykh izotopov, 30–36 (e-d. Moskalev, Yu. I.). Moscow. Translated in Distribution and biological effects of radioactive isotopes AEC-tr-6944 (Rev.), 35–43.
Zalikin, G. A., 1966b. The distribution of ^{233}Pa in the organism of rats in endotracheal, subcutaneous and peroral introduction. Med. Radiol. 11, 67–70.
Zalikin. G. A., 1969. On the distribution of protactinium-233 in the body of rats. In: Moskalev, Yu. I., ed. Radioaktivnye izotopy I organizm. Translated in Radioactive isotopes and the body. AEC-tr-7195, 136–146.

21. NEPTUNIUM (Z=93)

21.1. Chemical Forms in the Workplace

(607) Neptunium is an actinide element which occurs mainly in oxidation states IV, V and VI. Neptunium may be encountered in industry in a variety of chemical and physical forms, including oxides (NpO_2, Np_3O_8), nitrates, chlorides, fluorides, oxalates and carbonates. Less common forms such as bromides, iodides, sulphides or nitrides are also encountered in some specific situations.

(608) Neptunium-237, the most stable isotope of neptunium, is a by-product of nuclear reactors and plutonium production and it can be used as a component in neutron detection equipment.

Table 21.1. Isotopes of neptunium addressed in this report.

Isotopes	Physical half-life	Decay mode
Np-232	14.7 m	EC, B+
Np-233	36.2 m	EC, A
Np-234	4.4 d	EC, B+
Np-235	396.1 d	EC, A
Np-236	1.54E+5 y	EC, B-, A
Np-236m	22.5 h	EC, B-
Np-237[a]	2.144E+6 y	A
Np-238	2.117 d	B-
Np-239[a]	2.356 d	B-
Np-240	61.9 m	B-
Np-241	13.9 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

21.2. Routes of Intake

21.2.1. Inhalation

Absorption Types and parameter values

(609) No studies were found in the literature relating to lung retention of neptunium (Np) in man following accidental intakes other than environmental exposure to nuclear weapons fallout. Information on absorption from the respiratory tract is available from experimental studies with neptunium in several chemical forms including nitrate and oxide. Nearly all *in vivo* studies were carried out in rats. In most cases tissue distribution, but not excretion, data were reported, which limits the ability to derive absorption parameter values. Thompson (1982) reviewed the literature available at that time.

(610) Absorption parameter values and Types, and associated f_A values for particulate forms of neptunium are given in

(611) Table 21.**2**. Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values:

- For rats: the rat model for particle transport in the respiratory tract of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002) and information relating to the study (e.g. early excretion) for deposition in the respiratory tract; a simplified version of the Gastro-Intestinal Tract Model (ICRP, 1979) with a single large intestine compartment; the Np systemic model for man (ICRP, 1993) was simplified and calibrated using rat data from Stradling et al. (2000) and Lyubchanskiy and Levdik (1972).

(612) Rates for the lung, gut or systemic models were also modified when the fit with "default" values was not considered sufficiently good. In the studies of relatively insoluble forms of neptunium (oxide and contaminated dust) analysed here, s_r was not well defined: its value was assumed to be 3 d^{-1}, the general default value for Type M and S materials. No information was found that enabled bound state parameter values for neptunium to be estimated. In analyses carried out here to estimate values of the dissolution parameters (f_r, s_r and s_s) it was assumed that the bound state could be neglected, i.e. the bound fraction $f_b = 0.0$.

Neptunium nitrate ($Np(NO_3)_x$)

(613) According to Thompson (1982) several publications in the Russian literature appear to refer to a single series of experiments involving intratracheal administration to rats of ^{237}Np(V, VI) nitrate and of ^{237}Np(IV) oxalate (e.g. Levdik et al. 1972a,b). None report data on the kinetics of neptunium retention in, or absorption from, the lungs, but Thompson inferred from calculated doses a biological retention half-time in the lungs (T_b) of 100 – 200 d for both compounds, indicating Type M behaviour. Details were, however, reported of the distribution of neptunium within the lungs from autoradiographic studies. The results indicate that lung retention was mainly in particulate form rather than bound (see section on bound state below).

(614) Lyubchanskiy and Levdik (1972) followed the tissue distribution of ^{237}Np up to 512 d after inhalation of ^{237}Np(V,VI) nitrate (and oxalate, see below) by rats. There was considerable rapid absorption (more than for the oxalate): at the first measurement (0.25 d) ~70% of the initial lung deposit (ILD) had deposited in the systemic tissues, mostly in the skeleton. Lung clearance was relatively slow thereafter: retention falling to ~13% ILD at 32 d and ~1% ILD at 512 d. Analysis carried out here showed that the results could be fit with absorption parameter values as follows: f_r was well defined at ~0.7, s_r was not well defined, but >10 d^{-1}; and s_s was not well defined but <0.002 d^{-1}.

(615) Sullivan et al. (1986) followed the tissue distribution of ^{237}Np up to 750 d after inhalation of ^{237}Np nitrate by rats, at three exposure levels: High, Medium and Low, with inhaled masses of about 0.5, 0.25 and 0.17 mg ^{237}Np respectively per rat. The authors fit lung retention by a three-component exponential function: with T_b = 1 d (~78% ILD); 35 d (~21% ILD) and roughly 10,000 d (0.8% ILD). There was some rapid absorption: ~3% ILD was found in the skeleton immediately after exposure and ~15% ILD at 4 d. Analysis carried out here showed that the results for all three groups could be fit with absorption parameter values as follows: f_r was well defined at ~0.6, s_r was fairly well defined, at ~10 d^{-1}; and s_s was not well defined but <0.01 d^{-1}.

(616) Stradling et al. (2000) followed the biokinetics of ^{237}Np for 180 d after instillation of Np nitrate into rats. Analysis carried out here showed that the results could be fit with absorption parameter values as follows: f_r was well defined at ~0.8, s_r was not well defined, but >10 d^{-1}; and s_s was not well defined but <0.005 d^{-1}.

(617) The results for neptunium nitrate, coming from three independent studies, are more comprehensive than for any other relatively soluble form of neptunium. They are consistent in giving values of f_r of about 0.7. They are also consistent in giving relatively high values of s_r, of the order 10 d^{-1}; and moderate (if uncertain) values of s_s, of the order 0.001 – 0.01 d^{-1}. These results are therefore used as the basis for assigning the default rapid dissolution rate for neptunium (see below). Inhalation exposure to neptunium nitrate is not unlikely. The results are consistent with assignment to Type M, but the values assessed for f_r and s_r are very different from the Type M default values. Specific parameter values of $f_r = 0.7$, $s_r = 30$ d^{-1} and $s_s = 0.005$ d^{-1} are used here for neptunium nitrate.

Neptunium oxalate ($Np(C_2O_4)_2$))

(618) Lyubchanskiy and Levdik (1972) followed the tissue distribution of ^{237}Np up to 650 d after inhalation of $^{237}Np(IV)$ oxalate (and nitrate, see above) by rats. There was some rapid absorption, but less than for the nitrate: at the first measurement (0.25 d) ~20% ILD had deposited in the systemic tissues, mostly in the skeleton. Lung clearance was relatively slow thereafter: retention falling to ~30% ILD at 32 d and ~1% ILD at 650 d. Analysis carried out here showed that the results could be fit with absorption parameter values which were reasonably well defined as follows: f_r ~0.8, s_r ~2 d^{-1}; and s_s ~0.0015 d^{-1}. These results are consistent with assignment to Type M. Although absorption parameter values for neptunium oxalate based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for neptunium oxalate are not used here. Instead, it is assigned to Type M.

Neptunium citrate

(619) Moskalev et al. (1972) followed the biokinetics of ^{237}Np for 32 d after intratracheal instillation into rats. There was some rapid absorption: at the first measurement (1 d) ~9% ILD had deposited in the skeleton. Absorption continued slowly: at 32 d ~59% ILD remained in the lungs, with ~25% in the skeleton. The authors fit lung retention by a two-component exponential function: 31% with T_b = 4 d; and 69% with T_b = 133 d. A complementary intravenous (IV) injection experiment was carried out. The authors noted that following deposition in the lungs, most systemic deposition was in the skeleton, whereas after IV injection, most was deposited in the liver and spleen. This was attributed to colloid formation after IV injection. Analysis carried out here gave only broad estimates of absorption parameter values. With s_s fixed at 0.005 d^{-1}, f_r was estimated at ~0.2, and s_r was not well defined, but > 1 d^{-1}. These results give assignment to Type M.

Neptunium oxide (NpO_2)

(620) Lizon et al. (1996) reported preliminary results (tissue distribution up to 92 d) of a study of the behaviour of ^{237}Np in rats that inhaled $^{237}NpO_2$. Results were presented as fractions of initial deep lung deposit (IDLD) based on the lung content at the first measurement, 7 d. Average IDLDs were ~0.1 and 0.2 kBq in the two groups studied. Lung retention from 7 to 92 d was fit by a single exponential function with T_b = 68 d. The skeleton contained ~1% IDLD with little change from 7 to 92 d: liver and kidneys contained smaller amounts. In analyses carried out here for this, and other studies on neptunium oxide, s_r was not well defined: its value was assumed to be 3 d^{-1}, the general default value for Type M and S materials. Analysis carried out

here showed that the results could be fit with absorption parameter values as follows: f_r was well defined at 0.012; and s_s was well defined at 3 x 10^{-4} d^{-1}. These results give assignment to Type S.

(621) Guezingar et al. (1998) investigated the particle distribution in the lungs following inhalation of $^{237}NpO_2$ by rats, with average IDLD of 4.4 kBq. Lung retention was followed in each rat by external x-ray spectrometry. The authors fit lung retention from 7 to 500 d by a two-component exponential function: 60% with T_b = 65 d and the rest with T_b = 467 d. These results indicate Type S behaviour: there was insufficient information to estimate absorption parameter values. The high IDLD may well have resulted in impaired lung clearance by particle transport, as observed by Dudoignon et al. (1999, 2001) at similar exposure levels.

(622) Dudoignon et al. (1999, 2001) investigated lung carcinogenesis in rats following inhalation of $^{237}NpO_2$ by rats, with average IDLD ranging from 0.1 to 7 kBq. Lung retention was followed in each rat by external x-ray spectrometry. The authors fit lung retention from 7 to ~500 d by a two-component exponential function. For an IDLD of 0.2 kBq (the lowest exposure level), ~70% IDLD was retained with T_b ~30 d and the rest with T_b ~200 d. The half-time of the long-term retention phase increased with increasing IDLD. These results indicate Type S behaviour.

(623) Ramounet et al. (2000) followed the lung retention and tissue distribution of ^{237}Np in rats following inhalation of two industrial $^{237}NpO_2$ dusts: in one group (IDLD 0.9 kBq) to 365 d, and in the other (IDLD 5.8 kBq) to 90 d. The authors fit lung retention by a two-component exponential function. For both groups, ~80% IDLD was retained with T_b ~30 d and the rest with T_b ~200 d. The authors noted that this was similar to reported retention of insoluble non-toxic particles in rats. Most of the transfer to blood occurred in the first week after inhalation, estimated to be ~0.4% and ~0.8% IDLD for the first and second groups respectively. Assuming a value of s_r = 100 d^{-1}, the authors estimated values of f_r = 0.001 and 0.002 respectively, and a value of s_s = 1x10^{-5} d^{-1} for both groups. Analysis carried out here (assuming a value of s_r = 3 d^{-1}) showed that the results could be fit with absorption parameter values as follows: for both exposure levels f_r was well defined at 0.003 and 0.006 respectively; only an upper limit for s_s was well defined at ~1 x 10^{-4} d^{-1} for both exposure levels. All these results give assignment to Type S.

(624) Stradling et al. (2000) and Bailey et al. (1999) reported measurements of the lung retention and tissue distribution of ^{237}Np to at least 140 d after inhalation of $^{237}NpO_2$ by rats, with average IDLD ranging from 0.1 to 4 kBq. About 2% ILD was absorbed in the first few days, and little thereafter. Analysis carried out here (assuming a value of s_r = 3 d^{-1}) showed that the results could be fit with absorption parameter values as follows: f_r was well defined at 0.04; but s_s was not well defined at ~4 x 10^{-4} d^{-1} (<0.002 d^{-1}). These results indicate Type S behaviour. Two *in vitro* tests were conducted on the same materials. In one, using a lung fluid simulant, 0.05–0.2% dissolved in 180 d, with ~30% of total dissolution in the first 7 d. In the other, using Gamble's solution, 0.05–0.2% dissolved in 180 d. These results give assignment to Type S.

(625) Although absorption parameter values for NpO_2 based on in-vivo data were derived, they were not well defined: NpO_2 is therefore assigned to Type S.

Neptunium in contaminated dust

(626) Bair and Case (1961) followed the biokinetics of ^{237}Np for 30 d following inhalation by rats of an industrial material containing ^{237}Np. Summaries were reported by Ballou et al.

(1962), who also conducted complementary intravenous injection and gavage experiments, and by Bair et al. (1963). Because of the low specific activity, a large mass of dust (10 mg) was inhaled, containing 60% aluminium, 20% iron and 16% uranium. Lung retention of ^{237}Np was about 7% and 2% ILD, at 1 d and 3 weeks, respectively, after inhalation. About 4% ILD was transported to systemic tissues or excreted in urine. The authors noted that the biokinetics might be affected by the large mass and possible chemical toxicity of the dust inhaled. Analysis carried out here (assuming a value of s_r = 3 d^{-1}) showed that the results could be fit with absorption parameter values as follows: f_r was not well defined, but no more than a few percent; s_s was well defined at ~0.04 d^{-1}. The results indicate Type M behaviour.

Nuclear weapons fallout

(627) Erfurd et al. (1986) measured concentrations of ^{237}Np and ^{239}Pu in lung and liver samples from individuals with no known occupational exposure to any actinide element. The average ^{237}Np/^{239}Pu atom ratio was measured was 0.04, considerably lower than that in global fallout (~0.7). The authors concluded that the ratios measured in the tissues suggest that Np has been lost preferentially to Pu in the lung, and that the Np lost from the lungs was not concentrated in the liver. Overall this indicates Type M or S behaviour.

Rapid dissolution rate for neptunium

(628) As described above, the results of studies with neptunium nitrate are considered to provide the best basis for assigning the default rapid dissolution rate for neptunium. The results of one study gave a value for s_r of ~10 d^{-1}; those of the other two gave 10 d^{-1} as a lower limit. As these estimates are close to the general default value of 30 d^{-1}, this value is adopted here for all Type F forms of neptunium.

Extent of binding of neptunium to the respiratory tract

(629) According to Thompson (1982), Levdik et al. (1972b) reported details of the microdistribution of neptunium within the lungs from autoradiographic studies involving intratracheal administration to rats of ^{237}Np(V, VI) nitrate and of ^{237}Np(IV) oxalate. At early times, the nitrate showed a more diffuse distribution than the oxalate, but after 7 d both forms appeared mainly as aggregates associated with macrophages of the alveolar septum, with desquamated cells of the alveolar and bronchial lumen, and less frequently in the bronchial epithelium. By 7 d after nitrate and 30 d after oxalate administration, accumulation of neptunium was noted along peribronchial and perivascular spaces, which was interpreted as being associated with elimination from the lung. From 6 to 12 months after administration accumulation was noted in reticular sinus cells and regional lymph nodes. This description indicates that lung retention was mainly in particulate form rather than bound. The data are insufficient to estimate the extent of any bound state. Although it is not clear that the bound state for neptunium is negligible, it is assumed by default that f_b = 0.

Table 21.2. Absorption parameter values for inhaled and ingested neptunium.

Inhaled particulate materials	Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A[b]
Specific parameter values[c]				
Neptunium nitrate	0.7	30	0.005	3.5×10^{-4}
Default parameter values[d]				
Absorption Type / Assigned forms				
F —	1	30		5×10^{-4}
M[d] Neptunium citrate, oxalate	0.2	3	0.005	1×10^{-4}
S Neptunium dioxide	0.01	3	1×10^{-4}	5×10^{-6}
Ingested materials[f]				
All chemical forms				5×10^{-4}

a It is assumed that for neptunium the bound state can be neglected, i.e., $f_b = 0.0$. The value of s_r for Type F forms of neptunium (30 d^{-1}) is element-specific (although numerically equal to the general default value). The values for Types M and S (3 d^{-1}) are the general default values.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the (rounded) product of f_r for the absorption Type and the f_A value for ingested soluble forms of neptunium (5×10^{-4}).

c See text for summary of information on which parameter values are based, and on ranges of parameter values observed in different studies. For neptunium nitrate, specific parameter values are used for dissolution in the lungs, but a default value of f_A (footnote b).

d Materials (e.g. neptunium citrate) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

e Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

f Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction fA for the secreted activity is the reference fA (=5x10-4) for ingestion of the radionuclide.

21.2.2. Ingestion

(630) The gastrointestinal absorption of neptunium is influenced by its initial chemical form (nitrate, citrate, bicarbonate…), mass and oxidation state (IV, V or VI) (ICRP, 2006).

(631) Popplewell et al. (1991) measured the absorption of ^{239}Np in five adult male volunteers by comparing urinary excretion after oral and intravenous administration as citrate; The mean f_1 value obtained was 2×10^{-4} for Np with a range of 10^{-4} to 3×10^{-4}.

(632) Animal data on the absorption of Np have been reviewed in Harrison (1991) and *Publication 100* (ICRP, 2006).

(633) The first measurements of Np absorption involved administration of mg quantities of ^{237}Np to rats and f_1 values of about 1×10^{-2} were obtained (Ballou et al., 1962; Sullivan and Crosby, 1975, 1976). Subsequent experiments established that absorption at lower concentrations in a number of animal species was an order of magnitude or more lower. Métivier et al. (1983, 1986) observed that absorption was about 10^{-3} in baboons given 15-66 ng

^{239}Np as the nitrate and about 1 x 10^{-2} at a dose of 40-100 µg ^{237}Np. Harrison et al. (1984) reported in rats values of 3 x 10^{-3} for a 500 µg dose of ^{237}Np as the nitrate and 3 x 10^{-4} for 0.5 ng of ^{239}Np. Ham et al. (1994) reported a f_1 value of 2 x 10^{-3} after administration to primates (C. jacchus) of 13 µg ^{237}Np(V)-citrate by gastric intubation.

(634) In *Publication 30* (ICRP, 1980), absorption was taken to be 1 x 10^{-2} based on measurements on rats given high masses of ^{237}Np. In *Publication 48* (ICRP, 1986), the effect of mass was discussed and a general value for actinides of 10^{-3} was applied to Np. This value was also adopted in *Publication 56* (ICRP, 1989). However, in this report available data provided a sufficient basis for the use of a general value of 5 x 10^{-4} for all actinides other than U.

(635) An f_A value of 5 x 10^{-4} is adopted here for all chemical forms of Np.

21.2.3. Systemic distribution, retention and excretion of neptunium

21.2.3.1. Data

(636) The rate of urinary excretion of ^{239}Np was determined in five healthy adult male human subjects over 9-10 days following intravenous injection of this radionuclide in citrate solution (Popplewell et al., 1991). Cumulative urinary excretion during this period accounted for 23–42% of administered ^{237}Np. This is a considerably higher rate of urinary excretion than has been estimated for most other actinide elements in human subjects or laboratory animals.

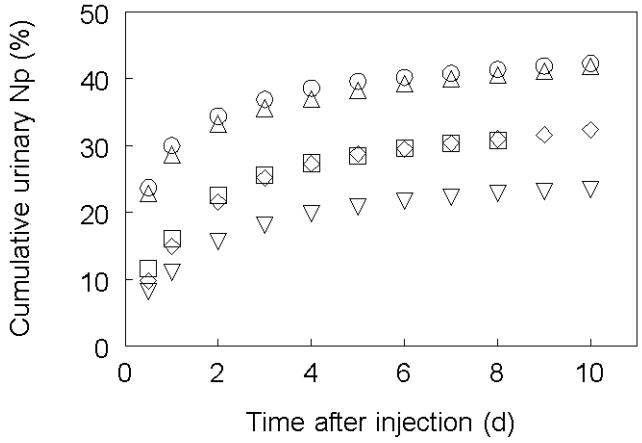


Fig. 21.1. Cumulative urinary excretion of ^{239}Np by five healthy adult male humans following intravenous injection with ^{239}Np citrate (data of Popplewell et al., 1991).

(637) The systemic biokinetics of neptunium has been studied in a variety of laboratory animals including baboons (Cohen, 1987; Ralston et al., 1986), monkeys (Durbin et al., 1986, 1989), tamarins (Cohen, 1987), swine (Sullivan and Gorham, 1982), rabbits (Buldakov et al., 1972), and rodents (Ballou et al., 1962; Moskalev et al., 1972; Lyubchanskii and Levdik, 1972; Morin et al., 1973; Volf and Wirth, 1986; Paquet et al., 1996, 2000; Ramounet et al., 1998; Sontag et al., 1997). Collective data from animal studies indicate the following typical initial distribution of neptunium in adults: about half of absorbed or injected neptunium is deposited in

the skeleton, 10% or less is deposited in the liver, about 5% is deposited in kidneys and other soft tissues, a small percentage is excreted in feces, and the remainder is rapidly excreted in urine.

(638) The externally viewed removal half-time of neptunium from the liver is no more than a few weeks in mice and rats and a few months in non-human primates (Cohen, 1987; Durbin 1989), but these animals generally lose actinides from the liver at a much greater rate than do humans. Data for rabbits injected subcutaneously with neptunium (Buldakov et al., 1972) are consistent with a rate of loss from liver to blood on the order of 0.5–1.0 y^{-1}. Comparative environmental and human autopsy data for ^{237}Np and ^{239}Pu (Efurd et al., 1984, 1986) are consistent with the assumption that neptunium is removed at a faster rate than plutonium from the human liver.

(639) The behavior of neptunium in the skeleton appears to be similar to that of other studied actinide elements, excluding uranium. Neptunium is deposited on bone surfaces, and formation of aggregates in bone marrow following bone remodeling is evident (Nenot et al., 1972; NCRP, 1988). The division between trabecular and cortical portions of the skeleton is closer to that of americium and alkaline earth elements than that of plutonium. Similarities between the gross skeletal distribution of neptunium and alkaline earth elements have been noted, particularly in the osteogenic part of bone (Nenot et al., 1972; Durbin et al., 1986).

21.2.3.2. Biokinetic model

(640) The biokinetic model for systemic neptunium applied in this report is described in Section 18.2.3.

21.2.3.3. Treatment of progeny

(641) The treatment of radioactive progeny of neptunium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

21.3. Individual monitoring

^{237}Np

(642) Measurements of ^{237}Np concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main techniques used for *in vitro* bioassay are alpha spectrometry and ICP-MS. The decay product ^{233}Pa grows into equilibrium with ^{237}Np within several tens of days and transforms into ^{233}U, as alpha-emitter with a long half-life. ^{233}Pa can be measured more easily than ^{237}Np and can serve as an indicator of contamination with ^{237}Np. *In vivo* lung measurements of ^{237}Np may be used to determine intakes of the radionuclide for routine monitoring. Whole body measurement may be used as an additional technique for special investigations. The main technique for *in vivo* measurements is gamma spectrometry.

Table 21.3. Monitoring techniques for ^{237}Np.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{237}Np	Urine Bioassay	α spectrometry	0.6 mBq/L	0.1 mBq/L
^{237}Np	Urine Bioassay	ICP-MS[a]	1.0×10^{-12} g/L	4.0×10^{-15} g/L
^{237}Np	Faecal Bioassay	α spectrometry	1 mBq/24h	1 mBq/24h
^{237}Np	Lung Measurement[b]	γ-ray spectrometry	25 Bq	13 Bq
^{237}Np	Whole Body Measurement[c]	γ-ray spectrometry	400 Bq	200 Bq

a Inductively Coupled Plasma Mass Spectrometry (ICP-MS),
b Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
c Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

^{239}Np

(643) *In vivo* lung measurements of ^{239}Np are used to determine intakes of the radionuclide for routine monitoring. Measurements of ^{237}Np concentrations in urine and faeces may be used to determine intakes of the radionuclide. Whole body measurement may be used as an additional technique for special investigations. The main technique is gamma spectrometry.

Table 21.4. Monitoring techniques for ^{239}Np.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{239}Np	Urine Bioassay	γ-ray spectrometry	18 Bq/L
^{239}Np	Faecal Bioassay	γ-ray spectrometry	18 Bq/24h
^{239}Np	Lung Measurement[a]	γ-ray spectrometry	10 Bq
^{239}Np	Whole Body Measurement[b]	γ-ray spectrometry	200 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe) and counting time of 15 minutes.

21.4. Dosimetric data for neptunium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Bailey, M. R., Etherington, G., Stradling, G. N. et al., 1999. Inhalation of radionuclides. Final report January 1996 - June 1999 of Contract F14PCT950026. NRPB-M1103, Chilton, National Radiological Protection Board.

Bair, W.J., and Case, A.C, 1961. Preliminary studies of inhaled dust containing neptunium-237. Hanford Laboratories Report HW-70949 (UC-48, Biology and Medicine).

Bair W.J., Tombropoulos E.G., Park J.F., 1963. Distribution and removal of transuranic elements and cerium deposited by the inhalation route. In: Diagnosis and treatment of radioactive poisoning: 319-344. (Vienna: IAEA) IAEA-SR-6/28.

Ballou, J.E., Bair, W.J., Case, A.C., Thompson, R.C., 1962. Studies with neptunium in the rat. Health Phys. 8, 685–688.

Buldakov, L. A., Nifatov, A. P., Filippova, L. G., Khalturin, G. V., 1972. Subcutaneous administration of transuranic elements (neptunium 237, plutonium 239, and americium 241). In: Biological effects of radiation from external and internal sources, ed. by Yu. I. Moskalev, V. S. Kalistratova. Moscow: Meditsina; 359–367.

Cohen, N., 1987. Radioactivity studies. Final Report. COO-3382-23. U.S. Department of Energy. DOE/EV/03382-T1.

Dudoignon, N., Guezingar-Liebard, F., Guillet, K., et al., 1999. Lung carcinogenesis in rats after inhalation exposure to (237)NpO2. Radiat. Res. 152, S31–S33.

Dudoignon, N., Guillet, K., Rateau, G., Fritsch, P., 2001. Survival, lung clearance, dosimetry and gross pathology of rats exposed to either NpO2 or PuO2 aerosols. Int. J. Radiat. Biol. 77, 979–990.

Durbin, P. W., Jeung, N., Bucher, J. J., 1986. Initial distribution of neptunium-237 in a monkey. In: Biology and medicine division annual report 1986, LBL-22300; Berkeley, CA: Lawrence Berkeley Laboratory, Univ. of California, 78–86.

Durbin, P. W., Schmidt, C. T., Jeung, N., 1989. Distribution and excretion of neptunium in an adult cynomolgus monkey two years after intramuscular injection of 237NpO2NO3. In: Thirty-fourth annual meeting of the Health Physics Society; Abstracts of papers presented at the meeting, June 25-29, 1989, Albuquerque, New Mexico, S59.

Efurd, D. W., Knobeloch, G. W., Perrin, R. E., Barr, D. W., 1984. An estimate of Np-237 production during atmospheric testing. Health Phys. 47, 786–787.

Efurd, D. W., Perrin, R. E., McInroy, J. F., 1986. Neptunium-237 in human tissue samples. Health Phys. 51, 665–666.

Guezingar, F., Dudoignon, N., Le Foll, L., et al., 1998. Evaluation of acitinide oxide distribution within rat lungs after inhalation exposure: preliminary results using solid track detector autoradiography. Radiat. Prot. Dosim. 79, 401–404.

Ham, J.G., Harrison, J.D., Popplewell, D.S., et al., 1994. The gastrointestinal of neptunium, plutonium and americium in a primate (C.jacchus). Sci. Total Environ. 145, 1–6.

Harrison, J.D., 1991. The gastrointestinal absorption of the actinide elements. Science Total Environ. 100, 43–60.

Harrison, J.D., Popplewell, D.S., David, A.J., 1984. The effect of concentration and chemical form on the gastrointestinal absorption of neptunium. Int. J. Radiat. Biol. 46, 269–277.

ICRP, 1979. Limits for intakes of radionuclides by workers, ICRP Publication 30, Part 1. Ann. ICRP 2(3/4).

ICRP, 1980. Limits on intakes of radionuclides for workers. ICRP Publication 30, Part 2. Ann. ICRP 4(3/4).

ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).

ICRP, 1989. Age-dependent doses to members of the public from intake of radionuclides. Part 1. ICRP Publication 56. Ann. ICRP 20(2).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides. Part 2. ICRP Publication 67. Ann. ICRP. 23(3/4).

ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. ICRP Supporting Guidance 3. Ann. ICRP 32(1/2).

ICRP, 2006. Human alimentary tract model for radiological protection. ICRP publication 100. Ann. ICRP 36(1/2).

ICRP, 2015. Occupational intakes of radionuclides. Part 1. ICRP Publication 130. Ann. ICRP 44(2)

Levdik, T.I., Lemberg, V.K., Lyubchanskii, E.R., 1972b. Dynamics of morphological changes and microdistribution of neptunium-237 in the rat following intratracheal administration of the isotope. In: Biological Effects of Radiation From External and Internal Sources (Ed. by Moskalev, Y.I., Kalistratova, V.S.), 229–239. Meditsina, Moscow. (Translated in US Atomic Energy Commission Document AEC-Tr-7457, 342–351.)

Levdik, T.I., Lemberg, V.K., Lyubchanskii, E.R., Buldakov, L. A., Pesternikov V. M., 1972a. Biological effectiveness of ^{237}Np. Health Phys. 22, 643–645.

Lizon, C., Massiot, P., Le Naour, H., et al., 1996. Biological behavior of ^{237}Np after inhalation of NpO_2 in the Rat: preliminary results. In: IRPA 9, Proceedings of the 9th International Congress of the International Radiation Protection Association, Vienna, Hofburg, Austria, 451–453.

Lyubchanskiy, E.R., Levdik, T.I., 1972. Neptunium 237 Metabolism after inhalation thereof. In: Biological Effects of Radiation From External and Internal Sources. Translation AEC-Tr-7457 (Ed. by Y.I.Moskalev & V.S.Kalistratova), 204-214. Moscow, Meditsina.

Metivier, H., Bourges, J., Fritsch, P., Nolibe, D., Masse, R., 1986. Gastrointestinal absorption of neptunium in primates: Effect of ingested mass, diet and fasting. Radiat. Res. 106, 190–200.

Metivier, H., Masse, R., Lafuma, J., 1983. Effect de la masse sur l'absorption intestinale du neptunium V chez le singe et le rat. Radioprot. 18, 13–17.

Morin, M., Nenot, J. C., Lafuma, J., 1973. The behavior of Np-237 in the rat. Health Phys. 24, 311–315.

Moskalev, Y. I., Rudnitskaya, E. I., Zalikin, G. A., Petrovich, I. K., 1972. Distribution and biological effects of neptunium-237. In: Biological Effects of Radiation From External and Internal Sources.(Translated in US Atomic Energy Commission Document AEC-Tr-7457, 330–341.) (Ed. by Y.I.Moskalev & V.S.Kalistratova), 220–229. Meditsina, Moscow.

Mueller, W. A., Linzner, U., 1983. Distribution and dosimetry studies after incorporation of Np-239 (Pu-239) in mice. Health Phys. 44, 577-580.

NCRP, 1988. Neptunium: Radiation protection considerations. NCRP Report No. 90. National Council on Radiation Protection and Measurements, Bethesda, MD

NCRP, 2007. Development of a Biokinetic Model for Radionuclide-Contaminated Wounds for Their Assessment, Dosimetry and Treatment. NCRP Report No. 156. National Council on Radiation Protection and Measurements, Bethesda, MD

7112 Nenot, J. C., Masse, R., Morin, M., Lafuma, J., 1972. An experimental comparative study of
7113 the behaviour of Np-237, Pu-238, Pu-239, Am-241 and Cm-242 in bone. Health Phys.
7114 22, 657–665.
7115 Paquet, F., Montegue, B., Ansoborlo, E., et al., 2000. Efficacy of 3,4,3-LIHOPO for reducing
7116 neptunium retention in the rat after simulated wound contamination. Int. J. Radiat.
7117 Biol. 76, 113–117.
7118 Paquet, F., Ramounet, B., Metivier, H., Taylor, D. M., 1996. The effect of the mass and initial
7119 chemical form of neptunium on its molecular associations in blood and liver. Radiat.
7120 Res. 146, 306–312.
7121 Popplewell, D.S., Harrison, J.D., Ham, G.J., 1991. Gastrointestinal absorption of neptunium
7122 and curium in humans. Health Phys. 60, 797–805.
7123 Ralston, L. G., Cohen, N., Bhattacharyya, M. H., et al., 1986. The metabolism and
7124 gastrointestinal absorption of neptunium and protactinium in adult baboons. In:
7125 Bulman, R. A.; Cooper, J. R., eds. Speciation of fission and activation products in the
7126 environment. London: Elsevier Applied Science Publishers.
7127 Ramounet, B., Abram, M.C., Rateau, G., Grillon, G., Fritsch., P., 2000. Actinides behaviour
7128 after inhalation exposure of rats to industrial NpO2. In IRPA 10, Proceedings of the
7129 10th International Congress of the International Radiation Protection Association,
7130 'Harmonisation of Radiation, Human Life, and the Ecosystem. Hiroshima, Japan, May
7131 14-19, 2000. P-3a-188.
7132 Ramounet, B., Matton, S., Grillon, G., Fritsch, P., 1998. Early biokinetics of actinides after
7133 intravenous administration of soluble forms of Pu(IV), Np(IV), and Np(V). J. Alloys
7134 and Compounds 271–273, 103–105.
7135 Scott, K.G., Overstreet, R., Jacobson, L., et al., 1947. The metabolism of carrier-free fission
7136 products in the rat. Manhattan District Declassified Document. MDDC-1275.
7137 Sontag, W., Wirth, R., Luz, A., Schaffer, E., Volf, V., 1997. Dosimetry and pathology of
7138 237Np in female rats. Hum. Exp. Toxicol. 16, 89–100.
7139 Stradling, G. N., Bailey, M. R., Birchall, A., et al., 2000. Clearance of radioactivity deposited
7140 in the respiratory tract to blood: Progress in a multinational interspecies comparison
7141 project. J. Radioanal. Nucl. Chem. 243, 323–337.
7142 Sullivan, M. F., Gorham, L. S., 1982. Further studies on the absorption of actinide elements
7143 form the gastrointestinal tract of neonatal animals. Health Phys. 43, 509–519.
7144 Sullivan, M. F., Crosby, A.L., 1975. Absorption of uranium-233, neptunium-237, plutonium-
7145 238, americium-241, curium-244, and einsteinium-253 from the gastrointestinal tract
7146 of newborn and adult rats. In: Pacific Northwest Laboratory Annual Report for 1974,
7147 Pt. 1. Biomedical Sciences. BNWL-1950, 105.
7148 Sullivan, M. F., Crosby, A.L., 1976. Absorption of transuranic elements from rat gut. In:
7149 Pacific Northwest Laboratory Annual Report for 1975, Pt. 1. Biomed. Sci. BNWL-
7150 2000, 91.
7151 Sullivan, M. F., Ruemmler, P. S., Buschbom, R.L., 1986. Neptunium-237 inhalation in rats.
7152 Health Phys. 51, 745–753.
7153 Thompson, R. C., 1982. Neptunium--the neglected actinide: a review of the biological and
7154 environmental literature. Radiat. Res. 90, 1–32.
7155 Volf, V., Wirth, R., 1986. Rapid communication. Effective chelation therapy after
7156 incorporation of neptunium-239 in rats. Int. J. Radiat. Biol. 50, 955–959.
7157 Wirth, R., Volf, V., Long term retention of Np-237 in rats. 1984. Int. J. Radiat. Biol. 46, 787–
7158 792.

22. PLUTONIUM (Z=94)

22.1. Chemical Forms in the Workplace

(644) Plutonium is an actinide element which occurs in various oxidation states (III to VII), but mostly in oxidation state (IV). Plutonium may be encountered in a variety of chemical and physical forms, including metal, carbides, hydroxides, oxides (PuO_2), including mixed oxide reactor fuel (MOX), chlorides, oxalates and nitrates, and also organic forms such as tributyl-phosphate (TBP). ^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Pu are the main isotopes of plutonium, and ^{239}Pu is the main fissile material used for the production of nuclear weapons.

(645) Some studies indicate that the biokinetics of plutonium depends on the total mass of circulating plutonium. This leads to significant differences between isotopes (e.g. ^{238}Pu and ^{239}Pu) when their biokinetics is expressed in terms of activity, due to differences in specific activity (and thus in total plutonium mass (Guilmette et al., 1992).

Table 22.1. Isotopes of plutonium addressed in this report.

Isotope	Physical half-life	Decay mode
Pu-232	33.7 m	EC, A
Pu-234	8.8 h	EC, A
Pu-235	25.3 m	EC, A
Pu-236	2.858 y	A, SF
Pu-237	45.2 d	EC, A
Pu-238[a]	87.7 y	A, SF
Pu-239[a]	2.411E+4 y	A
Pu-240[a]	6.564E+3 y	A, SF
Pu-241[a]	14.35 y	B-, A
Pu-242	3.75E+5 y	A, SF
Pu-243	4.956 h	B-
Pu-244	8.00E+7 y	A, SF
Pu-245	10.5 h	B-
Pu-246	10.84 d	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

22.2. Routes of Intake

22.2.1. Inhalation

(646) There is extensive information available on the behaviour of plutonium after deposition in the respiratory tract from animal experiments (mainly in rats, dogs and baboons), in-vitro dissolution studies, some accidental human intakes, and one human volunteer study. *Publication 19* (1972) reviewed information then available on inhalation of plutonium. It

summarised the results of over forty in-vivo experiments, about half of which were on plutonium dioxide, several on the nitrate, and the others on a wide range of laboratory forms. *ICRP Publication 48* (ICRP, 1986) addressed the behaviour of plutonium entering the body by inhalation in the context of the *Publication 30* Lung Model (ICRP 1979). It placed emphasis on more recent data, supplementing those studies already covered in *Publications 19* and *31* (ICRP 1972, 1980) (The latter was mainly concerned with the biological effects of inhaled radionuclides.) Because the various oxide forms had been the most thoroughly studied, they were given special attention and used to illustrate the effects of important variables influencing the distribution and retention of radionuclides in the respiratory tract, including: impairment of clearance by radiation effects and other pathology; the temperature of oxide formation; particle size; specific activity (^{238}Pu vs. ^{239}Pu); and the presence of other metals. Of the more soluble forms, the nitrate and tri-butyl phosphate complex were considered in detail as being of most importance for occupational exposure.

(647) *Publication 71* (ICRP, 1995) provided a brief review of the literature relating to inhaled plutonium compounds in the context of the HRTM, and with emphasis on forms to which members of the public might be exposed as a result of environmental releases. More recently, HRTM absorption parameter values have been derived from the results of animal and in-vitro studies for a wide range of compounds encountered in the nuclear fuel industry. Davesne et al. (2010) carried out a comprehensive review, re-interpreting experimental data in many cases to derive values for f_r, s_r, and s_s for each chemical form (assuming f_b = 0, see below). Emphasis is given here to studies which provide information on HRTM absorption parameter values for forms of most importance for occupational exposure. The Task Group has here re-analysed the data from most of the studies and utilised some extended data sets that were not available to Davesne et al. (2010).

(648) Absorption parameter values for important particulate forms of plutonium are given in: Tables 22.2 and 22.3 for plutonium nitrate; Table 22.4 for plutonium-239 dioxide; Table 22.5 for plutonium-uranium mixed oxides (MOX); and Table 22.6 for plutonium-238 dioxide Recommended absorption parameter values and Types, and associated f_A values for particulate forms of plutonium are given in Table 22.9.

(649) Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values. Data from the human studies were interpreted using the revised HRTM (ICRP, 2015), the Gastro-Intestinal Tract Model (ICRP, 1979) or the Human Alimentary Tract Model (HATM, ICRP, 2006), and the systemic model for plutonium described in section 22.2.3. Data from a study of the biokinetics of inhaled plutonium nitrate in monkeys (Brooks *et al*., 1992) were interpreted using the revised HRTM (ICRP, 2015) and the systemic model for humans described in section 22.2.3. Respiratory tract deposition fractions were determined from measured bioassay data.

(650) The rat studies were interpreted using the respiratory tract model described in ICRP Supporting Guidance 3 (ICRP, 2002), and a simple gastro-intestinal and systemic model (Smith, 201X). This model was derived from data on the retention and excretion of intravenously (IV) injected plutonium citrate in rats (Bailey et al., 1999), from rat gavage studies of insoluble forms of gadolinium (Pellow et al., 2016a) and terbium (Hodgson et al., 2004) and from published data on rat digestive tract transit times (Enck et al., 1989; Quini et al. 2012; Schoonjans et al. 2002).

(651) In analysis of many of the rat studies there were large uncertainties in the values of s_r and f_r, partly due to the (negative) correlation between them: a good fit to a dataset can be obtained with a range of values of each, if suitable data do not constrain one or the other. For

example, analyses of measurements by Stather and Priest (1977) of ^{238}Pu and ^{239}Pu after instillation of a solution of the nitrates gave a large difference between the estimated values of s_r, even though the data sets were similar (see below). Therefore, a single fixed s_r value for rats (1 d^{-1}) was derived (Smith, 201x) from the individual s_r values estimated for a subset of the studies where sufficient early retention data were available (Table 22.8). Data from each study were then re-analysed using this fixed s_r value to obtain more robust f_r and s_s values (Table 22.2).

(652) The structure of the rat respiratory tract model (ICRP, 2002) was also used to analyse data from the dog studies. The particle transport rates from the TB and ET compartments and the deposition fractions in the TB_{slow} and TB_{fast} compartments were the default values used in the rat model (ICRP, 2002). The particle transport rates from the AI compartments and the deposition fractions in the AI compartments were obtained from measurements on dogs supplied by Kreyling (1990) and are reported by Pellow et al. (2016a). The gastro-intestinal and systemic models for the dog described in Mewhinney and Diel (1983) were used.

Absorption Types and parameter values

(653) Two studies of occupational exposure to plutonium nitrate in humans (Puncher et al., 2016b,c) and one experimental study in dogs (Pellow et al., 2016b; Puncher et al., 2016a) provide strong evidence for the existence of a long-term retained component in the respiratory tract, for which the bound state provides the simplest explanation. The assessed values for the bound state parameters (f_b = 0.002; s_b = 0 d^{-1}) were applied in the analysis of the results of all the plutonium studies reported in this section. A detailed discussion on binding of plutonium in the respiratory tract and on the choice of the values for f_b and s_b is provided below in the section: 'Extent of binding of plutonium in the respiratory tract'.

(654) Due to the large number of studies of the biokinetics of inhaled and instilled plutonium, results for each chemical form are generally presented for each species studied in turn.

Plutonium citrate

(655) Ballou et al. (1972) followed the biokinetics of ^{239}Pu in Beagle dogs for 100 days after inhalation of plutonium citrate (pH 3.5). Complementary experiments were also carried out where plutonium citrate was administered orally and intravenously. After inhalation, about 60% of the initial lung deposit (ILD) cleared within 7 days, and this was attributed to deposition in the upper respiratory tract (URT). The content of the skeleton increased from ~6% ILD at 1 d to ~40% ILD for t > 50 d, exceeding that in the lungs (~30% ILD). Analysis here gave: f_r = 0.3, s_r = 0.5 d^{-1}, s_s = 0.005 d^{-1}, and assignment to Type M.

(656) Stather and Howden (1975) investigated the effect of chemical form on the biokinetics of plutonium in rats after intra-tracheal instillation of plutonium citrate (pH 6.5) and nitrate. Rats were killed at times up to 180 days and ^{239}Pu content was measured in lungs, liver, remaining carcass, urine and faeces. Lung retention as a fraction of the estimated ILD was lower for citrate than for nitrate, and in particular showed faster transfer to systemic tissue in the first day and the first week. Analysis here for the citrate gave: f_r = 0.8, s_r = 2 d^{-1}, s_s = 0.008 d^{-1}, and assignment to Type M. Analysis here for the nitrate gave: f_r = 0.6, s_r = 1.4 d^{-1}, s_s = 0.003 d^{-1}. To obtain more robust f_r and s_s values for comparison purposes, the data were re-analysed here with fixed s_r = 1 d^{-1} (see above), which gave: f_r = 0.8 and s_s = 0.007 d^{-1} for the

citrate, and f_r = 0.6 and s_s = 0.001 d^{-1} for the nitrate, indicating that absorption of citrate was higher in both the rapid and slow phases.

(657) Smith et al. (1977) followed the biokinetics of ^{239}Pu in rats for 17 d after intra-tracheal instillation of plutonium citrate (0.01M nitric acid / 2% sodium citrate). The lung content fell from 27% ILD at 18 hours to 10% and 7.4% ILD at 6 and 17 days respectively, whilst the content in systemic tissues increased from 59% to 75% and 73% ILD respectively. Analysis here gave: f_r = 0.9, s_r = 2 d^{-1} with fixed s_s = 0.001 d^{-1}, and assignment to Type M, but very close to the criterion for assignment to Type F. As retention was only measured for 17 days, the value of s_s is poorly defined. Analysis indicated only that its value is less than 0.01 d^{-1}.

(658) Although absorption parameter values for plutonium citrate based on in-vivo data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for plutonium citrate are not used here. Instead, it is assigned to Type M. However, the results were taken into account in the selection of the rapid dissolution rate for plutonium. They made only a small contribution to it, because more results are available for plutonium nitrate, including human volunteer data.

Pu chloride ($PuCl_3$)

(659) *Publication 19* (ICRP, 1972) includes one $PuCl_3$ inhalation experiment in its review: retention in lung and skeleton were broadly similar to those following inhalation of nitrate. It is not considered in detail here because exposure to $PuCl_3$ is unlikely. However, one account of accidental occupational exposure was found in the literature.

(660) Ramsden et al. (1970) reported an incident in which two workers inhaled an aerosol believed to be a mixture of ferrous chloride and plutonium chloride ($PuCl_3$) in a finely divided form (smoke or fume). The mass median diameter was estimated to be about 0.2 µm. Both men started faecal and urine sampling programmes immediately. Faecal ^{239}Pu activity in the first 5 days was so low that long term sampling was not undertaken. Urine sampling continued for four months, until the levels were below the limit of detection. Lung content was measured at 2 and 365 days and was below the limit of detection (3 nCi, ~100 Bq) at both times. Analysis here, taking a fixed value for s_r of 0.4 d^{-1}, gave f_r = 0.15 and s_s = 0.005 d^{-1}, and assignment to Type M.

(661) Although absorption parameter values for plutonium chloride based on in-vivo data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for plutonium chloride are not used here. Instead, it is assigned to Type M.

Plutonium nitrate ($Pu(NO_3)_4$)

(662) Plutonium nitrate in aqueous solution is widely encountered in nuclear fuel fabrication and reprocessing. There are numerous biokinetic studies on plutonium nitrate following intra-tracheal instillation into rats, and inhalation by rats, dogs, monkeys and people. The importance of the mass of plutonium deposited in the lung has been recognised for plutonium nitrate, as absorption can be inhibited by relatively high mass loadings, possibly because of colloid formation (Nolibé et al., 1989). High mass loadings rarely occur and so such effects are not considered to be of concern for routine exposures to plutonium.

Man

(663) Two human volunteers inhaled a mixed $^{237}Pu/^{244}Pu$ nitrate aerosol with a breathing pattern designed to maximise alveolar deposition (Etherington et al., 2003). Measurements were made of ^{237}Pu lung and liver retention by external counting up to about 4 months; and of ^{237}Pu and/or ^{244}Pu in blood and excreta for several years. The data were re-interpreted using the revised HRTM, the HATM and a modified version of the systemic model described in section 22.2.3, by means of a Bayesian analysis (Puncher and Etherington, 2016). Particle transport rates were determined from the measured data. Absorption parameter values were determined from a combined analysis for the two volunteers: $f_r = 0.2$, $s_r = 0.4$ d^{-1}, $s_s = 0.002$ d^{-1}, consistent with assignment to Type M.

(664) Puncher et al. (2016b) performed an analysis of the autopsy and bioassay data of United States Trans-Uranium and Uranium Registries (USTUR) donor 269, a plutonium worker who died 38 y after receiving a high (58 kBq) acute intake of plutonium nitrate by inhalation (James et al., 2007). The analysis also used the results of recent measurements (Tolmachev et al., 2016) on plutonium in the extra-thoracic (ET_2), bronchial, bronchiolar and alveolar-interstitial regions and in the thoracic lymph nodes for this donor. The data were found to be uninformative on the rapid absorbed fraction parameters, which were therefore fixed at $f_r = 0.17$ and $s_r = 1$ d^{-1}. The fixed s_r value was based on an assessment of s_r values from a limited number of in-vivo studies on plutonium nitrate and oxides in a variety of mammals, which were adequately described by lognormal distributions centred on 1 d^{-1}, whilst the f_r value was based on a similar assessment for plutonium nitrate only (Puncher et al., 2011). After the measured systemic (liver and skeleton) retention data were corrected to remove the effect of DTPA (diethylene triamine pentaacetic acid) treatment, the mean value for f_b was determined as 0.0037. There was no evidence for an s_b value other than zero. The estimated value for s_s was 0.0048 d^{-1}. Puncher et al. (2016b) is one of the two studies that provide the basis for the adoption of a bound state for plutonium, the other being Pellow et al. (2016b) (see below).

(665) Puncher et al. (2016c) performed an analysis of autopsy data (plutonium activity in skeleton, liver, lungs, and thoracic lymph nodes) from 20 former plutonium workers of the Mayak Production Association (MPA) exposed only to plutonium nitrates, and 20 workers exposed only to plutonium oxides. The mean value for f_b was determined as 0.0014. There was no evidence for an s_b value other than zero. The rapid fraction and rapid dissolution rate were fixed at values of 0.17 and 1 d^{-1} (see above) and the mean value determined for s_s was 2.5×10^{-4} d^{-1}.

Monkeys

(666) Brooks et al. (1992) investigated the distribution and the biological effects of inhaled ^{239}Pu nitrate in 20 male cynomolgus monkeys. Animals died or were sacrificed and amounts were measured in lungs, liver and skeleton at times between 4 days and 99 months. Amounts were also measured in urine and faeces collected daily up to 38 days. Projected ILDs were 40, 10, or 4 kBq. Three animals exposed to 40 kBq of ^{239}Pu died of radiation-related pulmonary pneumonitis and fibrosis, but inclusion or exclusion of these data did not significantly affect the absorption parameter analysis. The systemic model was adjusted to account for the shorter residence time of Pu in the liver. Analysis here gave: $f_r = 0.1$, $s_r > 0.1$ d^{-1}, $s_s = 0.003$ d^{-1}, and assignment to Type M.

Dogs

(667) Bair (1970) followed the biokinetics of ^{239}Pu for 300 d after inhalation of ^{239}Pu nitrate by dogs. Results were also reported by McClellan (1972) for comparison with results on americium and curium. Fifteen dogs inhaled an aerosol of a plutonium HNO_3 solution (0.14N for three dogs killed after one month and 0.27N for twelve dogs killed at times between 75 and 303 days). The lungs contained about 65% of the sacrifice body burden one month after exposure; skeleton and liver contained about 20% and 12% respectively. Autoradiographs showed much particulate plutonium in the lung, probably due to colloid formation in the aerosol droplets. The lung retention dropped to about 35% ILD at 200-300 days: about 2% ILD was transferred to tracheobronchial lymph nodes (TBLN), 25% to skeleton and 7% to liver. About 15% was excreted in faeces and 1% in urine. Analysis here gave: f_r = 0.3, s_r = 0.2 d^{-1}, s_s = 0.0013 d^{-1}, and assignment to Type M.

(668) Dagle et al. (1983) compared the biokinetics of plutonium in 24 Beagle dogs after nose-only inhalation of ^{238}Pu and ^{239}Pu nitrate (0.27N nitric acid solution), as part of a 15-year life span effects study (Dagle et al., 1993; PNL, 1994). Amounts in tissues and excreta were measured for dogs killed at times between 3 days and 12 months. The ILD was defined as the total tissue and excretion content minus the content in the first 3 days faecal excreta. Plutonium-238 cleared more rapidly from the lungs than ^{239}Pu: the lung content was 49% and 88% ILD respectively after 3 days. The lung and tissue content after one year were 2% and 72% for ^{238}Pu and 13% and 56% for ^{239}Pu. Given the similar amounts of administered activity, the difference between isotopes may be attributed to the lower specific activity/higher mass of ^{239}Pu and a possible increased formation of colloids, which are less readily translocated from lungs to blood. Analyses here gave: f_r = 0.8, s_r = 0.3 d^{-1}, s_s = 0.005 d^{-1} for ^{238}Pu, and f_r = 0.13, s_r = 0.14 d^{-1}, s_s = 0.004 d^{-1} for ^{239}Pu, both consistent with assignment to Type M.

(669) The data for ^{239}Pu, including long-term retention measurements, were analysed by Pellow et al. (2016b) and Puncher et al. (2016a). Lung clearance of ^{239}Pu was modelled using simplified and modified versions of the *Publication 66* HRTM and the revised HRTM (ICRP, 2015). The arithmetic mean of the posterior distribution for f_b, determined using a model based on the *Publication 66* HRTM, was 0.0023. The half time associated with this bound fraction was greater than 70,000 days, and so the uptake rate to blood from the bound state (s_b) was assigned a value of 0 d^{-1}. The rapid fraction and rapid dissolution rate were fixed at 0.17 and 1 d^{-1} (see study of USTUR donor 0269 above) and the arithmetic mean of the posterior distribution determined for s_s was 0.0023 d^{-1}.

Rats

(670) Absorption parameter values obtained from individual analyses of the data from each study are presented with the study descriptions below. Although biokinetic data from a large number of studies with laboratory rats are available, the information obtainable from each individual study on the rapid dissolution rate, s_r, is limited, mainly because of the limited amount of early retention data.

(671) Morin et al. (1972) compared the biokinetics of 238Pu and 239Pu in rats following inhalation and intravenous injection of Pu nitrate. Rats inhaled Pu in HNO_3 solution (pH 1). Amounts were measured in lung, systemic organs and in urinary and faecal excretion for 1 to 45 days and 1 to 90 days after inhalation for ^{238}Pu and ^{239}Pu, respectively. The lung clearance rate for ^{239}Pu was higher than that for ^{238}Pu: lung retention on days 1 and 45 was 96% ILD and 30% ILD for ^{238}Pu and 79% ILD and 30% ILD for ^{239}Pu. Individual analyses here gave: f_r = 0.13, s_r

= 0.2 d^{-1}, s_s = 0.005 d^{-1} for ^{238}Pu and f_r = 0.05, s_r = 9 d^{-1}, s_s = 0.002 d^{-1} for ^{239}Pu, both consistent with assignment to Type M.

(672) Nénot et al. (1972) compared retention of ^{238}Pu, ^{239}Pu, ^{241}Am and ^{242}Cm in the lungs and bone of rats following inhalation of the nitrates. Lung retention was measured in the period 2 to 42 d for ^{238}Pu and in the period 8 to 90 days for ^{239}Pu. Lung retention was broadly similar although ^{239}Pu cleared slightly more rapidly than ^{238}Pu: for ^{239}Pu, 30% ILD was retained at 45 days, while for ^{238}Pu, ~42% ILD was retained at 42 days. Individual analyses here gave: f_r = 0.14, s_r = 0.2 d^{-1}, s_s = 0.005 d^{-1} for ^{238}Pu and f_r = 0.04, s_r = 0.8 d^{-1}, s_s = 0.004 d^{-1} for ^{239}Pu, both consistent with assignment to Type M. No details of the inhalation exposure were given. However, the authors noted that some differences in retention could have been due to differences in mucociliary clearance and/or to the greater mass of ^{239}Pu than that of the other radionuclides, which suggests that the radionuclides were administered separately.

(673) Stather and Howden (1975) investigated the effect of chemical form on the distribution and excretion of plutonium after intra-tracheal instillation into the respiratory tract of rats as the citrate or nitrate. ^{239}Pu nitrate was administered in 0.01M nitric acid. The ^{239}Pu content of the lungs, liver and remaining carcass, and the urine and faeces were analysed. Lung retention as a fraction of the estimated ILD was higher for nitrate than for citrate for the six months follow-up, showing, in particular, slower transfer to systemic tissues in the first day and first week. Analysis here for the nitrate gave: f_r = 0.6, s_r = 1.4 d^{-1}, s_s = 0.003 d^{-1}, and assignment to Type M.

(674) Stather and Priest (1977) administered a solution of 0.01N nitric acid containing ^{238}Pu, ^{239}Pu and ^{241}Am nitrates to rats by intratracheal instillation. Groups were killed at times between 1 and 120 days. The lung, liver and carcass contents (%ILD) of ^{238}Pu and ^{239}Pu were similar. Lung content fell from about 70% ILD at 1 day to 40% and 7.3% at 7 and 120 days respectively. Content in systemic organs increased from 21% ILD at 1 day to about 40% at 120 days. Individual analyses here gave: f_r = 0.4, s_r = 80 d^{-1}, s_s = 0.007 d^{-1} for ^{238}Pu and f_r = 0.5, s_r = 0.4 d^{-1}, s_s = 0.004 d^{-1} for ^{239}Pu, both consistent with assignment to Type M.

(675) Ballou et al. (1977) studied long-term effects, retention and distribution of ^{239}Pu in rats exposed by nose-only inhalation to a ^{239}Pu nitrate aerosol (0.27N nitric acid). The amounts in lung, liver and skeleton were followed for over 900 days and analysed here for the rats which were not treated with Ca-DTPA. The first measurements, at 30 days, show a small transfer of plutonium from lung to systemic tissues. Ballou et al. (1977) described the lung retention as the sum of three exponentials with effective half-times (T_b) of 5, 35 and 155 days, associated with 60, 30 and 10% ILD, respectively. Analysis here resulted in satisfactory fits to the data only with a fixed s_r value (taken to be 1 d^{-1}, Table 22.2) giving f_r = 0.06, s_s = 0.004 d^{-1}, and assignment to Type M.

(676) Stradling et al. (1987) exposed rats by inhalation to a laboratory prepared mixed aerosol of ^{238}Pu and ^{241}Am nitrate. The ^{238}Pu ILD was determined from tissue analysis of rats killed immediately after exposure. Lung and organ retention was measured at times between 7, and 252 days. The Pu lung content had reduced to 64%, 36% and 2.3% ILD at 7, 28 and 252 days respectively while the systemic content increased up to about 20% at 252 days. Analysis here gave: f_r = 0.5, s_r = 0.1 d^{-1}, s_s = 0.002 d^{-1}, and assignment to Type M.

(677) Moody et al. (1993, 1994, 1998) exposed 35 rats, by nose-only inhalation, to a sample of diluted industrial process feed liquor, essentially Pu nitrate in 0.01M nitric acid (designated "Material A"). (The experiment complemented two involving intratracheal instillation into rats of particulate materials which were 10- to 20-year-old residues of nitrate absorbed on to ubiquitous building dust: see *Plutonium nitrate residues* section below.) The

ILD was estimated from analysis of tissues of rats killed 30 minutes after exposure. Further groups were killed at times between 7 and 365 days. The lungs, liver and remaining carcass (excluding gastrointestinal tract, the pelt and the extremities) were analysed for total plutonium activity. Lung content decreased from 49% to 1.8% ILD and the liver content decreased from 8.1% to 1.1% between 1 and 365 days. Analysis here gave: f_r = 0.6, s_s = 0.002 d^{-1}, and assignment to Type M.

(678) Pellow et al. (2016c) reported the results of measurements of the biokinetics of plutonium for 170 d after inhalation and intratracheal instillation of Pu nitrate into rats. In the inhalation experiment (Hodgson et al., 2003), rats were exposed for 40 minutes by nose-only inhalation to a ^{237}Pu nitrate aerosol. Groups were killed at 10-minute intervals during the exposure and at 10 and 30 minutes, 1, 3 and 6 hours and at times between 1 and 84 days. The average ^{237}Pu ILD of the rats killed immediately after exposure was 23% of the total amount in the body, including activity on the pelt. This fell to approximately 12% and 4% at 7 and 84 days respectively. The liver content initially rose from 0.3% to 1% at 7 days and then fell gradually to 0.5% at 84 days.

(679) In the complementary instillation experiments, 0.1 ml of plutonium nitrate in saline was instilled into the lungs of rats. Animals received ^{237}Pu and/or ^{238}Pu. Early results were based on ^{237}Pu alone or the average of ^{237}Pu plus ^{238}Pu. Later values were based on ^{238}Pu alone due to the short half-life of ^{237}Pu. Animals were killed at 10 and 30 minutes, 1, 3 and 6 hours and at times between 1 and 169 days. Initial clearance of material from the lungs was rapid with only 57, 29 and 19% remaining in the lungs at 1 hour and 1 and 7 days respectively and eventually falling to 4% at 169 days. The systemic content at these times was 22, 34, 35 and 26% ILD. Most of the activity cleared from the body via the faeces, cumulative excretion at 1, 7 and 169 days being 22, 31 and 60%, whereas no more than about 3% was excreted in urine by 169 days. In analyses here, independent estimates for inhalation gave: f_r = 0.13, s_r = 12 d^{-1}, s_s = 0.007 d^{-1}; and for instillation: f_r = 0.7, s_r = 20 d^{-1}, s_s = 0.003 d^{-1}, both consistent with assignment to Type M.

(680) The rapid fraction was larger following instillation than following inhalation. A higher rapid fraction following instillation of plutonium nitrate than following inhalation was noted by ICRP (2002, Section C.6.4), in a discussion of the advantages and disadvantages of different methods of administration of radionuclides to the respiratory tract for biokinetic studies. Several possible reasons were considered including differences in distribution and artefacts resulting from the presence of liquid.

(681) Results of the re-analysis of these experimental studies made here using a single fixed s_r value of 1 d^{-1} (see below) are presented in Table 22.2. The difference between absorption parameter values obtained from instillation and inhalation experiments, and in particular the difference in f_r values, is clearly shown by the median and range of values given in the Table.

Table 22.2. Case-specific f_r and s_s absorption parameter values for plutonium nitrate in rat studies reporting early retention data, estimated using a fixed s_r = 1 d^{-1}.

Administration	Absorption parameter values[a]		References
	f_r	s_s (d^{-1})	
Inhaled, ^{238}Pu	0.04	0.0085	Morin et al. (1972)
Inhaled, ^{239}Pu	0.19	0.0049	Morin et al. (1972)
Inhaled, ^{238}Pu	0.05	0.0041	Nénot et al. (1972)
Inhaled, ^{239}Pu	0.03	0.0042	Nénot et al. (1972)

Instilled	0.62	0.0013	Stather and Howden (1975)
Instilled, ^{238}Pu	0.52	0.0043	Stather and Priest (1977)
Instilled, ^{239}Pu	0.48	0.0045	Stather and Priest (1977)
Inhaled	0.06	0.0043	Ballou et al. (1977)
Inhaled, ^{238}Pu	0.22	0.0035	Stradling et al. (1987)
Inhaled	0.55	0.0018	Moody et al. (1993, 1994, 1998)
Instilled	0.74	5.2×10^{-5}	Pellow et al. (2016c)
Inhaled	0.24	0.0042	Pellow et al. (2016c)
Median	0.23	0.042	
Geom. mean		0.0026	
Min	0.030	5.2×10^{-5}	
Max	0.74	0.0085	
Instillation vs inhalation			
Median	0.57; 0.13	0.0028; 0.0042	
Geom. mean		0.0011; 0.0041	
Min	0.48; 0.030	5.2×10^{-5}; 0.0018	
Max	0.74; 0.55	0.0045; 0.0085	
Notes a. f_b and s_b were assumed to be 0.002 and 0 d^{-1} respectively			

(682) Estimates of absorption parameter values for plutonium nitrate derived above are summarised in Table 22.3. For rats, instillation studies are not included, because of possible artefacts as discussed above, and because there are ample results from inhalation experiments. With regard to the rapid phase it is considered that the human volunteer experiment provides the most reliable estimates of f_r (0.16) and s_r (0.39 d^{-1}) (Etherington et al., 2003; Puncher and Etherington, 2016). Not only does it involve human data, but the carefully controlled exposure and comprehensive early data (in-vivo, blood and excreta) enable good estimates to be made of f_r and s_r. The other human studies, and many of the animal experiments, lack early data and only provide estimates of s_s. For inhalation experiments in rodents it is difficult to obtain reliable excretion data during the first few days, because of likely cross-contamination of samples from material deposited on the pelt, etc.

Table 22.3. Estimated absorption parameter values for inhaled plutonium nitrate. Values in parentheses were fixed in analyses.

Species	Absorption parameter values			Reference	Comment
	f_r	s_r (d^{-1})	s_s (d^{-1})		
Man	0.16	0.39	0.0022	Etherington et al. (2003), Puncher and Etherington (2016)	Human volunteer experiment, only two subjects, but extensive data to 300 d.
Man	*(0.17)*	*(1)*	0.0048	Puncher et al. (2016d)	One USTUR subject, bioassay and autopsy data.
Man	*(0.17)*	*(1)*	0.00025	Puncher et al. (2016d)	Autopsy data only, for 20 subjects, first at 5 y after exposure.
Monkey	0.1	>0.1	0.0025	Brooks et al. (1992)	Monkeys: 20 followed up to 8 years, few early data.
Dog	0.27	0.17	0.0013	Bair (1970)	Extensive data to 300 d.

Dog	0.83	0.28	0.0048	Dagle et al. (1983)	^{238}Pu nitrate: data to 1 y.
Dog	0.13	0.14	0.0044	Dagle et al. (1983)	^{239}Pu nitrate: data to 1 y.
Dog	*(0.17)*	*(1)*	0.0023	Pellow et al. (2016b), Puncher et al. (2016a)	^{239}Pu nitrate: extensive data to 15 y.
Rat	0.06	*(1)*	0.0043	Ballou et al. (1977)	No early data, but later data to 2.5 y.
Rat	0.13	12	0.0068	Hodgson et al. (unpublished)	^{237}Pu: extensive data during exposure, and from 10 min to 84 d after.
Rat	0.13	0.20	0.005	Morin et al. (1972)	^{238}Pu: data 1 to 45 d
Rat	0.05	9.1	0.002	Morin et al. (1972)	^{239}Pu: data 1 to 90 d
Rat	0.14	0.16	0.0054	Nénot et al. (1972)	^{238}Pu: data 2 to 42 d
Rat	0.036	0.83	0.0041	Nénot et al. (1972)	^{239}Pu: data 8 to 90 d
Rat	0.47	0.098	0.0018	Stradling et al. (1987)	^{238}Pu: data 7 to 252 d
Rat	0.52	8	9×10^{-4}	Moody et al. (1993, 1994, 1998)	^{23X}Pu: data 30 min to 365 d

(683) With regard to f_r, there is considerable variation in the estimated values from animal experiments (Tables 22.2 and 22.3), with a range from about 0.05 to 0.8, which is broadly consistent with the value from the human volunteer experiment. As noted above, the scatter is partly due to the (negative) correlation between estimates of f_r and s_r. The value from the human volunteer experiment, rounded to 0.2, is chosen here.

(684) With regard to s_r, the results from the dog studies are close to that from the human volunteer experiment. Those from the rat experiments, however, range from about 0.05 to 10 d^{-1}, which is broadly consistent with the value from the human volunteer experiment.

(685) However, a much higher value (~10 d^{-1}) comes from the rat experiment with the most comprehensive early data, including measurements made immediately after exposure. This indicates that rather than a constant rate of absorption from the respiratory tract applying during the "rapid" phase (the first day or so) as assumed in the HRTM, the rate decreases with time from >10 d^{-1} to <1 d^{-1}. This could be represented more realistically in a compartment model structure by additional compartments. For example, Birchall et al. (1995) used the bound state compartment as a second component of absorption in order to represent the biokinetics after intratracheal instillation into rats of plutonium nitrate (see section on *Extent of binding of plutonium in the respiratory tract*, below). Because the rate of absorption of the rapid phase (even at 0.4 d^{-1}) is so great compared to particle transport rates from the AI region, with which it competes, the value of s_r has little effect on the total amount absorbed to blood from the lungs in the rapid phase. However, typically a similar amount of activity deposits in the ET airways, as deposits in the lungs. Because particle transport from ET_2 to the alimentary tract is assumed to be so rapid (100 d^{-1}), assumption of a low value of s_r (e.g. 0.4 d^{-1}) (and a low value of f_A) results in very little uptake from material deposited in the nose. However, if there were a large fraction absorbed at a higher rate (>10 d^{-1}), this would result in a correspondingly large uptake from material deposited in the nose. The use of a single low value of s_r based on overall uptake from the lungs might then result in an underestimate of uptake from the nose. Nevertheless, it is possible that even if the higher rate occurred in the AI region, it would not occur in the nose e.g. because of the presence of mucus and a thicker epithelium. In the human volunteer experiment the subjects inhaled through a mouthpiece, so there was minimal ET deposition. However, in the study by Brooks et al. (1992) the monkeys were exposed nose-only, and so although it lacks early data on which to assess the value of s_r, it provides an opportunity to test whether the

assumption of a single low value of s_r results in underestimation of overall uptake during nose-breathing. Analysis here applying the values f_r = 0.16, s_r = 0.39 d^{-1}, s_s = 0.0022 d^{-1}, from the human volunteer study to the results of the monkey experiment gave a reasonably good fit to the data, and therefore indicates that overall uptake is not significantly underestimated.

(686) With regard to the slow dissolution rate s_s, the estimate from the human volunteer experiment is not as definitive as the values for the rapid phase. In-vivo measurements of organ retention using ^{237}Pu (half-life 45.3 d) were limited to about 4 months, but the estimated rate of 0.0022 d^{-1} corresponds to a half-time of about a year, and so much of the material remained when detailed measurements stopped. (Measurements in blood and excreta using ^{244}Pu continued for several years.) There are also other important sources of information. The two animal experiments considered to be most reliable are the study of Brooks et al. (1992), in which measurements were made in primates for 9 y, and the ^{239}Pu study of Dagle et al. (1983) in which a large number of dogs were followed for up to 15 y. Estimates of the value of s_s from both are remarkably similar: 0.0025 and 0.0023 d^{-1}, respectively. Estimated values for rat studies range from 0.002 to 0.02 d^{-1}, but are given much lower weight in consideration of a representative value, both because the studies were in rodents, and because they were of shorter duration.

(687) Two other estimates were made from human studies. One is from analysis of the USTUR autopsy and bioassay data of a worker who received a high acute inhalation intake of plutonium nitrate (Puncher et al., 2016b). The estimated value of s_s is 0.0048 d^{-1}, which is about twice the estimates above. Factors giving it high weight are: a human study, detailed measurements, both bioassay and autopsy, and long duration (many years between exposure and autopsy). However, the measurements are on a single subject, who received an unusually high exposure and was treated with DTPA.

(688) The other estimate is from analysis of autopsy data from 20 former MPA workers considered to be exposed only to plutonium nitrate (Puncher et al., 2016c). The estimated value of s_s is 2.5 x 10^{-4} d^{-1}. This is much lower than those derived from the other human and animal studies considered above. Factors giving it high weight are: a human study, a large number of subjects, and long duration. However, the exposures are less well characterised than in the other studies considered, and there are no bioassay or other early data: the first MPA autopsy was at ~5 y after exposure. The possibility that the low value was due at least partly to the different time scale of the study was investigated here. The estimated rate of 0.0022 d^{-1} from the volunteer experiment corresponds to a half-time of about a year, and such a phase would have been completed by the time of the first autopsy. It was confirmed here that the MPA data did not exclude such a phase, by fitting an exponential retention function with three dissolution components (in addition to a bound state). With fixed values f_r = 0.2, s_r = 1 d^{-1}, and s_s = 0.0022 d^{-1}, analysis gave a fraction of 0.48 associated with the component dissolving at 0.0022 d^{-1}, and 0.32 dissolving at 1.3 x 10^{-4} d^{-1}. Such a large fraction (0.32) dissolving at such a low rate (1.3 x 10^{-4} d^{-1}), seems inconsistent with the results of the USTUR and long term dog and monkey studies. Indeed, recent re-analysis of the dog data does indicate that the large slow fraction is not compatible with the later data in that series, but is compatible with the human volunteer data because of the much shorter duration of data collection (40% is still in the lungs when the last lung measurement was taken) (M. Puncher, personal communication, 2015). It is not therefore included in the recommended specific parameter values for plutonium nitrate. However, it could be considered in assessments of high exposures. Dose assessments for a material with more dissolution components than the two included in the published HRTM can be made using software that implements the HRTM (and allows material specific parameter values to be

changed), by considering simultaneous intakes of more than one material, each with two components.

(689) In conclusion, estimated values of the slow dissolution rate s_s, from the human volunteer, and long-term monkey and dog inhalation experiments are remarkably similar: 0.0022, 0.0025 and 0.0023 d^{-1}, respectively. Estimates from the USTUR and MPA are considerably higher and lower, respectively. A rounded value of 0.002 d^{-1} is used here.

(690) Based on the studies above, specific absorption parameter values of f_r = 0.2, s_r = 0.4 d^{-1}, s_s = 0.002 d^{-1} are used here for plutonium nitrate. A specific absorption parameter value of $f_A = 1 \times 10^{-4}$ (see ingestion section) is also used.

Plutonium nitrate residues

(691) Stradling et al. (1987) exposed rats by inhalation and intra-tracheal instillation to the respirable fraction (particles less than 2 µm Stokes diameter, obtained by sedimentation) of a dust containing mainly ^{239}Pu. It had been separated from a mixture of atmospherically degraded plutonium, americium and natural uranium nitrates mixed and diluted with corrosion products from an experimental rig. After inhalation, amounts in lungs, systemic organs and in urinary and faecal samples were measured for animals killed at times between 2 and 365 days. The ^{239}Pu lung content was 41% and 3.1% IAD at 28 and 365 days, respectively. Analysis here gave: f_r = 0.4, s_r = 0.03 d^{-1}, s_s = 0.002 d^{-1}. After intra-tracheal instillation the lung content decreased from 94% ILD at 2 days to 37% ILD at 365 days. Between 2 and 365 days the liver content increased from 0.2 to 4.1% ILD and the carcass from 1.6 to 7.3% ILD. Analysis here resulted in satisfactory fits to the data only with a fixed s_r value: f_r = 0.02, s_r = 1 d^{-1}, s_s = 0.002 d^{-1}. Both sets of results give assignment to Type M.

(692) Moody et al. (1993, 1994, 1998) followed the tissue distribution of plutonium in rats for 365 days after intratracheal instillation of suspensions of two materials (designated B and C): both were 10- to 20-year old residues consisting of plutonium nitrate absorbed onto ubiquitous building dust and corrosion products. Both materials contained plutonium originating from plutonium nitrate liquor but were likely to contain partially oxidised forms. (The experiments were complemented by an inhalation study with recently separated plutonium nitrate liquor, "Material A": see Plutonium-239 nitrate section above.) For both materials the ILD was estimated by analysing aliquots of the suspension. Groups were killed at times between 3 and 365 days. The lungs, liver and total carcass were analysed for total plutonium-alpha activity. For Material B, the lung content decreased from 49% to 3.6% ILD between 1 and 365 days, whilst the liver content peaked at 2.4% at 28 days. Analysis here gave: f_r = 0.14 and s_s = 0.0012 d^{-1}. For Material C, the lung content decreased from 65% to 9.8% ILD between 1 and 365 days post exposure, whilst the liver content peaked at 1.8% at 168 days. Analysis here gave: f_r = 0.03 and $s_r = 9 \times 10^{-4}$ d^{-1}. Results for both materials are consistent with assignment to Type M, although Material C is close to the criterion for Type S.

Plutonium Tri-Butyl-Phosphate (Pu-TBP)

(693) Tri-n-Butyl-Phosphate (TBP) is used extensively as an extractant during fabrication of nuclear fuel and for the separation of uranium and plutonium during reprocessing (Purex process). Plutonium (IV) is extracted into the organic phase as the neutral complex $Pu(NO_3)_4 \cdot 2TBP$, referred to hereafter as Pu-TBP (Stradling et al., 1985). As in the case of

plutonium nitrate, absorption can be inhibited by relatively high mass loadings, possibly because of colloid formation (Nolibé et al., 1989; ICRP, 1986). Such mass effects are not considered to be of concern for routine exposures, but may have affected the experimental results below.

(694) Métivier et al. (1989a) exposed baboons (Papio papio) via an intratracheal tube to an aerosol of ^{239}Pu-TBP (30% Pu-TBP in n-dodecane). Animals were killed at times between 0.21 and 365 days. The ^{239}Pu content of the lungs, trachea, thoracic lymph nodes, femurs, humeri, liver and kidneys were analysed. Lung content fell from about 87% to 14% ILD between 0.21 and 365 days, while skeletal content increased from about 0.3 to 10% ILD. Cumulative faecal and urinary excretion were 68% and 8% ILD respectively at 365 days. In a complementary experiment, the biokinetics of systemic plutonium up to 365 days were determined in baboons after intravenous (IV) injection of the Pu-TBP solution. There was high retention in the lungs (73% of the injected activity at 2 days, and 17% at 365 days). It is possible that this was due to the formation of colloidal particles which were retained in pulmonary capillaries (see e.g. Warner and Brain, 1990; Leung et al., 1995). The distribution of the remaining activity was broadly similar to that predicted by a citrate-based systemic model. However, urinary excretion was reported to be three times higher than following (IV) injection of Pu citrate. Analysis here gave only a lower limit on s_r (> 10 d^{-1}), which was fixed at 30 d^{-1}(based on analysis of the study by Stradling et al., 1985, below) giving: f_r = 0.05, s_s = 0.002 d^{-1}, and assignment to Type M.

(695) Métivier et al. (1983) exposed rats by nose-only inhalation to an aerosol of Pu-TBP (30% Pu-TBP in n-dodecane). Plutonium in lung, liver and skeleton was measured at times between 6 hours and 400 days. About 70% ILD was excreted by fast mucociliary clearance; liver plus skeleton content at 8 days was about 0.5% ILD. In complementary experiments the biokinetics of plutonium were determined up to 30 days after intramuscular injection, and 6 days after intra-gastric administration of the Pu-TBP solution. The authors estimated gastrointestinal absorption to be ~1.5 × 10^{-4} of the administered plutonium. Analysis here, with s_r fixed at 30 d^{-1} (based on analysis of the study by Stradling et al., 1985, below), gave: f_r = 0.01, s_s = 0.0013 d^{-1}, and assignment to Type M.

(696) Stradling et al. (1985) exposed rats by nose-only inhalation to an aerosol of ^{238}Pu-TBP (30% TBP in n-dodecane). ILDs were only about 0.5 ng to ensure that they were not greatly in excess of those corresponding to human exposure at the annual limit. Groups were killed at times between 30 min and 120 days, and lungs, liver and remaining carcass (without pelt and gastro-intestinal tract), plus urine and faeces, measured. ILDs were estimated from the total activity in body tissue and excreta, ignoring that in feces in the first three days, which was considered to result mainly from ingested pelt contamination. Absorption from the lungs was very rapid: the ^{238}Pu contents of liver and carcass were about 10% ILD and 30% ILD at 30 minutes, but subsequent lung clearance was mainly by particle transport to feces. DTPA injections given to another group of rats were effective at enhancing ^{238}Pu lung clearance. The authors noted that the much slower absorption from the lungs, and ineffectiveness of DTPA, observed by Métivier et al. (1983, see above) might have been due to colloid formation. Stradling et al. (1983) had previously observed rapid absorption of ^{238}Pu (30% ILD in 1 day), following intratracheal instillation of a low mass of ^{238}Pu-TBP into hamsters. Analysis here with s_r fixed at 30 d^{-1}, (based on analysis by Davesne et al, 2010) gave: f_r = 0.5, s_s = 0.005 d^{-1}, and assignment to Type M.

(697) Specific absorption parameter values of f_r = 0.5, s_r = 30 d^{-1}, s_s = 0.005 d^{-1}, based on the study by Stradling et al. (1985), using inhalation of low masses, and f_A = 10^{-4} based on the

study by Métivier et al. (1983) are used here for Pu-TBP. As this is an organic form, it is understandable that the rapid dissolution rate should be faster than for ionic forms such as nitrate and citrate. The studies by Métivier et al. (1983, 1989a) suggest that a lower value of f_r (~0.02) might apply in the case of a high accidental intake: specific parameter values are not applied here because such intakes would require special investigation. The distribution of absorbed plutonium between systemic organs is broadly similar to that of ionic forms, and therefore it is considered that the plutonium systemic model described in Section 18.2.3. can be applied to Pu-TBP with caution. The greater transfer from blood to urine (compared to citrate) observed by Métivier et al. (1989a) following IV injection, is not implemented here, partly because of uncertainties associated with the experiment. Assumption of enhanced urinary excretion would make little difference to the inhalation dose coefficient, because urinary excretion would still be small compared to systemic deposition. However, systemic uptake (and intake) estimated from urinary excretion would be much lower, and could be underestimated if enhanced urinary excretion did not occur in practice.

Plutonium dioxide (PuO_2)

(698) Plutonium dioxide is the final product in the manufacture of fuel pellets, and is present in mixed oxide fuel (MOX) with uranium oxide. PuO_2 can be present in different physico-chemical forms: its production temperature can vary from 300 to 1800°C. Numerous studies in several animal species have been conducted, and measurements after accidental inhalation in man have been performed. Following exposure to PuO_2 aerosols, generally two distinct phases of absorption to blood from the respiratory tract are exhibited: a small rapidly-absorbed fraction, which is possibly related to ultrafilterable (<25 nm diameter) particles (ICRP, 1986; Smith et al., 1977, see also below) and the remainder, which is generally cleared with a half-time of the order of years or decades. Both the fraction rapidly absorbed and the long-term retention half-time can be influenced by the method of formation of the material and its history (ICRP, 1986).

Plutonium-239 dioxide

(699) Plutonium in the dioxide form used in the production of nuclear fuel is predominantly ^{239}Pu by activity, and for simplicity is here termed $^{239}PuO_2$. It may, however, contain varying amounts of other isotopes, notably: ^{238}Pu, ^{240}Pu, ^{241}Pu and ^{242}Pu. Plutonium-241 decays to ^{241}Am, which emits a 60-keV gamma ray that is more readily measured by external detectors than the low energy x-rays resulting from the decay of plutonium.

(700) In analyses of data on plutonium oxides and mixed oxides containing plutonium conducted here, the value for the rapid dissolution rate was fixed: $s_r = 1\ d^{-1}$ for rats and $s_r = 0.4\ d^{-1}$ for all the other species (see the *Rapid dissolution* section below).

Man

(701) Cases of accidental intake of plutonium oxides at the Rocky Flats Plant (RFP) show very long term lung retention of plutonium, and correspondingly low dissolution *in vivo*. Gr**e**goratto et al. (2010) analysed nine cases, which were considered in a previous study, based on lung measurements and reported in a National Institute for Occupational Safety and Health (NIOSH) Technical Document (ORAUT, 2007). Lung and urine measurements are available for up to 30-38 years. Six of the RFP cases were exposed to plutonium from a fire in October 1965

(Mann and Kirchner, 1967). The plutonium consisted of 'high-fired' PuO_2. Gregoratto et al. (2010) analysed the lung and urine data for the six workers and the median values were f_r = 0.005 and $s_s = 4 \times 10^{-6}$ d^{-1}, consistent with assignment to Type S.

(702) Avtandilashvili et al. (2012) reported bioassay data (lung, urine and faecal measurements) for USTUR donors 0202 and 0407, who are the two most highly exposed of the 18 USTUR Registrants who were involved in the 1965 RFP fire. They also reported ^{239,240}Pu post mortem tissue analyses for Case 0202. (No radiochemical analyses had yet been performed on Registrant 0407's tissue samples taken at autopsy.) They carried out a maximum-likelihood analysis of the results, using the AI particle transport model of Gregoratto et al. (2010), on which that of the updated HRTM (ICRP, 2015) is based, and derived material-specific absorption parameter values. For both Cases, about 1% was absorbed relatively rapidly, with half-times (T_b) of approximately 8 h (s_r = 1 d^{-1}, Case 0202) or 16 h (s_r = 2 d^{-1} Case 0407), respectively; and the remainder absorbed extremely slowly, with T_b approximately 400 y (Case 0202) or 360 y (Case 0407), respectively, giving $s_s = 5 \times 10^{-6}$ d^{-1} for both. Avtandilashvili et al. (2013) applied Bayesian inference techniques to the same data to obtain probability distributions for the parameter values. Central estimates of values of s_r were higher (about 2 d^{-1} for Case 0202; and 6 d^{-1} for Case 0407) than the point estimates obtained by Avtandilashvili et al. (2012), but those for s_s were similar. These values are consistent with assignment to Type S.

(703) Puncher et al. (2016d) analysed autopsy data from 20 Mayak workers exposed to plutonium-239/240 oxides. Urine data were not used because they were affected by large uncertainties. However, measurements of plutonium activity in skeleton, liver, lungs, and thoracic lymph nodes at death, ranging from 5 to 18 years post-exposure, and information from the workers' exposure histories (Birchall et al., 2016), were used in a Bayesian analysis to estimate the slow dissolution rate. A value of $s_s = 4.5 \times 10^{-5}$ d^{-1} was obtained, with f_r and s_r were fixed at 0.0026 and 1 d^{-1} respectively as the data were not informative for these parameters, being based on measurements at late times following exposure.

(704) Ramsden et al. (1970) reported measurements (external and excreta) made on a worker in an experimental plutonium fuels laboratory, following accidental inhalation of a compacted mixture of plutonium oxide and graphite, produced from the oxalate by calcining at 500°C, dry mixing and sintering at 1200°C. Faecal samples were obtained for the first 5 days and at times up to 470 days, and analysed for $^{239+240}$Pu and ^{238}Pu. The results indicated that the worker had also been exposed to a different material, which complicates any analysis. The two forms of plutonium are referred to as "low burn up" (5.4% ^{240}Pu by weight) and "high burn up" (14% ^{240}Pu by weight). Faecal data are provided for both materials. Urine measurements, started 2 weeks after the incident, were near the limit of detection and decreased with time. Lung measurements were made at six times between 15 and 566 days. Ramsden (1976) reported further lung measurements on this worker, up to 1500 d. Analysis here gave f_r = 0.006, $s_s = 7 \times 10^{-6}$ d^{-1}, and assignment to Type S.

(705) Ramsden (1976) also reported plutonium-in-lung measurements made on four other workers after single acute inhalation exposures to plutonium oxide in the same laboratory. Measurements were made up to times between 30 and 1000 days. In all cases lung retention was fit by a two-exponential function with an intermediate phase of half-time (T_b) about 10-50 days and a long-term phase with T_b up to 600 days. There is insufficient information to estimate absorption parameter values: the results suggest Type M or S behaviour.

(706) Ramsden (1976) and Ramsden et al. (1978) reported lung and excreta measurements made on a worker who was involved in a number of minor incidents involving inhalation of high-fired plutonium oxide over a 12-year period. Ramsden (1984) reported a further 7 years

lung retention data on the subject, during which period there was little, if any, clearance from the lungs. Analysis here gave an upper limit on the slow absorption rate: $s_s < 1 \times 10^{-4}$ d^{-1}, indicating Type S behaviour.

(707) Spitz and Robinson (1981) reported measurements of plutonium in excreta and in-vivo chest measurements of ^{241}Am for a worker exposed to plutonium released in air during routine operations with plutonium dioxide pellets in a glovebox. The isotopic composition of alpha-activity was 8%, 80%, and 12% for ^{238}Pu, $^{239+240}$Pu and ^{241}Am, respectively. The ^{241}Pu gave rise to measurable ingrowth of ^{241}Am. DTPA chelation therapy was performed five times within ten days after intake. Chest measurements of ^{241}Am, corrected for ingrowth, did not show any decrease during the 500 days follow-up (the data showed a small increasing trend with a 95% confidence interval [-3×10^{-4}, 2×10^{-4} d^{-1}] for the overall clearance rate) and no measurable amount of plutonium in urine excretion after three weeks nor detectable activity in faeces 280 days after exposure (the previous measurement is at 6 days). The authors estimated that less than 1% of the inhaled plutonium was excreted in urine and faeces, including the first week after intake and during the chelation therapy, indicating that the material was very insoluble in lungs: Type S behaviour.

(708) Carbaugh and La Bone (2003) analysed extensive data obtained over 6500 days as follow-up monitoring for a worker (HAN-1) who accidentally inhaled an aerosol of high-fired plutonium oxide (calcined at 600°C). In-vivo lung measurements of ^{241}Am showed very long term lung retention. No activity was detected in faecal samples at 600 and 2200 days and early urine samples showed only a very slight systemic uptake. This case has been previously analysed by Carbaugh and La Bone (2003); Fritsch (2007); Davesne et al. (2010); and Gregoratto et al. (2011). Information on the early rapid absorption phase was difficult to analyse because of the possible enhancement of urine excretion due to the administration of DTPA but all analyses found a slow particle transport clearance, more consistent with the revised HRTM (ICRP, 2015) than with the original HRTM (ICRP, 1994) and a slow dissolution rate, $s_s = 10^{-5}$ d^{-1}.

(709) Bihl et al. (1988a,b,c) reported on ten cases of inhaled plutonium at the Hanford nuclear site (including HAN-1), that showed extremely slow clearance from the lung and very little short-term or long-term absorption, and which they referred to as "Super Class Y plutonium". Evidence suggested that the chemical form was plutonium oxide. Except for HAN-1 above, there is insufficient information to estimate absorption parameter values. However, approximate lung retention half-times ranged from 5000 to >20,000 days: the results therefore suggest Type S behaviour, and that the behaviour observed in HAN-1 is not exceptional.

(710) Surendran et al. (1995) reported measurements of ^{241}Am in the lungs of a worker exposed to high burn-up plutonium, which showed a linear increase over a 6-year period. There was no detectable ^{241}Am in skeleton and liver, and negligible excretion. The authors noted that this case provided the first supporting evidence from another laboratory of "Super Class Y" plutonium" as observed for HAN-1.

Monkeys

(711) Métivier et al. (1978, 1989a) studied the radiation effects and lung clearance of ^{239}Pu after inhalation (through a mask) of $^{239}PuO_2$ by 64 immature baboons (*Papio papio*). The $^{239}PuO_2$ was prepared by calcining plutonium peroxide at 1000°C. The ILD was determined from in-vivo x-ray measurements one week later. Plutonium tissue distributions were determined at death, mostly between about 25 and 4000 d after exposure. Radiation

pneumonitis, pulmonary fibrosis and respiratory insufficiency were the primary causes of death. Bair et al. (1980) compared the lung clearance and radiation effects in this study (results available up to 1978) with corresponding results obtained in a separate study with Beagle dogs (see below). They concluded that lung clearance and effects were similar in the two species. Poncy et al. (1998) reported results on two baboons that died at 6900 and 8700 d. The lung clearance half-time for most baboons was between 600 and 3900 days. Activity in liver plus skeleton increased slowly to about 1% ILD at 2000 d. Analysis here gave f_r = <0.001, $s_s = 10^{-5}$ d^{-1}, and assignment to Type S

(712) LaBauve et al. (1980) exposed 16 immature rhesus monkeys via inhalation to $^{239}PuO_2$ aerosol labelled with ^{169}Yb. Monkeys were exposed in groups to four different initial lung burdens. In-vivo whole-body ^{169}Yb measurements were made up to 200 days and it was estimated that $^{239}PuO_2$ was retained in the body with an average effective half-time of 1000 days. Autopsy data are reported for four monkeys sacrificed 4 h and 30 days and for three monkeys which died at 430, 443 and 990 days (two from radiation pneumonitis, and the third from gastric torsion, presumably not related to Pu exposure). The data show little absorption, with less than 1% ILD in systemic organs and lung content decreasing between 400 and 1000 days from 73% to 42% ILD (one animal) with a major transfer to lymph nodes, from 5% to 36% ILD at 400 and 1000 days respectively. Analysis here gave: f_r = 0.001, $s_s = 6 \times 10^{-6}$ d^{-1}, and assignment to Type S.

(713) Stanley et al. (1980b) exposed monkeys (six cynomolgus and three rhesus), dogs, and rats by inhalation to aerosols of $^{239}PuO_2$, heat-treated at 850°C, as used in the fabrication of nuclear fuel. Measurements of activity in lung, TBLN, liver and skeleton were made at sacrifice at times between 4 hours, and 1.5 years. In monkeys, activity in lung (lymph nodes) was 30(13)% and 60(5)% ILD at 1 and 1.5 years, and 0.04% in liver after 1.5 years. No liver measurements are available at earlier times and the systemic model was adjusted to account for the shorter residence time of Pu in the liver as in the analysis of Brooks (1992). Analysis here gave: $f_r = 2 \times 10^{-3}$, $s_s = 2 \times 10^{-6}$ d^{-1} with significant uncertainties but consistent with assignment to Type S.

(714) Lataillade et al. (1995) exposed three pairs of baboons by tracheal intubation each to a different form of plutonium oxide: 1) an industrial PuO_2 (70% ^{239}Pu and 0.2% ^{238}Pu, heat-treated at 950°C; 2) a "reference" pure ^{239}Pu oxide obtained by calcining Pu peroxide at 1000°C, grinding it and reheating it at 1000°C; and 3) a mixed U-Pu oxide (see below in the MOX section). (Experiments with rats were also conducted, see below.) Baboons were kept for one year, urine was collected daily for the first 6 days and one week per month afterwards for the baboons exposed to the industrial Pu oxide. The ILD was estimated from in-vivo measurements of x-rays one week after exposure. Lung, thoracic lymph nodes, liver, kidneys, femora and humeri were measured at sacrifice and activity in skeleton was estimated as 5.9*(femora + humeri). Plutonium translocation to the systemic organs after one year was greater after inhalation of the "reference" ^{239}Pu oxide than after the inhalation of the industrial Pu oxide, about 0.85% and 0.05% ILD respectively. Analysis here for the industrial Pu oxide gave: f_r = 0.002, $s_s = 4 \times 10^{-6}$ d^{-1} with significant uncertainties but consistent with assignment to Type S.

Dogs

(715) Bair and McClanahan (1961) exposed four dogs by nose-only inhalation to an aerosol of $^{239}PuO_2$. Two were killed after 30 min and two after 39 weeks: plutonium in lungs

and systemic organs was measured. About 1.5% ILD was found in the systemic organs at 30 min. Urine and faeces were collected from the dogs kept for 39 weeks: the total urinary excretion was 1.3% and 1.6%. Analysis here gave: f_r = 0.2 and an undefined very low value for s_s, consistent with assignment to Type M.

(716) Bair and Willard (1963) exposed 48 Beagle dogs by nose-only inhalation to $^{239}PuO_2$ aerosols, prepared by calcining plutonium oxalate at 325°C, with three particle size distributions: MMD = 0.65, 3.3 and 4.3 □m (GSD = 2.3). Dogs were killed immediately after exposure, and after 1, 7, and 14 days. Activity expressed as percent of initial alveolar deposit (IAD) was measured in lungs, systemic organs and in urine and faeces. At 14 days the lung content was about 50%, 88% and 95% IAD, the systemic content plus urine cumulative excretion was 20%, 5% and 2% IAD for the aerosols with MMD = 0.65, 3.3 and 4.3 □m respectively, and indicate that dissolution increases with decreasing particle size. There is insufficient information to estimate absorption parameter values: the results suggest Type M behavior.

(717) Park et al. (1972) studied the biological effects and the disposition of inhaled $^{239}PuO_2$ in 70 Beagle dogs. Thirty were given a single exposure as described in Bair and Willard (1962) and the other 40 were given single exposures via a mask. The $^{239}PuO_2$ was formed from plutonium oxalate calcined in air at 300-350°C or 450°C. Sixty dogs died or were euthanised when death was imminent due to plutonium-induced pulmonary fibrosis and/or neoplasia 2-135 months post-exposure. After 8-10 y, approximately 10% IAD was retained in the lungs, 40-50% was translocated to the tracheobronchial and mediastinal lymph nodes, 10-15% to the liver, 5% to the skeleton and 5% to the abdominal lymph nodes. The pathology in these tissues may have influenced the clearance and translocation rates of the plutonium. Analysis here gave: f_r = 0.004, $s_s = 5 \times 10^{-5}$ d^{-1}, and assignment to Type S.

(718) Bair et al. (1980) exposed 43 Beagle dogs to $^{239}PuO_2$, prepared by calcining plutonium oxalate at 300–430°C. The aerosol was inhaled through a mask. The ILD was determined from the body burden at death and excreta collection from a subset of dogs. All the dogs died or were euthanised when moribund. Radiation pneumonitis, pulmonary fibrosis and respiratory insufficiency were the primary causes of death. Activity measurements are available from 55 to 1549 days for lung and from 80 to 1549 days for skeleton. Analysis here gave: $f_r = 3 \times 10^{-4}$, $s_s = 6.5 \times 10^{-5}$ d^{-1}, and assignment to Type S.

(719) Stanley et al. (1980b) exposed 18 Beagle dogs by inhalation to $^{239}PuO_2$ (see description of the experiment in *Monkey* section above). Dogs showed slower lung clearance than monkeys and a larger transfer to TBLN compared to monkeys and rats. Activity in lung (and lymph nodes) was 66 (21)% and 53 (19)% ILD at 1 and 1.5 years, and 0.27% in liver after 1.5 years. Analysis gave here: $f_r = 6 \times 10^{-4}$, $s_s = 9 \times 10^{-6}$ d^{-1}, and assignment to Type S.

(720) Diel et al. (1980a, 1992) investigated the lifespan dose effects and disposition of inhaled monodisperse 0.75-µm $^{239}PuO_2$ particles in Beagle dogs after single (48 animals) or repeated (39 animals) exposure. For dogs exposed once, lung retention of plutonium over nearly 10 years could be represented by the sum of two exponentials with T_b of 63 and 1130 days associated with 28% and 62% ILD respectively. Systemic tissue and urine measurements were not reported because the activities found in tissues other than the lung were less than 5% of the body burden: 99% of the body burden at one year after initial exposure and 95% at two years was in either the lung or the lung associated lymph nodes and 99% of excreted activity was in the feces. This limited information does not allow precise estimating of dissolution parameters but values of f_r of the order of 0.005 and s_s of the order of 5×10^{-5} d^{-1}, and assignment to Type S, are consistent with the observations.

(721) Guilmette et al. (1984, 1987) studied the retention and distribution of $^{239}PuO_2$ in Beagle dogs after inhalation of monodisperse aerosols with AMAD about 0.7, 1.5 or 3 □m. Guilmette et al. (1984) measured activity excreted in urine and feces and in lungs, thoracic lymph nodes, liver, and skeleton of dogs killed at times between 0.2 and 730 days. Guilmette et al. (1987) followed other animals which inhaled 1.5- or 3-□m aerosols over their life-span up to 3 years post-inhalation, with activity measured in the same tissues plus kidneys, spleen and other sets of lymph nodes. Analysis here gave: f_r = 3 x 10^{-4}, s_s = 10^{-5} d^{-1} for all three particle sizes, consistent with assignment to Type S.

(722) Park et al. (1990, 1986a) investigated the life-span dose effects and the disposition of inhaled $^{239}PuO_2$ in 130 Beagle dogs. The oxide was prepared by calcining the oxalate at 750°C for 2 hours. Dogs were given a single exposure to obtain six dose levels (generally lower than those used by Park et al., 1972), and were followed for up to 16 years. After 10 years, about 10% IAD was retained in the lungs, 40% was translocated to lymph nodes, and 10% to liver and skeleton combined. Analysis here gave: f_r = 0.001, s_s = 3 x 10^{-5} d^{-1}, and assignment to Type S. Park et al. (1990) carried out a similar study with $^{238}PuO_2$, which showed greater long-term transfer of plutonium to systemic tissues, and a much higher value of s_s (see below).

Rats

(723) Rhoads et al. (1986) exposed rats, by nose only inhalation, in groups of 35 to either high fired $^{239}PuO_2$ or to a mixed $^{239}Pu/^{244}Cm$ oxide. Groups were killed at times between 3 and 120 days. Activity was measured in lung, systemic organs and excreta. Less than 1% IAD was translocated to any of the systemic tissues. Lung clearance of plutonium was slightly slower for the mixed oxide than for the pure oxide. Analysis here for the pure oxide gave: f_r = 0.001 and s_s = 3 x 10^{-6} d^{-1}, and assignment to Type S.

(724) Stradling et al. (1987) exposed rats by inhalation to the respirable fraction of ^{239}Pu oxide (the product of corrosion of the metal under ambient conditions over a period of about 15 years). After inhalation, groups were killed at times between 3 and 365 days. The ^{239}Pu IAD was determined from rats killed on day 3. The lung content reduced to 10% IAD at 365 days. The carcass content rose from 0.06% at 3 days to 0.7% at 365 days. Analysis here gave: f_r = 0.0006, s_s = 9 x 10^{-5} d^{-1}, and assignment to Type S.

(725) Stradling et al. (1990) administered the respirable fraction of a PuO_2 dust (coded ALDP9, produced by ignition of the metal in air) to 40 rats by nose only inhalation, and to 10 rats by intratracheal instillation. The dust contained ^{241}Am oxide as a decay product of ^{241}Pu. After inhalation, the Pu contents of the lungs, liver and remaining carcass were measured. The ILD was obtained from tissue analysis of rats killed at 2 days. Further groups were killed at times between 7 and 730 days. Lung content decreased to 1.5% ILD whilst carcass content increased to 0.12% at 730 days. Analysis here gave: f_r = 4 x 10^{-4} and s_s = 5 x 10^{-5} d^{-1}. After instillation, groups were killed at 7 and 21 days. The Pu content of the lungs, liver, remaining carcass, urine and faeces were measured and the ILD was assessed from the total activity in the tissues and excreta. Lung content decreased from 78% to 47% ILD between 7 and 21 days. Analysis here gave: f_r = 4 x 10^{-4} and s_s = 3 x 10^{-5} d^{-1}: both values were similar to those obtained after inhalation, and consistent with assignment to Type S.

(726) Lataillade et al. (1995) exposed rats by inhalation to an aqueous solution of the respirable fraction of a reference industrial $^{239}PuO_2$ (heat treated at 950ºC). Groups were killed at times between 1 and 180 days: the Pu contents of the lungs, liver and skeleton (ten times the femora content) was measured. The IAD was estimated from lung contents measured at 1 day.

The lung content fell to about 12% IAD at 180 days. Analysis here gave: f_r = 0.008 and s_s = 5 x 10^{-4} d^{-1}, and assignment to Type S.

(727) Ramounet et al. (2000) exposed groups of 30 rats to an aerosol of industrial PuO_2 obtained after calcination. Groups were killed at times between 7 days and 9 months. The initial deep lung deposit (IDLD) was defined as the mean lung content at 7 days. The Pu content of the liver, kidneys and the two femora were measured (assumed to be 10% of the skeleton). The Pu content of the skeleton remained fairly constant at 0.7% IDLD. Analysis here gave: f_r = 0.0012, s_s = 3 x 10^{-5} d^{-1}, and assignment to Type S.

(728) Pellow et al. (2003) exposed 36 rats by inhalation (nose only) to an aerosol of $^{239}PuO_2$ obtained from an industrial production line, filtered to obtain particle sizes mostly between 0.2 and 3 µm. Groups of rats were killed immediately after exposure and at times between 1 and 365 days. Plutonium was measured in the lungs, liver, other tissues and the remaining carcass, and reported as a percentage of the total activity associated with each animal. The lung content fell from 9% immediately after exposure to 0.7% at 365 days. The carcass content remained constant at about 0.2% from 28 to 365 days. Analysis here gave: f_r = 0.06, s_s = 9 x 10^{-4} d^{-1}, and assignment to Type M.

(729) Pellow et al. (2003) administered the same material to 40 rats by intratracheal instillation. Rats were killed in groups of four at times between 1 hour and 28 days. Plutonium was measured in the lungs, liver, head (plus head-pelt), pelt, gastro-intestinal tract and remaining carcass. The ILD was estimated from animals for which there was a complete activity balance. The lung content reduced from 78% ILD at 1 hour to 33% at 28 days. Analysis here gave: f_r = 0.03, s_s = 0.003 d^{-1}, and assignment to Type M.

Mouse

(730) Morgan et al. (1988a) exposed mice by nose-only inhalation to $^{238}PuO_2$ (see below) and $^{239}PuO_2$, fired at temperatures of 550, 750, 1000 and 1250°C. Groups were killed at times between 1 and 24 months. Measurements were made of ^{238}Pu and ^{239}Pu in the lungs, lung-associated lymph nodes, liver and skeleton. Lung retention was independent of firing temperature for ^{239}Pu and translocation to liver and bone was smaller than for ^{238}Pu. Davesne et al. (2010), using fixed values for s_r = 100 d^{-1} and f_b = 0, estimated dissolution parameter values for the four ^{239}Pu aerosols: f_r = 9 x 10^{-5} (all four); and s_s = 7 x 10^{-6} d^{-1} (550°C); s_s = 5 x 10^{-6} (750°C); s_s = 5 x 10^{-6} d^{-1} (1000°C); and s_s =1 x 10^{-5} d^{-1} (1250°C), all consistent with assignment to Type S.

Table 22.4. Estimated absorption parameter values for inhaled plutonium-239 dioxide. Values in parentheses were fixed in analyses.

Species	Absorption parameter values[a] and duration T of study				References
	f_r	s_r (d^{-1})	s_s (d^{-1})	T (y)	
Man	0.006	(0.4)	7 x 10^{-6}	4	Ramsden et al. (1970)
Man	(0.001)	(9.9, 100)	1 x 10^{-5}	18	Carbaugh and La Bone (2003)
Man	0.005	(100)	4 x 10^{-6}	30-38	Gregoratto et al. (2010)
Man	0.01	2	5 x 10^{-6}	18, 43	Avtandilashvili et al. (2012, 2013)
Man	(0.0026)	(1)	4.5 x 10^{-5}	18	Puncher et al. (2016d)
Baboon	<0.001	(0.4)	10^{-5}	3.5	Métivier et al. (1978, 1989a)
Monkey	0.002	(0.4)	2 x 10^{-6}	1.5	Stanley et al. (1980b)

Monkey	0.001	(0.4)	6×10^{-6}	2.5	LaBauve et al. (1980)
Baboon	0.002	(0.4)	4×10^{-6}	1	Lataillade et al. (1995)
Dog	0.2	(0.4)	-	0.75	Bair and McClanahan (1961)
Dog	0.004	(0.4)	5×10^{-5}	8-10	Park et al. (1972)
Dog	3×10^{-4}	(0.4)	7×10^{-5}	4.2	Bair et al. (1980)
Dog	6×10^{-4}	(0.4)	9×10^{-6}	1.5	Stanley et al. (1980b)
Dog	(3×10^{-4})	(0.4)	1×10^{-5}	3	Guilmette et al. (1984, 1987)
Dog	0.001	(0.4)	3×10^{-5}	16	Park et al. (1990)
Dog	0.005	(0.4)	5×10^{-5}	10	Diel et al. (1980a, 1992)
Rat	0.0011	(1)	3×10^{-6}	0.3	Rhoads et al. (1986)
Rat	0.0006	(1)	9×10^{-5}	1	Stradling et al. (1987)
Rat	4×10^{-4}	(1)	5×10^{-5}	2	Stradling et al. (1990)
Rat	0.008	(1)	5×10^{-4}	0.5	Lataillade et al. (1995)
Rat	0.012	(1)	3×10^{-5}	0.75	Ramounet et al. (2000)
Rat	0.06	(1)	9×10^{-4}	1	Pellow et al. (2003)
Mouse[b]	9×10^{-5}	(100)	7×10^{-6}	2	Morgan et al. (1988a)
Mouse[b]	9×10^{-5}	(100)	5×10^{-6}	2	Morgan et al. (1988a)
Mouse[b]	9×10^{-5}	(100)	5×10^{-6}	2	Morgan et al. (1988a)
Mouse[b]	9×10^{-5}	(100)	1×10^{-5}	2	Morgan et al. (1988a)
Man, baboon, monkey, dog					
Median	0.0020		1×10^{-5}		
Geom. mean	0.0023		1.2×10^{-5}		
Min	3×10^{-4}		2×10^{-6}		
Max	0.2		7×10^{-5}		
All species					
Median	0.0011		1×10^{-5}		
Geom. mean	0.0015		1.7×10^{-5}		
Min	9×10^{-5}		2×10^{-6}		
Max	0.2				

a f_b and s_b were assumed to be 0.002 and 0 d^{-1} respectively.
b From Davesne et al. (2010), Table 1.

(731) In-vitro dissolution studies performed by Eidson et al. (1983) and Rateau-Matton et al. (2004) gave absorption parameter values of the same order of magnitude with $f_r = 0.003$, $s_r = 0.7\ d^{-1}$ and $s_s = 0.8–7.0\ 10^{-5}\ d^{-1}$, all consistent with assignment to Type S.

(732) Estimates of absorption parameter values for plutonium-239 oxide derived above are summarised in Table 22.4. (Absorption parameter values from two rat instillation studies are not included, because they were of much shorter duration, and there are ample results from inhalation experiments.) In all studies the material was relatively insoluble in the lungs, with low values of f_r and s_s. Most sets of parameter values gave assignment to Type S.

(733) With regard to f_r, there is considerable variation in the estimated values from animal experiments, with a range from about 1 x 10^{-4} to 0.2, which encloses the range of values, 0.001 to 0.01, from the human cases. The geometric mean from the human studies, 0.004, is chosen here.

(734) As the rapidly-dissolved fraction was so small, in nearly all cases there was insufficient information to estimate the value of s_r, which was fixed in analyses conducted here at either 0.4 or 1 d^{-1}.

(735) With regard to the slow dissolution rate, s_s, it is considered that the information from human cases and dog and monkey studies should be given more weight than rat and mouse studies, partly because of the uncertainty associated with estimates of such low rates in experiments of limited duration.

(736) A number of accidental occupational intakes of plutonium oxides described above had shown long-term retention of plutonium in the lung exceeding that predicted by the original HRTM (ICRP, 1994) and default Type S slow dissolution rate. The results for the absorption parameter values reported in Table 22.4 have been obtained by using the revised HRTM (ICRP, 2015) or, by the authors of some of the studies, by slowing down the particle clearance within the original HRTM (ICRP, 1994).

(737) The most informative case study is the 35-year follow up of a group of workers who inhaled plutonium dioxide in the 1965 RFP fire (Mann and Kirchner 1967; ORAUT, 2007). The estimated value of s_s is 4 x 10^{-6} d^{-1}. Factors giving it high weight are: a group of workers exposed to a very similar aerosol in the same incident, detailed lung and urine measurements and very long duration.

(738) Two other informative case studies with long follow up reported here are Ramsden (1970) and Carbaugh and LaBone (2003). The estimated values of s_s are 1 x 10^{-5} and 7 x 10^{-6} d^{-1} respectively. Factors giving both studies high weight are: a human study, detailed lung and excretion measurements, long duration. A potential problem with these human data is that each involved only one subject: the biokinetics might be exceptional and have been selected for publication because retention was so long.

(739) Two other estimates were made from human studies. One is from analysis of autopsy data from 20 former MPA workers considered to be exposed only to plutonium oxide (Puncher et al., 2016d). The estimated value of s_s is 4.5 x 10^{-5} d^{-1}. Factors giving it high weight are: a human study, a large number of subjects, and long duration. However, the exposures are less well characterised than in the other studies considered, and there is very limited bioassay information.

(740) The other estimate is from analysis of the USTUR autopsy and bioassay data of two workers involved in the 1965 RFP fire and with the two highest exposures (Avtandilashvili et al., 2012, 2013). The estimated value of s_s in both cases is 5 x 10^{-6} d^{-1}. Factors giving it high weight are: a human study, detailed measurements, both bioassay and autopsy, and long duration (many years between exposure and autopsy). However, the measurements are on two subjects who received unusually high exposures (3 Gy to AI by 18 y post-intake, and 3 Gy to AI 43 y post-intake). One subject also had previous exposure to coal mine dust and was a smoker. The values of s_s for the humans studies range from 4 x 10^{-6} to 4.5 x 10^{-5}, with geometric mean 9 x 10^{-6} d^{-1}.

(741) The primate experiments reported here cannot be given high weight: the study of Métivier et al. (1989a) was intended primarily as a mortality study and lung function may have been impaired, with radiation pneumonitis, pulmonary fibrosis and respiratory insufficiency being the primary causes of death. The other studies, Stanley et al. (1980b), LaBauve et al.

(1980), and Lataillade et al. (1995), are of shorter duration (1 to 2.5 y) and with a small number of data, which gives more uncertain estimates of s_s. Nevertheless, the geometric mean value of the estimates of s_s is 5 x 10^{-6} d^{-1}, similar to the value from the human studies.

(742) The dog experiment considered to be most reliable with respect to long duration and relatively low doses is that of Park et al. (1990), which gave an estimated value of s_s of 1 x 10^{-5} d^{-1}. The geometric mean for the dog studies is 3 x 10^{-5} d^{-1}.

(743) Estimated values for rat and mice studies range from 3 x 10^{-6} to 9 x 10^{-4} d^{-1}, but are given much lower weight in consideration of a representative value, both because the studies were in rodents, and because they were of shorter duration. Geometric mean values of s_s are similar, about 1 x 10^{-5} d^{-1}, for human studies alone, large animal studies only, or all species.

Based on the studies above, specific absorption parameter values of f_r = 0.004 and s_s = 1 x 10^{-5} d^{-1}, with the default value of s_r = 0.4 d^{-1}, are used here for plutonium-239 dioxide. A specific absorption parameter value of f_A = 1 x 10^{-5} (see ingestion section) is also used.

Plutonium in mixed oxide (MOX: (UO_2 + PuO_2) or (U,Pu)O_2)

(744) Actinide-bearing mixed oxides (MOX) have been used as fuel in some pressurised water reactors (PWR). These materials are prepared using different fabrication processes, consisting either of a dry mix of plutonium and depleted uranium oxides, UO_2 + PuO_2, referred to as the MIMAS process (Haas et al., 1994; Massiot et al., 1998a); or co-precipitation of soluble forms of these actinides, (U,Pu)O_2, referred to as the SOLGEL process, where the powder forms are obtained by calcination or grinding (Massiot et al., 1998b; Stringer et al., 1984). Plutonium can form between about 2.5% and 7% by mass, with an isotopic composition depending on its history.

Man

(745) Foster (1991) reported measurements of plutonium activity in lungs, urine and feces made up to about 1000 days following inhalation of blended plutonium and uranium oxides (approximate ratio 1:2 by mass) by a worker in an industrial fuel production facility. Interpretation of the data was complicated by previous small exposures. The isotopic composition by alpha-activity of the material from analysis of a nasal smear and a nose blow sample was 7%, 55%, and 38% for ^{238}Pu, $^{239+240}$Pu and ^{241}Am, respectively. Analysis here of the data, corrected by the authors for the observed levels of retention and excretion prior to the last intake, gave f_r = 0.05, s_s = 2 x 10^{-5} d^{-1}, and assignment to Type S. Foster noted that inhalation studies in rats and hamsters had been carried out on material from this working area: but the materials studied showed very little absorption from the lung, giving lower values of both f_r and s_s (James et al., 1978, see below).

Monkey

(746) Stanley et al. (1980a) exposed monkeys (seven cynomolgus and two rhesus), dogs and rats by inhalation to aerosols of mixed uranium-plutonium oxides, heat-treated at 1750°C in the fabrication of nuclear fuel. Monkeys were killed at times between 4 hours, and 1.5 years. Measurements of activity in lung, TBLN, liver and skeleton were made: activity in lung (lymph nodes) was 44 (0.7)% and 38 (3)% ILD at 1 and 1.5 years, and 0.14% in liver after 1.5 years. Because of the small number of data and the very similar experimental conditions to those of Mewhinney and Eidson (1982), data were pooled for analysis (see below).

(747) Stanley et al. (1982) exposed monkeys (six cynomolgus and three rhesus), dogs and rats to an aerosol containing a mixture of UO_2 and 750°C heat-treated PuO_2 (77% and 23% by mass respectively). Powders produced during the routine ball milling of mixed oxides were collected from the floor of the glove-box at an industrial facility and used to generate an aerosol with a size distribution similar to those observed in samples collected at the industrial site. Monkeys were killed at times between 4 hours and 2 years. ILDs were calculated by adding the activity found in all tissues at death to that estimated to have been excreted from day 4 onwards. The material was relatively insoluble in the lungs of all species. Monkeys and rats cleared plutonium from their lungs faster than dogs. Very little plutonium translocated in the first 2 years to tissues other than TBLN. Because of the small number of data and the very similar experimental conditions to those of Mewhinney and Eidson (1982), data were pooled for analysis (see below).

(748) Mewhinney and Eidson (1982) exposed 6 cynomolgus monkeys, 12 dogs and 30 rats to aerosols derived from the industrial production of nuclear fuel, containing either mixed uranium-plutonium oxides heat-treated at 1750°C, or a mixture of UO_2 and 750°C heat-treated PuO_2. For each study, one monkey was killed shortly after exposure, at times between 64 days and and 4 years. Plutonium content was measured in lungs, TBLN and liver. Because of the small number of data and the very similar experimental settings to the two previous studies above, Stanley et al. (1980a) and Stanley et al. (1982), data were pooled for each type of MOX, and analysis here gave: $f_r = 0.0012$, $s_s = 5 \times 10^{-6}$ d^{-1} (1750°C); and $f_r = 3 \times 10^{-4}$, $s_s = 3 \times 10^{-6}$ d^{-1} (750°C), respectively, both giving assignment to Type S.

(749) Lataillade et al. (1995) exposed three pairs of baboons by tracheal intubation to different forms of plutonium oxide. One pair was exposed to a mixed U-Pu oxide (see above for the oxide cases and a description of the experimental procedure). Plutonium translocation to the systemic organs after one year was greater after inhalation of the mixed oxides, about 2.1% ILD, than after the inhalation of the industrial and reference Pu oxides, about 0.85% and 0.05% ILD respectively. Analysis here gave: $f_r = 0.03$, $s_s = 4 \times 10^{-4}$ d^{-1}, and assignment to Type S.

Dog

(750) Stanley et al. (1980a) exposed 18 Beagle dogs to aerosols of mixed U-Pu oxides (see above for description of the experiment). Dogs were killed at times between 4 hours and 2 years. Dogs showed slower clearance from lung and liver than monkeys and greater transfer to TBLN than monkeys or rats. Activity in lung (lymph nodes) was 53 (4)% and 38 (13)% ILD at 1 and 2 years, and 1.2% in liver after 1.5 years. Because of the small number of data and the very similar experimental conditions to those of Mewhinney and Eidson (1982), data were pooled for analysis (see below).

(751) Stanley et al. (1982) exposed 18 Beagle dogs to a mixture of UO_2 and PuO_2 aerosols (see above for description of the experiment). Dogs were killed at times between 4 hours and 2 years. ILD was estimated as for the monkeys. The lungs and TBLN contained at least 95% of the body content of Pu and Am at all times. Because of the small number of data and the very similar experimental conditions to those of Mewhinney and Eidson (1982), data were pooled for analysis (see below).

(752) Mewhinney and Eidson (1982) exposed 6 cynomolgus monkeys, 12 dogs and 30 rats to aerosols derived from the industrial production of nuclear fuel (see above for description of the experiment). For each study, dogs were killed shortly after exposure, and at times between 64 days and 4 years. Plutonium content was measured in lungs, TBLN and liver. Because of the

small number of data and the very similar experimental conditions to the two previous studies above, Stanley et al. (1980a) and Stanley et al. (1982), data were pooled for each type of MOX and analysis here gave: f_r = 0.0012, s_s = 5 x 10^{-5} d^{-1} (1750°C); and f_r = 0.001, s_s = 1.3 x 10^{-5} d^{-1} (750°C), respectively, both giving assignment to Type S.

Rat

(753) James et al. (1978) exposed rats and hamsters to an aerosol of $^{239}PuO_2$ (and $^{241}AmO_2$), calcined at 550ºC, before blending with UO_2 in the ratio 1:2 by mass. The material was obtained from glove boxes in an experimental fast reactor fuel fabrication laboratory (Strong et al., 1977; Foster, 1991, see above). James et al. reported measurements of retention of ^{239}Pu in lung, liver and 'remaining carcass' at times between 7 and 180 days in both species. Lung retention of ^{241}Am was very similar to that of ^{239}Pu over this period. Further data were reported by Stather et al. (1979a, 1984). For both species, the amounts of ^{239}Pu deposited in tissues from the blood were <0.1% ILD at 30 d and <0.4% ILD at the end of the study (360 or 540 days; Stather et al., 1979a). Analysis here gave f_r <10^{-4}, s_s = 5 x 10^{-6} d^{-1}, and assignment to Type S.

(754) Lataillade et al. (1995) exposed rats by inhalation to the respirable fraction of a mixed industrial plutonium-uranium oxide, $(U,Pu)O_2$ containing 20% (w/w) Pu (heat treated at 1680ºC). Groups of rats were killed at times between 1 and 180 days. The Pu content of the lungs, liver and skeleton was measured. The lung content fell to about 16% IAD at 150 days. Analysis here gave: f_r = 0.008, s_s = 5 x 10^{-4} d^{-1}, and assignment to Type S.

(755) Ramounet et al. (2000) followed the tissue distribution of plutonium in rats for 360 days after inhalation of MOX prepared by either the MIMAS or SOLGEL process. Both contained ~4% (w/w) Pu. Groups were killed at times between 7 days and 12 months, and for MIMAS also at 18 months. The Pu contents of the liver, kidneys and femora (assumed to make up 10% of the skeleton). There were some differences in systemic uptake. For MIMAS, skeletal content peaked at 0.25% at 180 days: the SOLGEL showed a similar trend but with higher values, with a peak of 1.2% at 270 days. Analysis here gave: f_r = 0.0011 and s_s = 3 x 10^{-5} d^{-1} for MIMAS; and f_r = 0.004 with fixed s_s < 5 x 10^{-4} d^{-1} for SOLGEL, both giving assignment to Type S.

(756) Ramounet-Le Gall et al. (2003) exposed two groups of 30 rats to industrial MOX aerosols containing 2.5% and 5% (w/w) plutonium. Rats were killed at times between 7 and 180 days. The IDLD (estimated one week after exposure) and the lung content at death were determined from in-vivo x-ray measurements. The Pu content in organs was measured at death by alpha spectrometry. The authors estimated absorption parameter values f_r and s_s for each rat using the cumulative transfer to blood (2 x skeleton) and the lung content, and a fixed value s_r=100 d^{-1}: f_r = 0.004 and s_s = 2 x 10^{-4} d^{-1} for 2.5% Pu-MOX; and f_r = 0.001 and s_s = 5 x 10^{-5} d^{-1} for 5% Pu-MOX, both giving assignment to Type S.

Table 22.5. Estimated absorption parameter values for inhaled plutonium in mixed oxide (MOX). Values in parentheses were fixed in analyses.

	Absorption parameter values[1] and duration T of study				References
	f_r	s_r (d^{-1})	s_s (d^{-1})	T (y)	
Man	0.05	(0.4)	2.4 x 10^{-5}	2.7	Foster (1991)
Cynomolgus	0.0012	(0.4)	5 x 10^{-6}	4	Stanley et al. (1980a)

monkey					Mewhinney and Eidson (1982)
Cynomolgus and rhesus monkeys	3×10^{-4}	(0.4)	3×10^{-6}	4	Stanley et al. (1982), Mewhinney and Eidson (1982)
baboon	0.03	(0.4)	4×10^{-4}	1	Lataillade et al. (1995)
Dog	0.0012	(0.4)	5×10^{-5}	4	Stanley et al. (1980a), Mewhinney and Eidson (1982)
Dog	0.001	(0.4)	1.3×10^{-5}	4	Stanley et al. (1982), Mewhinney and Eidson (1982)
Rat ins[2]	0.008	(1)	$< 5 \times 10^{-4}$	0.5	Lataillade et al. (1995)
Rat	0.0011	(1)	3×10^{-5}	1.5	Ramounet et al. (2000), MIMAS
Rat	0.004	(1)	5×10^{-4}	1	Ramounet et al. (2000), SOLGEL
Rat[3]	0.004	(100)	2×10^{-4}	0.5	Ramounet-Le Gall et al. (2003)
Rat[3]	0.001	(100)	5×10^{-5}	0.5	Ramounet-Le Gall et al. (2003)
Man, baboon, monkey, dog					
Median	0.0012		1.8×10^{-5}		
Geom. mean	0.0029		2.1×10^{-5}		
Min	3×10^{-4}		3×10^{-6}		
Max	0.05		4×10^{-4}		
All species					
Median	0.0012		4×10^{-5}		
Geometric mean	0.0028		4.1×10^{-5}		
Min	3×10^{-4}		3×10^{-6}		
Max	0.05		5×10^{-4}		

1. f_b and s_b were assumed to be 0.002 and 0 d^{-1} respectively
2. "ins" – material was instilled; otherwise material was inhaled
3. Parameter values published by the authors.

(757) In-vitro dissolution studies performed by Eidson et al. (1983) and Rateau-Matton et al. (2004) gave absorption parameter values of the same order of magnitude with f_r = 0.001 – 0.05, s_r = 0.12 – 0.58 d^{-1} and s_s = 0.46 – 1.6 x 10^{-4} d^{-1}, giving assignment to Type S.

(758) In all studies the material was relatively insoluble in the lungs, with low values of f_r and s_s. All sets of parameter values derived from in-vivo studies (Table 22.5) gave assignment to Type S (see text above). As the rapidly-dissolved fraction was so small, there was insufficient information to estimate the value of s_r, which was fixed in analyses here at either 0.4 or 1 d^{-1}. Values of f_r were in the range 3 x 10^{-4} to 0.05, with a median and geometric mean of 0.0012 and 0.0028 respectively. Most values of s_s were in the range 3 x 10^{-6} to 5 x 10^{-4} d^{-1} with a median and geometric mean of 4 x 10^{-5} d^{-1}. As for plutonium-239 dioxide, estimates from the studies in man and other large animals are considered more reliable than those from rat which were in rodents and of shorter duration. These give median and geometric mean values of 2 x 10^{-5} d^{-1}. Median values of both parameters are lower than the corresponding values for default Type S (f_r = 0.01 and s_s = 1 x 10^{-4} d^{-1}).

(759) These results are similar to those summarised above for plutonium-239 dioxide. Plutonium in MOX is therefore given the same material-specific parameter values here as plutonium-239 dioxide.

Plutonium-238 dioxide

(760) Plutonium-238 has a relatively short half-life of 87.7 years, and a correspondingly high specific activity and decay heat: 1 gram of ^{238}Pu generates about 0.5 watts of thermal power. Pure ^{238}Pu is produced by neutron irradiation of ^{237}Np, recovered from spent nuclear fuel. It produces little hazardous penetrating radiation, and so has found industrial applications in Radioisotope Thermoelectric Generators (RTGs), used for example in cardiac pacemakers and spacecraft, and Radioisotope Heater Units (RHU) used in spacecraft to heat critical components. In 1964 a satellite containing a Space Nuclear Auxiliary Power supply (SNAP-9A) failed to achieve orbit and disintegrated, dispersing about 1 kilogram of ^{238}Pu into the atmosphere. The ceramic dioxide form is generally used in such applications, being stable, with low solubility in water. Recent reviews of the applications and biokinetics of ^{238}Pu include those of NCRP (2001) and Suslova et al. (2012).

(761) However, it was found that $^{238}PuO_2$ in particulate form is more soluble *in vitro* and *in vivo* than $^{239}PuO_2$ formed under similar conditions, and that storage of $^{238}PuO_2$ particles in an aqueous medium results in a larger rapidly-absorbed fraction. Early observations, such as those of Raabe et al. (1973) and Patterson et al. (1974), that the in-vitro dissolution rate of $^{238}PuO_2$ particles was much higher than that of $^{239}PuO_2$ particles of similar size led to investigations of the mechanisms involved (NCRP, 2001).

(762) Park et al. (1974) compared the effects of storage of aqueous suspensions of $^{238}PuO_2$ and $^{239}PuO_2$ particles (both produced by calcining the oxalate at 750°C) on their physico-chemical properties, and on the biokinetics of plutonium after inhalation by dogs. In freshly prepared suspensions of both forms, the fraction that was 'ultrafilterable' (using 2.4-nm pore-size membrane) was 0.2%. This increased to 25% in the $^{238}PuO_2$ after 6 months storage ('aging'), but remained at 0.2% in the $^{239}PuO_2$ after 16 months. X-ray diffraction of 19-month-old $^{239}PuO_2$ suspensions and 'fresh' (72-hour-old) $^{238}PuO_2$ suspensions showed the expected peaks, but a $^{238}PuO_2$ suspension stored for 9 months did not, indicating altered crystal structure. A few months after inhalation by dogs, the ^{238}Pu distribution after inhalation of 'fresh' $^{238}PuO_2$ suspension was similar to that of ^{239}Pu after inhalation of an 'aged' $^{239}PuO_2$ suspension: nearly all plutonium in the body was in lungs. There was somewhat greater transfer of ^{238}Pu to liver and skeleton, but far more after inhalation of an 'aged' $^{238}PuO_2$ suspension. They noted that in other studies in dogs and rats, greater transfer of plutonium to skeleton had been observed after inhalation of $^{238}PuO_2$ than after inhalation of $^{239}PuO_2$ (see below). This suggested that changes occurred to $^{238}PuO_2$ particles during suspension in water leading to a more soluble form, and similar changes might well occur *in vivo*. As this did not occur with $^{239}PuO_2$ suspensions, it suggested that it might be due to the higher specific activity of ^{238}Pu and so might also occur with other high specific activity actinides.

(763) Fleischer (1975) and Fleischer and Raabe (1977, 1978) carried out experiments involving analysis of fission tracks produced by neutron irradiation of $^{239}PuO_2$ particles, and developed models of radiation damage to PuO_2 particles. (For a summary, see NCRP, 2001.) They concluded that PuO_2 particles, "dissolve" in water as a result of damage by the nucleus recoiling after alpha decay, which produces "subparticles" (particle fragments). They observed that far more plutonium atoms were ejected from particles in water than in a vacuum, and concluded that the presence of water might result in loosening of fragments or etching along the recoil damage track. This process has sometimes been termed radiolytic fragmentation.

(764) Stradling et al. (1978a) investigated sized fractions of $^{238}PuO_2$ particles, prepared by calcining the oxalate at 750°C (see the section below on *Plutonium dioxide nanoparticles*). It was shown that the <25-nm fraction consisted only of 1-nm diameter particles. 'Aging' increased the proportion of 1-nm particles in suspension from ~2% at 1 day to ~40% at 270 days. After intratracheal instillation into rats, there was negligible absorption up to 21 days from the fractions of $^{238}PuO_2$ particles >25 nm, but high absorption from the 1-nm fraction of both 'fresh' and 'aged' suspensions. The authors concluded that the higher in-vivo dissolution of $^{238}PuO_2$ than of $^{239}PuO_2$ is due to radiolytic fragmentation and formation of 1-nm particles.

(765) To investigate fragmentation of $^{238}PuO_2$ particles *in vivo*, Diel and Mewhinney (1983) studied autoradiographs of lung sections from Beagle dogs sacrificed between 4 days and 2 years after inhalation of monodisperse $^{238}PuO_2$ (aerodynamic diameter, d_{ae} = 1.7 µm; GSD = 1.1). The amount of activity in fragments, as a fraction of that in intact particles, increased from about 1% at a month to about 5% at 1 – 2 years. (Similar results were obtained by Diel and Mewhinney, 1980, in hamsters following inhalation of a monodisperse $^{238}PuO_2$ aerosol.) The study complemented that in which Mewhinney and Diel (1983) followed the biokinetics in dogs for 4 years after inhalation of $^{238}PuO_2$ aerosols (see below). The authors developed a complex simulation model that described absorption from lungs to blood, taking account of the increasing dissolution rate resulting from the increase in surface area due to fragmentation, and applied it to represent the tissue distribution and excretion of ^{238}Pu in the dogs. Guilmette et al. (1994) and Hickman et al. (1995) developed the model further, adapted it to man, and applied it to urinary bioassay data from workers who inhaled ^{238}Pu aerosols (see below).

(766) In some of the studies outlined below, urinary excretion rates that increased with time were observed, indicating that the dissolution rate in the lungs increased with time. The 'default' HRTM representation of particle dissolution, with rapid and slowly dissolving fractions, can only represent decreasing dissolution rates (although in some circumstances a urinary excretion rate that increases with time can be predicted). However, the 'alternative' HRTM representation of particle dissolution (OIR Part 1, Fig 3.5b, ICRP, 2015) can do so, and is used here. In this, material deposited in the respiratory tract is assigned to compartments labelled ‘Particles in initial state’ in which it dissolves at a constant rate s_p. Material is simultaneously transferred (at a constant rate s_{pt}) to a corresponding compartment labelled ‘Particles in transformed state’ in which it has a different dissolution rate, s_t. With this system, the initial dissolution rate is approximately s_p and the final dissolution rate is approximately s_t. Thus, with a suitable choice of parameter values, including $s_t > s_p$, an increasing dissolution rate can be represented. Fits were also made to the data using the 'default' model with rapid and slowly dissolving fractions (Table 22.6), but, as noted later, generally they fit urine data less well, and in some cases very poorly. Note that the values of f_r and s_s (s_r was fixed) were derived from the data independently of the values of s_p, s_{pt} and s_t, and were not calculated from them using Equation 3.1 of OIR Part 1. They were used to assign the material in each study to Type M or S.

Man

(767) Guilmette et al. (1994) and Hickman et al. (1995) reported urinary excretion of ^{238}Pu for seven workers, up to 18 years after inhalation exposure in the same incident. The inhaled material was described as “plutonium ceramic”, likely to be a PuO_2 material containing a molybdenum binder for the fabrication of heat source pellets. The measurements of ^{238}Pu in

urine showed an unusual pattern: shortly after the exposure they were near the limit of detection, but they increased in the following months, reaching a plateau. One of the workers died 18 years after the incident, and was a USTUR donor (Case 0259): post-mortem measurements of ^{238}Pu in his tissues have been reported (James et al., 2003, below). This combination of long-term urinary excretion measurements on a group of workers, combined with autopsy data on one of them, provides an exceptionally comprehensive set of human data. Analysis here of the seven cases, including autopsy data for one of them, gave shared parameter values: s_{pt} = 0.0026 d^{-1} and s_t = 6 x 10^{-4} d^{-1} (s_p = 1 x 10^{-6} d^{-1}, fixed as in the analysis by James et al, 2003, below). Alimentary tract absorption was fixed at f_A = 5 × 10^{-8}, based on the results of Smith (1970), who measured absorption of ^{238}Pu following intra-gastric administration to pigs of crushed $^{238}PuO_2$ microspheres (as used in RTG). For completeness, analysis was carried out here using rapid and slow dissolution compartments, which gave f_r = 0.0 and s_s = 5 × 10^{-4} d^{-1} (s_r fixed at 0.4 d^{-1}) and assignment to Type S. However, the urinary excretion pattern was not well represented.

(768) James et al. (2003) analysed ^{238}Pu in tissues of a whole body donor (USTUR Case 0259) who accidentally inhaled plutonium (predominantly ^{238}Pu) in the form of a highly insoluble ceramic $^{238}PuO_2$-molybdenum. Along with six other workers exposed at the same time (Hickman et al., 1995, above), this donor excreted little or no ^{238}Pu in his urine for several months. Subsequently, however, and with no further intakes, the urinary excretion of ^{238}Pu increased. James et al were able to model the urinary excretion pattern by applying the HRTM representation of particle dissolution using particles in initial and transformed states with parameter values s_p = 10^{-6} d^{-1}, s_{pt} = 0.00189 d^{-1} and s_t = 2.57 x 10^{-4} d^{-1}. Combined with the *Publication 67* (ICRP, 1993) plutonium systemic model, it predicted well the total ^{238}Pu activity retained in the body, and the distribution between lungs and systemic organs. Small adjustments to several rate constants in these models provided precise predictions of the absolute amounts of ^{238}Pu in the individual tissues. Analysis here, using the revised HRTM and plutonium systemic model (ICRP, 2015) gave: s_{pt} = 0.0022 d^{-1} and s_t = 4.3 x 10^{-4} d^{-1} (s_p = 1x10^{-6} d^{-1} fixed as in James et al. (2003), and f_A = 5 × 10^{-8}, based on the results of Smith1970).

(769) Fleming and Hall (1978) analysed data from a worker exposed to airborne 'high-fired' $^{238}PuO_2$. Activity in chest and in urinary and faecal excretion was measured up to one year. The chest retention measurements showed a half-time of about 1000 days. Analysis here gave s_p = 7 x 10^{-4} d^{-1}, s_{pt} = 0.01 d^{-1} and s_t = 0.002 d^{-1}. A reasonable fit was also obtained with f_r = 4 x 10^{-4} and s_s = 0.0011 d^{-1} (giving assignment to Type M), but the urine data were less well represented.

(770) Newton et al. (1983) studied the retention of $^{238}PuO_2$ and $^{241}AmO_2$ in the lungs of a worker between 7 and 869 days after the simultaneous exposure to aerosols of both oxides. The PuO_2 had been prepared by calcination at 750^{o}C and ^{238}Pu accounted for 94% of the activity. After the initial fast mucociliary clearance ^{238}Pu showed only a long-term retention with a biological half-life of about 800 days with clearance predominantly by systemic or lymphatic uptake. Little information was given about urinary excretion: it was only stated that urinary and faecal excretions were roughly similar and accounted for about 15% of the ^{238}Pu cleared from the lungs between 7 and 700 days. In contrast, most of the ^{241}Am was cleared within 50 days and the small remaining fraction was cleared with a half-life similar to that of ^{238}Pu (see *Americium* section in this report). Analysis here for $^{238}PuO_2$ was limited by the lack of urine data: only upper limits on absorption rates could be derived. Analysis with s_{pt} fixed at 0.005 d^{-1} (a central value based on the other results in Table 22.6) gave s_p = <1 × 10^{-4} d^{-1}, and s_t <1 × 10^{-4} d^{-1}. Analysis here also gave f_r < 0.004 and s_s < 1 x 10^{-4} d^{-1}, and assignment to Type S.

Dog

(771) Mewhinney and Diel (1983) followed the biokinetics of ^{238}Pu in dogs after inhalation of three monodisperse aerosols (AMAD = 0.7, 1.7 or 2.7 □m and GSD <1.2), or a polydisperse aerosol (AMAD = 1.4 □m and GSD = 1.5) of $^{238}PuO_2$. Droplets containing $^{238}Pu(OH)_4$ in HCl were dried at 350°C, then fired at 1150°C. (Note that in this case the 'firing' was of very short duration.) Dogs were killed at times between 2 hours and 4 years. Activity was measured in lungs, systemic organs and in urine and faeces. Mewhinney and Diel noted an increased rate of transport of ^{238}Pu out of the lung from 64 through 512 days after inhalation. This was interpreted as due to an increased rate of dissolution as particles fragmented because of the high specific activity of ^{238}Pu. In analyses here, values of s_{pt} were not well defined, and were optimised as a shared parameter for the four experiments: s_{pt} = 0.0079 d^{-1}. Values of s_p are about 0.001 d^{-1}, and of s_t about 0.004 d^{-1}. Individual values are given in Table 22.6. Analysis here also gave f_r < 1 x 10^{-4} and values of s_s between 9 x 10^{-4} and 0.005 d^{-1} (Table 22.6, most giving assignment to Type M): fits to lung and feces data were satisfactory, but ^{238}Pu in systemic organs and urine was overestimated up to about 500 days. The dissolution parameter values are higher than those derived from the data of Hickman et al above, indicating that this material dissolved more rapidly in the lungs.

(772) Park et al. (1990) investigated the life-span dose effects and the disposition of inhaled $^{238}PuO_2$ in 137 Beagle dogs. The oxide was prepared by calcining the oxalate at 700°C and subjecting it to steam in argon exchange at 800°C for 96 hours in order to be used as fuel in space-nuclear-power systems. Dogs were given a single exposure to obtain six dose levels and were followed for 16 years. After 10 years, less than 1% IAD was retained in the lungs, 3–4% was translocated to lymph nodes, and 15–20% to both liver and skeleton. Analysis here (using lung, liver and skeleton data) gave: s_p = 4.1 x10^{-4} d^{-1}, s_{pt} = 0.0013 d^{-1} (with s_t fixed at 7 x10^{-4} d^{-1}). An equally good fit was obtained with f_r = 0.0015, s_s = 6 x 10^{-4} d^{-1}, giving assignment to Type S. The dissolution parameter values are similar to those derived from the data of Hickman et al. (1995) above.

Mouse

(773) Morgan et al. (1988a) followed the tissue distribution of ^{238}Pu and ^{239}Pu in mice after nose-only inhalation of $^{238}PuO_2$ and $^{239}PuO_2$, fired at temperatures of 550°C and 750°C ('low-fired'), 1000°C and 1250°C ('high-fired') for 2 hours (see the *Plutonium-239 dioxide* section above). Mice were killed at 1 day to determine the average IAD. Further groups were killed at times between 3 and 24 months for tissue analysis. Fecal, but not urine samples were obtained. Translocation to liver and skeleton decreased with firing temperature and was about an order of magnitude higher than for ^{239}Pu. With the 'low-fired' materials, the skeletal content reached ~2% IAD within 6 months, with little further change. With the 'high-fired' materials it increased throughout the 2 years, but only reached ~1% IAD. In analyses carried out here, systemic model parameter values were shared between the four inhalation studies and one on the biokinetics of plutonium following intra-peritoneal injection of the citrate into mice (Ellender et al., 1995). Results are given in Table 22.6. For the 'high-fired' materials, estimated values of s_t are less than those of s_p, and therefore show no evidence for an increasing dissolution rate. To estimate values f_r and s_s, that of s_r was optimised as a shared parameter across the four inhalation studies, giving 0.75 d^{-1}; the fits were as good as those obtained with the initial/

transformed particle model. The results (Table 22.6) give assignment to Types M and S for the 'low-fired' and 'high-fired' $^{238}PuO_2$ respectively.

(774) Based mainly on the human studies (Hickman et al., 1995; James et al., 2003) above, specific absorption parameter values: s_p = 1 x10^{-6} d^{-1}, s_{pt} = 0.0026 d^{-1}, s_t = 6 x10^{-4} d^{-1} and f_A = 1 x 10^{-7} are used here for 'ceramic' $^{238}PuO_2$, as used in Radioisotope Thermoelectric Generators.

(775) Based mainly on the dog studies (Mewhinney and Diel, 1983) above, specific absorption parameter values: s_p = 0.001 d^{-1}, s_{pt} = 0.008 d^{-1} and s_t = 0.004 d^{-1} are used here for 'non-ceramic' $^{238}PuO_2$. A specific absorption parameter value of f_A = 1 x 10^{-5} (see *Ingestion* section) is also used.

(776) Stradling et al. (1978a) observed that while the extrapulmonary tissue distribution of the ^{238}Pu absorbed after intratracheal instillation of 1-nm $^{238}PuO_2$ was similar to that of Pu-citrate, urinary excretion in the first day was a few times higher (see the section below on *Plutonium dioxide nanoparticles*). This implies that application of plutonium systemic models based on citrate (as used here) to early urinary excretion after 1-nm $^{238}PuO_2$ deposition or formation in the lungs would overestimate systemic organ deposition. It is therefore notable that good agreement was found between estimates of organ contents based on urinary excretion and post-mortem measurements made on USTUR donor 0259 reported by James et al. (2003), which was confirmed by analyses here. Similarly, good fits were obtained here to tissue retention and excretion data following inhalation of $^{238}PuO_2$ by dogs, reported by Mewhinney and Diel (1983). Therefore no enhancement to urinary excretion of ^{238}Pu transferring from the lungs to blood is applied here.

Table 22.6. Estimated absorption parameter values for inhaled plutonium in $^{238}PuO_2$. Values in parentheses were fixed in analyses. AMAD and firing (calcining) temperatures are given where known, usually for laboratory-produced aerosols.

Species	Dura-tion	AMAD	Firing Temp-erature	Absorption parameter values							Reference
	y	µm	°C	s_p (d^{-1})	s_{pt} (d^{-1})	s_t (d^{-1})	f_r [c]	s_r [c] (d^{-1})	s_s [c] (d^{-1})	Type	
Man	18			(1 x10^{-6})	0.0026	6 x10^{-4}	0	-	5 x 10^{-4}		Hickman et al. (1995)
Man	1			7 x10^{-4}	0.0097	0.002	4 x10^{-4}	(0.4)	0.0011	M	Fleming and Hall (1978)
Man	2.4		750	<1 x10^{-4}	(0.005)	<1 x 10^{-4}	<0.004	(0.4)	<1 x 10^{-4}	S	Newton et al. (1983)
Dog	4	0.7[a]	1150	7 x10^{-4}	0.0079[b]	0.003	1 x 10^{-4}	(0.4)	0.003	M	Mewhinney and Diel (1983)
	4	1.7[a]		6 x10^{-4}		0.006	1 x 10^{-4}	(0.4)	9 x 10^{-4}	S	
	4	2.7[a]		0.0010		0.004	1 x 10^{-4}	(0.4)	0.005	M	
	4	1.4		0.0011		0.002	1 x 10^{-4}	(0.4)	0.002	M	
Dog	13	1.8	700	4.1 x 10^{-4}	0.0013	(7 x 10^{-4})	0.0015	(0.4)	6 x 10^{-4}	S	Park et al. (1990)
Mouse	2	1.6	550	6 x 10^{-4}	0.011	0.0044	3 x 10^{-4}	0.75[b]	0.0032	M	Morgan et al. (1988a)
		1.6	750	0.0017	0.0043	0.0026	5 x 10^{-4}		0.0023	M	
		1.4	1000	0.0024	0.057	4.9 x 10^{-4}	0.0075		8 x 10^{-4}	S	
		1.5	1250	0.0051	0.50	3.1 x 10^{-4}	0.0088		4 x 10^{-4}	S	

Notes:
a: monodisperse aerosols
b: shared parameter value
c: Values estimated for f_r, s_r and s_s are given for completeness and comparison purposes. However in some cases they greatly underestimate urinary excretion and systemic uptake at early times: see text

Plutonium dioxide nanoparticles

(777) As noted in OIR Part 1 (ICRP, 2015), it was recognised in *Publication 66* (ICRP, 1994, Annex E Section E.2.2) that there was evidence that particles smaller than a few nanometres are readily transported into the blood: “Smith et al. (1977) and Stradling et al.

(1978a,b) found that 1 nm particles of $^{239}PuO_2$ or $^{238}PuO_2$ were readily translocated from the lungs to the blood in rats, but there was negligible translocation of particles larger than 25 nm. This is consistent with observations that the intercellular clefts in pulmonary blood capillaries do not exceed 4 nm (Lauweryns and Baert, 1977)." The concept was not new in 1977. For example, Anderson et al. (1970) noted that part of the rapid urinary excretion observed after accidental inhalation of ^{238}Pu was: "thought to be due to refractory particles of colloidal dimensions which were transferred very rapidly to the systemic system...".

(778) As described above, high-fired plutonium-239 dioxide particles dissolve extremely slowly in the lungs, although a small fraction of the ILD, usually less than 1%, is absorbed rapidly. Studies of the lung clearance of inhaled sodium-plutonium oxide aerosols, summarised in the section below, *Plutonium dioxide formed in the presence of sodium*, showed much higher rapidly absorbed fractions, up to 50%. Investigations indicated that this was related to the fraction of particles that penetrated a 100-nm filter, then referred to as the 'ultrafilterable' fraction, and probably to particles within it of about 1-nm diameter (e.g. Stather et al., 1979b; Stradling et al., 1980). Particles with physical diameters less than 100 nm are now described as 'ultrafine particles' or 'nanoparticles'. In recent years, there has been enormous growth in interest in nanoparticles, their applications, and their toxicology. NCRP established Scientific Committee 2-6 to develop a report on the current state of knowledge and guidance for radiation safety programmes involved with nanotechnology (Hoover et al., 2015).

(779) Studies conducted to investigate the properties and lung clearance of the 'ultrafine fraction' of PuO_2 aerosols, and ultrafine PuO_2 aerosols, are summarised here. Studies of the inhalation of aerosols formed from plutonium mixed with sodium and other metals (except MOX) are summarised below.

(780) As described below, Brightwell and Carter (1977) followed the tissue distribution of ^{239}Pu in mice after inhalation of aerosols produced by the 'exploding wire' technique, in which a capacitor bank is discharged through a metal wire or foil, leading to vaporisation and condensation, to form an oxide fume. According to Smith et al. (1977), previous studies had shown that the properties of aerosols produced in this way are similar to those of oxides formed by other high temperature methods. Brightwell and Carter compared plutonium vaporised alone, or with sodium in atomic ratio Na:Pu between 1.5:1 and 16:1. Electron microscopy of filter samples from the exposure chamber showed that the pure $^{239}PuO_2$ consisted of chain-like aggregates which did not disperse in water; but at a Na:Pu ratio of 16:1, the particles appeared as a typical hygroscopic sodium oxide fume, and exposure to water left a residue containing many PuO_2 particles less than 10-nm diameter.

(781) Stather et al. (1975) followed the tissue distribution of ^{239}Pu in rats after inhalation of aerosols produced by the 'exploding wire' technique, with or without sodium present at a Na:Pu ratio of 20:1 (see below). They also carried out experiments in which the aerosol was collected with an 'impinger' (inertial impaction into distilled water) and sized fractions of the suspension were obtained by sequential filtering. The tissue distribution and cumulative urinary and fecal excretion of ^{239}Pu were determined at 7 days after intratracheal instillation into rats. For comparison, similar experiments were carried out with plutonium nitrate and citrate. The 'transportable fraction' (systemic uptake) was estimated from the 'extrapulmonary tissue deposit' (ETD = skeleton + liver + soft tissues). For material passing through filters with pore size 200 nm or larger, the ETD was <1% ILD. However, for material penetrating a 100-nm filter (for pure $^{239}PuO_2$ this was only ~0.3% of the original suspension), the ETD was ~20% ILD. Similar transportable fractions were measured with material penetrating a 25-nm filter from aerosols generated with Na:Pu ratios up to 87:1. Deposition in the liver accounted for ~16% ETD, for

the suspensions as well as for the nitrate and citrate, indicating that it was in a monomeric form. However, cumulative urinary excretion at 7 days ranged from 5 – 10% ETD for the suspensions, somewhat higher than for nitrate and citrate (~4% ETD).

(782) Stather et al. (1977a) measured the ultrafilterable fraction of plutonium from aerosols generated from a range of Pu-Na mixtures: it was <1% for Na:Pu ratios up to 1:1, and increased with sodium content up to a maximum of ~55% for ratios of 20:1 to 87:1.

(783) Smith et al. (1977) fractionated, by sequential filtering, a suspension of $^{239}PuO_2$ particles produced from plutonium foil using the exploding wire technique, into size ranges <25 nm; 25–200 nm (0.2 µm); and 0.2–1.2 µm. Further filtration of the <25 nm fraction (~0.1% of the total $^{239}PuO_2$), supported by electron microscopy, indicated that the particle size was uniform and ~1-nm diameter. They measured tissue distribution and excretion of ^{239}Pu at 18 hours, 6 and 17 d after intratracheal instillation of the three fractions, and, for comparison, Pu citrate solution. (See *Plutonium citrate* section above.) For the 1-nm $^{239}PuO_2$ and citrate, there was rapid absorption of ~70% ILD, and similar distributions between extra-pulmonary tissues (liver, blood, remaining carcass) and faecal excretion at all times. Analysis here for 1-nm $^{239}PuO_2$ gave $f_r = 0.8$ and $s_r = 3\ d^{-1}$. The lack of long-term measurements prevented a reliable assessment of s_s.

(784) However, for 1-nm $^{239}PuO_2$, urinary excretion in 18 hours was higher (~5% ILD) than for citrate (~1.5% ILD). Lung contents were similar (~30% ILD) at 1 day, but fell more slowly for the 1-nm $^{239}PuO_2$, (~25% and ~20% ILD at 6 and 21 days) than for the citrate (10% and 7% ILD, respectively). In contrast, there was no detectable systemic uptake of the 25 – 200 nm and 0.2–1.2 µm $^{239}PuO_2$ fractions, and ~90% ILD remained in the lungs at 17 days. In similar complementary experiments, all three $^{239}PuO_2$ fractions and Pu citrate were administered to rats by intravenous (IV) injection (measurements were also made at 50 days). Tissue distributions were similar for the 1-nm $^{239}PuO_2$ and citrate. However, for 1-nm $^{239}PuO_2$, urinary excretion at 18 hours was much higher than for citrate: ~10% and 1.5% injected activity (IVA), respectively. In contrast, for the larger-sized fractions, most of the ^{239}Pu was deposited in liver and spleen (~85% and 5% IVA) and retained there. Ca-DTPA administered 1 hour after IV injection had no effect on urinary excretion of ^{239}Pu administered as particles >25 nm, but significantly increased urinary excretion at 7 days after administration of 1-nm $^{239}PuO_2$ (from 13% to 43% IVA), similar to the effect on Pu-citrate (from 3% to 35% IVA). Investigations of the chemical form of plutonium in blood and urine *in vitro*, and in animals intravenously injected, indicated that a form "intermediate" between PuO_2 and Pu citrate was present, and possibly associated with the enhanced urinary excretion. (Ultimately the Pu was complexed by transferrin (~95%) and citrate (~5%) in blood and by citrate in urine.) It was estimated that 1-nm diameter PuO_2 particles contain about 25 plutonium atoms, most of which lie at the surface, and so are accessible to react with citrate ions *in vivo*.

(785) Stradling et al. (1978b) carried out a study similar to that of Smith et al. (1977), except that the particles were produced (by the exploding wire technique), with sodium present at Na:Pu ratios of 3:1 and 20:1. The amounts of plutonium in the 1-nm fraction were 1.6% and 48% respectively, much higher than for plutonium alone (~0.1%, Smith et al 1977), but were also negligible in the size range 4–25 nm. They measured tissue distribution and excretion of plutonium at 1, 6 and 21 d after intratracheal instillation of the 1-nm fraction from both aerosols, and, for comparison, Pu citrate solution. For all three there was rapid absorption of ~70% ILD, and similar distribution between extra-pulmonary tissues. However, for 1-nm $^{239}PuO_2$, urinary excretion in 1 day was higher (~7% ILD) than for citrate (~1.5% ILD). Lung contents were similar for all three (~30% ILD) at 1 day, but fell more slowly for the 1-nm

$^{239}PuO_2$, (~25% and ~20% ILD at 6 and 21 days) than for the citrate (7% and 5% ILD, respectively). Analysis here for 1-nm $^{239}PuO_2$ gave f_r = 0.7, s_r = 3 d^{-1} and s_s = 0.015 d^{-1}, and f_r = 0.7, s_r = 3 d^{-1} and s_s = 0.019 d^{-1}, respectively. These values are similar to those derived from the results of Smith et al. (1977) above. In similar complementary experiments, the materials were administered to rats by IV injection. Again, tissue distributions were similar, and for 1-nm $^{239}PuO_2$, urinary excretion in 1 day was much higher than for citrate: ~10% and 2% IVA, respectively. Investigations of the chemical form of plutonium in blood and urine indicated that a complex "intermediate" between PuO_2, and Pu citrate was present, and accounted for the high urinary excretion. The findings thus supported those of Smith et al. 1977, and indicated that the behaviour of the 1-nm $^{239}PuO_2$, was related to its size, not the initial presence of sodium in the aerosol.

(786) Stradling et al. (1978a) similarly investigated sized fractions of $^{238}PuO_2$ particles, prepared by calcining the oxalate at 750°C. As for the $^{239}PuO_2$ produced by the exploding wire technique, ultrafiltration and electron microscopy showed that the <25-nm fraction consisted only of 1-nm diameter particles. 'Aging' (storing the $^{238}PuO_2$ in aqueous suspension: see *Plutonium-238 dioxide* section) increased the proportion of 1-nm particles in the suspension from ~2% at 1 day to ~40% at 270 days. The biokinetic behaviour was similar to that of $^{239}PuO_2$ suspensions (see above). After intratracheal instillation into rats, there was negligible absorption (<0.5% ILD) up to 21 days from the 25–200 nm and 0.2–1.2 µm fractions, but high absorption from the 1-nm fraction of either 'fresh' (1-day) and 'aged' (32 weeks) suspensions: the extrapulmonary tissue distribution was similar to that of Pu-citrate. Analysis here for 1-nm $^{238}PuO_2$ gave f_r = 0.6, s_r = 3 d^{-1}, and s_s = 0.016 d^{-1}; and f_r = 0.6, s_r = 3 d^{-1}, and s_s = 0.010 d^{-1}, respectively for fresh and aged suspensions.

(787) The authors considered that the findings supported the view that the higher in-vivo dissolution of $^{238}PuO_2$ than of $^{239}PuO_2$ is due to radiolytic fragmentation and formation of 1-nm particles. As for 1-nm $^{239}PuO_2$ particles, urinary excretion was higher than for Pu-citrate: to account for this, the authors proposed that a fraction of 1-nm particles passed from lungs to blood and urine, which was possible because the pore diameters of the alveolar epithelium (0.12 –2 nm) and the glomerular membrane (up to 7 nm) could allow the passage of such particles. However, as described in the *Plutonium-238 dioxide* section, studies in which measurements of urinary excretion and tissue distribution are available, following inhalation of $^{238}PuO_2$ by men and dogs, do not support the assumption of enhanced urinary excretion of nanoparticles transferred from lungs to blood compared to a citrate-based systemic model.

(788) Cooper et al. (1979) studied the reactions of 1-nm $^{238}PuO_2$ particles prepared as described by Stradling et al. (1978a), with rat lung fluid *in vivo* and *in vitro*, in order to elucidate the mechanisms by which plutonium is transferred to blood. For the in-vivo experiments, 1-nm $^{238}PuO_2$ particles were administered by intratracheal instillation into rats, and ^{238}Pu-labelled lung fluid removed by lung lavage; for the in-vitro experiments, lung fluid was removed by lavage and incubated with an aqueous suspension of 1-nm $^{238}PuO_2$ particles. In both cases the lung fluid was fractionated by gel-permeation chromatography and sucrose density gradient centrifugation. It was concluded that the $^{238}PuO_2$ particles reacted rapidly with pulmonary surfactant *in vitro*: after 2 hours incubation ^{238}Pu-labelled pulmonary surfactant was the major ^{238}Pu-bearing species. The biokinetics of ^{238}Pu was measured at 1, 6 and 21 days after intratracheal instillation into rats of several forms. Urinary excretion at 1 day was higher (5.5% ILD) for 1-nm $^{238}PuO_2$ than for Pu-citrate (1.5% ILD) and much higher (17% ILD) for ^{238}Pu-labelled pulmonary surfactant. It was concluded that the formation of plutonium-labelled pulmonary surfactant could account for the faster translocation of plutonium from lungs to

blood and high urinary excretion of 1-nm PuO_2 relative to plutonium citrate. In similar experiments, Cooper et al. (1980) compared the reactions of 1-nm $^{238}PuO_2$ particles with rat lung fluid, with those of 1-nm $^{244}CmO_2$. Previous studies (Stradling et al., 1979) had shown that for $^{244}CmO_2$ the presence or formation of 1-nm particles in the lungs was an important factor influencing transfer to blood. However, the physical and chemical properties of the 1-nm $^{244}CmO_2$ particles, and their transfer mechanisms, were found to be different from those of $^{238}PuO_2$. Electrophoresis showed that the 1-nm $^{238}PuO_2$ are positively charged, whereas the $^{244}CmO_2$ particles are negatively charged. The latter did not combine with surfactant, which is also negatively charged. The authors proposed that the 1-nm $^{244}CmO_2$ particles diffuse passively through pores in the alveolar epithelium.

(789) Kanapilly (1977) carried out a review of the alveolar microenvironment and material transport across the air-blood barrier, and concluded that nanometer-size insoluble particles such as PuO_2 might be transported from the alveoli into the blood by a pinocytotic mechanism similar to protein transport.

(790) Kanapilly and Diel (1980) generated ultrafine $^{239}PuO_2$ aerosols by vaporising a chelate prepared with THD (2,2,6,6, tetramethyl-3,5-heptane dione): $Pu(THD)_3$. The vapour was oxidised at 280°C to obtain the desired particle size, then fired at 1150°C. Electron microscopy showed the aerosol to consist of compact clusters of primary particles <10-nm diameter. X-ray diffraction confirmed that the structure was 'standard' $^{239}PuO_2$. In-vitro tests were carried out on aerosol samples. Dissolution of the ultrafine PuO_2 varied considerable between the four solvents used, but the highest was only 0.3% over 16 days (in 0.1M HCl). This was much less than expected for such small particles, based on their high specific surface area and dissolution rate constants measured for micron-sized $^{239}PuO_2$. The biokinetics of ^{239}Pu was followed for 16 days after inhalation of an aerosol with primary particle diameter 9±5 nm, and it was estimated that <1% ILD was absorbed in that time. The authors assessed that this was no more than would be expected for micron-sized $^{239}PuO_2$. Thus the high absorption observed elsewhere for 1-nm particles was not seen with 9-nm particles in this study.

(791) Reflecting current interest in potential exposure to radioactive nanoparticles, Cash (2014) carried out a study to assess: (1) whether the biological behaviour and associated dosimetry of PuO_2 nanoparticles (<100-nm diameter) might differ significantly from the default assumptions in current dosimetric models based on particles in the micrometer size range; and (2) how any differences might influence health protection of persons potentially exposed to PuO_2 nanoparticles. Cash derived biokinetic information for PuO_2 nanoparticles from the studies by Smith et al. (1977) and Stradling et al. (1978a) summarised above. She used simulation software to develop respiratory tract and systemic models from the experimental data that took account of the rapid absorption from lungs to blood, and the relatively high urinary excretion. She found that the use of default ICRP models led to large overestimates of assessed intake and dose from bioassay samples for PuO_2 nanoparticles, compared to models based on the experimental data.

(792) Specific parameter values are adopted here for 1-nm PuO_2 (either $^{238}PuO_2$ or $^{239}PuO_2$) because there is evidence that they are formed in condensation aerosols in which plutonium is mixed with a metal with a soluble oxide (see below), and their behaviour is very different from that of larger PuO_2 particles. Specific parameter values for 1-nm PuO_2 (either $^{238}PuO_2$ or $^{239}PuO_2$) derived above from experiments in which particle suspensions were instilled into rats are approximately: $f_r = 0.7$; $s_r = 3\ d^{-1}$ and $s_s = 0.01\ d^{-1}$. However, it is considered that the mechanisms involved in the rapid absorption of the plutonium in this form would apply only in the AI region. To reduce calculated absorption from the upper respiratory

tract (ET and BB regions), a lower value of s_r is adopted instead (0.4 d^{-1}, the default for soluble forms of plutonium). Because this competes with much higher rates of particle transport (10 d^{-1} in BB and 100 d^{-1} in ET, see Part 1, Fig. 3.4, ICRP, 2015), little absorption takes place in these regions. Since the experiments were of short duration (21 days), s_s was not well determined. However, the slow phase of absorption was clearly lower than for citrate. Estimates of s_s for citrate are in the range 0.005 – 0.007 d^{-1} (see *Plutonium citrate* section above): a value of 0.005 d^{-1} (Type M default value) is adopted here. Thus for 1-nm PuO_2, material-specific parameter values of f_r = 0.7; s_r = 0.4 d^{-1} and s_s = 0.005 d^{-1} are adopted here. In the absence of any measured values of f_A for 1-nm PuO_2, the default f_A value for inhaled materials is applied: i.e., the (rounded) product of f_r (0.7) and the f_A value for ingested soluble forms of plutonium (1×10^{-4}), i.e. 1×10^{-4} (rounded).

(793) The greater transfer from blood to urine (typically about a factor of three) compared to plutonium citrate, is not implemented here, because it was not confirmed in the case of $^{238}PuO_2$, where a similar enhanced urinary excretion was indicated from instillation experiments, but not observed following inhalation. Assumption of enhanced urinary excretion would make little difference to the inhalation dose coefficient, because urinary excretion would still be small compared to systemic deposition. However, systemic uptake (and intake) estimated from urinary excretion would be much lower, and could be underestimated if enhanced urinary excretion did not occur in practice.

Plutonium dioxide aerosols formed in the presence of sodium

(794) Some fast breeder reactor designs use liquid sodium as a coolant. The possibility that, under certain conditions, mixtures of plutonium, uranium and sodium could be released into the environment, prompted experimental studies on the biokinetics of ^{239}Pu formed in a condensation aerosol from vaporised mixtures of metallic sodium and plutonium (Na-Pu).

(795) Métivier et al. (1976b) studied the biokinetics of ^{239}Pu present in an aqueous solution formed from combustion of a mixture of sodium and plutonium oxides (Na:Pu ratio 20:1) pre-heated to 450°C. The tissue distribution, urinary and faecal excretion were measured at times up to 30 days after intramuscular injection of the suspension into rats and up to 6 months in baboons (*Papio papio*). A larger fraction of activity was transferred from the injection site to the systemic circulation than after injection of an acidic nitrate solution, up to 20% in rats and 40% in baboons. Skeletal retention was always higher than liver retention. Urine was the main route of early excretion but faecal excretion was preponderant after a week in rats and a month in baboons. DTPA treatment was found to be less effective than after Pu nitrate injection. The plutonium and sodium aqueous solution was also administered to rats by inhalation. Rats were killed at times between 30 minutes and 14 days and the contents of the lung, liver, skeleton, blood, urine and faeces measured. At the end of the one hour long inhalation, about 20% Pu ILD was absorbed to blood. Afterwards, up to 6% ILD and 14% ILD respectively were retained in liver (after 30 min) and in skeleton (after 4 days) respectively. Lung retention fell to 11% ILD after 14 days, while 80% ILD had been excreted in faeces, mostly through muco-ciliary clearance. The authors discuss the results in two articles (Métivier et al 1976a, Métivier et al 1976b) and suggest that the increased absorption and transfer to skeleton is not explained here by small particle sizes but by the production of diffusible hexavalent and heptavalent plutonium forms, strongly bound to a protein complex which reduces the efficacy of DTPA treatment.

(796) Brightwell and Carter (1977) followed the tissue distribution of ^{239}Pu in mice up to 35 days after inhalation of aerosols produced by the 'exploding wire' technique (see section above on *Plutonium dioxide nanoparticles*). They compared plutonium vaporised alone, or with sodium in atomic ratio Na:Pu between 1.5:1 and 16:1. Lung clearance, and transfer to liver and skeleton, increased with increasing Pu:Na ratio. At 7 days, the liver + skeleton content was only 0.06% ILD for pure $^{239}PuO_2$, as expected, but about 8% ILD at a Na:Pu ratio of 16.

(797) Stather et al. (1975) followed the tissue distribution of ^{239}Pu in rats up to 28 days after inhalation of aerosols produced by the 'exploding wire' technique, with or without sodium present. At 28 days the 'extrapulmonary tissue deposit' (ETD = skeleton + liver + soft tissues) was about 0.1% ILD for pure $^{239}PuO_2$, and ~4% ILD at a Na:Pu ratio of 20:1. The authors noted that deposition in the liver accounted for ~16% ETD, indicating that it was in a monomeric form.

(798) Stather et al. (1977a) measured the tissue distribution of ^{239}Pu in hamsters 30 days after inhalation of aerosols (produced by the 'exploding wire' technique) of $^{239}PuO_2$, alone or with sodium present. For pure $^{239}PuO_2$ the ETD was ~0.06% ILD, similar to that seen in mice and rats (see above). In the presence of sodium the ETD was far higher, between 6% and 38% ILD at Na:Pu ratios between 7:1 and 270:1, but there was no correlation with the ratio. (Stather et al., 1979b, reported the result for an Na:Pu ratio of 27:1, for which the ETD was 34% ILD.) Autoradiographs of the lungs showed a much more diffuse deposit after inhalation of the Na-Pu aerosol than after inhalation of pure $^{239}PuO_2$, but no differences that could be correlated with the transportable fraction.

(799) In further experiments, Stather et al. (1977a, 1978a) measured the tissue distribution of ^{239}Pu in hamsters at times up to 550 days after inhalation of pure $^{239}PuO_2$, or with sodium at a Na:Pu ratio of 27:1; and up to 365 days with sodium at a Na:Pu ratio of 104:1. For the pure $^{239}PuO_2$, the ETD at 7 days was 0.06 (±0.02)% ILD and increased slowly, reaching ~0.4% by 550 days. For the Na-Pu (27:1) aerosol the ETD increased from ~20% ILD at 7 days to ~30% at 28 days, with little change thereafter. For the Na-Pu (104:1) aerosol the ETD was lower: ~7% ILD from 7 to 365 days. The plutonium contained ~10% ^{241}Am (by alpha activity): measurements following inhalation of the pure $^{239}PuO_2$, and the Na-Pu (27:1) aerosol showed somewhat higher absorption of the ^{241}Am than of the ^{239}Pu, but not enough to change the ^{239}Pu: ^{241}Am ratio in the lungs. The authors concluded that the Na-Pu aerosols consisted of a soluble fraction that is rapidly absorbed into blood, and an insoluble fraction that is cleared very slowly by particle transport. In a complementary study, Stather and Rodwell (1978) found that following inhalation by hamsters of a Na-Pu (27:1) aerosol, administration of Ca-DTPA reduced both the lung and ETD contents of ^{239}Pu and ^{241}Am (measured at 30 days) significantly. This indicates that even if the soluble form consists initially of $^{239}PuO_2$ nanoparticles, the ^{239}Pu and ^{241}Am within them was available to complexing with DTPA.

(800) Thus it appears that Na-Pu aerosols behave as a mixture of 1-nm PuO_2 (see above) and "normal" plutonium-239 dioxide, with the proportions depending on the Na:Pu ratio. Specific parameter values are not given here for any “reference” Na:Pu ratio. If an estimate can be made of the proportion of 1-nm PuO_2 out of the total PuO_2 present in the aerosol, according to the circumstances of the exposure, then assessments can be made using the dose coefficients and bioassay functions given here for 1-nm PuO_2 and high-fired PuO_2

Plutonium dioxide formed in presence of other metals

(801) Stather et al. (1977b, 1979b) applied the 'exploding wire' technique to mixtures of plutonium with other metals which could be associated with plutonium in accidents in the nuclear industry: uranium, potassium, calcium, and aluminium. They measured lung retention, and as a measure of absorption, the ETD, at 30 days after inhalation of the aerosols by hamsters. For pure $^{239}PuO_2$, the ETD was 0.06 (±0.01)% ILD. It was somewhat higher for U-Pu and Al-Pu aerosols: 0.2% ILD for U-Pu (1:1), 0.5% for U-Pu (4:1) and 0.5% for Al-Pu (4:1). It was considerably higher, 3% ILD, for Ca-Pu (20:1); and 25% for K-Pu (36:1), similar to values for Na-Pu aerosols. The trend reflected the solubility of the predominant species in the aerosol matrix. For the U-Pu aerosols, tissue distributions were measured up to 360 days: continuing absorption was slow, but somewhat higher than for pure $^{239}PuO_2$.

(802) Métivier et al. (1980) studied the biokinetics of ^{239}Pu formed from vaporised mixtures of metallic plutonium and magnesium, because magnesium is used in many metallurgical and chemical processes, and, like sodium, is highly inflammable in air. Rats inhaled an aerosol generated by the arc ignition of a plutonium-magnesium alloy (atomic ratio Mg:Pu = 66:1). Rats were killed at times between 1 and 30 days, and the contents of the lung, spleen, kidneys, blood, femora were measured (the skeletal burden was estimated as 10 times the femora burden). The IAD was estimated from the lung content at four days after inhalation. Lung content fell to ~60% IAD at 30 days. There was significant deposition in skeleton (~2% IAD) at 1 day, increasing to ~8% IAD at 30 days. Early treatment with DTPA was effective at enhancing excretion. Analysis here (with s_r fixed at 1 d^{-1}) gave f_r = 0.05, s_s = 0.007 d^{-1}, and assignment to Type M.

(803) Rhoads et al. (1986) exposed rats, by nose-only inhalation, to high fired $^{239}PuO_2$ (see above), ^{244}Cm oxide, or to a mixed Pu-Cm oxide prepared by calcining the oxalates together at 750°C. The mass ratio of Pu:Cm was 1385:1, and the alpha-activity ratio ~ 1:1. The purpose of the experiments was to determine whether the kinetics of these two radionuclides changed from those in the single compounds when they were calcined together. Rats were killed at times between 3 and 120 days. Activities were measured in lung, systemic organs and excreta. Less than 1% IAD of ^{239}Pu was translocated to any of the systemic tissues . Clearance of ^{239}Pu from the lungs was slightly slower for the mixed oxide than for the pure oxide. Analysis here gave (with s_r fixed at 1 d^{-1}): f_r = 0.003, $s_s < 2 \times 10^{-3}$ d^{-1}, and assignment to Type S. The ^{244}Cm cleared more slowly from the mixed oxide than from the ^{244}Cm oxide, but much faster than the ^{239}Pu (see *Curium* section in this report).

Miscellaneous industrial dusts

Magnox storage pond residues

(804) Cooling pond storage of spent fuel from a Magnox reactor (magnesium-alloy clad uranium metal) could result in workplace contamination through suspension in air of sediment formed by corrosion. Stradling et al. (1989c) measured the tissue distribution in rats of $^{238+239}$Pu, ^{241}Am, ^{144}Ce, and ^{137}Cs, after intratracheal instillation of a suspension of residues present in a sample of pond water (see *Americium* section in this report, and *Caesium* section in OIR Part 2). The particles consisted almost entirely of uranium, but the potential hazard was considered to be mainly from $^{238+239}$Pu and ^{241}Am. Groups were killed at times between 28 and 360 days, and the lung, liver and carcass contents measured. Lung content fell from about 46% ILD at 28 days to 5% ILD at 360 days, whilst the carcass content rose from about 3% to 8.5%

ILD. Analysis here (with s_r fixed at 1 d^{-1}) gave: f_r = 0.04, s_s = 0.002 d^{-1}, and assignment to Type M.

Residues from refining process

(805) Stradling et al. (1987) measured the tissue distribution in rats of ^{239}Pu (and ^{241}Am: see *Americium* section in this report) after inhalation or intratracheal instillation of the respirable fraction of residues obtained from a plutonium electro-refining process. It was considered that plutonium could be present in the residue as Pu^{3+} chloride and finely divided metal. After inhalation, the ILD was determined by analysing tissues from rats killed at 3 days. Groups were killed at times between 10 and 365 days, and the ^{239}Pu content of the lungs, liver and remaining carcass measured. The lung content fell to 6% at 365 days. The carcass content rose from 1.2% at 3 days to 1.6% at 84–365 days. For intratracheal instillation, the ILD was determined by analysing aliquots of the suspension. Rats were killed at times between 1 and 84 days. Urine and faeces were collected. The lung content reduced to 39% at 84 days. The carcass content rose from 1.3% at 1 day to 1.7% at 84 days. Analysis here for both experiments gave: f_r = 0.02, s_s = 3 x 10^{-4} d^{-1}, and assignment to Type S.

Oxide mixtures of plutonium with uranium, beryllium and aluminium

(806) Stradling et al. (1990) (also reported by Moody et al., 1991; Stradling and Moody, 1995) investigated the biokinetics of ^{239}Pu (and ^{241}Am: see *Americium* section in this report) in four site-specific industrial dusts after deposition in the rat lung by inhalation or intratracheal instillation (Table 22.7). One was PuO_2 (coded ALDP9, see *Plutonium-239 dioxide* section above). The others consisted of:

- a mixed oxide of PuO_2, UO_2 and Al_2O_3 (estimated relative atomic proportions 1.0Pu: 2.0U: 13Al) produced by oxidation of a molten mixture of the metals (ALDP10);
- a mixed oxide dust containing $^{239}PuO_2$, $^{235}U_3O_8$ and BeO (1.0Pu: 3.1U: 26Be) produced by combustion of the metals separately (ALDP11);
- a mixed oxide dust containing $^{239}PuO_2$ and BeO (1.0Pu: 46Be) produced by combustion of the metals separately with prolonged sintering at 900 – 1050ºC to give 'high-fired' oxides (ALDP13).

(807) In each case, the respirable fraction was obtained by sedimentation in alcohol. For inhalation, the ILD was obtained from tissue analysis of rats killed at 2 days. Further groups were killed at times between 7 and 730 days and the lung, liver and carcass contents measured. Following instillation, urine and feces were also measured. In two experiments groups were killed at 7 and 21 days, in the third, at times between 7 and 365 days. Absorption parameter values derived here are given in Table 22.7. However, estimates of s_s from the 21-day instillation studies are considered less reliable than the others because of their short duration. Results for ALDP10 give assignment to Type M, the others to Type S.

Table 22.7. Summary of experimental data and derived absorption parameter values for some plutonium-metal oxides (Stradling et al., 1990).

Material code	ALDP10	ALDP11	ALDP13
Metals present with plutonium	U, Al	U, Be	Be
Inhalation			
Duration, days	730	730	730

Lungs, %ILD at 7 (730 d)	81 (1.5)	88 (2.8.)	81 (1.6)
Carcass %ILD at 7 (730 d)	1.5 (12)	0.12 (0.5)	0.11 (0.4)
f_r	0.023	0.0018	0.0026
s_s, x 10^{-4} d^{-1}	17	0.9	1.3
Instillation			
Duration, days (T_f)	21	21	365
Lungs, %ILD at 7 (T_f) days	73 (52)	84 (63)	71 (7)
Carcass,%ILD at7 (T_f) days	1.3 (3.3)	0.12 (0.14)	0.13 (0.26)
f_r	$<10^{-4}$	0.0018	0.0029
s_s, x 10^{-4} d^{-1}	45	0.9	0.8

Unknown compounds

(808) Reports in the literature of monitoring following accidental occupational exposures demonstrate the very wide range of dissolution characteristics that plutonium can exhibit in situations such as mixed laboratory waste or long-term contamination.

(809) La Bone et al. (1992) reported an occupational case of ^{238}Pu inhalation due to a contaminated shipping container. The worker received Zn-DTPA treatment shortly after the incident and her urine excretion was monitored over more than 500 d after intake. No information was obtained on the chemical form or the particle size distribution of the aerosol. However, the measurements of ^{238}Pu in urine suggested a high solubility of the inhaled material and a poor effectiveness of DTPA treatment. The analysis of the case by the authors, confirmed by a group of experts, indicated that the bioassay data were best modeled assuming an intake of very fine (0.4 µm AMAD) and very soluble (Class D i.e. Type F in the framework of the current HRTM) plutonium.

(810) Blanchin et al. (2008) reported two occupational cases of exposure to mixtures of plutonium isotopes and ^{241}Am. The first subject inhaled an aerosol from a MOX pot that had been stored for many years. A chemical analysis revealed high chloride concentration most likely linked to the deterioration of the polyvinyl chloride envelope on the pot. The second subject inhaled an aerosol formed from old acid (nitrate, chloride and oxalate) solutions in a glovebox. Both workers were treated with Ca-DTPA and monitored by measurements of ^{241}Am in lungs, ^{241}Am, ^{238}Pu and $^{239+240}$Pu in urine and faecal samples. They were followed up to 50 d and 210 d after their respective incidents. The measurement results appeared inconsistent with Types M and S. In both cases, the authors obtained a best fit to the data by assuming Type F, an AMAD of 0.1 µm and no significant effect of DTPA treatment.

(811) Wernli and Eikenberg (2007) reported the follow-up of a worker who inhaled a mixture of plutonium isotopes and ^{241}Am following a glove box accident in which waste material related to nuclear fuel overheated. No information was obtained on the chemical form or the particle size distribution of the aerosol. The radionuclide composition of the fuel samples used in the solution that overheated and was dispersed in the accident is known, and is given as per cent of the total alpha activity: 9% ^{238}Pu, 55% ^{239}Pu, 26% ^{240}Pu, 10% ^{241}Am, 750% ^{241}Pu (beta activity). There has been an extensive series of follow-up measurements on the subject. The data collected over nearly 30 years include measurements of plutonium in bronchial mucus and nasal swabs, plutonium and ^{241}Am in faeces and urine, and ^{241}Am in chest, lymph nodes, bone and liver. About 60% ILD was retained in lungs from 30 d to 180 d post-intake. The amount does not decrease appreciably for over twenty years but a significant fraction of the

^{241}Am retained after 1000 d is due to ingrowth from ^{241}Pu. Analyses of the data available at various times have been reported (e.g. ICRP, 2002 Annex E; IAEA, 2007; Wernli and Eikenberg, 2007). In the most recent analysis, Wernli et al. (2015) fit the plutonium and ^{241}Am data simultaneously, taking into account the ingrowth of ^{241}Am from ^{241}Pu. Assuming f_b=0.002 and s_b=0 d^{-1}, they obtained parameter values for plutonium of f_r = 0.003, s_r = 0.4 d^{-1}, and s_s = 8 x 10^{-5} d^{-1}, giving assignment to Type S. The dissolution rates s_r and s_s were not significantly different for plutonium and ^{241}Am (although the value of s_r for plutonium was not well defined), but the value of f_r (0.003) was lower than that estimated for ^{241}Am (0.08).

Plutonium in dust and soils

(812) There have been a number of studies of plutonium released into the environment. Although generally related more to public than to occupational, exposure, information is included here for completeness. Some might also be relevant to occupational exposure at contaminated site.

Plutonium in nuclear weapons fallout

(813) Numerous measurements have been made of the concentration of ^{239}Pu, resulting from the atmospheric testing of nuclear weapons, in tissues (notably lung, liver, skeleton and tracheo-bronchial lymph nodes) taken at autopsy from non-occupationally exposed people (e.g. Fisenne et al., 1980; McInroy et al., 1981; Bunzl and Kracke, 1983; Popplewell et al., 1985). Comparisons with levels predicted from measured air concentrations using the then current ICRP models were broadly consistent with Class Y (Bennett, 1976; ICRP, 1986). *Publication 66* (ICRP, 1994, Table E.25) summarised information relating to concentrations in lungs and lymph nodes of non-occupationally exposed persons, which demonstrated the long-term retention of fallout plutonium in these tissues.

(814) Jones and Prosser (1997) compared published results with levels predicted from measured air concentrations using the HRTM and the *Publication 67* plutonium systemic model. They found good agreement for concentrations in liver and bone assuming Type M absorption, and for concentrations in lung and lymph nodes assuming Type S absorption. This suggests that good overall agreement would be obtained assuming a rapid fraction similar to that for Type M (~0.1) and a slow dissolution rate similar to that for Type S (~10^{-4} d^{-1}) defaults in the original HRTM (ICRP, 1994).

Plutonium in estuarine sediment

(815) A large fraction of the actinides discharged to sea from the Windscale (now Sellafield) nuclear fuel reprocessing plant rapidly became associated with sediments, some of which were deposited on shorelines such as those of the nearby Ravenglass Estuary, from which they could become resuspended in air by the action of tides, waves, and winds.

(816) Stather et al. (1978b) followed the biokinetics, after intratracheal instillation into rats and hamsters, of ^{239}Pu and ^{241}Am associated with a suspension of Ravenglass sediment. Particles greater than 10 µm were removed by sedimentation. Because the specific activity of the sample was considered too low for in-vivo measurements, ^{239}Pu and ^{241}Am were added to the suspension: it was confirmed that they attached rapidly. Tissue distributions and cumulative excretion were measured in rats at 7 and 14 days; tissue distributions in rats and hamsters at 28

days. The ^{239}Pu lung content decreased to 53% ILD at 7 days, with most of the clearance to systemic tissues: only ~10% ILD went to feces. It then decreased more slowly: to ~35% ILD at 28 days. Lung clearance of ^{241}Am was similar but somewhat slower. (See *Americium* section in this report.) Tissue distributions in hamsters at 28 days were similar to those in rats. Analysis here gave: $f_r = 0.36$, $s_s = 0.008$ d^{-1}, and assignment to Type M.

(817) Morgan et al. (1988b, 1990) followed the biokinetics, after intratracheal instillation into rats, of ^{238}Pu, $^{239(+240)}$Pu and ^{241}Am associated with a suspension of Ravenglass sediment. Unlike Stather et al. (1978b), they did not 'spike' the sediment with additional activity, but administered a much larger mass: ~25 mg. As it was undesirable to administer so much in a single dose, it was fractionated into five 5-mg portions given over 7 weeks. Tissue distributions were determined in rats killed at 2 days after the final instillation and at times between 47 and 548 days. The lung content at 2 days was taken to be the initial lung (alveolar) deposit (IAD). Lung retention of all three radionuclides decreased with a half-time of ~240 days, much slower than seen in rats administered low masses of insoluble particles (ICRP, 2002), and demonstrating, as expected, that the high mass led to 'overload': impaired alveolar clearance by particle transport (see e.g. Muhle et al., 1990). What effect, if any, 'overload' has on dissolution and absorption is not known. Some transfer to liver and skeleton (2 – 4% IAD) occurred during the 7-week administration period. For plutonium, there was little further change in liver content, but that of the skeleton increased to about 20% IAD by 90 days. Values for ^{241}Am were lower, but not significantly. (See *Americium* section in this report.) The authors noted that absorption of actinides was lower than observed by Stather et al. (1975), but whether this was due to differences in speciation between 'spiked' and 'naturally' labelled sediment, or to 'overload' was not known. Analysis here gave: $f_r = 0.08$ and $s_s = 0.0025$ d^{-1} for ^{238}Pu; $f_r = 0.06$ and $s_s = 0.0025$ d^{-1} for $^{239(+240)}$Pu, and assignment to Type M for both.

Palomares nuclear weapon accident

(818) On 17 January 1966, there was an aviation accident above the town of Palomares in south-eastern Spain. Four thermonuclear bombs carried by one of the planes fell, and on impact, the nuclear fuel in two of them partially ignited. This gave rise to an aerosol which contaminated approximately 230 hectares of underbrush, farmland and urban areas (Iranzo et al., 1987). Biokinetic studies of ^{239}Pu and ^{241}Am associated with contaminated dust were conducted in order to improve the basis for assessing internal doses and interpreting bioassay data (Stradling et al., 1993, 1996, 1998; Espinosa et al., 1998). A soil sample was fractionated and four fractions investigated: 'total soil;' '125–250 µm'; '20–40 µm'; '<5 µm'. The three larger fractions were ground and the respirable fraction (defined as <5 µm aerodynamic diameter) of each obtained by sedimentation in ethanol. Because of the low specific activity, about 7 mg of dust was administered by intratracheal instillation to each rat in three aliquots over a 5-day period. Groups were killed at times between 7 and either 330 or 365 days after the first administration, and ^{239}Pu (and ^{241}Am in the 125–250 µm and <5 µm fractions) measured in the lungs, liver and carcass. In the four experiments, the ^{239}Pu lung content fell from about 70% ILD at 7 days, to between 22 and 32% ILD at the last measurement. Lung clearance of ^{241}Am was somewhat faster (19–27% ILD retained at the last measurement), (see *Americium* section in this report). It was noted that the retention half-times (220–310 days) were longer than typically observed for insoluble particles in rats, but this was not unexpected because the large mass administered would have impaired alveolar particle transport ('overload': see above). The

estimated amount of ^{239}Pu absorbed into blood by 7 days ranged from 0.5% ILD (125–250 µm fraction) to 3.4% ILD (<5 µm fraction). Thereafter, absorption was similar: a further 2–4% ILD absorbed between 7 days and 1 year. Absorption of ^{241}Am was somewhat greater. Analysis here gave parameter values for ^{239}Pu as follows; all give assignment to Type S:

Table 22.8. Parameter values for ^{239}Pu.

Fraction	<5 µm	20–40 µm	125–250 µm	Total soil
f_r	0.05	0.02	0.007	0.02
s_s, x 10^{-4} d^{-1}	6	7	3	5

Maralinga

(819) Between 1953 and 1963 nuclear weapons trials were conducted at Maralinga in South Australia. These included "minor trials" involving chemical explosions and the dispersal of radioactive materials, which in some cases included plutonium. As a result, residual activity remains, and studies were conducted to assess the radiation exposure to people living a semi-traditional lifestyle in the area (Johnston et al., 1992; Haywood and Smith, 1992; Burns et al., 1995).

(820) Stradling et al., (1989b, 1992, 1994) followed the biokinetics of ^{239}Pu and ^{241}Am (see *Americium* section in this report) present in the respirable fraction of three samples of contaminated dusts from Maralinga, after their deposition in the rat lung. One sample (Q380) was supplied with a nominal AMAD of 5 µm. For the other two (TM100 and TM101) the respirable fraction was separated by sedimentation in alcohol. All three dusts were administered to groups of 36 rats by intratracheal instillation. To administer sufficient activity, several mg were deposited in three aliquots over a 5-day period. It is considered that the large mass administered impaired alveolar particle transport ('overload': see above). ILDs were determined by analysing the suspensions administered. Groups were killed at times between 7 and 365 days after the initial instillation, and the ^{239}Pu content of the lungs, liver and carcass measured. For Q380, TM100 and TM101 the lung contents fell to 26%, 27% and 17% ILD at 365 days, and estimated total amounts absorbed to blood were 6%, 1% and 10% ILD. The biokinetics of ^{239}Pu (and ^{241}Am) in rats was also followed after inhalation of TM101. The ILD was determined by analysing tissues of rats killed 30 minutes later. Groups were killed at times between 7 and 365 days and ^{239}Pu was measured in lungs, liver and carcass. Lung content fell from 70 to 3% ILD between 7 and 365 days. Lung clearance was faster than following instillation, indicating that although the ILD mass (0.4 mg) was relatively high, there was less, if any, impairment of clearance. Estimated total amounts absorbed to blood were 0.4% and 0.5% ILD at 7 and 365 days. Analysis here gave parameter values for ^{239}Pu as follows; results for TM100 give assignment to Type M, the others to Type S:

Table 22.9. Parameter values for ^{239}Pu.

Sample	Q380	TM100	TM101	TM101
Administration	Instillation	Instillation	Instillation	Inhalation
f_r	0.02	0.01	0.007	0.007
s_s, x 10^{-4} d^{-1}	7	15	0.6	0.6

(821) It is of interest that in these studies the plutonium remained mainly in insoluble forms even after two or three decades of environmental exposure. Mewhinney et al., (1987) found with in-vitro dissolution tests, that alternate wet-dry cycling, simulating that occurring under environmental conditions such as intermittent rainfall in an otherwise arid climate, led to much faster dissolution. The enhancement in total dissolution ranged from two to ten times during each wet-dry cycle compared to studies involving continuous immersion in the same solvents.

Rapid dissolution rate

(822) In seventeen *in vivo* studies of the biokinetics of inhaled soluble plutonium compounds (citrate and nitrate), sufficient early retention data were available to allow estimates of s_r to be made. These comprised one human volunteer, one monkey, three dog, and twelve rat studies. The results of individual analyses performed using data from these studies are summarised in Table 22.10. All analyses were performed using $f_b = 0.002$, and $s_b = 0\ d^{-1}$. In order to judge the effect of assuming this small bound fraction on estimates of f_r, s_r and s_s, the analysis for one study (Stather and Howden, 1975) was repeated with $f_b = 0$. Very minor differences in the estimated absorption parameter values were found (0.1 – 1%). For the specific purpose of analysing data from the rat studies (Table 22.2), a best estimate value of 1 d^{-1} was estimated from the results for the twelve rat studies (Smith, 20xx).

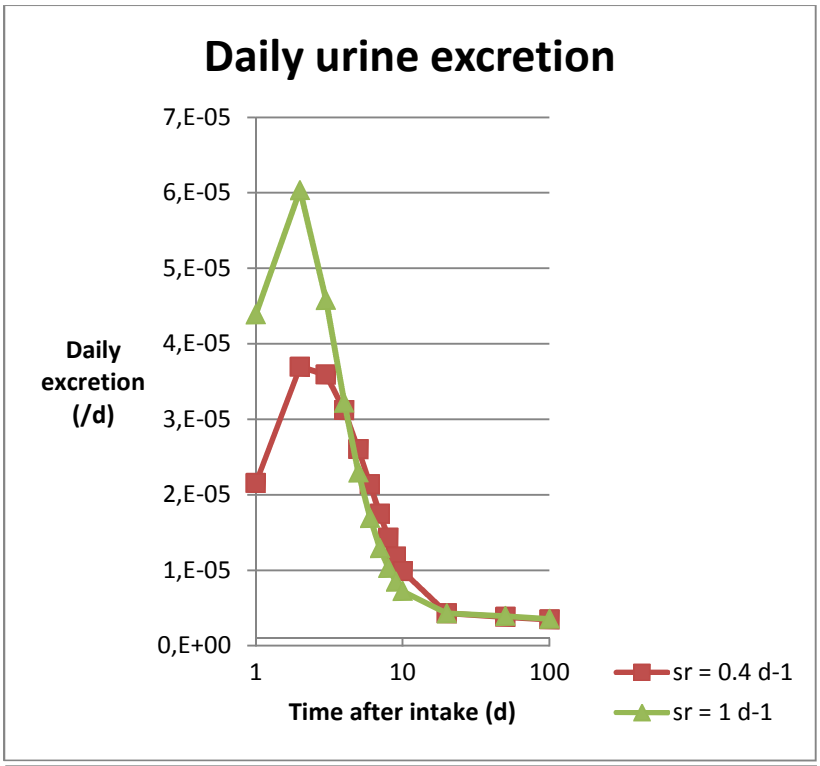
Table 22.10. Case-specific absorption parameter values estimated for soluble compounds in studies reporting early retention data

Materials and administration	Animal species	Absorption parameter values[a]		References
		f_r	s_r (d^{-1})	
nitrate	Man	0.16	0.39	Etherington et al. (2002, 2003) Puncher et al. (2016)
nitrate	Monkey	0.1	>0.1	Brooks et al. (1992)
nitrate, ^{238}Pu	Dog	0.83	0.28	Dagle et al. (1983)
nitrate, ^{239}Pu	Dog	0.13	0.14	Dagle et al. (1983)
nitrate	Dog	0.27	0.17	Bair (1970)
nitrate, ^{238}Pu	Rat	0.13	0.2	Morin et al. (1972)
nitrate, ^{239}Pu	Rat	0.05	9	Morin et al. (1972)
nitrate, ^{238}Pu	Rat	0.14	0.16	Nénot et al. (1972)
nitrate, ^{239}Pu	Rat	0.04	0.83	Nénot et al. (1972)
Nitrate, ins	Rat	0.59	1.4	Stather and Howden (1975)
nitrate, ^{238}Pu, ins	Rat	0.36	78	Stather and Priest (1977)
nitrate, ^{239}Pu, ins	Rat	0.49	0.36	Stather and Priest (1977)
nitrate, ^{238}Pu	Rat	0.47	0.1	Stradling et al. (1987)
nitrate	Rat	0.52	8	Moody et al. (1993, 1994, 1998)
nitrate	Rat	0.13	12	Pellow et al. (2016c)
nitrate, ins	Rat	0.69	17	Pellow et al. (2016c)
citrate	Dog	0.25	0.47	Ballou et al., 1972

citrate, ins	Rat	0.76	2.3	Stather and Howden (1975)
Nitrate only; all species				
Median		0.22	0.39	
Geometric mean		0.22	1.1	
Min		0.04	0.1	
Max		0.83	78	
Nitrate only; rats only				
Median		0.36	1.4	
Geometric mean		0.23	1.9	
Min		0.04	0.1	
Max		0.69	78	
Nitrate only; rats only; instillation vs inhalation				
Median		0.54; 0.13	9.2; 0.83	
Geometric mean		0.52; 0.14	5.1; 1.1	
Min		0.36; 0.04	0.36; 0.1	
Max		0.69; 0.52	78; 12	
Notes. a. f_b and s_b were assumed to be 0.002 and 0 d^{-1} respectively				

(823) In selecting a default s_r value for plutonium from the results for the various species, a high weighting is given to the value determined for the human volunteer study (Puncher et al., 2016), see *plutonium nitrate* section above. This value is broadly consistent with the values determined for the monkey study and the dog studies. Conversely, the values determined for the rat studies are very broadly distributed, although the best estimate value for rats of 1 d^{-1} remains close to the value determined for the human volunteer study. From a consideration of these results, giving increased weight to results for humans, an s_r value for plutonium of 0.4 d^{-1} is recommended.

(824) Consideration was given to rounding the value of s_r from 0.4 d^{-1}, to 1 d^{-1}, to reflect uncertainty in the estimate. Although overall uptake from the lungs is insensitive to the value of s_r, it does affect the pattern of urinary excretion over the first few days, and therefore estimates of dose per content. Fig. 22.1 shows that (for a Reference Worker exposed briefly to a 5-□m AMAD ^{239}Pu nitrate aerosol) urinary excretion in the first day is predicted to be approximately twice as high assuming a value of s_r of 1 d^{-1}, than assuming 0.4 d^{-1}; this is compensated by lower excretion from about 5 – 10 d, after which rates are similar. As a result, the calculated dose per excretion on the first day after intake is about twice as high assuming a value of s_r of 0.4 d^{-1} as it is assuming 1 d^{-1}. Measurements of urine samples taken on the first day after exposure are particularly important in assessing the consequences of accidental intakes and it is important not to underestimate the dose per daily urine. It was therefore decided not to round the value to 1 d^{-1}.



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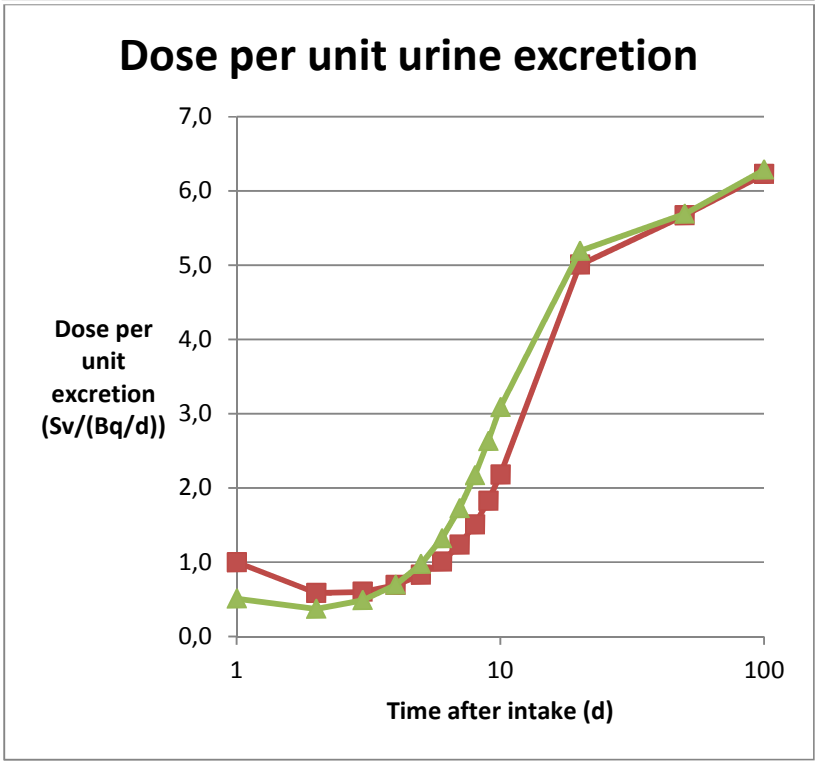

9004
9005
9006 Fig. 22.1. Effect of the value of s_r on (a) daily urinary excretion (b) dose per daily excretion
9007 (Reference worker exposed briefly to a 5-µm AMAD ^{239}Pu nitrate aerosol)
9008
9009

(825) Because this value (0.4 d^{-1}) is lower than the general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S forms of plutonium.

Extent of binding of plutonium in the respiratory tract

(826) Early applications of the HRTM to plutonium nitrate made use of a short-term bound fraction (ICRP, 2002, Annexe E Section E2). For example, Birchall et al. (1995) analysed the results of experiments in which the biokinetics of ^{239}Pu was followed for 180 d after instillation of plutonium nitrate into the pulmonary region of the lungs of rats (Stather and Howden, 1975; Stather and Priest, 1977). At 30 minutes, 1 d and 7 d respectively, lung retention was ~77%, 65% and 45% ILD, and deposition in the carcass ~9%, 20% and 30% ILD. Absorption over this period was represented by a high rapid dissolution rate (s_r ~50 d^{-1}), and bound fraction (f_b ~0.5, with s_b ~0.2 d^{-1}). However, while it enabled good fits to be made to the experimental data, including this bound fraction had little effect on dose.

(827) More recent studies indicate the presence of a small, but very long-term bound state for plutonium (e. g. James et al., 2007; Nielsen et al., 2012), which could potentially increase equivalent doses to the lungs significantly, particularly if it occurs in the bronchial (BB) and bronchiolar (bb) regions. Consideration is therefore only given here to such a long-term bound state. Because binding occurs after dissolution of the inhaled material, it is assumed to be independent of the initial chemical form. Three studies have investigated the specific issue of the presence or absence of a long-term bound state for inhaled plutonium nitrate, and its likely magnitude.

(828) The first study (Pellow et al., 2016b; Puncher et al., 2016a) involved analysis of lung retention data from a 15-year life span effects study (Dagle et al., 1993; PNL, 1994) in which groups of Beagle dogs inhaled different concentrations of ^{239}Pu nitrate aerosol. Lung clearance of ^{239}Pu was modelled using simplified and modified versions of the original HRTM (ICRP, 1994) and the revised HRTM (ICRP, 2015). A Bayesian analysis using Markov Chain Monte Carlo calculations was performed, and inclusion of a small bound fraction was found to be required to produce model predictions of lung retention that were consistent with the lung retention data. The arithmetic mean of the posterior distribution for f_b, determined using a model based on the *Publication 66* HRTM, was 0.0023 (95% confidence interval (CI) = 6 x 10^{-4} to 0.007). The half time associated with this bound fraction was greater than 200 y, and so the uptake rate to blood from the bound state (s_b) was assigned a value of 0 d^{-1}. This study is considered to provide strong evidence for the existence of a long-term retained component in the respiratory tract, for which the bound state provides the simplest explanation.

(829) In the second study, Puncher et al. (2016b) performed a reanalysis of the autopsy and bioassay data of United States Trans-Uranium and Uranium Registries (USTUR) donor 269, a plutonium worker who received a high (58 kBq) acute intake of plutonium nitrate by inhalation. This is the only USTUR case studied to date that involved exposure only to plutonium nitrate, and therefore the only one which can be used to assess bound state parameter values for inhaled plutonium. The original investigation of the case (James et al., 2007) inferred a bound fraction of around 0.08 from the unexpectedly high lung retention, and low (thoracic lymph node content):(lung content) ratio at the time of death, many years after intake. For the reanalysis, the revised HRTM was used to predict the measured quantities, and a Bayesian analysis using Markov Chain Monte Carlo calculations was performed that accounted for uncertainties in model parameter values, including those for clearance by particle transport, which were not

considered in the original analysis. The reanalysis also used the results of recent measurements (Tolmachev et al., 2016) on plutonium in the ET_2, BB, bb and AI regions and in the thoracic lymph nodes for donor 269. The results indicate that a small bound fraction is required to explain the data, largely because plutonium was present in the ET_2, BB and bb airways at the time of death. However, it is not known whether the plutonium present in these tissues was associated with the epithelium, as assumed in the dosimetric model for the bound fraction, or in underlying tissues, such as lymphatic channels. Métivier et al. (1989b) observed (following inhalation of $^{239}PuO_2$ by baboons) for some animals a high ^{239}Pu content in the trachea, which "was probably due to micro lymph nodes embedded in the external part of the trachea, removed with difficulty during autopsy". After the measured systemic (liver and skeleton) retention data were corrected to remove the effect of DTPA treatment, the mean value for f_b was determined as 0.0037 (95% CI = 0.0037 to 0.0039). There was no evidence for an s_b value other than zero. Lung measurements from a further two USTUR donors (631 and 745) have recently become available; these also show significant plutonium activity remaining in the ET_2, BB and bb airways, in addition to the AI region and in the thoracic lymph nodes, more than 40 years after high acute exposures to plutonium nitrate. These are currently being analysed using the same methodology applied to donor 269 (Puncher, 2015, personal communication).

(830) In the third study (Puncher et al., 2016c), autopsy data (plutonium amount in skeleton, liver, lungs, and thoracic lymph nodes) from 20 former MPA plutonium workers exposed only to plutonium nitrates and 20 workers exposed only to plutonium oxides were analysed. These analyses were carried out as part of a three-year study, commissioned by USDOE, to develop a methodology (Birchall et al., 2016) and then to derive internal doses for 8000 MPA workers. As for the studies described above, Bayesian analyses were performed using Markov Chain Monte Carlo calculations. Given the evidence for a long-term bound state provided by the two studies described above, the analyses were performed assuming that a bound state is present, with the value of f_b to be determined. The revised HRTM was used, with uniform prior distributions on f_b and s_s, together with log-normal prior distributions on particle transport rates and breathing parameters with median values set at the reference HRTM values (ICRP, 2015, Fig. 3.4). The posterior distributions determined for the particle transport parameters were largely consistent with the HRTM reference values, although the analysis suggested possibly a lower rate from ALV to INT, particularly for the oxides (2×10^{-5}). The mean value for f_b was determined as 0.0014 (95% CI = 1.1×10^{-4} to 0.003). There was no evidence for an s_b value other than zero. The mean value determined for s_s for plutonium nitrate was 2.5×10^{-4} d^{-1} (95% CI = 2.1×10^{-4} to 2.8×10^{-4} d^{-1}). It should be noted, however, that the same data could be explained when f_b was fixed at zero, and this also largely unaffected the estimate of s_s. This result was consistent with the fact that the distribution obtained in the analysis where f_b was varied, was a normal distribution, left truncated at zero.

(831) Strong evidence for the existence of a bound state comes from the reanalysis of the Beagle dog data (Pellow et al., 2016b; Puncher et al. 2016a) and of USTUR Case 269, with estimated values of f_b of 0.0023 and 0.0037, respectively. On the assumption that a bound state exists, the best estimate from the MPA worker study is 0.0014 (Puncher et al., 2016c). The re-analysis of USTUR Case 269 (Puncher et al., 2016b) indicates that if a bound state exists, then material in the ET_2, BB, and bb regions as well as material in the AI region is subject to binding. From the perspective of radiation protection, the assumption that the data from these studies represent a small bound state rather than a second long-term particle dissolution component provides an appropriate degree of conservatism. The evidence provided by the three studies therefore indicates a value for f_b of about 0.2%, to be applied to the whole of the

respiratory tract except for ET_1, for all plutonium compounds. There is no evidence to indicate an s_b value other than 0 d^{-1}. This small long-term bound state results in an additional contribution to the committed equivalent dose coefficient for the lungs from inhaled ^{239}Pu nitrate of about 20%.

Table 22.11. Absorption parameter values for inhaled and ingested plutonium.

Inhaled particulate materials	Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A[f]
Specific parameter values[b]				
Plutonium nitrate, $Pu(NO_3)_4$	0.2	0.4	0.002	1×10^{-4}
Plutonium Tri-Butyl-Phosphate (Pu-TBP)	0.5	30	0.005	1×10^{-4}
Plutonium-239[c] dioxide, $^{239}PuO_2$	0.004	0.4	1×10^{-5}	1×10^{-5}
Plutonium in mixed oxide (MOX: (UO_2 + PuO_2) or $(U,Pu)O_2$)	0.002	0.4	2×10^{-5}	1×10^{-5}
Plutonium-238 dioxide, $^{238}PuO_2$ ceramic	d	d	d	5×10^{-8}
Plutonium-238 dioxide, $^{238}PuO_2$ non-ceramic	e	e	e	1×10^{-5}
Plutonium dioxide 1-nm nanoparticles, 1-nm PuO_2	0.7	3	0.005	1×10^{-4}
Default parameter values[f,g]				
Absorption Type — Assigned forms				
F —	1	0.4	—	1×10^{-4}
M[h] Plutonium citrate	0.2	0.4	0.005	2×10^{-5}
S —	0.01	0.4	1×10^{-4}	1×10^{-6}
Ingested materials				
Soluble forms (nitrate, chloride, bicarbonates,..)				1×10^{-4}
Insoluble forms (oxides, ..)				1×10^{-5}
All other unidentified chemical forms				5×10^{-4}

a It is assumed that for plutonium a bound fraction $f_b = 0.002$ with an uptake rate $s_b = 0$ d^{-1} is applied throughout the respiratory tract, except in the ET_1 region. The values of s_r for Type F, M and S forms of plutonium (0.4 d^{-1}) are element-specific.

b See text for summary of information on which parameter values are based, and on ranges of parameter values observed for individual materials. For plutonium specific parameter values are used for dissolution in the lungs, and in most cases, where information is available, for absorption from the alimentary tract. However, for plutonium dioxide nanoparticles, the default value of f_A is used (footnote f).

c Plutonium in the dioxide form used in the production of nuclear fuel is predominantly ^{239}Pu by activity, and for simplicity is here termed $^{239}PuO_2$. It may, however, contain varying amounts of other isotopes, notably: ^{238}Pu, ^{240}Pu, ^{241}Pu and ^{242}Pu.

d See text: $s_p = 1 \times 10^{-6}$ d^{-1}, $s_{pt} = 0.0026$ d^{-1}, $s_t = 6 \times 10^{-4}$ d^{-1} with $f_A = 5 \times 10^{-8}$, for ceramic forms.

e See text: $s_p = 0.001$ d^{-1}, $s_{pt} = 0.008$ d^{-1}, $s_t = 0.004$ d^{-1} with $f_A = 1 \times 10^{-5}$, for non-ceramic forms.

f For inhaled material deposited in the respiratory tract and subsequent cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the (rounded) product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of plutonium (1×10^{-4}).

g Materials (e.g. plutonium citrate) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

h Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

22.2.2. Ingestion

(832) Gastrointestinal absorption of plutonium is influenced by its initial oxidation state. Popplewell et al. (1994) and Ham and Harrison (2000) measured the absorption of ^{244}Pu administered in citrate solution with a mid-day meal to five volunteers. The values obtained were in the range of 10^{-4} to 10^{-3}, with a mean value of 6×10^{-4}.

(833) Animal data on the absorption of Pu in species including rodents, pigs, dogs and primates was extensively reviewed in *Publication 48* (ICRP, 1986) and by Harrison (1983, 1991). The chemical form ingested is an important factor affecting absorption. The lowest values obtained are for the oxide, ranging from about 2×10^{-4} (Sullivan, 1980) to about 3×10^{-8} (Smith, 1970). This large range for the oxides probably reflects the solubility of the oxide preparations, affected by the temperature of production (Mewhinney et al., 1976), the proportion of small particles present (Stather et al., 1975), and the specific activity of the isotope (Fleischer and Raabe, 1977). The lowest oxide values were obtained by Smith (1970) in studies where intact or crushed $^{238}PuO_2$ ceramic microspheres as used in RTG were administered to pigs. High levels of lung deposition were observed following feeding of the crushed microspheres and were attributed to inhalation of material resuspended from feces. If allowance is made for those high lung levels, reasonably comparable values in the order of $5x10^{-8}$ are obtained for both intact and crushed $^{238}PuO_2$ microspheres. Mixed Pu-sodium oxides contain a higher proportion of very small particles (about 1 nm diameter) than the pure oxides (Stather et al., 1975) and suspensions of ^{238}Pu oxide are more prone than those of ^{239}Pu oxide (6.27×10^{8} and 2.25×10^{6} kBq g^{-1}, respectively) to radiolytic breakdown to small particles (Fleischer and Raabe, 1977). Comparisons of the behaviour of inhaled Pu oxide and mixed U/Pu oxides in rats and baboons showed that, although solubility in the lung was low in each case, transfer of Pu to liver and bone was about two to three times greater for the mixed oxide (Lataillade et al., 1995). Conway et al. (2009) analysed the *in vitro* dissolution of hot particles from soils sampled at two locations within the Semipalatinsk Nuclear Test Site: Tel'kem 1 (TK1) and 2 (TK2). From particle sampled in TK2, 0.1% to 2% Pu activity was extracted in 2-hour digestion by a simulated stomach solution, and less than 0.04% additional Pu activity was extracted in 4-hour digestion by a simulated small intestine solution. From particles isolated at TK1, 3% to 27% alpha activity was extracted in 2-hour digestion by a simulated stomach solution, and 3.3% additional alpha activity was extracted by the simulated small intestine solution.

(834) The range in values of uptake for Pu administered to animals as the nitrate, chloride or bicarbonate is not as large as for the oxide. In general, the results are between 10^{-4} and 10^{-5}. Fasting has been shown to increase absorption by up to an order of magnitude. For example, absorption in mice fasted for 8 hours before and 8 hours after the administration of ^{236}Pu bicarbonate was about 10^{-3} compared with 2×10^{-4} in fed animals (Larsen et al., 1981). High values of 10^{-3} to 2×10^{-3} have been reported for uptake of ^{237}Pu nitrate given as a single dose to rats and mice (Sullivan, 1981; Sullivan et al., 1982). These results were taken as evidence of increased absorption at low masses. However, in experiments to determine the effect of chronic ingestion at low concentrations, a value of 3×10^{-5} was obtained for the nitrate in rats (Weeks et al., 1956) and 10^{-5} for the bicarbonate in hamsters (Stather et al., 1981). It would appear that in general ingested mass and valence are not important factors affecting absorption. However, at high masses of Pu(V), absorption may be increased by an order of magnitude as demonstrated by Métivier et al. (1985) in studies using baboons.

(835) The absorption of Pu administered to animals as organic complexes or incorporated into food materials is generally greater than for inorganic forms (ICRP, 1986). For example, most of the reported values for Pu citrate are in the range $6x10^{-5}$ to $6x10^{-4}$ compared with the range of 10^{-5} to 10^{-4} for the nitrate. An organic form of importance in reprocessing is Pu-tributylphosphate for which Métivier et al. (1983) measured absorption in rats as about 10^{-4} to 2×10^{-4}.

(836) In *Publication 30* (ICRP, 1979), the recommended absorption values were 10^{-5} for oxides and hydroxides and 10^{-4} for all other forms. In *Publication 48* (1986), values of 10^{-5} for oxides and hydroxides and 10^{-4} for nitrates were recommended. In addition, on the basis of animal data, a value of 1×10^{-3} was recommended for all other forms of Pu and was taken to apply as a general value for all actinides other than U. This value was also adopted in *Publication 56* (ICRP, 1989). However, in this report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all actinides other than U.

(837) f_A of 1×10^{-5} for oxides and hydroxides and 1×10^{-4} for nitrates, chlorides and bicarbonate forms are adopted here. For unidentified chemical forms, an f_A of 5×10^{-4} is adopted here as a default value for direct ingestion.

22.2.3. Systemic distribution, retention and excretion of plutonium

22.2.3.1. Summary of the database

Data for human subjects

(838) In the mid-1940s, 18 seriously ill persons were injected with tracer amounts of Pu citrate or nitrate to investigate the relation of the systemic burden and excretion rate of Pu (Langham et al., 1950; Langham, 1959). The life expectancies of the subjects of the "Langham study" were judged to be short at the time of injection, but eight were still alive after 8 y and four survived at least 3 decades (Rowland and Durbin, 1976). Measurements of activity in blood and excreta were made frequently during the early weeks after injection, and a few additional excretion measurements were made for two of the subjects through 4.5 y (Langham et al., 1950; Durbin, 1972). The concentration of Pu in tissues was determined in samples collected at autopsy from subjects dying in the first 15 months after injection (Langham et al., 1950; Durbin, 1972). Langham and coworkers estimated on the basis of the autopsy results that on average 66% of Pu entering blood deposited in the skeleton and 23% deposited in the liver. Durbin (1972) reanalysed the data to account for the non-uniformity of Pu in bone samples and estimated that about 50% of the systemic burden was contained in the skeleton and 30% was contained in the liver at 4-457 d after injection.

(839) Excretion data from the Langham study were used by ICRP as the primary basis for bioassay models (e.g. power functions or sums of exponential terms) for Pu until the 1990s, when the systemic model of *Publication 67* was adopted as both a dosimetric and bioassay model (ICRP, 1993, 1997). Parameter values of the *Publication 67* model describing the short- and intermediate-term behavior of Pu, including its urinary and faecal excretion rates and initial division between bone and liver, were heavily influenced by data from the Langham study. However, modeling of the long-term distribution and excretion of Pu was guided largely by excretion and autopsy data for Pu workers (Leggett, 1985; Leggett and Eckerman, 1987; Kathren et al., 1988; McInroy et al., 1989; McInroy and Kathren, 1990; Kathren and McInroy, 1991), which differed greatly from projections based on the Langham data with regard to long-term urinary and faecal excretion rates.

(840) Much additional excretion and autopsy data for Pu workers have been published since the completion of *Publication 67* (e.g. Khokhryakov et al., 1994, 2000; Suslova et al., 1996, 2002, 2009, 2012; Ehrhart and Filipy, 2001; Filipy, 2001, 2003; James and Brooks, 2006). Newer (post-1993) information on the systemic behavior of Pu also includes results of two studies involving intravenous administration of Pu isotopes to healthy volunteers. One of

the studies, initiated at the Harwell Laboratory in Great Britain, involved six adult males and six adult females (Talbot et al., 1993, 1997; Warner et al., 1994; Newton et al., 1998; D. Newton, private communication). The other, conducted at the National Radiological Protection Board (NRPB) in Great Britain, involved five adult males (Popplewell et al., 1994; Ham and Harrison, 2000; J. Harrison, private communication). Data from the Harwell study include measurements of urinary and fecal excretion rates up to 5 y, the concentration of Pu in blood up to 6 y, external measurements of Pu in the liver for more than a year after injection, and limited measurements on other tissues. In the NRPB subjects, the urinary excretion rate was determined over two decades after injection.

(841) Comparisons of the post-1993 data with information underlying the *Publication 67* (ICRP, 1993) model show reasonable consistency with regard to blood clearance (Fig. 22.2), total-body retention, daily urinary and faecal excretion (Fig. 22.3 and Fig. 22.4), the time-dependent fraction of systemic plutonium in skeleton plus liver, and the long-term division of Pu between skeleton and liver. However, the newer information provides a different picture of certain aspects of the early behavior of Pu, most notably the initial division between the liver and skeleton. For example, in the subjects of the Harwell injection study, peak estimates of the liver content based on external counts averaged more than 70% of the administered activity (Fig. 22.5), compared with earlier indications that the liver typically accumulates 30% or less of the Pu reaching blood. The expanded set of autopsy data for Pu workers indicates that there is considerable variability in the division of activity between the liver and skeleton at all measurement times (Fig. 22.6), with the skeleton containing more Pu than the liver in some cases and less in others (Schofield and Dolphin, 1974; McInroy et al., 1989; Suslova et al., 1996, 2002; Ehrhardt and Filipy, 2001). The central tendencies of the autopsy data (means or medians of the skeleton and liver contents as a percentage of the systemic content) indicate, however, that the liver typically is the more important repository soon after exposure and that there is a gradual shift of activity from the liver to the skeleton (Fig. 22.6).

Data for laboratory animals

(842) The systemic behavior of Pu has been studied in many different animal types including baboons, monkeys, dogs, swine, rats, mice, hamsters, rabbits, tree shrews, and sheep (Durbin, 1972, 1973, 2011; Taylor, 1984). As is the case for humans, the various animal species generally have shown high deposition and tenacious retention in the skeleton, as well as a high initial concentration in the liver. However, considerable differences among species are seen regarding the residence time of Pu by the liver. For example, the residence time in liver is measured in days, weeks, or months in rats, monkeys, and baboons but in years or decades in hamsters, dogs, and pigs, as well as in humans (Taylor, 1984). The short retention time in the liver seen in many species appears to be primarily the result of a high rate of biliary secretion of Pu.

(843) The beagle dog has proved to be a particularly useful laboratory model for humans with regard to the behavior of plutonium, as it shows qualitatively similar behavior and broadly similar quantitative behavior to humans with regard to liver kinetics as well as deposition and retention of Pu in bone (Leggett, 1985, 2001). Data for beagles have played an important role in the development of a number of biokinetic models for Pu including the systemic model used in this report. For example, the biological half-time for Pu in bone marrow (0.25 y) assumed here, as well as in precursors to the present model (Leggett, 1985; ICRP, 1989, 1993), was derived from long-term studies of the gradual transfer of Pu from bone to marrow in beagles and the subsequent kinetics of Pu in marrow (Jee, 1972; Wronski et al., 1980).

22.2.3.2. Biokinetic model

(844) The biokinetic model for systemic plutonium applied in this report is described in Section 18.2.3.

22.2.3.3. Treatment of progeny

(845) The treatment of radioactive progeny of plutonium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

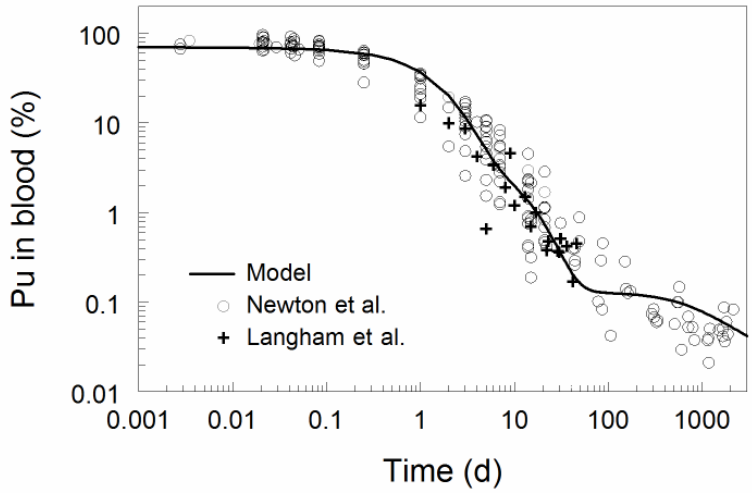

Fig. 22.2. Time-dependent blood content of intravenously administered Pu as measured in human injection studies (Langham et al., 1950; Newton et al., 1998) and generated by the model used in this report.

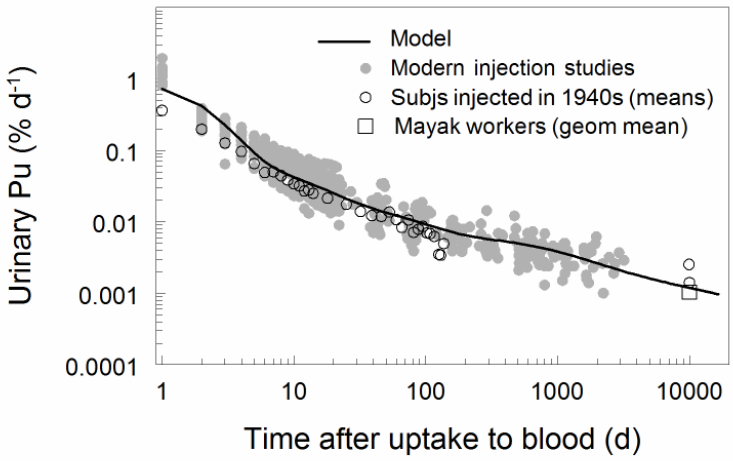

Fig. 22.3. Urinary excretion of Pu predicted by the model used in this report and measured in human injection studies and Mayak workers (Langham et al., 1950; Durbin, 1972; Rundo et al., 1976; Talbot et al, 1993, 1997; Popplewell et al., 1994; Warner et al., 1994; Khokhryakov et al., 1994, 2000; Newton et al., 1998; Ham and Harrison, 2000; J. Harrison, private communication; D. Newton, private communication).

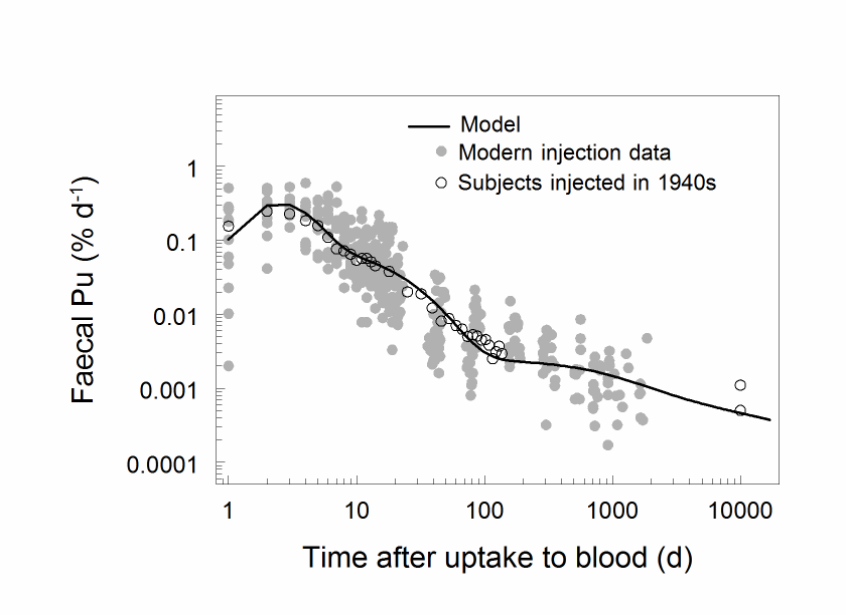

Fig. 22.4. Faecal excretion of Pu as predicted by the model used in this report and measured in human injection studies (Langham et al., 1950; Durbin, 1972; Rundo et al., 1976; Talbot et al., 1993, 1997; Newton et al., 1998; D. Newton, private communication).

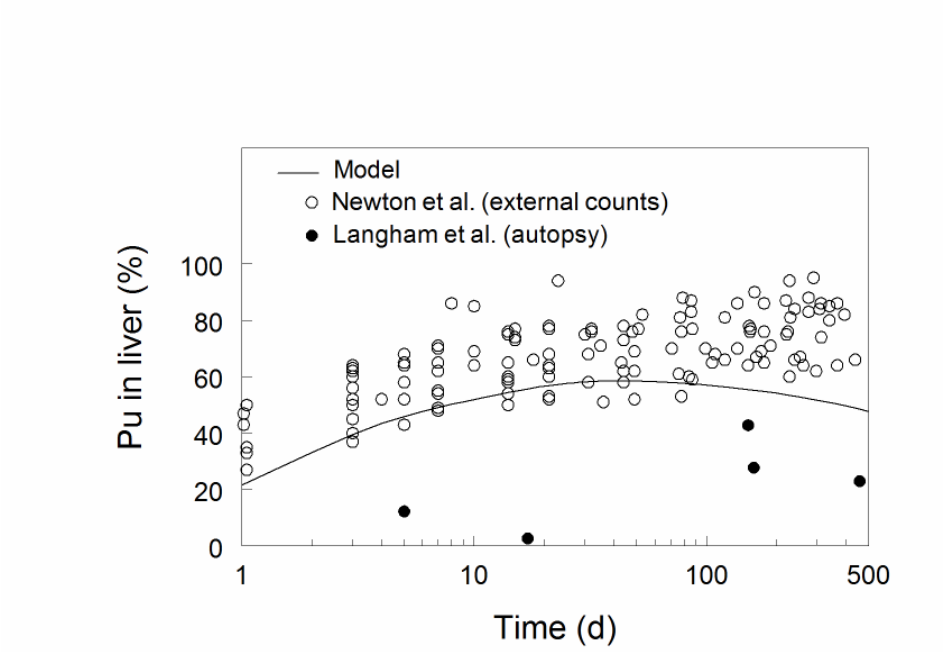

Fig. 22.5.Content of Pu in the liver as predicted by the model used in this report and measured in human injection studies (Langham et al., 1950; Newton et al., 1998).

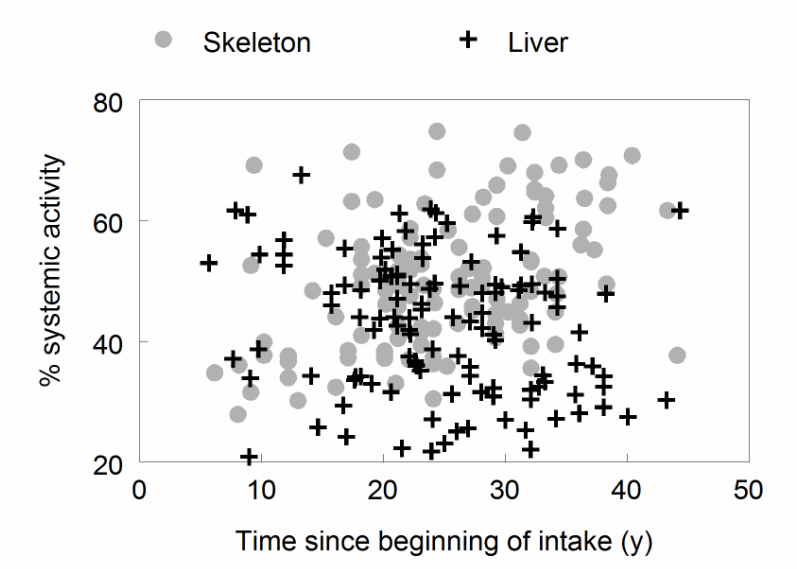

Fig. 22.6. Division of Pu between liver and skeleton in occupationally exposed subjects, based on data of Schofield and Dolphin, 1974; McInroy et al., 1989; Suslova et al., 1996, 2002; and Filipy, 2001 (after Leggett, 2005).

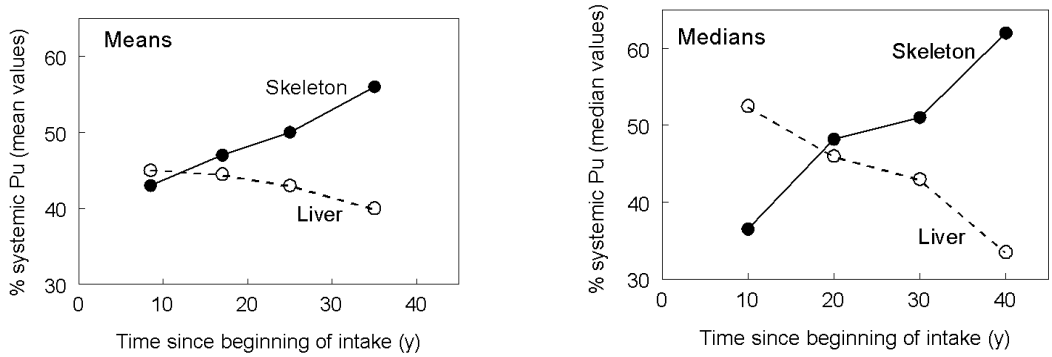

Fig. 22.7. Shift with time in the systemic distribution of Pu as indicated by central estimates of the skeleton and liver contents (% systemic Pu), based on data reported by Suslova et al. (2002) for Mayak workers (after Leggett, 2005).

22.3. Individual monitoring

^{238}Pu

(847) Measurements of ^{238}Pu concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main technique used for *in vitro* bioassay is alpha spectrometry. *In vivo* lung measurements of ^{238}Pu may be used as an additional technique for special investigations. The main technique for *in vivo* measurement is x-ray spectrometry.

Table 22.12. Monitoring techniques for ^{238}Pu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{238}Pu	Urine Bioassay	α spectrometry	0.3 mBq/L	0.05 mBq/L
^{238}Pu	Faecal Bioassay	α spectrometry	2 mBq/24h	0.2 mBq/24h
^{238}Pu	Lung Measurement[a]	x-ray spectrometry	1000 Bq	300 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

^{239}Pu/^{240}Pu

(848) Measurements of ^{239}Pu concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main techniques used for *in vitro* bioassay are alpha spectrometry and ICP-MS; which is the more sensitive and preferable technique to be applied. Industrial sources of plutonium usually consist of a mixture of

plutonium isotopes and ^{241}Am from ingrowth of ^{241}Pu. *In vivo* lung measurement of ^{241}Am may permit evaluation of intake of the mixture or it can, in certain circumstances, be used as a marker for plutonium. For quantitative interpretation, the radionuclide ratios in the inhaled material should be determined either by analysis of material collected in the working environment or by analysis of faecal excretion.

Table 22.13. Monitoring techniques for ^{239}Pu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{239}Pu	Urine Bioassay	α spectrometry	0.3mBq/L	0.05 mBq/L
^{239}Pu	Urine Bioassay	ICP-MS[a]	100 x10^{-15} g/L	1.0 x10^{-15} g/L
^{239}Pu	Urine Bioassay	ICP-SFMS[b]	9.0x10^{-15} g/L	1.0x10^{-15} g/L
^{239}Pu	Faecal Bioassay	α spectrometry	2 mBq/24h	0.2 mBq/24h
^{239}Pu	Lung Measurement[c]	x-ray spectrometry	4000 Bq	600 Bq
^{239}Pu	Lung Measurement[c]	□-ray spectrometry of ^{241}Am	10 Bq	4 Bq

[a] Inductively Coupled Plasma Mass Spectrometry (ICP-MS),
[b] Sector field inductively coupled plasma mass spectrometry (ICP-SFMS)
[c] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

^{241}Pu

(849) Measurements of ^{241}Pu concentrations in urine are used to determine intakes of the radionuclide. The main technique used for urinalysis is liquid scintillation.

Table 22.14. Monitoring techniques for ^{241}Pu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{241}Pu	Urine Bioassay	Liquid Scintillation	10 Bq/L	0.03 Bq/L

^{242}Pu

(850) Measurements of ^{242}Pu concentrations in urine and feces are used to determine intakes of the radionuclide. The main technique used is alpha spectrometry.

Table 22.15. Monitoring techniques for ^{242}Pu.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{242}Pu	Urine Bioassay	α spectrometry	0.2 mBq/L
^{242}Pu	Faecal Bioassay	α spectrometry	0.2 mBq/24h

22.4. Dosimetric data for plutonium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Anderson, H. F., Sheehan, W. E., Mann, J. R., et al., 1970. Evaluation of accidental personnel exposure to plutonium-238: whole body counting and bioassay results. Health Phys. 18, 631–639.

Avtandilashvili, M., Brey, R., Birchall, A., 2013. Maximum likelihood analysis of bioassay data from long-term follow-up of two refractory PuO_2 inhalation cases. Health Phys. 103, 70–79.

Avtandilashvili, M., Brey, R., James, A.C., 2012. Application of Bayesian inference to bioassay data from long-term follow-up of two refractory PuO_2 inhalation cases. Health Phys. 104, 394–404.

Bailey, M.R., Etherington, G., Stradling, G.N., et al., 1999. Inhalation of radionuclides: final report of contract F14PCT950026 on research carried out under the auspices of the Nuclear Fission Safety Programme of the European Commission, NRPB-M1103. Chilton, UK: National Radiological Protection Board. Available from G Etherington, george.etherington@phe.gov.uk

Bair, W. J., McClanahan, B. J., 1961. Plutonium Inhalation Studies. Archives of Environmental Health: An International Journal, 2, 648–655.

Bair, W.J., 1970. Plutonium inhalation studies. Battelle Pacific Northwest Laboratory, Report BPNL-1221.

Bair, W.J., Metivier, H., Park, J.F., 1980. Comparison of early mortality in baboons and dogs after inhalation of $^{239}PuO_2$. Radiat. Res. 82, 588–610.

Bair, W.J., Willard, D.H., 1962. Plutonium inhalation studies. IV. Mortality in dogs after inhalation of $Pu^{239}O_2$. Rad. Res. 16, 811–821.

Bair, W.J., Willard, D.H., 1963. Plutonium inhalation studies-III: effect of particle size and total dose on deposition, retention and translocation. Health Phys. 9, 253–266.

Ballou, J. E., Dagle, G. E., McDonald, K. E., Buschbom, R. L., 1977. Influence of inhaled Ca-DTPA on the long-term effects of inhaled Pu nitrate. Health Phys. 32, 479–487.

Bennett, B.G., 1976. Transuranic element pathways to man. In: Transuranium Nuclides in the Environment STI/PUB/410, 367–383. International Atomic Energy Agency, Vienna.

Ballou, J.E., Park, J.F., Morrow, W.G., 1972. On the metabolic equivalence of ingested, injected and inhaled ^{239}Pu citrate. Health Phys. 22, 857–862.

Bihl, D.E., Carbaugh, E.H., Sula, M.J., et al., 1988b. Human data supporting a super Class Y form of plutonium (abstract). Health Phys. 54, S4.

Bihl, D.E., Lynch, T.P., Carbaugh, E.H., et al., 1988a. Problems with detection of intakes of very insoluble plutonium. Presented at the Thirty Fourth Annual Conference on Bioassay, Analytical, and Environmental Radiochemistry, Las Vegas, Nevada, October 17–21, 1988. PNL-SA-15981. National Technical Information Service, Springfield, Virginia.

Bihl, D.E., Lynch, T.P., Carbaugh, E.H., et al., 1988c. Methods to improve routine bioassay monitoring for freshly separated, poorly transported plutonium. PNL-6695, Pacific Northwest Laboratory Richland, Washington. National Technical Information Service, Springfield, Virginia.

Birchall, A., Bailey, M. R., Jarvis, N. S. 1995. Application of the new ICRP respiratory tract model to inhaled plutonium nitrate using experimental biokinetic data. In: Proceedings of the International Conference on Radiation Dose Management in the Nuclear Industry, Windermere, UK, 9–11 October, 1995. 216–223. British Nuclear Energy Society.

Birchall, A., Vostrotin, V., Puncher, M., et al., 2016. The Mayak Worker Dosimetry System (MWDS-2013) for internally deposited plutonium: An overview. Radiat. Prot. Dosim. (Special Issue, 2016, in preparation)

Blanchin N., Bérard P., Blanchardon E., et al., 2008. Assessing internal exposure in the absence of an appropriate model: two cases involving an incidental inhalation of transuranic elements. Radioprotection 43, 515–532.

Brightwell, J., Carter, R.E., 1975. Comparative measurements of the short-term lung clearance and translocation of PuO_2 and mixed Na_20+ PuO_2 aerosols in mice, in: Inhaled Particles (Edited by Walton W. H.), 285–302 (Oxford: Pergamon Press).

Brooks, A.L., Guilmette, R.A., Hahn, F.F., et al., 1992. Distribution and biological effects of inhaled $^{239}Pu(NO_3)_4$ in cynomolgus monkeys. Radiat. Res. 130, 79–87.

Bunzl, K., Kracke, W., 1983. Fallout $^{239/240}$Pu and ^{238}Pu in human tissues from the Federal Republic of Germany. Health Phys. 44, Suppl. 1, 441–449.

Burns, P.A., Cooper, M.B., Lokan K.H, et al., 1995. Characteristics of plutonium and americium contamination at the former U.K. atomic weapons test ranges at Maralinga and Emu. Appl. Radiat. Isot. 46, 1099–1107.

Carbaugh, E.H., La Bone, T.R., 2003. Two case studies of highly insoluble plutonium inhalation with implications for bioassay. Radiat. Prot. Dosim., 105, 133–138.

Cash L.J., 2014, Risk-informed decision-making for potential inhalation of plutonium-239 and -238 dioxide nanoparticles: use of default assumptions and material-specific data for assessing dose. Baltimore, MD: Johns Hopkins University; Dissertation (LA-UR 13-29329).

Cooper, J., Stradling, G. N., Smith, H., et al., 1979. The reactions of 1.0 nanometre diameter plutonium-238 particles with rat lung fluid. Int. J. Radiat. Biol. 36, 453–466.

Dagle, G.E., Adee, R.R., Buschbom, R.L., et al., 1993. Inhaled plutonium nitrate in dogs. Pacific Northwest Laboratory Annual Report for 1992 to the DOE Office of Energy Research. Part 1 Biomedical sciences. PNL-8500 Pt 1., Battelle Memorial Institute, Pacific Northwest Laboratories, 9–15.

Davesne, E., Paquet, F., Ansoborlo, E. et al., 2010. Absorption of plutonium compounds in the respiratory tract, J. Radiol. Prot. 30, 5–21.

Dagle, G.E., Cannon, W.C., Stevens, D.L., et al., 1983. Comparative distribution of inhaled ^{238}Pu and ^{239}Pu nitrates in beagles. Health Phys. 44, 275–277.

Diel, J. H., Guilmette, R. A., Muggenburg, B.A., Hahn, F.F., Chang, I.Y., 1992. Influence of dose rate on survival time for $^{239}PuO_2$-induced radiation pneumonitis or pulmonary fibrosis in dogs. Radiat. Res. 129, 53–60.

Diel, J.H., Hahn F.F., Guilmette R.A., Lundgren D.L., 1980a. Repeated inhalation exposure of Beagle dogs to aerosols of $^{239}PuO_2$ IV. Inhalation Toxicology Research Institute Annual Report 1979–80, LMF-84, 146–148. Lovelace Biomedical & Environmental Research Foundation, Albuquerque, New Mexico.

Diel, J.H., Mewhinney, J.A., 1980. Breakup of inhaled $^{238}PuO_2$ particles in the lungs of hamsters and dogs. Inhalation Toxicology Research Institute Annual Report 1979–80, LMF-84, 17–19. Lovelace Biomedical & Environmental Research Foundation,

Albuquerque, New Mexico.
Diel, J.H., Mewhinney, J.A., 1983. Fragmentation of inhaled $^{238}PuO_2$ particles in lung. Health Phys. 44, 135–143.
Durbin P. W., 1972. Plutonium in man: A new look at the old data. In: B. J. Stover and W. S. S. Jee, eds. Radiobiology of Pu; Salt Lake City, UT: J. W. Press, 469–530.
Durbin, P. W., 1975. Plutonium in mammals: Influence of plutonium chemistry, route of administration, and physiological status of the animal on initial distribution and long-term metabolism. Health Phys. 29, 495–510.
Durbin, P. W., 2011. Actinides in animals and man. Chapter 31 in: The chemistry of the actinide and transactinide elements, 4th edition, Vol. 5, Morss, L. R., Edelstein, N. M., Fuger, J., Katz, J. J. (Eds.) Springer, 3339–3474.
Ehrhart, S. M., Filipy, R. E., 2001. USTUR Annual Report for February 1, 2000 through January 31, 2001. United States Tranuranium and Uranium Registries. USTUR-0177-01. Washington State University.
Eidson, A.F., Mewhinney, J.A., 1983. *In vitro* dissolution of respirable aerosols of industrial uranium and plutonium oxide fuels. Health Phys. 45, 1023–1037.
Ellender, M., Haines, J.W., Harrison, J.D., 1995. The distribution and retention of plutonium, americium and uranium in CBA/H mice. Hum. Exp. Toxicol. 14, 38–48.
Enck, P., Merlin, V., Erckenbrecht, J. F. et al., 1989. Stress effects on gastrointestinal transit in the rat. Gut, 30, 455–459.
Espinosa, A., Aragon, A., Stradling, N., Hodgson, A., Birchall, A., 1998. Assessment of doses to adult members of the public in Palomares from inhalation of plutonium and americium. Radiat. Prot. Dosim. 79, 161–164.
Etherington, G., Shutt, A.L. Stradling, G.N., et al., 2002. A study of the human biokinetics of inhaled plutonium nitrate. Ann. Occup. Hyg. 46, 350–352.
Etherington, G., Stradling, G. N., Hodgson, A. et al., 2003. Anomalously high excretion of Pu in urine following inhalation of plutonium nitrate? Radiat. Prot. Dosim. 105, 321–324.
Filipy, R. E., 2001. Analyses of whole body donations. USTUR annual report for February 1, 2000 through January 31, 2001, 12–17.
Filipy, R. E., 2003. Estimation of actinide body burdens on the basis of tissue samples collected at autopsy. USTUR annual report for the period February 1, 2002 – January 31, 2003, 32–35.
Fisenne, I.M., Cohen, N., Neton, J.W., et al., 1980. Fallout plutonium in human tissues from New York City. Radiat. Res. 83, 162–168.
Fleischer, R.L., 1975. On the "dissolution" of respirable PuO_2. Health Phys. 29, 69–73.
Fleischer, R.L., Raabe, O.G., 1977. Fragmentation of respirable PuO_2 particles in water by alpha decay – a mode of dissolution. Health Phys. 32, 253–257
Fleischer, R.L., Raabe, O.G., 1978. On the mechanism of "dissolution" in liquids of PuO_2 by alpha decay. Health Phys. 35, 545–548.
Fleming, R.R., Hall, R.M., 1978. Two ^{238}Pu inhalation incidents. Du Pont Savannah River Plant Report. DPSPU 78–30–4, 1–9.
Foster, P.P., 1991. Study of a plutonium oxide fuel inhalation case. Radiat. Prot. Dosim. 38, 141–146.
Fritsch, P., 2007. Uncertainties in doses calculated according to ICRP recommendations after inhalation of $^{239}PuO_2$ and early chest monitoring. Radiat. Prot. Dosim. 125, 553–556.
Gregoratto, D., Bailey, M. R., Marsh, J. W., 2010. Modelling particle retention in the alveolar-interstitial region of the human lungs. J. Radiol. Prot., 30, 491–512.

Gregoratto, D., Bailey, M. R., Marsh, J. W., 2011. Particle clearance in the alveolar-interstitial region of the human lungs: model validation. Radiat. Prot. Dosim. 144, 353–6.

Guilmette, R.A., Diel, J.H., Muggenburg, B.A., et al., 1984. Biokinetics of inhaled $^{239}PuO_2$ in the beagle dog: effect of aerosol particle size. Int. J. Radiat. Biol., 45, 563–581.

Guilmette, R.A., Griffith, W.C., Hickman, A.W., 1994. Intake assessment for workers that inhaled ^{238}Pu aerosols. Radiat. Prot. Dosim., 53, 127–131.

Guilmette, R.A., Hickman, A.W., Griffith, W.C., 1992. The effect of isotope on the dosimetry of inhaled plutonium oxide. In: Proc. 8th IRPA conference, Montreal, Canada, 900–903.

Guilmette, R.A., Muggenburg, B.A., Hahn, F.F., et al., 1987. Dosimetry of ^{239}Pu in dogs that inhaled monodisperse aerosols of $^{239}PuO_2$. Radiat. Res. 110, 199–218.

Haas, D., Vandergheynst, A., Van Vliet, J., et al., 1994. Mixed-oxide fuel fabrication technology and experience at the Belgonucléaire and CFCa plants and further developments for the Melox plant. Nuclear Technology 104, 60–82.

Ham, G. J., Harrison, J. D, 2000. The gastrointestinal absorption and urinary excretion of Pu in male volunteers. Radiat. Prot. Dosim. 87, 267–272.

Harrison, J. D., 1983. The gastrointestinal absorption of plutonium, americium and curium. Radiat. Prot. Dosim. 5, 19–35.

Harrison, J. D., 1991. The gastrointestinal absorption of the actinide elements. Science Total Environ. 100, 43–60.

Haywood, S. M., Smith, J. G., 1992. Assessment of potential doses at the Maralinga and Emu test sites. Health Phys. 63, 641–650.

Hickman, A. W., Griffith, W. C., Roessler, G. S. et al., 1995. Application of a canine ^{238}Pu biokinetics/dosimetry model to human bioassay data. Health Phys. 68, 359–370.

Hodgson, A., Kreyling, W. G., Newton, D., et al., 2004. Interspecies Comparison of Lung Clearance of 160Terbium Oxide. NRPB-DA/4/2003, National Radiological Protection Board, Chilton.

Hodgson, A., Shutt, A. L., Etherington, G., et al., 2003. Comparison of predicted with observed biokinetics of inhaled plutonium nitrate and gadolinium oxide in humans. Radiat. Prot. Dosim. 105, 91–94.

Hoover, M. D., Myers, D. S., Cash, L. J., et al., 2015. Application of an informatics-based decision-making framework and process to the assessment of radiation safety in nanotechnology. Health Phys. 179–194.

IAEA, 2007. IAEA-TECDOC-1568. Intercomparison Exercise on Internal Dose Assessment, Vienna, International Atomic Energy Agency.

ICRP, 1972. The metabolism of compounds of plutonium and other actinides. ICRP Publication 19. Pergamon Press, Oxford.

ICRP, 1979. Limits on intakes of radionuclides for workers. ICRP Publication 30, Part 1. Ann. ICRP 2(3/4).

ICRP, 1980. Biological effects of inhaled radionuclides. ICRP Publication 31. Ann. ICRP 4(1/2).

ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).

ICRP, 1989. Age-dependent doses to members of the public from intake of radionuclides. Part 1. ICRP Publication 56. Ann. ICRP 20(2).

ICRP, 1991. 1990 Recommendations of the International Commission on Radiological Protection, ICRP Publication 60. Ann. ICRP 21(1–3).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).

ICRP, 1994. Human respiratory tract model for radiological protection. ICRP Publication 66. Ann. ICRP 24(1–3).

ICRP 1994. Dose coefficients for intakes of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

ICRP, 1995. Age-dependent doses to members of the public from intake of radionuclides: Part 4. Inhalation dose coefficients. ICRP Publication 71. Ann. ICRP 25(3/4).

ICRP, 1997. Individual monitoring for internal exposure of workers. ICRP Publication 78. Ann. ICRP 27(3/4).

ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. Supporting Guidance 3. Ann. ICRP 32(1–2).

ICRP, 2006. Human alimentary tract model for radiological protection. ICRP Publication 100. Ann. ICRP 36(1/2).

ICRP 2015. Occupational intakes of radionuclides. Part 1. ICRP Publication 130. Ann. ICRP 44 (2).

Iranzo, E., Salvador, S., Iranzo, E., 1987. Air concentrations of ^{239}Pu and ^{240}Pu and potential radiation doses to persons living near Pu-contaminated areas in Palomares, Spain. Health Phys. 52, 453–461.

James, A.C., Stather, J.W., Strong J. C., et al., 1978. National Radiological Protection Board, Annual Research and Development Report 1978, NRPB/R&D 2, 57–64. National Radiological Protection Board, Chilton, UK.

James, A. C., Brooks, B. G., 2006. The United States Transuranium and Uranium Registries (USTUR): Learning from plutonium and uranium workers. JAEA-Conf 2007-002. Tokai Research & Development Center, JAEA, Japan.

James, A.C., Filipy R.E., Russell, J.J., et al., 2003. USTUR Case 0259 whole body donation: a comprehensive test of the current ICRP models for the behavior of inhaled $^{238}PuO_2$ ceramic particles. Health Phys. 84, 2–33.

James, A.C., Sasser, L.B., Stuit, D.B., et al., 2007. USTUR whole body case 0269: demonstrating effectiveness of iv Ca-DTPA for Pu. Radiat. Prot. Dosim. 127, 449–455

Jee, W. S. S., 1972. Pu-239 in bones as visualized by photographic and neutron-induced autoradiography. In: Radiobiology of plutonium (Stover, B. J.; Jee, W. S. S., eds), 171–193. Salt Lake City, UT: The J. W. Press.

Johnston, P.N., Lokan, K.H., Williams, G.A., 1992. Inhalation doses for aboriginal people reoccupying former nuclear weapons testing ranges in South Australia. Health Phys. 63, 641–650.

Jones, K. A., Prosser, S. L., 1997. A comparison of ^{239240}Pu post-mortem measurements with estimates based on current ICRP models. In: Proceedings of the Conference on Low Level Measurements of Actinides and Long-lived Radionuclides, Cherbourg, France. J. Radioanal. Nucl. Chem. 226, 129–133.

Kanapilly, G. M, Diel, J. H., 1980, Ultrafine $^{239}PuO_2$ aerosol generation, characterization and short-term inhalation study in the rat. Health Phys. 39, 505–519.

Kanapilly, G. M., 1977, Alveolar microenvironment and its relationship to the retention and transport into blood of aerosols deposited in the alveoli, Health Phys. 32, 89–100.

Kathren, R. L., McInroy, J. F, 1991. Comparison of systemic plutonium deposition estimates from urinalysis and autopsy data in five whole-body donors. Health Phys. 60, 481–488.

9602 Kathren, R. L., McInroy, J. F., Reichert, M. M., Swint, M. J, 1988. Partitioning of Pu-238,
9603 Pu-239 and Am-241 in skeleton and liver of U.S. Transuranium Registry autopsy cases.
9604 Health Phys. 54, 181–188.
9605 Khokhryakov, V. F., Menshikh, Z. S., Suslova, K. G., et al., 1994. Plutonium excretion model
9606 for the healthy man. Radiat. Prot. Dosim. 53, 235–239.
9607 Khokhryakov, V. F., Suslova, K. G., Filipy, R. E., et al., 2000. Metabolism and dosimetry of
9608 actinide elements in occupationally exposed personnel of Russia and the United States:
9609 A summary progress report. Health Phys. 79, 63-71.
9610 Kreyling, W. G. 1990. Interspecies comparison of lung clearance of "insoluble" particles. J.
9611 Aerosol Med. 3, Suppl. 1, S93–S111.
9612 La Bone, T. R., Carbaugh, E.H., Griffith, W.C., Guilmette, R.A.,. Skrable, K.W. 1992.
9613 Evaluation of Savannah River Site Internal Dosimetry Registry Case 664(U). ESH-
9614 HPT- 920178. Westinghouse Savannah River Company, Aiken, South Carolina.
9615 LaBauve, R. J, Brooks, A.L., McClellan, R.O., et al., 1980. Cytogenetic and other biological
9616 effects of $^{239}PuO_2$ inhaled by the rhesus monkey. Radiat. Res. 82, 310–335.
9617 Langham W. H.. 1959. Physiology and toxicology of plutonium-239 and its industrial medical
9618 control. Health Phys. 2, 172–185.
9619 Langham, W. H., Bassett, S. H., Harris, P. S., Carter, R. E, 1950. Distribution and excretion of
9620 Pu administered to man, Los Alamos Scientific Laboratory, LA-1151.
9621 Larsen, R. P., Bhattacharyya, M.H., Oldham, R.D., et al., 1981. Continued studies of the
9622 gastrointestinal absorption of plutonium in rodents. In: Annual Report for Radiological
9623 and Environmental Research Division, Argonne National Laboratory, Illinois. ANL–
9624 81–85 (Pt.II), 105–116.
9625 Lataillade, G., Verry, M., Rateau, G., 1995. Translocation of Pu from rat and monkey lung
9626 after inhalation of industrial plutonium oxide and mixed U and Pu oxide. J. Radiat.
9627 Biol. 67, 373–380.
9628 Lauweryns, J. M., Baert, J.H., 1977. Alveolar clearance and the role of the pulmonary
9629 lymphatics. Am. Rev. Respir. Dis. 115, 625–683.
9630 Leggett, R. W., 1984. Bioassay Data and a Retention-Excretion Model for Systemic
9631 Plutonium, ORNL/TM-8795, NUREG/CR-3346.
9632 Leggett, R. W., 1985. A model of the retention, translocation, and excretion of systemic Pu,
9633 Health Phys. 49, 1115–1137.
9634 Leggett, R. W., 1992. A retention-excretion model for americium in humans, Health Phys. 62,
9635 288–310;
9636 Leggett, R. W., 2001. Reliability of the ICRP's dose coefficients for members of the public. 1.
9637 Sources of uncertainty in the biokinetic models. Radiat. Protect. Dosim. 95, 199–213.
9638 Leggett, R. W., Eckerman, K. F., Khokhryakov, V. F., et al., 2005. Mayak worker study: An
9639 improved biokinetic model for reconstructing doses from internally deposited
9640 plutonium. Radiat. Res. 164, 111–122.
9641 Leggett, R. W., Eckerman, K. F., 1987. A method for estimating the systemic burden of Pu
9642 from urinalyses, Health Phys. 52, 337–346.
9643 Leggett, R. W., 2003. Reliability of the ICRP's dose coefficients for members of the public.
9644 III. Plutonium as a case study of uncertainties in the systemic biokinetics of
9645 radionuclides. Radiat. Prot. Dosim. 106, 103-120.
9646 Leung, T. W. T., Lau, W. Y., Ho, S. K. W., et al., 1995. Radiation pneumonitis after selective
9647 internal radiation treatment with intraarterial ^{90}yttrium-microspheres for inoperable
9648 hepatic tumors. J. Radiat. Oncol. Biol. Phys. 33, 919–924.

Mann, J. R., Kirchner, R. A., 1967. Evaluation of lung burden folllowing acute inhalation exposure to highly insoluble PuO2. Health Phys. 13, 877–82

Massiot, P., Leprince, B., Lizon, C., et al., 1998a. Chemical composition of inhalable MOX powders prepared according to a SOLGEL process: an energy dispersive X-ray analysis of individual particles. J. Alloys Compd. 271–273, 38–41.

Massiot, P., Leprince, B., Lizon, C., et al., 1998b. Physico-chemical characterisation of inhalable MOX particles according to industrial process. Radiat. Prot. Dosim. 79, 43–48.

McClellan, R.O., 1972. Progress in studies with transuranic elements at the Lovelace Foundation. Health Phys. 22, 812–822.

McInroy, J. F., Kathren, R. L, 1990. Plutonium content in marrow and mineralized bone in an occupationally exposed person. Radiat. Prot. Dosim. 32, 245–252.

McInroy, J. F., Kathren, R. L., Swint, M. J, 1989. Distribution of Pu and americium in whole bodies donated to the United States Transuranium Registry. Radiat. Prot. Dosim. 26, 151–158.

McInroy, J.F., Boyd, H.A., Eustler, B.C., 1981. Deposition and retention of plutonium in the United States general population. In: Wrenn, M.E. (Ed.) Actinides in Man and Animals, Proceedings of the Actinide Workshop, Snowbird, Utah, October 15–17, 1979. 161–179. RD Press, Salt Lake City, Utah.

Métivier H., Masse R., Nenot J. C., et al., 1976b. Etude experimentale de la contamination par un melange issu de la combustion du sodium en presence d'oxyde de plutonium, in: Diagnosis and Treatment of Incorporated Radionuclides, 107–117 (Vienna: IAEA).

Métivier, H., 1976a. Devenir biologique des melanges d'aerosols d'oxyde de sodium et de plutonium, Radioprotection 11, 271.

Métivier, H., Madic, C., Bourges, J. et al., 1985. Valency five, similarities between plutonium and neptunium in gastrointestinal uptake. In: Bulman, R.A, Cooper, J.R. (Eds.) Speciation of Fission and Activation Products in the Environment. Elsevier Applied Science Publishers, London. 175–178.

Métivier, H., Piechowski, J., Duserre, C., et al., 1989a. Biological behaviour of plutonium inhaled by baboons as plutonium n-tributylphosphate complex. Comparison with ICRP models. Radiat. Prot. Dosim. 26, 287–292.

Métivier, H., Masse, R., Lafuma, J., 1983. Metabolism of plutonium introduced as tri-N-butyl phosphate complex in the rat and removal attempts by DTPA. Health Phys. 44, 623–634.

Métivier, H., Masse, R., Rateau, G., et al., 1980. Experimental study of respiratory contamination by a mixed oxide aerosol formed from the combustion of a plutonium magnesium alloy. Health Phys. 38, 769–776.

Métivier, H., Masse, R., Rateau, G., et al., 1989b. New data on the toxicity and translocation of inhaled $^{239}PuO_2$ in baboons. Radiat. Prot. Dosim. 26, 267–172.

Métivier, H., Nolibé, D., Masse, R., et al., 1978. New data on toxicity and translocation of inhaled $^{239}PuO_2$ in baboons. Health Phys. 35, 401–404.

Mewhinney, J. A., Eidson, A. F., 1982. Models of retention, distribution and excretion of Pu, Am and U by Beagle dogs, cynomolgmuso monkeys and Fischer-344 rats following inhalation of industrial aerosols NUREG/CR 3313, LMF-105, 21-32. Inhalation Toxicology Research Institute. Lovelace Biomedical & Environmental Research Foundation, Albuquerque, New Mexico.

Mewhinney, J. A., Eidson, A. F., Wong, V. A, 1987. Effect of wet and dry cycles on

dissolution of relatively insoluble particles containing Pu. Health Phys. 53, 377–384.
Mewhinney, J. A., Diel, J. H., 1983. Retention of inhaled $^{238}PuO_2$ in beagles: A mechanistic approach to description. Health Phys. 45, 39–60.
Mewhinney, J. A., Muggenburg, B. A., McClellan, R. O., et al., 1976. The effect of varying physical and chemical characteristics of inhaled plutonium aerosols on metabolism and excretion. In: Proc. Int. Seminar on Diagnosis and Treatment of Incorporated Radionuclides. Vienna, IAEA. 87–97.
Moody, J. C., Birchall, A., Bailey, M. R., et al., 1998. Application of the ICRP Publication 66 respiratory tract model to three industrial plutonium nitrate materials. NRPB-M777. Chilton, National Radiological Protection Board.
Moody, J. C., Stradling, G. N., Gray, S., 1991. The biokinetics of four $^{239}Pu/^{241}Am$ dioxide bearing dusts in the rat after inhalation: The implications for occupational exposure. J. Aerosol Sci. 22, 805–808.
Moody, J. C., Stradling, G. N., Wilson, I. M., et al., 1993. Biokinetics of plutonium in the rat after the pulmonary deposition of three nitrate bearing materials: implications for human exposure. NRPB-M427, Chilton, National Radiological Protection Board.
Moody, J.C., Stradling, G.N., Britcher, A., 1994. Biokinetics of three plutonium nitrate bearing materials: implications for human exposure. Radiat. Prot. Dosim. 53, 169–172.
Morgan, A., Black, A. Holmes, A., et al., 1988b. Studies of environmental radioactivity in Cumbria. Part 14. Solubility in the rat lung of actinides associated with silt from the Ravenglass estuary and their translocation to liver and bone. AERE–R 12351. DOE Report DOE/RW/88.097.
Morgan, A., Black, A., Knight, D., et al., 1988a. The effect of firing temperature on the lung retention and translocation of Pu following the inhalation of $^{238}PuO_2$ and $^{239}PuO_2$ by CBA/H mice. Health Phys. 54, 301–310.
Morgan, A., Holmes, A., Pratley, F.W., 1990. Solubility in the rat lung of actinides associated with estuarine silt from West Cumbria. J. Radiol. Prot. 10, 135–142.
Morin, M., Nenot, J. C., Lafuma, J., 1972. Metabolic and therapeutic study following administration to rats of 238Pu nitrate: a comparison with 239Pu. Health Phys. 23, 475–480.
Muhle, H., Creutzenberg, O., Bellmann, B., et al., 1990. Dust overloading of lungs: Investigations of various materials, species differences and irreversibility of effects. J. Aerosol Med. 3, Suppl. 1, S111–S128.
NCRP, 2001. Scientific Basis for Evaluating the Risks to Populations from Space Applications of Plutonium. NCRP Report No. 131. National Council on Radiation Protection and Measurements, Bethesda MD.
Nenot, J. C., Masse, R., Morin, M., Lafuma, J., 1972. An experimental comparative study of the behaviour of 237Np, 238Pu, 239Pu, 241Am and 242Cm in bone. Health Phys. 22, 657–665.
Newton, D., Taylor, B. T., Eakins, J. D., 1983. Differential clearance of plutonium and americium oxides from the human lung. Health Phys. 44, Suppl. 1, 431–439.
Newton, D., Talbot, R. J., Kang, C., Warner, A. J., 1998. Uptake of Pu by the human liver. Radiat. Prot. Dosim. 80, 385–395.
Nielsen, C. E., Wilson, D. A., Brooks, A. L., et al., 2012. Microdistribution and long-term retention of $^{239}Pu\ (NO_3)_4$ in the respiratory tracts of an acutely exposed plutonium worker and experimental beagle dogs. Cancer Res. 72, 5529–5536.
Nolibé, D., Dusserre, C., Gil, I., et al., 1989. Biological behaviour of plutonium given as a

trilaurylamine complex. Comparison with plutonium-tributylphosphate. Radiat. Prot. Dosim. 26, 303–306.

ORAUT (Oak Ridge Associated Universities Team), 2007. Estimating doses for plutonium strongly retained in the Lung. ORAUT–OTIB–0049.

Park, J. F., Catt, D. L., Craig, D. K, et al., 1974. Solubility changes of ^{238}Pu oxide in water suspension and effect on biological behavior after inhalation by Beagle dogs. In: Proceedings of the Third International Congress of the International Radiation Protection Association. Oak Ridge, TN: U.S. Atomic Energy Commission, Office of Information Services, Technical Information Center, 719–724.

Park, J.F., Bair, W.J., Busch, R.H., 1972. Progress in beagle dog studies with transuranium elements at Battelle-Northwest. Health Phys. 22, 803–810.

Park, J.F., Buschbom, R.L., Dagle, G.E., et al., 1990. Inhaled plutonium oxide in dogs. Pacific Northwest Laboratory Annual Report for 1989 to the DOE Office of Energy Research. PNL-7200, Part 1, Biomedical Sciences. 11–28. Richland, Washington. Available from National Technical Information Service, Springfield, Virginia.

Patterson, J. H., Nelson, G. B., Matlack, G. M., 1974. The Dissolution of ^{238}Pu in Environmental and Biological Systems LA-5624. Los Alamos National Laboratory, Los Alamos, New Mexico.

Pellow, P. G. D., Puncher, M., Hodgson, A., Etherington, G., 2016b, in preparation. Estimation of plutonium nitrate absorption from the lungs of the Beagle dog using data from an exposure effects study. PHE-CRCE report.

Pellow, P. G. D., Hodgson, A., 2016c. in preparation. The biokinetics of plutonium deposited in the rat lung as the nitrate. PHE-CRCE report.

Pellow, P. G. D., Hodgson, S. A., Gregoratto, D., Hodgson, A., 2016a, in preparation. Biokinetics of gadolinium-153 oxide after inhalation or instillation. PHE-CRCE report.

PNL, 1994. PNL Report Appendix A. Dose effect studies with inhaled plutonium in Beagles: Inhaled plutonium nitrate in dogs. Richland, USA Pacific Northwest Laboratory A3-A11, PNL report for 1993 to the DoE Office of Energy Research.

Poncy, J. L., Massiot, P., Rateau, G., et al. (1998) Long-term pulmonary retention of inhaled actinide oxides in non-human primates. Radiat. Prot. Dosim. 79, 259–263.

Popplewell, D. S., Ham, G. J., Lands, C., 1994. Transfer of Pu across the human gut and its urinary excretion. Radiat. Prot. Dosim. 53, 241-244.

Popplewell, D. S., Ham, G. J., Johnson, T. E., Barry, S. F., 1985. Plutonium in autopsy tissues in Great Britain. Health Phys. 49, 304–309.

Popplewell, D. S., Ham, G. J., McCarthy, W., et al., 1994. Transfer of plutonium across the human gut and its urinary excretion. In: Proc. Workshop on Intakes of Radionuclides: Detection, Assessment and Limitation of Occupational Exposure. Radiat. Prot. Dosim. 53, 241–244.

Puncher M., Birchall, A., Sokolova, A.B., et al., 2016c. MWDS 2013: Plutonium binding in the lungs – an analysis of Mayak Workers. Radiat. Prot. Dosim. (Special Issue, 2016, in preparation).

Puncher, M., Birchall, A., Sokolova, A. B., et al., 2016d. MWDS 2013: Plutonium dissolution in the lungs - an analysis of Mayak workers. Radiat. Prot. Dosim. (Special Issue, 2016, in preparation).

Puncher, M., Birchall, A., Bull, R. K., 2011. Uncertainties on Lung Doses from Inhaled Plutonium. Radiat. Res. 176, 494–507.

Puncher, M., Birchall, A., Nielsen, C.E., et al., 2016b. MWDS 2013: A re-analysis of USTUR Case 269 to determine plutonium binding in the lungs. Radiat. Prot. Dosim. (Special Issue, 2016, in preparation).

Puncher, M., Etherington, G., 2016, in preparation. An experimental study of inhaled plutonium nitrate in humans and the characterisation of its biokinetic behaviour using Bayesian analysis.

Puncher, M., Pellow P. G. D., Hodgson, A., et al., 2016a. MWDS 2013: A Bayesian analysis to quantify pulmonary binding of plutonium in beagle dogs. Radiat. Prot. Dosim. (Special Issue, 2016, in preparation).

Quini, C. C., Américo, M. F., Corá, L. A., et al., 2012. Employment of a noninvasive magnetic method for evaluation of gastrointestinal transit in rats, J. Biol. Eng. 6, 6.

Raabe, O.G., Kanapilly, G.M., Boyd, H.A., 1973. Studies of the *in vitro* solubility of respirable particles of ^{238}Pu and ^{239}Pu oxides and an accidentally released aerosol containing ^{239}Pu. In: Inhalation Toxicology Research Institute Annual Report 1972–1973. Albuquerque, NM: Lovelace Foundation for Medical Education and Research; Report No. LF-46, 24–30.

Ramounet–Le Gall, B., Abram, M-C., Rateau, G., et al., 2003. *In vivo* measurement of Pu dissolution parameters of MOX aerosols and related uncertainties in the values of the dose per unit of intake. Radiat. Prot. Dosim. 105, 153–156.

Ramounet, B., Matton, S., Guezingar-Liebard, F., et al., 2000. Comparative biokinetics of plutonium and americium after inhalation of PuO_2 and mixed oxides (U, Pu)O_2 in rat. J. Radiat. Biol. 76, 215–222.

Ramsden, D., 1976. Assessment of plutonium in lung for both chronic and acute exposure conditions. In: Diagnosis and Treatment of Incorporated Radionuclides. Proceedings of a Seminar held by the International Atomic Energy Agency and the World Health Organization, December 8–12, 1975, Vienna, 139–161. International Atomic Energy Agency, Vienna, Austria.

Ramsden, D., 1984. A modified lung model to match observed lung and urinary data following the inhalation of plutonium oxide – the problems of long term retention in the pulmonary lymph nodes. In: Smith, H. and Gerber, G. (Eds.) Lung Modelling for Inhalation of Radioactive Materials. EUR 9384. CEC, Brussels, Belgium, 281–286.

Ramsden, D., Bains, M.E.D., Fraser, D.C., 1970. In-vivo and bioassay results from two contrasting cases of plutonium-239 inhalation. Health Phys. 19, 9–17.

Ramsden, D., Bains, M.E.D., Frazer, D.C., 1978. A case study of multiple low level exposure to plutonium oxide. Health Phys., 34, 649–659.

Rateau-Matton, S., Ansoborlo, E., Hodgson, A., 2004. Comparative absorption parameters of Pu and Am from PuO_2 and mixed oxide aerosols measured after *in vitro* dissolution test and inhalation in rats. Int. J. Radiat. Biol. 80, 777–785.

Rhoads, K., Killand, B. W., Mahaffey, J. A., et al., 1986. Lung clearance and translocation of ^{239}Pu and ^{244}Cm in rats following inhalation individually or as a mixed oxide. Health Phys. 51, 633–640.

Rowland R. E., Durbin P. W., 1976. Survival, causes of death, and estimated tissue doses in a group of human beings injected with plutonium. In: Jee, W. S. S., ed., The Health effects of plutonium and radium. Salt Lake City, UT: The J. W. Press, 329–341.

Rundo, J., Starzyk, P. M., Sedlet, J., et al., 1976. The excretion rate and retention of plutonium 10,000 days after acquisition. In: Diagnosis and treatment of incorporated radionuclides, Proceedings of a seminar, 8-12 Dec 1975, 15-22 (Vienna: IAEA);.

Schofield, G. B., Dolphin, G. W. 1974. U.K. Experience on the medical aspects of radiological protection of workers handling Pu. Ann. Occup. Hyg. 17, 73–83.

Schoonjans, R., Van Vlem, B., Van Heddeghem, N., et al., 2002. The ^{13}C-octanoic acid breath test: validation of a new noninvasive method of measuring gastric emptying in rats. Neurogastroenterol. Mot. 14, 287–293.

Smith, H., Stradling, G. N. Loveless, B. W., et al., 1977. The *in vivo* solubility of plutonium-239 dioxide in the rat lung. Health Phys. 33, 539–551.

Smith, J. R. H., 20xx, in preparation. A simple model of plutonium systemic biokinetics in laboratory rats and its use for the determination of lung absorption parameter values. PHE-CRCE report.

Smith, V. H., 1970. Fate of ingested $^{238}PuO_2$ in miniature swine. In: Pacific Northwest Laboratory Annual Report for 1969. Pt.1. Biomedical Sciences. Richland, Wash. BNWL-1306. 63–65.

Spitz, H.B., Robinson, R., 1981. Deposition of plutonium in the lungs of a worker following an accidental inhalation exposure. In: Wrenn, M.E. (Ed.) Actinides in Man and Animals, Proceedings of the Actinide Workshop, Snowbird, Utah, October 15–17, 1979. 115–135 RD Press, Salt Lake City, Utah.

Stanley, J.A., Eidson, A.F., Mewhinney, J.A., 1980a. Deposition, retention and dosimetry of inhaled mixed uranium-plutonium oxides (heat-treated at 1750°C) in Fischer-344 rats, beagle dogs and cynomolgous monkeys. In: Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Progress Report July 1978–June 1979, LF–71, US Nuclear Regulatory Commission Document No. NUREG/CR-1458, 47–53. Inhalation Toxicology Research Institute, Lovelace Biomedical & Environmental Research Institute, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Stanley, J.A., Eidson, A.F., Mewhinney, J.A., 1980b. Deposition, retention and dosimetry of inhaled plutonium dioxide (heat-treated at 850 C) in Fisher-344 rats, Beagle dogs and cynomolgus monkeys. In: Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Report July 1978–June 1979, US Nuclear Regulatory Commission Document No NUREG/CR-1458. (Albuquerque, NM: Inhalation Toxicology Research Institute) 55–60.

Stanley, J.A., Eidson, A.F., Mewhinney, J.A., 1982. Distribution, retention and dosimetry of plutonium and americium in the rat, dog and monkey after inhalation of an industrial-mixed uranium and plutonium oxide aerosol. Health Phys. 43, 521–530.

Stather, J. W., Brightwell J., Rodwell, P., et al., 1977b. A study of the lung clearance of mixed oxide aerosols formed from the oxidation of plutonium, in combination with uranium, calcium, potassium or aluminium. National Radiological Protection Board, Annual Research and Development Report 1976. NRPB-R&D 1, 39–40. National Radiological Protection Board, Chilton, UK.

Stather, J. W., James, A. C., Brightwell, J., et al., 1979a. The clearance of plutonium from the respiratory system of rodents after inhalation as the oxide. National Radiological Protection Board, Annual Research and Development Report 1978, NRPB/R&D 3, 52–58. National Radiological Protection Board, Chilton, UK.

Stather, J. W., Rodwell, P., Brightwell J., et al., 1977a. The clearance of plutonium and americium from lungs of rodents following the inhalation of oxide aerosols of these actinides either alone or in combination with sodium oxide. National Radiological Protection Board, Annual Research and Development Report 1976. NRPB-R&D 1,

35–38. National Radiological Protection Board, Chilton, UK.

Stather, J.W., Brightwell J., Rodwell, P., et al., 1978a. The clearance of plutonium and americium from the lungs of rodents following the inhalation of oxide aerosols of these actinides either alone or in combination with sodium oxide. National Radiological Protection Board, Annual Research and Development Report 1977, NRPB/R&D 2, 49–54. National Radiological Protection Board, Chilton, UK.

Stather, J.W., Harrison, J.D., David, A.J. et al., 1981. The gastrointestinal absorption of plutonium in the hamster after ingestion at low concentrations in drinking water. Health Phys. 41, 780–783.

Stather, J.W., Stradling, G.N., James, A.C., et al. 1984. The lung retention of actinide bearing industrial dusts. In: Smith, H. and Gerber, G. (Eds.) Lung Modelling for Inhalation of Radioactive Materials. EUR 9384. CEC, Brussels, Belgium, 127–134.

Stather, J.W., Howden, S., 1975. The effect of chemical form on the clearance of ^{239}Pu from the respiratory system of the rat. Health Phys. 28, 29–39.

Stather, J.W., Howden, S., Carter, R.F., 1975. A method for investigating the metabolism of the transportable fraction of plutonium aerosols. Phys. Med. Biol. 20, 106–124.

Stather, J.W., James, A.C., Brightwell, J., et al., 1979b. The clearance of plutonium and americium from the respiratory system of rodents after the inhalation of oxide aerosols of these actinides either alone or in combination with other metals. Proceedings of the Symposium on Biological Implications of Radionuclides Released from Nuclear Industries. March 26–30, 1979. Vienna, Austria. International Atomic Energy Agency, 3–25.

Stather, J.W., James, A.C., Rodwell, P., 1978b. Measurement of *in vitro* and *in vivo* rates of dissolution of actinides associated with sediment samples. National Radiological Protection Board, Annual Research and Development Report 1977, NRPB/R&D 2, 141–145. National Radiological Protection Board, Chilton, UK.

Stather, J.W., Priest, N.D., 1977. The pulmonary clearance and the comparative metabolism of plutonium-238, plutonium-239, americium-241 and curium-242 in the rat. National Radiological Protection Board, Annual Research and Development Report 1976. NRPB-R&D 1, 46–48. National Radiological Protection Board, Chilton, UK.

Stather, J.W., Rodwell, P., 1978. The use of DTPA as a treatment for plutonium inhaled in mixed oxide aerosols of plutonium and sodium. National Radiological Protection Board, Annual Research and Development Report 1977, NRPB/R&D 2, 112–114. National Radiological Protection Board, Chilton, UK.

Stradling, G. N., Cooper, J. R., Smith, H., et al., 1979. The mobility of curium-244 dioxide in the bronchially intubated rat. Int. J. Radiat. Biol. 36, 19–32.

Stradling, G. N., Stather, J. W., Ham, S. E., Sumner, S. A., Cooper, J. R., 1983. The efficacy of Zn DTPA for the decorporation of 238Pu-TBP injected into the lungs of hamsters. Health Phys. 44, 645–649.

Stradling, G.N., Stather, J.W., Sumner, S.A., et al., 1985. The metabolism and decorporation of plutonium after inhalation of tributyl phosphate complex by the rat. Health Phys. 49, 499–502.

Stradling, G. N., Gray, S. A., Moody, J. C., et al., 1990. Studies on the biokinetics of four industrial actinide-bearing aerosols after deposition in the rat lung: implications for occupational exposure. NRPB-M264. Chilton, National Radiological Protection Board.

Stradling, G. N., Ham, G. J., Smith, H., et al., 1978a. Factors affecting the mobility of plutonium-238 dioxide in the rat. Int. J. Radiat. Biol. 34, 37–47.

Stradling, G. N., Hodgson, S.A., Hodgson, A., et al., 1998. Dose coefficients and assessment of intake after inhalation of contaminated dusts from Palomares. Radiat. Prot. Dosim. 79, 179–182.

Stradling, G. N., Hodgson, S. A., Hodgson, A., et al., 1996. Dose coefficients and assessment of intake after inhalation of contaminated dusts at Palomares. NRPB-M692. Chilton, National Radiological Protection Board.

Stradling, G. N., Loveless, B. W., Ham, G. J., et al., 1978b. The biological solubility in the rat of plutonium present in mixed plutonium sodium aerosols. Health Phys. 35, 229–235.

Stradling, G. N., Moody, J. C., 1995. Use of animal studies for assessing intakes of inhaled actinide-bearing dusts. J. Radioanal. Nucl. Chem. 197, 309–329.

Stradling, G. N., Smith, H., Cooper, J. R., 1980. Factors affecting the mobility of actinide oxides and their influence on radiological protection. In: Proc. 19th Annual Hanford Life Sciences Symposium, Oct. 22–24 1979, Richland, Washington. DOE Symposium Series 53. Springfield, VA: National Technical Information Service. 209–223.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1987. Studies on the metabolic behaviour of industrial actinide-bearing aerosols after deposition in the rat lung: an experimental basis for interpreting chest monitoring data and assessing ALIs for workers. Human Toxicology 6, 365–375.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1989b. Biokinetics of plutonium-239 and americium-241 in the rat after the pulmonary deposition of contaminated dust from soil samples obtained from the former nuclear test site in Maralinga: Implications for human exposure. NRPB-M197. Chilton, National Radiological Protection Board.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1989c. Assessment of intake of an actinide-bearing dust from the pond storage of spent Magnox fuel. Biological Assessment of Occupational Exposure to Actinides. Proceedings of a Workshop held at Versailles, France, Versailles, France. Radiat. Prot. Dosim. 26, 201–206.

Stradling, G.N., Stather, J.W., Gray, S.A., et al., 1992. Radiological implications of inhaled ^{239}Pu and ^{241}Am in dusts at the former nuclear test site in Maralinga. Health Phys. 63, 641–650.

Stradling, G.N., Stather, J.W., Gray, S.A., et al., 1994. Biokinetics of inhaled plutonium-239 and americium-241 present in contaminated dusts at Maralinga. Inhaled Particles VII. Ann. Occup. Hyg. 38, 257–263.

Stringer, B., Russell, P.J., Davies, B.W. et al., 1984. Basic aspects of gel-precipitation route to nuclear fuel. Radiochimica acta, 36, 31–36.

Strong, J.C., James, A.C., Hodgson, A., et al., 1977. Sampling of actinide aerosols inside glove boxes at a mixed oxide fuel fabrication plant. National Radiological Protection Board, Annual Research and Development Report 1976. NRPB-R&D 1, 22–25. National Radiological Protection Board, Chilton, UK.

Sullivan, M. F., 1980. Absorption of actinide elements from the gastrointestinal tract of rats, guinea pigs and dogs. Health Phys. 38, 159–171.

Sullivan, M. F., 1981. Influence of plutonium mass on absorption from the gastrointestinal tract of adult and neonatal rodents. In: Pacific Northwest Laboratory Annual Report for 1980. Pt.1. Biomedical Sciences. Richland, Wash. PNL-3700, 185–186.

Sullivan, M. F., Miller, B. M., Ryan, J. L., 1982. Gut-related radionuclide studies. In: Pacific Northwest Laboratory Annual Report for 1981. Pt.1. Biomedical Sciences. Richland,

Wash. PNL-4100, 119–122.
Surendran, T., Haridasan, T. K., Sharma, R. C., 1995. Observations on unusually long retention half-times for Class Y actinides in human lungs and their implications. Bull. Radiol. Prot. 18, 252–257.
Suslova, K. G., Filipy, R. E., Khokhryakov, V. F., Romanov, S. A., Kathren, R. L., 1996. Comparison of the dosimetry registry of the Mayak Industrial Association and the United States Transuranium and Uranium Registries: A preliminary report. Radiat. Prot. Dosim. 67, 13–22.
Suslova, K. G., Khokhryakov, V. F., Tokarskaya, Z. B., et al., 2002. Extrapulmonary organ distribution of plutonium in healthy workers exposed by chronic inhalation at the Mayak Production Association. Health Phys. 82, 432–444.
Suslova, K. G., Sokolova, A. B., Krahenbuhl, M. P., Miller, S. C., 2009. The effects of smoking and lung health on the organ retention of different plutonium compounds in the Mayak PA workers. Radiat. Res. 171, 302–309.
Suslova, K. G., Sokolova, A. B., Krahenbuhl, M. P., Miller, S. C., 2012. Plutonium-238: accumulation, tissue distribution and excretion in Mayak workers after exposure to plutonium aerosols. Health Phys. 102, 251–262.
Suslova, K. G., Khokhryakov, V. F., Sokolova, A. B., et al., 2012. ^{238}Pu: a review of the biokinetics, dosimetry, and implications for human exposures. Health Phys. 102, 251–262.
Talbot, R. J., Newton, D., Dmitriev, S. N., 1997. Sex-related differences in the human metabolism of Pu. Radiat. Prot. Dosim. 71, 107–121.
Talbot, R. J., Newton, D., Warner, A. J., 1993. Metabolism of injected Pu in two healthy men. Health Phys. 65, 41–46.
Taylor, D. M., 1984. The retention of plutonium and americium in liver: an interspecies comparison. Radiation Risk Protection. 1, 431–434. 6th International Radiation Protection Association Congress, Berlin.
Tolmachev, S.Y., Nielsen, C.E., Avtandilashvili, M., et al., 2016. Mayak Worker Dosimetry System (MWDS 2013): Soluble plutonium distribution in the lungs of an occupationally exposed USTUR case. Radiat. Prot. Dosim. (Special Issue, 2016, in preparation).
Warner, A. J., Talbot, R. J., Newton, D. 1994. Deposition of Pu in human testes. Radiat. Prot. Dosim. 55, 61–63.
Warner, A. E., Brain, J. D., 1986. Intravascular pulmonary macrophages: A novel cell removes particles from blood. Am. J. Physiol. 250, R728–R732.
Weeks, M. H., Katz, J., Oakley, W. D., et al., 1956. Further studies on the gastrointestinal absorption of plutonium. Radiat. Res. 4, 339–347.
Wernli, C., Eikenberg, J., 2007. 20-year follow-up of a Pu/Am inhalation case. Radiat. Prot. Dosim. 125, 506–512.
Wernli, C., Eikenberg, J., Marzocchi, O., et al., 2015. 30-year follow-up of a Pu/Am inhalation case. Radiat. Prot. Dosim. 164, 57–64.
Wronski, T. J., Smith, J. M., Jee, W. S. S., 1980. The microdistribution and retention of injected Pu-239 on trabecular bone surfaces of the beagle: implications for the induction of osteosarcoma, Radiat. Res. 83, 74-89.

23. AMERICIUM (Z=95)

23.1. Chemical Forms in the Workplace

(851) Americium is an actinide element which occurs in oxidation states (III to VI) but mostly in oxidation state (III). Lanthanides such as Eu(III) or Gd(III) are good chemical analogues of Am(III). Americium may be encountered in industry in a variety of chemical and physical forms, including hydroxides, oxides (AmO_2), chlorides, oxalates, nitrates and citrates, and together with plutonium compounds, including as mixed oxide reactor fuel (MOX).

(852) Americium-240 and ^{241}Am are the two major isotopes of plutonium found in nuclear reactors.

Table 23.1. Isotopes of americium addressed in this report.

Isotope	Physical half-life	Decay mode
Am-237	73.0 m	EC, A
Am-238	98 m	EC, B+, A
Am-239	11.9 h	EC, A
Am-240	50.8 h	EC, A
Am-241[a]	432.2 y	A
Am-242	16.02 h	B, EC
Am-242m	141 y	IT, A
Am-243[a]	7.37E+3 y	A
Am-244	10.1 h	B-
Am-244m	26 m	B-
Am-245	2.05 h	B-
Am-246	39 m	B-
Am-246m	25.0 m	B-
Am-247	23.0 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

23.2. Routes of Intake

23.2.1. Inhalation

Absorption Types and parameter values

(853) There is a substantial amount of information available on the behaviour of americium (Am) after deposition in the respiratory tract from animal experiments, *in vitro* dissolution studies, and some accidental human intakes. *Publication 48* (ICRP, 1986) reviewed the biokinetics of americium, including data from animal studies and reported human exposure cases. The results indicated that for all americium compounds investigated, the americium was absorbed into blood with half times of several tens of days, in broad agreement with the definition of a Class W compound. *Publication 71* (ICRP, 1995) provided a brief review of the

literature relating to inhaled americium compounds in the context of the HRTM, and with emphasis on forms to which members of the public might be exposed as a result of environmental releases.

(854) Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values: the Human Respiratory Tract Model (ICRP, 1994a, OIR Part 1), the Gastro-Intestinal Tract Model (ICRP, 1979), the Human Alimentary Tract Model (ICRP, 2006), the human systemic model for Am (ICRP, 1993), the Am model for the dog of Luciani et al. (2006), the rat model for particle transport in the respiratory tract of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002) and the function describing the whole body retention of injected Am in the rat from Ménétrier et al. (2008). Unless specific data indicated otherwise, in analyses carried out here, s_r, f_b, and s_b were fixed at the values assessed for americium below: $s_r = 1\ d^{-1}$, $f_b = 0.01$, and $s_b = 1 \times 10^{-4}\ d^{-1}$. As described in the general actinide section, absorption parameter values based on plutonium ($s_r = 0.4\ d^{-1}$ $f_b = 0.002$; $s_b = 0\ d^{-1}$) are applied in this document to the transplutonium elements for radiation protection purposes. Absorption parameter values and Types, and associated f_A values for particulate forms of americium, are given in Table 23.3.

Americium citrate

(855) Lyubchanskiy and Nifatov (1972) measured the tissue distribution of ^{241}Am in rats at times up to 650 d after inhalation of ^{241}Am citrate or nitrate. At 32 d after inhalation of the citrate, about 5% of the initial lung deposit (ILD) was retained in the lungs and more than 40% ILD had been absorbed into blood. Analysis of the citrate data carried out here gave $f_b = 0.006$ (s_b assumed to be $1 \times 10^{-4}\ d^{-1}$ by default), $f_r = 0.7$, $s_r = 0.7\ d^{-1}$ and $s_s = 0.04\ d^{-1}$, giving assignment to Type F.

(856) Crawley and Goddard (1976) followed the tissue distribution and excretion of ^{241}Am and ^{242}Cm administered either as nitrates or citrates to rats by instillation into the nasopharyngeal (NP), tracheobronchial (TB) and pulmonary (P) regions of the respiratory system for 7 d. At one week after instillation of ^{241}Am citrate into the pulmonary region, only 7% ILD was retained in lungs while more than 80% ILD had been absorbed to blood. This is consistent with assignment to Type F. Following deposition in the NP or TB region, there was less retention in both lung and extrapulmonary tissues, because of faster mucociliary clearance. Analysis carried out here of data on citrate deposited in the pulmonary region gave $f_r = 0.8$ and $s_r = 4\ d^{-1}$. The data from deposition in the NP and TB regions were not detailed enough for further analysis and the limited time scale of the experiment (one week) prevented a reliable estimate of s_s in any case.

(857) Stradling et al. (1978) investigated the mobility of Am dioxide in the rat over 106 d after pulmonary instillation (see below). Am citrate was also administered as a control to four rats for each of four time periods considered. At three weeks post instillation, 4% ILD was retained in lungs and 61% ILD had been absorbed into blood, consistent with assignment to Type F. The analysis of citrate data here gave $f_b = 0.007$ (s_b assumed to be $1 \times 10^{-4}\ d^{-1}$ by default), $f_r = 0.9$, $s_r = 6\ d^{-1}$ and $s_s = 0.02\ d^{-1}$.

(858) Although absorption parameter values for americium citrate based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for americium citrate are not used here. Instead, it is assigned to Type F. However, the results contributed to the selection of the rapid dissolution rate for americium.

Americium chloride

(859) Zalikin et al. (1968) studied the distribution of ^{241}Am in rats for a month after intratracheal administration as chloride. After 32 d, 9% ILD was retained in the lungs and more than 44% had been absorbed into blood. Analysis here gave: $f_r = 0.5$, $s_r = 0.8$ d^{-1} and $s_s = 0.01$ d^{-1}, consistent with assignment to Type M.

(860) Il'in et al. (1975) studied the biokinetics of ^{241}Am in rats for 64 d after inhalation of ^{241}Am chloride. The radionuclide transferred from the lung to other tissues with a half-time of about 8 d. At 32 d, 5% ILD was in lungs and more than 40% ILD had been absorbed. Analysis here gave: $f_r = 0.2$, $s_r = 1$ d^{-1}, $s_s = 0.07$ d^{-1}, giving assignment to Type F.

(861) Zalikin and Popov (1977) studied the biokinetics of ^{241}Am in rats over two months after inhalation or intratracheal administration of the isotope as a chlorous salt solution. After 8 d, 34% ILD had been transferred to systemic tissues, and at 32 d, 5-7% ILD remained in lungs. The separate analysis here of the instillation and inhalation data gave respectively $f_r = 0.4$, $s_r = 1$ d^{-1}, $s_s = 0.02$ d^{-1}; and $f_r = 0.2$, $s_r = 8$ d^{-1}, $s_s = 0.06$ d^{-1}, both giving assignment to Type M.

(862) Although absorption parameter values for americium chloride based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for americium chloride are not used here. Instead, it is assigned to Type M. However, the results contributed to the selection of the rapid dissolution rate for americium.

Americium nitrate

(863) One exposure case has been described in which a worker received a combination of wound and inhalation exposures to ^{241}Am in nitric acid, presumably a nitrate form (Robinson et al., 1983). In this case, the lung retention was described as 86% associated with a 1.8-d half-time, 13% with a 27-d half-time and 1% with a 170-d half-time. The follow-up of the contamination was updated for the lifetime of the worker, during 11 years after the accident, by Breitenstein and Palmer (1989) and the results of an autopsy were reported afterwards by McInroy et al. (1995). However, the interpretation of these data is complicated by a significant wound intake, by the DTPA decorporation therapy employed and by the lasting skin contamination. The analysis here of lung retention, systemic retention and cumulative excretion gave: $f_r = 0.1$, $s_r = 0.2$ d^{-1} and $s_s = 8 \times 10^{-4}$ d^{-1}, consistent with assignment to Type M.

(864) Tseveleva and Yerokhin (1969) studied the tissue distribution of ^{241}Am in rats for 9 months after intraperitoneal or intratracheal administration of a nitric acid solution. One month after intratracheal administration, 6% ILD was retained in the lungs while more than 28% ILD had been transferred to blood. After 180 d, 3.5% ILD remained in the lungs. Analysis here of the data from intratracheal administration gave: $f_r = 0.6$, $s_r = 0.2$ d^{-1} and $s_s = 0.005$ d^{-1}, consistent with assignment to Type M.

(865) Nénot et al. (1971) compared the tissue distribution of Am in rats at 1, 10 and 90 d after inhalation of a nitrate aerosol or after intramuscular injection of a sulphate solution, with or without DTPA treatment. At 10 d after inhalation without treatment, 9% ILD was retained in lungs and about 57% ILD had been transferred to blood. At 90 d after inhalation, 4% ILD remained in lung. Analysis of the data here gave: $f_r = 0.7$, $s_r = 1$ d^{-1} and $s_s = 0.007$ d^{-1}, consistent with assignment to Type M.

(866) Nénot et al. (1972) compared the biokinetics of several actinides following intramuscular injection or pulmonary administration to rats as nitrates, over three months. At 30 d after inhalation, 17% ILD of ^{241}Am had been transferred to blood, while more than 8% was

still retained in lungs. After 90 d, 25% ILD was in bone and 4% ILD was in lung. This is consistent with assignment to Type M. The analysis of the Am nitrate data here gave f_r = 0.2 and s_s = 0.03 d^{-1}. However, these values are subject to significant uncertainty since the limited data regarding the time-dependent overall body burden do not allow a fully reliable fit of the model.

(867) Lyubchanskiy and Nifatov (1972) measured the tissue distribution of ^{241}Am in rats at times up to 650 d after inhalation of ^{241}Am citrate or nitrate. At 32 d after inhalation of the nitrate, lung retention was only 5% ILD, with absorption of more than 52% ILD to blood, suggesting Type F behaviour, close to the criterion for Type M. Analysis here gave f_b = 0.006, s_b = 2x10^{-4} d^{-1}, f_r = 0.7, s_r = 0.8 d^{-1} and s_s = 0.04 d^{-1}.

(868) Buldakov et al (1972) studied the biokinetics of ^{241}Am and ^{239}Pu in dogs for two years after inhalation of the nitrates. At 180 d, 27% ILD of ^{241}Am was retained in the lungs and 59% ILD in the liver and skeleton. This is consistent with assignment to Type M. Analysis of the Am data here gave f_r = 0.2, s_r = 3 d^{-1} and s_s = 0.005 d^{-1}.

(869) Crawley and Goddard (1976) studied the tissue distribution and excretion of ^{241}Am and ^{242}Cm in citrate or nitrate solutions 1 and 7 d after administration to rats by instillation into the NP, TB and pulmonary regions of the respiratory system. At 7 d, 72% initial pulmonary deposit of ^{241}Am nitrate was in lungs while 25% had been absorbed. Following deposition in the NP or TB region, there was less retention in both lung and extrapulmonary tissues, because of faster mucociliary clearance. The analysis here of the data from Am nitrate deposited in the pulmonary region gave f_r = 0.2 and s_r = 3 d^{-1}. The data from deposition in the NP and TB regions were not detailed enough for further analysis and the limited time scale of the experiment (one week) prevented a reliable estimate of s_s in any case.

(870) Stather and Priest (1977) studied the biokinetics of Pu, Am and Cm in rats for 120 d after pulmonary instillation as nitrates. In a first experiment with Pu and Am, 20% ILD and 6% ILD of ^{241}Am were retained in lungs after 30 and 120 d respectively. In a second experiment with Am and Cm, 13% ILD and 2% ILD of ^{241}Am were retained in lungs after 30 and 120 d respectively. This is consistent with assignment to Type M. The data were analysed in Annex E.7 of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002). A somewhat different analysis was conducted here, notably assuming the parameter values for the americium bound fraction defined above. This gave f_r = 0.5, s_r = 0.2 d^{-1} and s_s = 0.008 d^{-1} for the first experiment, and f_r = 0.7 and s_s = 0.01 d^{-1} for the second experiment.

(871) Ballou and Gies (1978) followed the clearance from rat lung to liver, kidney and skeleton of a nitric acid solution of Am for 200 d after nose-only inhalation of particles with three different AMADs. At 30 d post-inhalation about 9% ILD was retained in lungs and about 40% ILD had been transferred to other tissues, indicating Type M behaviour. The joint analysis of the data here gave f_r = 0.7 and s_s = 0.03 d^{-1}, consistent with assignment to Type M.

(872) Buldakov and Kalmykova (1979) studied the biokinetics of ^{241}Am in dogs up to 7 years after inhalation of a nitrate aerosol. The authors fit multi-exponential functions of time to their results of organ retention and urinary and faecal excretion. For example, 54% ILD was eliminated from the lungs with a half-time of 0.72 d, 17.5% ILD with 19.7 d, and 5.2% with 1035 d. The biokinetic functions provided by the authors were consistent with the following parameter values: f_r = 0.9, s_r = 0.2 d^{-1} and s_s = 0.001 d^{-1}, giving assignment to Type F.

(873) Stradling et al. (1987) compared their studies of industrial dusts with inhalation experiments they conducted on rats exposed to actinide nitrates and followed up to 252 d. After 28 d, 27% ILD of ^{241}Am was retained in lungs and 22% ILD had transferred to blood. After 168

d, 5% ILD was in lungs and 27% ILD had been absorbed to blood. This is consistent with assignment to Type M. Analysis here of these Am nitrate data gave $f_r = 0.2$ and $s_s = 0.004$ d^{-1}.

(874) Absorption parameter values for americium nitrate based on *in vivo* data are available from several studies. The results are variable: most are consistent with assignment to Type M, but some to Type F. Some values are very different from the default values for Type M or Type F. The estimated values of f_r range from 0.1 to 0.9 (median 0.6), greater than the default value for Type M (0.2). Estimated values of s_r range from 0.2 to 3 d^{-1} (median 0.5 d^{-1}), similar to the default value for plutonium (0.4 d^{-1}). Estimated values of s_s range from 8 x 10^{-4} to 0.04 d^{-1} (median 0.006 d^{-1}), similar to the default value for Type M (0.005 d^{-1}). Inhalation exposure to americium nitrate is not unlikely. Specific parameter values of $f_r = 0.6$, $s_r = 0.4$ d^{-1} and $s_s = 0.005$ d^{-1} are used here for americium nitrate.

Americium dioxide

(875) Several cases of known human inhalation exposure to oxide forms of americium have been reported. However, some are of limited value here because the *in vivo* measurements were not begun until months or years after the likely exposure times. Generally, most (≥80%) of the ^{241}Am lung contents were stated to have cleared from the lung with half-times of tens of days, and the remainder with half-times of the order of hundreds and/or thousands of days.

(876) Sanders (1974) described a case of accidental inhalation by a worker of mixed oxides of ^{244}Cm (75% of activity) and ^{241}Am (25% of activity). The worker was monitored by chest measurement, urine and fecal analyses for up to 410 d, and treated with DTPA. The isotopic ratio appeared to remain constant with time in faeces and presumably in lung. According to the author and based on a model of ICRP (1959), 37% of the intake was deposited in the lung. In the first 7 d post inhalation, 1.5% ILD was transported to the rest of body, 90% ILD was excreted in faeces and 8% ILD remained in lungs. The remaining lung activity was cleared with a 28-d half-time, 96% to the rest of body, 4% to faeces. Although the interpretation of the data was complicated by the DTPA treatment, analysis here gave $f_r = 0.1$ and $s_s = 0.02$ d^{-1}, consistent with assignment to Type M.

(877) Edvardsson and Lindgren (1976) followed the elimination of ^{241}Am from a worker exposed to an aerosol of americium oxide, for 100 d, by *in vivo* measurements in lung and whole body geometries and by urine and faeces analyses. About 80% of the intake was eliminated in the first week. The remaining activity in lung was cleared with a half-time of about 17 d. Analysis here gave values of $f_b = 0.005$, $f_r = 0.3$ and $s_s = 0.05$ d^{-1} and assignment to Type M.

(878) Fry (1976) studied the retention of ^{241}Am in two workers by *in vivo* measurement from about 6 months to 4 years after accidental inhalation of Am oxide. At the first measurement, about half of the body content was located in the thorax and it slowly cleared with a half-time of at least 900 d. Analysis here of the lung and whole body retention data gave $f_r = 0.5$ and $s_s = 2$ x 10^{-4} d^{-1} for both subjects, consistent with assignment to Type M.

(879) Toohey and Essling (1980) reported the late *in vivo* measurement of ^{241}Am in the lung and whole body of a worker at 2, 8, 10 and 12 years following inhalation of the dioxide. The authors estimated the lung content at 2 years as 16% of the total activity, which would suggest Type M behaviour. Between 5% and 10% ILD remained in the lung region after 12 years. DTPA chelation therapy administered from 2 to 9 years contributed to the excretion of over one-half ILD. Analysis here gave $f_r = 0.5$ and $s_s = 0.0001$ d^{-1}, consistent with assignment to Type M.

(880) Newton et al. (1983) reported the 870-d follow-up of a case of accidental inhalation exposure of a worker to aerosols of both $^{238}PuO_2$ and $^{241}AmO_2$. Half of the ILD of each nuclide was removed during the first few days by ciliary clearance mechanisms. Most of the residual ^{241}Am was cleared relatively quickly, with a half-time of about 11 d while a small proportion was subject to long-term retention with a half-time of about 900 d. Analysis here gave $f_r = 0.2$ and $s_s = 6 \times 10^{-4}$ d^{-1}, consistent with assignment to Type M.

(881) Truckenbrodt et al. (2000) presented the results and interpretation of *in vivo* measurement of ^{241}Am in the lung, skeleton and liver of a worker exposed approximately 26 years earlier by repeated inhalation of Am oxide, and urine and faeces bioassay analyses performed at the same time period. Using ICRP (1997) series biokinetic models, the authors estimated $f_r = 0.001$ and $s_s = 3 \times 10^{-4}$ d^{-1}, consistent with assignment to Type S.

(882) Bull et al. (2003) assessed a case of $^{241}AmO_2$ powder inhalation by a worker on the basis of a nose blow, lung and whole-body measurement two hours after the incident, faecal and urine sampling over 37 d. An intake of about 200 Bq was estimated but the urine bioassay results below the limit of detection were in contradiction with ICRP (1997) default lung parameter values for Am. To make the model prediction consistent with the observations, the authors used modified Type S model parameter values, setting f_r to 10^{-5} and f_1 to 10^{-4} or f_1 to 10^{-5} and f_r to 10^{-4} or a modified systemic model.

(883) Kathren et al. (2003) reported the follow-up of a worker for 6 years after accidental acute inhalation of ^{241}Am assumed to be in oxide form. Lung, skeleton and liver *in vivo* measurements were supplemented with four urine analyses. The authors described the lung clearance by two exponentials with half-times of 110 and 10,000 d. Although some inconsistency with the reference systemic model for Am (ICRP, 1993) was observed, data analysis here gave $f_r = 0.3$ and $s_s = 7 \times 10^{-4}$ d^{-1}, consistent with assignment to Type M.

(884) Carbaugh et al. (2010) reported three cases of worker inhalation exposure to ^{241}Am oxide. The workers were followed over about 300 d by *in vivo* lung measurements of ^{241}Am, fecal and urine analysis over about three months, and were treated with DTPA. One or two *in vivo* liver and skeleton measurements were performed on each subject. The DTPA therapy makes the interpretation of data uncertain, but parameter values of $f_r = 0.01$, 0.2 and 0.03; and $s_s = 0.01$, 0.006 and 0.007 d^{-1} respectively were assessed here for the three workers, which are all consistent with assignment to Type M.

(885) Lung retention data for ^{241}Am inhaled or instilled in various chemical forms by several species of experimental animals have been published, including rats, hamsters, dogs and monkeys. In addition, Mewhinney and Muggenburg (1985) studied the influence of age at inhalation on the biokinetics of $^{241}AmO_2$ in beagles. In the studies of americium oxides, the lung retention data have usually shown 70–90% clearance with half times from 10 to 30 d. One exception was the clearance of ^{241}Am from monkeys in which 32% ILD cleared with a 0.1-d half-time. The second clearance component was on the order of hundreds of days.

(886) McClellan (1972) reported the progress of studies on the biokinetics of transuranic elements in rodents and dogs at the Lovelace Foundation, Albuquerque. The figures presented included data on retention of ^{241}Am in lung, liver and skeleton over 1000 d after inhalation by dogs of the dioxide, as well as urinary excretion data for 3 weeks. $^{241}AmO_2$ appeared to leave the lung much more rapidly than plutonium dioxide or even plutonium nitrate with a consequent two-order of magnitude difference in urinary excretion rate at early times post-inhalation. Most of the ^{241}Am leaving the lung was translocated to skeleton and liver. Analysis here gave $f_r = 0.9$, $s_r = 0.1$ d^{-1} and $s_s = 8 \times 10^{-4}$ d^{-1}, consistent with assignment to Type F, but very close to the criterion for Type M.

(887) When investigating the respiratory carcinogenesis in rats after inhalation of actinides, Lafuma et al. (1974) observed the same lung clearance for ^{241}Am nitrate and dioxide: 99% ILD being cleared with a 12.5-d half-time and 1% with a 250-d half-time, suggesting Type M behaviour.

(888) Craig et al. (1975, 1979) followed the disposition of ^{241}Am in dogs for up to 810 d after a single inhalation exposure to $^{241}AmO_2$ at three levels of initial body burden: low (190 Bq), medium (7.4 kBq) and high (70 kBq). Urine and faeces were analysed as well as tissue distribution after sacrifice. The lung retention of Am was ~60% ILD at 10 d, ~50% ILD at 30 d and ~3% at 810 d, with mainly translocation to liver and skeleton: ~50% ILD had been absorbed to blood after 30 d. This is consistent with assignment to Type M. The joint analysis of all data here gave $f_r = 0.5$ and $s_s = 0.001$ d^{-1}.

(889) Mewhinney et al. (1976) studied the distribution of ^{241}Am in the lung, liver and skeleton of hamsters for up to 670 d after inhalation of $^{241}AmO_2$ as monodisperse aerosols of 0.8 µm, 1.7 µm and 3.3 µm aerodynamic diameters (d_{ae}) and as a polydisperse aerosol of 1.3 µm AMAD. The measured lung retention indicated that AmO_2 behaved as a relatively soluble material. The half-time of the long-term component increased with aerosol size from 92 d for 0.8 µm to 162 d for 3.3 µm. It represented less than 30% ILD for the 0.8 and 1.7 µm groups but more than 55% ILD for the 1.3 µm and 3.3 µm groups. Lung retention was of the order of 26%–60% ILD at 30 d and 3%–22% ILD at 180 d, with retention in skeleton and liver amounting to 15%–45% ILD at 30 d and 20%–45% ILD at 180 d. These results are consistent with assignment to Type M for all particle sizes. The analysis of data for the 0.8 µm, 1.7 µm, 3.3 µm and 1.3 µm groups here gave $f_r = 0.2$, 0.2, 0.4 and 0.3 respectively and $s_s = 0.004$, 0.005, 0.003 and 0.004 d^{-1} respectively.

(890) Stradling et al. (1978) investigated the effect on Am lung clearance of particle size and age of a dioxide form over 106 d after pulmonary instillation into rats. Rapid movement of Am from lungs to blood was observed for all aerosols, AmO_2 behaving as a soluble compound comparable to the citrate control. At 21 d, 3% – 20% ILD was retained in lungs and 57% – 79% had been absorbed to blood, indicating Type F or Type M behaviour. Analysis here (assuming $s_s = 10^{-4}$ d^{-1}) gave for a freshly prepared Am oxide: $f_r = 0.6$ and $s_r = 1$ d^{-1} (giving assignment to Type M) for particles of size less than 0.025 µm, $f_r = 0.9$; and $s_r = 4$ d^{-1} (giving assignment to Type F) for particle size range 0.025–1.2 µm. For an AmO_2 suspension aged for 4 months in water, analysis here gave $f_r = 0.9$ and $s_r = 3$ d^{-1} for particles of size less than 0.025 µm; and $f_r = 0.7$ and $s_r = 3$ d^{-1} for particles in the size range 0.025–1.2 µm, giving assignment to Type M.

(891) Stather et al (1979) studied the clearance from the lungs of hamsters after inhalation of actinide oxides, either alone or in combination with other metals. For Am dioxide, at 30 d, 66% ILD was still in lungs while 19% ILD was in extrapulmonary tissues. At 274 d, 13.5% ILD was in lungs and 45% ILD was in other tissues. Analysis here gave $f_r = 0.06$ and $s_s = 0.005$ d^{-1}, consistent with assignment to Type M.

(892) Mewhinney et al. (1978, 1982) and Mewhinney and Griffith (1983) studied the tissue distribution of Am in dogs following inhalation of monodisperse (0.75, 1.5 and 3.0 µm d_{ae}) and polydisperse (1.8 µm AMAD) $^{241}AmO_2$ aerosols over six years. A short-term retention half-time for 80% ILD ranged from 7 to 39 d, increasing with the aerosol size. A second component of retention appeared as 20% ILD retained with a half-time of 165–180 d. At 730 d after inhalation, about 2% ILD remained in lung. A small third component of 0.6–0.7% ILD showed a long effective half-time of 5000 – 5500 d. The effective retention half-time for this fraction was longer than expected for insoluble particles subject to mechanical clearance (particle transport): see section on "Extent of binding of americium to the respiratory tract". From the

observed rate of ^{241}Am accumulation in liver and skeleton, dissolution appeared to dominate lung clearance. At 4 and 6 years after inhalation, ~20% ILD was present in either liver or skeleton. The analysis conducted here gave values of absorption parameters for the groups exposed to aerosol sizes 0.75 µm, 1.5 µm, 3.0 µm and 1.8 µm respectively: f_b = 0.01 (assigned by default), 0.02, 0.01 and 0.03; f_r = 0.4, 0.4, 0.2 and 0.3; s_s = 0.02 d^{-1}, 0.007 d^{-1}, 0.005 d^{-1} and 0.01 d^{-1} respectively, and assignment to Type M for all aerosol sizes.

(893) Sanders and Mahaffey (1983) studied the content and carcinogenicity of ^{241}Am in the lung and skeleton of rats over about 880 d after a single inhalation exposure to $^{241}AmO_2$. About 55% ILD was cleared from lung with a half-time of 0.5 d, 37% with a half-time of 7 d and 8% with a half-time of 580 d. This resulted in retentions of ~5% ILD in lung and in bone at both 30 d and 180 d post-inhalation. Analysis here gave f_r = 0.4 and s_s = 0.001 d^{-1}, consistent with assignment to Type M.

(894) Mewhinney and Muggenburg (1985) investigated the influence of species and age on lung retention, tissue distribution and excretion of ^{241}Am by following its retention in lung, liver and skeleton of dogs of three age groups, and of adult monkeys, for two years after a single inhalation exposure to aerosols of $^{241}AmO_2$. The retention of ^{241}Am in lungs of aged dogs was greater than for immature and young adults dogs through about 200 d after exposure. It was 35%–80% ILD after 30 d and 13%–40% ILD after 130 d while the retention in liver and skeleton amounted to 7%–27% ILD at 30 d and 26%–58% ILD after 130 d. This is consistent with assignment to Type M. For the purpose of the present document, all dog data were analysed together and gave f_r = 0.2 and s_s = 0.004 d^{-1}. Monkeys exhibited a rapid initial clearance of 32% ILD with 0.1-d half-time. At 30 d, 55% ILD was retained in lung and 13% ILD had been transferred to liver and skeleton. After 180 d, the retention was 37% ILD in lungs and 18% ILD in liver and skeleton. This is also consistent with assignment to Type M. By about one year, the percentages of ILD remaining in lung were comparable for dogs and monkeys. The analysis here of monkey data gave f_r = 0.2 and s_s = 0.001 d^{-1}.

(895) Malátová et al. (2007) studied the *in vitro* dissolution of ^{241}Am, mainly as the dioxide, from an aerosol collected at a workplace, in the synthetic serum ultrafiltrate described by Eidson and Mewhinney (1983). The mean values from three experiments indicated f_r = 0.2, s_r = 4 d^{-1}, s_s = 0.002 d^{-1} and assignment to Type M. These experimentally determined parameter values were applied by Fojtik et al. (2013) in the analysis of a contamination case detected during routine monitoring of a worker exposed to $^{241}AmO_2$ from the same producer. A good fit of the model to urine, faeces, skeleton, lung and whole body measurement results collected over 5 years was then obtained.

(896) Although absorption parameter values for americium oxide based on *in vivo* data were derived, wide ranges of values of f_r (10^{-5} – 0.9) and s_s (10^{-4} – 0.05 d^{-1}) were obtained in different studies. Nevertheless, most studies support the assignment to Type M. Furthermore, the median values obtained here from 32 analyses: f_r = 0.3, s_r = 3 d^{-1}, s_s = 0.004 d^{-1} are very close to the default parameter values of Type M. Therefore specific parameter values for americium oxide are not used here. Instead, it is assigned to Type M. However, the results contributed to the selection of the bound state parameter value for americium.

Plutonium oxide forms

(897) A significant effort was invested in the dose reconstruction for workers exposed to plutonium (Pu) at the Mayak Production Association, Russia (Vasilenko et al., 2007). To document lung absorption, the transportability of industrial Pu aerosols were categorised by

solubility factors for soluble compounds (nitrate), moderately soluble compounds and insoluble compounds (dioxide and metal) (Khokhryakov et al., 1998). Suslova et al. (2013) reviewed the biokinetics of ^{241}Am, associated with Pu, and built up from the decay of ^{241}Pu, on the basis of 290 autopsy cases, bioassay data and whole body counting of exposed Mayak workers. For the three transportability categories, about 14 years after exposure, the fraction of body Am retained in the lung was slightly less than that of Pu, but the difference was not statistically significant. Sokolova et al. (2013) confirmed that applying the Pu absorption parameters to Am resulted in a limited overestimation of the Am lung burden by 48% on average over 456 autopsied cases, suggesting a slightly faster lung clearance for Am than for Pu.

(898) An informal feedback from French decommissioning worksites is that the dissolution kinetics of an Am and Pu mixture is intermediate between the Type M of Am oxide and the Type S of Pu oxide (SFMT, 2011). The results of animal studies indicate that the availability of ^{241}Am for absorption to blood depends on the solubility characteristics of the major chemical components of the matrix in which the ^{241}Am is present.

(899) James et al. (1978) studied the clearance from the lungs of rats of ^{239}Pu and ^{241}Am inhaled as dioxides calcined at 550°C and blended with uranium dioxide in the ratio Pu:U 1:2 by mass. The data indicated Am lung retention of 49% ILD at 30 d after inhalation and 12% ILD at 180 d. This is consistent with assignment to Type M but close to the criterion for Type S.

(900) Stather et al. (1979) also studied the clearance from hamster lung of oxide fumes of plutonium and americium mixed with sodium (Na:Pu atomic ratio 27:1) or potassium (K:Pu atomic ratio 36:1). At 30 d, 44% ILD of Am within Na:Pu and 19% ILD of Am within K:Pu remained in the lungs. At 180 d, 27% ILD of Am within Na:Pu remained in the lungs while 33% was in other tissues. This would indicate Type M for both mixtures and f_r = 0.4 and s_s = 0.003 d^{-1} for Am within Na:Pu. Such behaviour is clearly different from other Pu oxide compounds (see plutonium inhalation section).

(901) Stanley et al. (1982) studied the clearance from lung and distribution in other tissues of Pu and Am after inhalation exposure to a mixture of UO_2 and 750°C heat-treated PuO_2 obtained from ball milling in rats, dogs and monkeys. The UO_2-PuO_2 aerosol was relatively insoluble in the lungs of all species. Monkeys and rats cleared Pu and Am from their lungs faster than dogs. Very little Pu and Am translocated within the first 2 years after exposure to tissues other than tracheobronchial lymph nodes. Am systemic burdens below 5% ILD in dogs and monkeys and lung burden of 16% ILD in rats after 1 year indicate assignment to Type S. Analysis here of the americium data gave f_r = 0.004 and s_s = 4 x 10^{-5} d^{-1} for dogs, f_r = 0.002 and s_s = 1 x 10^{-4} d^{-1} for monkeys, f_r = 0.1 and s_s = 1 x 10^{-4} d^{-1} for rats, all consistent with assignment to Type S.

(902) Eidson and Mewhinney (1983) assessed the dissolution characteristics of representative industrial mixed-oxide (U, Pu and Am) powders obtained from fuel fabrication enclosures by *in vitro* dissolution tests over 30 d in two different solutions. No strong influence of the temperature history of the mixed-oxides or of the solvent was demonstrated. The dissolution of Am was slightly higher than that of Pu and much lower than that of U. Less than 10% dissolution at 30 d in any case indicates Type M or S. The absorption parameters values derived here from the two dissolution components observed by the authors for Am in the different combinations of plutonium oxide compound and solvent are summarised in Table 23.2.

Table 23.2. Absorption parameter values for Am within forms of plutonium oxide derived from Eidson and Mewhinney (1983).

Solvent	SUF [a]				0.1 M HCl		
Material containing Am	f_r	s_r, d^{-1}	s_s, d^{-1}		f_r	s_r, d^{-1}	s_s, d^{-1}
PuO_2 calcined at 750°C mixed with UO_2 and ball milled	0.02	0.4	4×10^{-5}		0.04	7	2×10^{-4}
PuO_2 calcined at 850°C, mixed with UO_2 and organic binders and suspended during the pellet pressing operation	0.006	0.7	1×10^{-4}		0.008	3	1×10^{-4}
Single phase solid solution $(U,Pu)O_{1.96}$ produced by grinding pellets sintered at 1750°C	0.07	0.6	8×10^{-5}		0.05	3	9×10^{-4}
PuO_2 calcined at 850°C and blended with other lots of feed PuO_2	0.004	[b]	1×10^{-4}		0.004	3	1×10^{-4}

a Synthetic serum ultrafiltrate (SUF) solution containing DTPA
b Not observed

(903) Ramounet et al. (2000) and Ramounet-Le Gall et al. (2002) compared the biokinetics of Pu and Am in rats over 540 d after inhalation of industrial PuO_2 from calcination and after inhalation of mixed oxides (MOX): MIMAS involved dry oxide mixing; SOLGEL was obtained from a co-precipitation procedure. About 80% of the actinides were cleared with a half-time of 30 d and the remainder with a half-time of 200 d. Rateau-Matton et al. (2004) analysed the resulting *in vivo* data with the approach applied here and studied the *in vitro* dissolution of the three compounds in the same synthetic serum ultrafiltrate as Eidson and Mewhinney (1983). All results were consistent with assignment to Type S. In the same laboratory, Sérandour and Fritsch (2008) observed *in vivo* an increased solubility for an old PuO_2 studied more than 15 years after its fabrication, giving assignment to Type M. The absorption parameter values derived by the authors for Am in the different forms of plutonium oxide are summarised in Table 23.3.

Table 23.3. Absorption parameter values for Am within forms of plutonium oxide, rounded from Rateau-Matton et al. (2004) and Sérandour and Fritsch (2008).

	In vivo				*In vitro*		
Material containing Am	f_r	s_r, d^{-1}	s_s, d^{-1}		f_r	s_r, d^{-1}	s_s, d^{-1}
MOX from MIMAS process	7×10^{-4}	0.4	4×10^{-5}		0.05	0.4	2×10^{-4}
MOX from SOLGEL process	0.001	0.9	4×10^{-4}		0.1	0.2	1×10^{-4}
PuO_2	0.01	0.5	5×10^{-5}		0.04	1.2	3×10^{-5}
old PuO_2	0.1	[a]	0.004		[a]	[a]	[a]

a Not observed

(904) Although absorption parameter values for americium in forms of plutonium oxide based on *in vivo* data were derived, wide ranges of values of f_r (7×10^{-4} – 0.1) and s_s (3×10^{-5} –

0.004 d^{-1}) were obtained in different studies. Nevertheless, most of them support the assignment to Type S. Furthermore, the median values obtained here: f_r = 0.02, s_r = 0.7 d^{-1}, s_s = 1 x 10^{-4} d^{-1} are very close to the default parameter values of Type S. (An element-specific value of s_r = 1 d^{-1}, is adopted here for Type S americium.) Therefore specific parameter values for americium in plutonium oxide are not used here. Instead, it is assigned to Type S. However, it is noted that the dissolution kinetics of Am may well depend on the state of the PuO_2 matrix, notably after aging or mixture with other metals.

Unspecified forms

(905) Jeanmaire and Ballada (1970) followed two researchers contaminated with a soluble ^{241}Am salt by the measurement of ^{241}Am in lungs and in excreta for nearly one year after inhalation. The lung retention (R) decreased approximately as a power function of time (T): $R = T^{-0.9}$. After a month, only 5 – 6% ILD was left in lungs, suggesting Type F behaviour. The analysis of the data here was complicated by DTPA therapy and by the pooling of urinary and faecal excretion, but gave values of f_r = 0.6, s_s = 0.04 d^{-1}, f_b = 0.03 and f_r = 0.8, s_s = 0.03 d^{-1}, f_b = 0.02 respectively for the two researchers, both consistent with assignment to Type F.

(906) Cohen et al. (1979) reported 8 years of follow-up of a father and his son who were unknowingly contaminated in their home about 6 years before, at the ages of 50 and 4 years. *In vivo* measurements of the ^{241}Am burden in lung, liver and skeleton were performed. A significant decrease of the activity in lung was observed over the 8 years: 38% for the adult and more than 95% for the adolescent. The interpretation of the measurements was complicated by the little knowledge of the conditions of exposure, by a pentetate chelation therapy and by the growth of the adolescent. However, values of f_r = 0.6 and 0.7, respectively; s_s = 2 x 10^{-4} and 4 x 10^{-4} d^{-1}, respectively, were determined here for the adult and adolescent. These values are consistent with assignment to Type M.

(907) Wernli et al. (2014) reported the 30-year follow-up of a worker who inhaled a mixture of plutonium isotopes and ^{241}Am following a glove box accident in which waste material related to nuclear fuel overheated. Absorption parameter values for ^{241}Am fit by the authors (assuming f_b=0.002 and s_b=0 d^{-1}) were f_r = 0.08, s_r = 0.4 d^{-1}, and s_s = 8 x 10^{-5} d^{-1}, consistent with assignment to Type S. For additional information on this case see the description in the plutonium inhalation section of this document..

(908) Thomas et al. (1972) studied the retention and excretion of ^{241}Am in five dogs after inhalation of an aerosol formed by passing droplets of ^{241}Am oxide dissolved in hydrochloric and oxalic acids through a heating column at 600°C. Urine and faeces were collected and analysed for 60 d; whole body measurement was performed over about 1000 d. Following sacrifice shortly after inhalation, or from 127 to 1022 d afterwards, the ^{241}Am content was measured in lung, lymph nodes, skeleton, liver, kidney and thyroid. At 180 d, less than 4% ILD was retained in lung while more than 30% ILD was transferred to systemic tissues. Continuing high urinary excretion in the first two months pointed to a large fraction of activity being absorbed at a moderate rate. Analysis here gave f_r = 0.9, s_r = 0.08 d^{-1}, s_s = 0.005 d^{-1} and f_b = 0.01, consistent with assignment to Type M.

(909) Stradling et al. (1987) studied the biokinetics of ^{239}Pu and ^{241}Am in site-specific industrial dusts after deposition in the rat lung. Residues from a purification process, highly enriched with ^{241}Am as a chloride, were administered to rats either by inhalation or by intratracheal instillation and followed up to one year. After instillation, ^{241}Am was cleared from the lungs with a half-time of 16 d. After inhalation, a second half-time of 90 d was observed.

Lung retentions of ~30% ILD at 28 d (with ~25% ILD absorbed to blood) and less than 15% ILD at 168 d (with more than 28% ILD absorbed to blood) were consistent with assignment to Type M. The separate analysis here of inhalation and intratracheal instillation data gave consistent values of $f_r = 0.2$, $s_s = 0.003$ d^{-1} and $f_r = 0.2$, $s_s = 0.008$ d^{-1} respectively. ^{241}Am in an atmospherically degraded mixture of Pu, Am and U nitrates from a process line, intimately mixed and highly diluted with inactive debris, was retained in lung as 51% ILD at 168 d after intratracheal instillation while 12% had been absorbed to blood. The analysis here of data from 74 to 365 d gave $f_r = 0.06$ and $s_s = 5 \times 10^{-4}$ d^{-1}, consistent with assignment to Type S.

(910) Stradling et al. (1989) followed the biokinetics of ^{241}Am over a year after intratracheal instillation into rats of irradiated Magnox fuel from a storage pond. At 168 d, 14% ILD was retained in lungs and the same amount had been absorbed to blood. This indicates intermediate behaviour between Types M and S. The analysis of data here gave $f_r = 0.03$ and $s_s = 0.002$ d^{-1}, consistent with assignment to Type M.

Environmental forms

(911) Americium is ubiquitously present in most plutonium-bearing materials as well as unprocessed nuclear waste materials that have undergone substantial neutron irradiation. As such, it is probable that exposures to americium environmental contamination will involve americium as a trace radioactive contaminant of other matrices, which may also contain other radionuclides. See the *Plutonium* section in this document for further information on the studies summarised below.

(912) Stather et al. (1978b) followed the biokinetics, after intratracheal instillation into 17 rats (and 6 hamsters), of ^{239}Pu and ^{241}Am associated with a suspension of Ravenglass sediment. Particles greater than 10 µm were removed by sedimentation. Because the specific activity of the sample was considered too low for in-vivo measurements, ^{239}Pu and ^{241}Am were added to the suspension: it was confirmed that they attached rapidly. Tissue distributions and cumulative excretion were measured in rats at 7 and 14 days; tissue distributions in rats and hamsters at 28 days. The ^{241}Am lung content decreased to 76% ILD at 7 days, with most of the clearance to systemic tissues: only ~8% ILD went to feces, and to ~45% ILD at 28 days. Lung clearance of ^{239}Pu was similar but somewhat faster. Tissue distributions in hamsters at 28 days were similar to those in rats. There is insufficient information to estimate s_r or s_s. Analysis here gave: $f_r = 0.2$, $s_s < 0.003$ d^{-1}, and assignment to Type M.

(913) Morgan et al. (1990) studied the solubility of Pu and Am associated with estuarine silt from West Cumbria, England, by intratracheal instillation of 5 doses in 7 weeks and follow-up of lung, skeleton and liver content over 550 d. Most of the actinides were cleared from the lung with a half-time of about 240 d. At 220 d post intake, 59% ILD of ^{241}Am remained in the lungs while ~12% had been transferred to liver and skeleton. Analysis here gave $f_r = 0.02$ and $s_s = 0.001$ d^{-1}, consistent with assignment to Type M.

(914) Stradling et al. (1992) investigated the biokinetics of Pu and Am present in three dust samples from the former nuclear weapons test site at Maralinga, South Australia, for one year after intratracheal instillation into rats. For two samples, the lung retention of ^{241}Am at one year was more than 23% ILD and the total absorption to blood was less than 6% ILD, consistent with assignment to Type S. For the third sample, 19% ILD was retained in lungs at one year when 16% ILD was absorbed to blood, indicating intermediate behaviour between Types M and S. The analysis performed here provided values of $f_r = 0.01$ and $s_s = 4 \times 10^{-4}$ d^{-1}; $f_r = 0.008$ and $s_s = 8 \times 10^{-5}$ d^{-1}; and $f_r = 0.05$ and $s_s = 0.001$ d^{-1} respectively for these three samples. An

inhalation experiment performed with the second sample led to the same conclusions. The first two sets of parameter values are consistent with assignment to Type S, the third to Type M.

(915) Stradling et al. (1998) determined the absorption parameters in the rat lung of Pu and Am present in soil samples from the site of the aviation accident and conventional explosions of nuclear weapons at Palomares, Spain. One year after intratracheal instillation, 22 – 27% ILD of ^{241}Am was still in lungs, 6 – 14% ILD had been absorbed to blood. This indicates Type S (possibly Type M) behaviour. The authors evaluated f_r = 0.08 and s_s = 4 x 10^{-4} d^{-1} for the particle size fraction < 5 µm; and f_r = 0.007 and s_s = 4 x 10^{-4} d^{-1} for the fraction 125 – 250 µm. Both sets of parameter values are consistent with assignment to Type S.

Rapid dissolution rate

In fifteen studies of inhaled soluble compounds (chlorides, citrates and nitrates), sufficient early retention data were available to allow an estimate of the rapid dissolution rate s_r. The results of analysis here are summarised in Table 3: Values of s_r ranging from 0.2 to 7 d^{-1} with a median of 1 d^{-1}, were obtained by fitting a rat respiratory tract model (ICRP 2002) to the experimental data. This is close to the default value of 0.4 d^{-1} adopted for plutonium compounds. Consequently a default value of s_r = 0.4 d^{-1} is proposed for the rapid dissolution rate of americium compounds.

Table 23.4. Case-specific absorption parameter values estimated here for soluble compounds in studies reporting early retention data.

Inhaled particulate materials	Animal species	Absorption parameter values		References
		f_r	s_r (d^{-1})	
chloride	rat	0.2	1	Il'in et al. (1975)
		0.5	0.8	Zalikin et al. (1968)
		0.4	1	Zalikin and Popov (1977)
		0.2	7	
citrate	rat	0.8	4	Crawley and Goddard (1976)
		0.7	0.7	Lyubchanskii and Nifatov (1972)
		0.9	6	Stradling et al. (1978)
nitrate	rat	0.2	3	Crawley and Goddard (1976)
		0.5	0.2	ICRP (2002)
		0.7	0.8	Lyubchanskii and Nifatov (1972)
		0.7	1	Nénot et al. (1971)
		0.6	0.2	Tseveleva and Yerokhin (1969)
	dog	0.2	3	Buldakov et al. (1972)
		0.9	0.2	Buldakov and Kalmykova (1979)

	human	0.1	0.2	Robinson et al. (1983)
Median		0.5	1	
Geometric mean		0.4	1	
Min - max		0.2 – 0.9	0.2 – 7	

Extent of binding of americium to the respiratory tract

(916) As noted above, Mewhinney et al. (1978, 1982) and Mewhinney and Griffith (1983) studied the tissue distribution of Am in Beagle dogs following inhalation of monodisperse (3.0 µm, 1.5 µm and 0.75 µm AMAD) and polydisperse (1.8 µm AMAD) $^{241}AmO_2$ aerosols over six years. They noted the long-term pulmonary retention of a small fraction, of the order of 1% (0.5% to 2%), of the ILD. The effective retention half-time (about 5000 d) for this fraction was longer than expected for insoluble particles subject to mechanical clearance (particle transport). Taya et al. (1994) aimed at characterizing the binding nature of the small fraction of americium retained for a long time in the beagle lung after inhalation of americium nitrate by homogenization-fractionation of lung lobes and autoradiography. Dissolved americium was then observed to be associated with connective tissues. In studies with $^{241}AmO_2$, the autoradiography of monodisperse particles revealed the progressive appearance of single tracks with time in the lungs as the AmO_2 particles dissolved in situ. At different times after exposure, which were proportional to particle size, the particles became less and less frequent, and eventually could no longer be found when the activity retained in lung became close to stable. Only the single tracks, which were primarily associated with parenchymal interstitium, then remained. The magnitude of the bound fraction may thus be inferred from the lung retention described by Mewhinney and Griffith (1983) for monodisperse $^{241}AmO_2$ particles, assigning the long-term retained fraction of about 1.5% ILD to the bound compartment.

(917) A similar long-term retention of about 1.5% ILD was previously observed in dogs, more than two years after Am inhalation, by Thomas et al. (1972). The follow-up by Jeanmaire and Ballada (1970) for more than 200 d of two accidental cases of human exposure to a soluble salt of Am suggests slightly higher bound fractions of 2–3% ILD. However, the analysis of data from Lyubchanskiy and Nifatov (1972) on the retention of soluble Am nitrate and citrate in rat lungs for nearly two years suggests a slightly lower value of about 0.6%. Based on these considerations, the bound fraction for americium is assessed to be $f_b = 0.01$ and $s_b = 10^{-4}$ d^{-1}. There is no evidence of long-term retention of americium deposited in relatively soluble form in the ET, BB or bb regions. Such a small long-term bound state in the alveolar region results in an additional contribution to the committed equivalent dose coefficient for the lungs from inhaled ^{241}Am of about 75%, about 15%, less than 1%, and about 25% for Absorption Types F, M, S, and for Am nitrate respectively.

(918) Nevertheless, as described in the general actinide section, absorption parameter values for the bound state based on plutonium are applied in this document to the transplutonium elements for radiation protection purposes. Thus, a bound fraction $f_b = 0.002$ and a rate of uptake $s_b = 0$ d^{-1}, are applied throughout the respiratory tract except in the ET_1 region.

Table 23.5. Absorption parameter values for inhaled and ingested americium.

Inhaled particulate materials	Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A[b]
Specific parameter values[c]				
Americium nitrate	0.6	0.4	0.005	3×10^{-4}
Default parameter values[d,e]				
Absorption Type / Assigned forms				
F — Citrate	1	0.4	–	5×10^{-4}
M[e] — Oxide, chloride	0.2	0.4	0.005	1×10^{-4}
S — Americium associated with plutonium oxide	0.01	0.4	1×10^{-4}	5×10^{-6}
Ingested material[f]				
All compounds				5×10^{-4}

a It is assumed that for americium a bound fraction $f_b = 0.002$ with $s_b = 0$ d^{-1} is applied throughout the respiratory tract except in the ET_1 region. The values of s_r for Type F, M and S forms of americium (0.4 d^{-1}) are element-specific.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of americium (5×10^{-4}).

c See text for summary of information on which parameter values are based, and on ranges of parameter values observed in different studies. For americium nitrate, specific parameter values are used for dissolution in the lungs, but a default value of f_A (footnote b).

d Materials (e.g. americium oxide) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values or because specific parameter values would not be significantly different from the default (see text).

e Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

f Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction fA for the secreted activity is the reference fA (=5×10^{-4}) for ingestion of the radionuclide.

23.2.2. Ingestion

(919) Compared to plutonium and neptunium, limited data are available on the absorption of americium.

(920) The only human data on the absorption of Am are those from Hunt et al. (1986, 1990) who carried out two studies on the absorption of plutonium and americium by volunteers eating shellfish winkles collected on the Cumbrian coast near to the nuclear-fuel reprocessing plant at Sellafield. The overall absorption value obtained for americium was 1×10^{-4} with a range of 4×10^{-5} to 3×10^{-4}.

(921) Animal data on the absorption of Am was reviewed in *Publication 48* (ICRP, 1986), Harrison (1991, 1995) and *Publication 100* (ICRP, 2006). Results for absorption after administration to rats ranged from about 1.2 to 6×10^{-4} for Am nitrate (Sullivan and Crosby,

1975; Ballou et al., 1978; Sullivan, 1980) 0.9 to 1 x 10^{-4} for Am oxide (Sullivan and Crosby, 1975; Sullivan, 1980) and 6 to 7 x 10^{-4} for Am citrate (Sullivan et al., 1985).

(922) Results for other species are in the same range. They ranged from 10^{-5} to 10^{-3} for Am citrate in swine (Eisele and Erickson, 1985; Eisele et al., 1987), 1.7 to 3 x 10^{-4} for Am nitrate in guinea pig (Sullivan et al, 1980), and from 0.6 x 10^{-4} (oxide) to 5 x 10^{-4} (nitrate) in hamsters (Stather et al., 1979; Harrison et al., 1981). In other studies performed on dairy animals, absorption of Am chloride in cows and Am nitrate in goats was estimated to be 2 x 10^{-4} and 2.6 x 10^{-4} respectively (Howard et al., 2009). After ingestion of dusts from the former nuclear weapons site of Maralinga, absorption values measured in rats and guinea pigs ranged from 3 x 10^{-6} to 5 x 10^{-5} (Harrison et al., 1994).

(923) Several factors such as fasting and diet are known to modify the gastrointestinal absorption of americium. In rats, an iron deficient diet may increase the absorption of Am nitrate by a factor 2 to 3 (Sullivan and Ruemmler, 1988).

(924) In *Publication 30* (ICRP, 1979), an absorption value of 5 x 10^{-4} was recommended. In *Publication 48* (1986), a general value of 1 x 10^{-3} for actinides was used. This value was also adopted in *Publication 56* (ICRP, 1989). However, in this report available data provided a sufficient basis for the use of a general value of 5 x 10^{-4} for all actinides other than U.

(925) An f_A value of 5 x 10^{-4} is adopted here for all chemical forms of Am.

23.2.3. Systemic distribution, retention and excretion of americium

23.2.3.1. Summary of the database

Human studies

(926) The biokinetics of systemic americium has been investigated in workers exposed to ^{241}Am or its parent ^{241}Pu, which is tenaciously retained in systemic tissues and decays to ^{241}Am with a half-time of 14.4 y. Reported data for workers include urinary and faecal levels of ^{241}Am, external measurements of ^{241}Am in bone and liver of living subjects, and ^{241}Am in a liver, bone, and other tissues collected at autopsy.

(927) Data for direct intake of relatively pure ^{241}Am (i.e., not mixed with a significant amount of its parent ^{241}Pu) are preferred for modelling americium kinetics but are available for only a few subjects, some of whom received chelation therapy (Wrenn et al., 1972; Whalen and Davies, 1972; Fry, 1976; Rosen et al., 1980; Heid and Robinson, 1985; Breitenstein and Palmer, 1989; Doerfel and Oliveira, 1989; Malátová et al., 2003, 2010). More extensive observations are available for workers whose systemic ^{241}Am burden may have resulted largely from decay of systemic ^{241}Pu (Kathren et al., 1988, 1997; Lynch et al., 1989; Popplewell and Ham, 1989; McInroy et al., 1989; Kathren and McInroy, 1992; Suslova et al., 2013). Data for the latter cases suggest that ^{241}Am migrates from ^{241}Pu over time, resulting in a skeleton to liver activity ratio (ratio of total activity in the skeleton to that in liver) that is typically much larger for ^{241}Am than for its parent ^{241}Pu. However, ^{241}Am produced in bone and perhaps at some soft-tissue sites (e.g. in reticulendothelial cells) may remain with ^{241}Pu for an extended period. Thus, ^{241}Am produced *in vivo* by decay of ^{241}Pu may reflect some combination of the systemic behaviour of americium and that of plutonium.

(928) There are broad similarities in the systemic behaviour of plutonium and initially pure americium but also notable differences, particularly in their long-term distributions. For both elements there is early uptake of about 70-90% of the injected amount by the liver and skeleton,

with the liver initially containing the greater portion on average in mature humans and in most but not all of the studied laboratory animals. Notable differences in the systemic behaviours of these two elements include an initially higher rate of urinary excretion of americium and faster removal of americium from the liver. There are also differences in the sites of deposition of americium and plutonium on bone surfaces and perhaps associated differences in the net rate of removal of these elements from bone.

(929) Sokolova et al. (2013, 2014) assessed the potential contributions of direct intake and *in vivo* production of ^{241}Am to its total body content in a group of workers at the Mayak Production Association. The analysis was based on estimated quantities of ^{241}Am and ^{241}Pu at various work locations over time. The investigators concluded that through the early 1970s the body burdens of ^{241}Am in these workers were likely to have arisen almost entirely from internally deposited ^{241}Pu. For later years there was estimated to be an increasing contribution from direct intake of ^{241}Am resulting from its continual production from decaying ^{241}Pu in spent nuclear fuel stored at the site. They estimated that ^{241}Am produced *in vivo* accounted for roughly 70% of the body burden in the workers by the year 2000.

(930) Americium-241 has been measured in the total body or selected tissues of many Transuranium and Uranium Registry (USTUR) donors with occupational exposures to ^{241}Pu or mixtures of ^{241}Pu and ^{241}Am and in a few cases to relatively pure forms of ^{241}Am. The exposures typically occurred 2-4 decades before death. The ratio of the ^{241}Am content of the skeleton to that of the liver was estimated by the authors of the present report for 101 USTUR cases (Kathren et al., 1988, 1996a, 1996b, 1997; McInroy et al., 1989; Filipy and Kathren, 1996 ; Filipy, 2001, 2002, 2003) under the assumption that reported ^{241}Am concentrations for bone samples were representative of the entire skeleton. The estimated skeleton to liver ratio ranged from 1.2 to 89 with a mean of 15 and median of 7.8. For seven whole body donors (McInroy et al., 1989; Filipy, 2003) the ^{241}Am contents of the skeleton, liver, and other soft tissues represented on average 74.2%, 7.9%, and 17.9% , respectively, of systemic ^{241}Am. Median values were 77.7%, 6.5%, and 13.5%, respectively. Blanchardon et al. (2007) reviewed USTUR data in an effort to derive a typical fractional content of ^{241}Am in non-liver soft tissues from the variable data for the studied tissues. They concluded that the most reliable data, as judged mainly from the sampling process for massive tissues and the level of activity in the samples, indicated that non-liver soft tissues typically contain roughly 15% of the systemic ^{241}Am.

(931) A detailed autopsy study of the tissue distribution of ^{241}Am was conducted for a radiochemist (USTUR Case 102) thought to have been exposed through contamination of a wound while working with an unsealed ^{241}Am source during the period 1952-54, about 25 y before his death (Breitenstein et al., 1985; Heid and Robinson, 1985; McInroy et al., 1985; Durbin and Schmidt, 1985). The first indication that an intake had occurred was detection of radioactivity in a urine sample collected in 1958 as part of a routine surveillance programme. No chelation therapy was performed, although Ca-EDTA was used on one occasion to cause sufficient excretion of activity to identify the radionuclide. The skeleton, liver, kidneys, and other soft tissues contained 82.3%, 6.4%, 0.25%, and 11.0%, respectively, of the systemic burden. About 80% of skeletal activity was contained in compact bone together with the portion of trabecular bone containing fatty marrow, and the remaining 20% was in trabecular bone containing red marrow. Activity was distributed among bone groups as follows: skull, 13.6%; vertebrae, 10.6%; arms and hands, 13.2%; legs and feet, 46.0%; ribs, 5.7%; pelvis, 7.2%; remaining bones, 3.7% (Lynch et al., 1989). The large portion of activity found in the lower extremities may be unusual as the subject's legs contained a considerably larger portion of skeletal mineral than measured in age-matched controls, presumably as a result of the subject's

long-term strenuous programme of running and bicycling (Durbin and Schmidt, 1985; Lynch et al., 1989). Durbin and Schmidt (1985) noted evidence of a gradual trend toward uniform distribution of ^{241}Am in the skeleton and extrapolated the findings for this subject to the following distribution in an adult with a typical distribution of bone mineral: cranium, 17.9%; vertebrae, 12.2%; arms and hands, 15.2%; legs and feet, 38.2%; ribs, 6.3%; pelvis, 6.3%; remaining bones, 3.9%.

(932) Malátová et al. (2003, 2010) measured ^{241}Am in urine and faeces and externally in the skull in seven workers over a period of about 12 y, starting roughly 11-25 y after their imprecisely known times of exposure to ^{241}Am. The source of contamination presumably was AmO_2 powder, used in the production of AmBe neutron sources, smoke alarms, and other ^{241}Am sources. The estimated content of ^{241}Am in the skull was extrapolated to the total skeleton based on the assumption that the skull contains 12.5% of skeletal ^{241}Am. This assumption is based on autopsy measurements of ^{241}Am in bones of four workers (Lynch et al., 1989), three with long-term exposures to plutonium isotopes and one with a brief exposure to ^{241}Am (USTUR Case 102, discussed above). The investigators compared their findings with predictions of the model for systemic americium in adults adopted in *Publications 67* (1993) and applied to workers in *Publications 68* (1994) and 78 (1997). The data are consistent with the urinary to faecal excretion ratio predicted by that model but indicate a lower than predicted ratio of daily urinary ^{241}Am to skeletal ^{241}Am. For example, urinary to skeletal ratios based on the model are about twofold greater on average than estimates of Malátová et al. at roughly 20 y after exposure. Growing differences between average estimates and model predictions are seen after about 22-23 y post exposure, but the increasing discrepancies may arise in part from increased variability in the urinary excretion data and changes in the composition and size of the study group. Uncertainties in the derived urinary to skeletal ratios arise from a number of sources, the most important of which appear to be the fraction of skeletal ^{241}Am in the skull, the externally determined content of ^{241}Am in the skull, and variability in urinary ^{241}Am. It seems doubtful, however, that the methods and assumptions of Malátová and coworkers would consistently underestimate the true urinary to skeletal ^{241}Am ratio by as much as a factor of 2.

(933) Suslova et al. (2013) studied the distribution and excretion of ^{241}Am and plutonium isotopes in workers at the Mayak Production Association. Presumably a substantial portion of ^{241}Am in the studied workers was produced *in vivo* by decay of internally deposited ^{241}Pu. Autopsy data were obtained for 290 workers who died on average 14.7 y ± 12 y (standard deviation) after the end of employment. Urine bioassay measurements were performed about 23-26 y after the end of employment for 47 workers who started work at Mayak from 1949-1964, a period of high inhalation exposures. Subjects of the autopsy study were divided into two groups on the basis of cause of death and histopathological findings in the liver. Group 1 consisted of 33 subjects who died from suicide, accident, or acute cardiovascular problems. Group 2 consisted of 257 subjects with various liver diseases or other chronic illnesses over an extended period before death. For Group 1 the skeleton, liver, kidneys, and other soft tissue contained on average 69.3%, 23.1%, 0.44%, and 7.2%, respectively, of systemic ^{241}Am; and 46.4%, 46.0%, 0.17%, and 7.4%, respectively, of systemic plutonium. For Group 2 the skeleton, liver, kidneys, and other soft tissue contained on average 80.6%, 11.1%, 0.17%, and 8.1%, respectively, of systemic ^{241}Am; and 65.3%, 25.8%, 0.16%, and 8.7%, respectively, of systemic plutonium. The ratio of daily urine excretion of ^{241}Am to total systemic ^{241}Am based on autopsy measurements averaged 1.57×10^{-5} for seven reasonably healthy workers and 2.92×10^{-5} for 15 unhealthy workers. The ratio of daily urine excretion of ^{241}Am to total systemic ^{241}Am based on whole body counting of 29 reasonably healthy workers was 1.8×10^{-5}. For

comparison, the model for systemic americium in adults adopted in *Publication 67* predicts a "urinary to systemic" ratio of 2.4×10^{-5} at 25 y and 2.2×10^{-5} at 35 y after acute intake of ^{241}Am to blood.

Animal studies

(934) The behaviour of americium in blood has been studied in a variety of animals including baboons (Rosen et al., 1972; Cohen and Wrenn, 1973;, Guilmette et al., 1980), monkeys (Durbin, 1973), beagles (Bruenger et al., 1969), sheep (McClellan et al., 1962), rats (Turner and Taylor, 1968; Belyaev, 1969), cows (Sutton et al., 1978), and goats (Sutton et al., 1978). Nearly all americium in blood is found in the plasma fraction. As is the case for plutonium and neptunium, most circulating americium soon becomes bound to plasma proteins, primarily transferrin and citrate. However, the affinity constants are much lower for americium than for plutonium or neptunium, resulting in much faster removal of americium from blood (Paquet and Stather, 1997). Roughly 5-10% of intravenously injected americium remains in blood at 1 h, 0.1 1.5% at 24 h, and 0.03-0.5% at 48 h. Much of the activity that leaves blood in the first hour after injection returns to blood over the next few hours.

(935) Data for rats suggest that a third or more of americium leaving blood in the first few minutes after injection entered soft tissues and extracellular fluids and that much of this returned to blood over the next few hours (Belyaev, 1969; Durbin, 1973). In baboons, a substantial portion of systemic americium remained in the non-liver soft tissues at 1 d (Guilmette et al., 1980).

(936) Following parenteral administration of ^{241}Am citrate to baboons (Rosen et al., 1972; Cohen and Wrenn, 1973), monkeys (Durbin, 1973), and beagles (Lloyd et al., 1970), cumulative urinary excretion over the first 3 weeks amounted to ~10% of the administered activity. In beagles the urinary excretion rates over the first three weeks were similar for americium and curium isotopes (Lloyd et al., 1970; Lloyd et al., 1974). Similar urinary excretion rates were observed for americium and curium in rats following parenteral administration (Durbin, 1973).

(937) In animals of all ages, most systemic Am (typically 80% or more) accumulates in the skeleton and liver within a few days after parenteral injection (Lloyd et al., 1970; Rosen et al., 1972; Durakovic et al., 1973; Moskalev, 1977; Stevens et al., 1977; Guilmette et al., 1980). In monkeys (Durbin, 1973) and beagles (Lloyd et al., 1970) the liver and skeleton contained about 50% and 30%, respectively, of the systemic activity in the first few days or weeks after injection. In baboons (Guilmette et al., 1980) the liver and skeleton contained about 30% and 40%, respectively, of systemic activity in the early weeks after injection.

(938) The systemic biokinetics of americium varies somewhat among species, due largely to differences in the handling of americium by the liver. The studied animal species fall into two main groups with regard to the behaviour of americium in the liver (Taylor, 1984; Durbin and Schmidt, 1985). A group including rats, mice, macaque monkeys, and baboons shows a short residence time in the liver and a relatively high rate of removal of activity from the liver in bile. A second group including dogs and hamsters shows much slower removal from the liver with relatively low loss via biliary secretion. Biological half-times of americium in the liver typically are on the order of 5-15 d in rats and mice, 30-150 d in baboons and monkeys, and a few years in dogs and hamsters. Long-term studies on dogs (Lloyd et al., 1970, Mewhinney et al., 1982) indicate that a large portion of the initial liver burden gradually transfers to the skeleton.

(939) Hamilton (1948) described the sites of bone deposition of americium and curium in rodents as indistinguishable from those of the trivalent elements cerium, promethium, and actinium but different from sites of deposition of the tetravalent elements plutonium, thorium, and zirconium. Later studies involving a variety of animal species indicate that americium deposits on all types of bone surfaces, including resorbing and forming surfaces (Herring, 1962; Lloyd et al., 1972; Durbin, 1973; Priest et al., 1983). Deposition on bone surfaces is more uniform than that of plutonium, although there are gradations in the intensity of the americium label. In dogs and monkeys, initial concentrations on surfaces tended to decrease in the order: resorbing surfaces > resting surfaces > growing surfaces (Herring, 1962; Lloyd et al., 1972; Durbin, 1973). Americium deposits to a greater extent than plutonium on cortical vascular channels (Hamilton, 1948; Herring et al., 1962).

(940) Priest et al. (1983) studied the systemic behaviour of ^{241}Am in rats over the first month after administration, with emphasis on its behaviour in bone. After 1 d the total body contained about 90% of the injected activity. At that time the liver and skeleton contained roughly one-half and one-third, respectively, of the injected amount. The liver content declined with a half-time of about 12 d. Most of the loss from the liver presumably entered the gastrointestinal content in bile, but a gradual increase in the skeletal content over the observation period indicated that part of the activity removed from the liver re-entered the circulation. Activity entering the skeleton deposited on all types of bone surfaces including vascular canals within cortical bone but was preferentially deposited on resorbing surfaces. Bone accretion resulted in burial of surface deposits. Bone resorption caused removal of ^{241}Am from surfaces and its accumulation in phagocytic cells in bone marrow. Transfer of ^{241}Am from the bone marrow back to bone surfaces ("local recycling") appeared to occur. Some "systemic recycling" of resorbed activity (i.e., transfer from bone surface to blood and redeposition on bone surface) may also have occurred. Within the skeleton the largest increases in the ^{241}Am content over the observation period were found for bones with relatively low resorption rates.

(941) Comparison of the long-term gross distributions of skeletal americium and plutonium in dogs indicated more similarities than differences (Lloyd et al., 1972). A notable difference was that the skeletal distribution of plutonium changed little with time after injection while the distribution of americium changed noticeably over time. In particular, three bones with high trabecular content (vertebrae, tail, and sternum) exhibited a decreasing fraction of total skeletal americium with increasing time.

23.2.3.2. Biokinetic model

(942) The biokinetic model for systemic americium applied in this report is described in Section 18.2.3.

23.2.3.3. Treatment of progeny

(943) The treatment of radioactive progeny of americium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

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Table 23.6. Transfer coefficients in the biokinetic model for systemic americium.

From	To	Transfer coefficient (d^{-1})
Blood	Liver 1	11.6
Blood	ST0	10.0
Blood	ST1	1.67
Blood	ST2	0.466
Blood	Cortical bone surface	3.49
Blood	Trabecular bone surface	3.49
Blood	Kidneys 1	0.466
Blood	Right colon content	0.303
Blood	Kidneys 2	0.116
Blood	Testes	0.0082
Blood	Ovaries	0.0026
Blood	Urinary bladder content	1.63
Liver 1	Blood	0.00185
Liver 0	SI content	0.000049
ST0	Blood	1.386
ST1	Blood	0.0139
ST2	Blood	0.000019
Cortical bone marrow	Blood	0.00253
Cortical bone marrow	Cortical bone surface	0.00507
Cortical bone surface	Cortical bone marrow	0.0000821
Cortical bone surface	Cortical bone volume	0.0000411
Cortical bone volume	Cortical bone marrow	0.0000821
Red marrow	Blood	0.0076
Trabecular bone surface	Red marrow	0.000493
Trabecular bone surface	Trabecular bone volume	0.000247
Trabecular bone volume	Red marrow	0.000493
Kidneys 1	Urinary bladder content	0.099
Kidneys 2	Blood	0.00139
Testes	Blood	0.00019
Ovaries	Blood	0.00019

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23.3. Individual monitoring

^{241}Am

(944) Measurements of ^{241}Am concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main techniques used for *in vitro* bioassay are alpha spectrometry and ICP-MS; which is the more sensitive and preferable technique to be applied. *In vivo* lung measurement of ^{241}Am may allow evaluating the intake of radionuclide if the measurement system is sensitive enough. Measurements of ^{241}Am in skeleton and liver are feasible following significant intakes and may be used to determine systemic uptake. The main technique for *in vivo* measurement is gamma spectrometry.

Table 23.7. Monitoring techniques for ^{241}Am.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{241}Am	Urine Bioassay	α spectrometry	0.3mBq/L	0.05 mBq/L
^{241}Am	Urine Bioassay	ICP-MS[a]	$100x10^{-15}$ g/L	$1.0 x10^{-15}$ g/L
^{241}Am	Urine Bioassay	γ-ray spectrometry	0.5 Bq/L	
^{241}Am	Faecal Bioassay	α spectrometry	2 mBq/24h	0.5 mBq/24h
^{241}Am	Lung Measurement[b]	γ-ray spectrometry	8 Bq	2 Bq
^{241}Am	Skeleton Measurement (Knee)[c]	γ-ray spectrometry	10 Bq	
^{241}Am	Skeleton Measurement (Skull)[d]	γ-ray spectrometry	18 Bq	

[a] Inductively Coupled Plasma Mass Spectrometry (ICP-MS).
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[c] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes.
[d] Skull measurement of ^{241}Am is not generally used in routine monitoring of workers. The Monte Carlo programme Visual Monte Carlo was used to simulate the photon emission, to calculate the calibration factor for the geometry and radionuclide, and to calculate the detection limit in the skull.

^{243}Am

(945) Measurements of ^{243}Am concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main techniques used for *in vitro* bioassay are alpha spectrometry and ICP-MS; which is the more sensitive and preferable technique to be applied. *In vivo* lung measurement of ^{243}Am may allow evaluating the intake of radionuclide if the measurement system is sensitive enough. Measurements of ^{243}Am in skeleton and liver are feasible following significant intakes and may be used to determine systemic uptake. The main technique for *in vivo* measurement is gamma spectrometry.

Table 23.8. Monitoring techniques for ^{243}Am.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit

^{243}Am	Urine Bioassay	α spectrometry	0.2 mBq/L	
^{243}Am	Urine Bioassay	ICP-MS[a]	$50x10^{-15}$ g/L	$1x10^{-15}$ g/L
^{243}Am	Faecal Bioassay	α spectrometry	0.2 mBq/24h	
^{243}Am	Lung Measurement[b]	γ-ray spectrometry	4 Bq	
^{243}Am	Skeleton Measurement (Knee)[c]	γ-ray spectrometry	10 Bq	
^{243}Am	Skull Measurement[d]	γ-ray spectrometry	10 Bq	

[a] Inductively Coupled Plasma Mass Spectrometry (ICP-MS)
[b] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.
[c] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes.
[d] Skull measurement of ^{243}Am is not generally used in routine monitoring of workers. The Monte Carlo programme Visual Monte Carlo was used to simulate the photon emission, to calculate the calibration factor for the geometry and radionuclide, and to calculate the detection limit in the skull.

23.4. Dosimetric data for americium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Ballou, J. E., Price, K. R., Gies, R. A., Doctor, P. G., 1978. The influence of DTPA on the biological availability of transuranics. Health Phys. 34, 445–50.

Ballou, J. E., Gies, R. A., 1978. Inhalation toxicology of $^{241}Am(NO_3)_3$. Pacific Northwest Laboratory Annual Report for 1977 to the DOE Assistant Secretary for Environment, PNL–2500 Part 1, Biomedical Sciences, 3.36–3.37. Richland, Washington. Available from National Technical Information Service, Springfield, Virginia.

Belyaev, Yu. A., 1971. Americium-241 distribution in rats and the effect of complexing substances on its elimination. In: Radioactive isotopes and the body, ed. by Yu. I. Moskalev. Izdatel'stvo Meditsina, Moscow, 1969. Translation AEC tr 6944, 168-174.

Blanchardon, E., Leggett, R. W., Eckerman, K. F., 2007. Some elements for a revision of the americium reference biokinetic model. Radiat. Prot. Dosim. 127, 131–135.

Breitenstein, B. D., Palmer, H. E., 1989. Lifetime follow-up of the 1976 americium accident victim. Radiat. Prot. Dosim. 26, 317-322.

Breitenstein, B. D., Newton, C. E. Norris, H. T. 1985. The U.S. Transuranium Registry report on the 241Am content of a whole body. Part 1: Introduction and history of the case. Health Phys. 49, 559–567.

Bruenger, F. W., Stevens, W., Stover, B. J., 1969. Americium-241 in the blood: *in vivo* and *in vitro* observations. Radiat. Res. 37, 349–360.

Buldakov, L. A., Kalmykova, Z. I., 1979, Postinhalation kinetics of metabolism of americium 241 and absorbed doses in organs. Translated from Radiobiologiya, 19, 462–467. Document No DOE-tr–4/15, 171–176.

Buldakov, L. A., Kalmykova, Z. I., Nifatov, A. P.,et al., 1972. Metabolism and biological effects of inhaled ^{241}Am and ^{239}Pu in dogs. Health Phys. 22, 873–874.

10939 Bull, R. K., Morrison, R. T., Talbot, R., Roberts, G. A., 2003. An intake of americium oxide
10940 powder: Implications for biokinetic models for americium Radiat. Prot. Dosim. 105,
10941 369–373.
10942 Carbaugh, E. H., Lynch, T. P., Cannon, C. N., Lewis, L. L., 2010. Case study: Three acute
10943 ^{241}Am inhalation exposures with DTPA therapy. Health Phys. 99, 539–546.
10944 Cohen, N., LoSasso, T., Wrenn, M. E., 1979. Metabolism of americium-241 in a man: An
10945 unusual case of internal contamination of a child and his father. Science 206, 64–66.
10946 Cohen, N., Wrenn, M. E., 1973. Metabolic characteristics of Am 241 in the adult baboon.
10947 Radiat. Res. 55, 129–143.
10948 Craig, D. K., Cannon, W. C., Catt, D. L., et al., 1975, Distribution of ^{241}Am and ^{244}Cm in dogs
10949 after inhalation of the oxides. Pacific Northwest Laboratory Annual Report for 1974 to
10950 the USAEC Division of Biomedical and Environmental Research. BNWL-1950, Part
10951 1, Biomedical Sciences. 17–18. Richland, Washington. Available from National
10952 Technical Information Service, Springfield, Virginia.
10953 Craig, D. K., Park, J. F., Power, G. J. and Catt, D. L., 1979. The disposition of americium-
10954 241 oxide following inhalation by beagles. Radiat. Res. 78, 129–143.
10955 Crawley, F. E. H., Goddard, E. A., 1976. The translocation of 241-americium and 244-curium
10956 from the respiratory system of a rat. Health Phys. 30, 191–197.
10957 Doerfel, H., Oliveira, C. A. N., 1989. *In vivo* measurement of Am-241 organ burdens:
10958 Techniques and results of measurements after an incident in an industrial research
10959 institute. Radiat. Prot. Dosim. 26, 189–193.
10960 Durakovic, A. B., Hollins, J. G., Storr, M. C., 1973. The influence of age and sex on the
10961 metabolism of americium by rats. Health Phys. 24, 541–546.
10962 Durbin, P. W., Schmidt, C. T., 1985. The U.S. Transuranium Registry report on the ^{241}Am
10963 content of a whole body. Part V: Implications for metabolic modelling. Health Phys.
10964 49, 623–661.
10965 Durbin, P.W., 1973. Metabolism and biological effects of the transplutonium elements. In:
10966 Uranium, Plutonium, Transplutonium Elements (Ed. by H.C.Hodge, J.N.Stannard &
10967 J.B.Hursh), 739–883. Berlin, Springer Verlag.
10968 Edvardsson, K. A., Lindgren, L., 1976. Elimination of americium-241 after a case of
10969 accidental inhalation. In: Diagnosis and Treatment of Incorporated Radionuclides.
10970 Proceedings of a Seminar held by the International Atomic Energy Agency and the
10971 World Health Organization, December 8–12, 1975, Vienna, 497–502. International
10972 Atomic Energy Agency, Vienna, Austria.
10973 Eidson, A.F., Mewhinney, J.A., 1983. *In vitro* dissolution of respirable aerosols of industrial
10974 uranium and plutonium mixed-oxide nuclear fuels. Health Phys. 45, 1023–1037.
10975 Eisele, G. R., Bernard, S. R., Nestor, C. W., 1987. Gastrointestinal absorption of americium -
10976 241 by orally exposed swine: comparison of experimental results with predictions of
10977 metabolic models. Radiat.Res. 112, 62–73.
10978 Eisele, G. R, Erickson, B. H., 1985. Gonadal retention and localization of 241Am in orally
10979 exposed swine. Health Phys. 49, 1276–1279.
10980 Filipy, R. E., 2001. Analyses of whole body donations. USTUR annual report for February 1,
10981 2000 through January 31, 12–17.
10982 Filipy, R. E., 2002. USTUR case 0425. USTUR annual report for the period February 1, 2001
10983 – January 31, 2002, 18–19.
10984 Filipy, R. E., 2003. Estimation of actinide body burdens on the basis of tissue samples
10985 collected at autopsy. USTUR annual report for the period February 1, 2002 – January

31, 2003, 32–35.
Filipy, R. E., Kathren, R. L., 1996. Changes in soft tissue concentrations of plutonium and americium with time after human occupational exposure. Health Phys. 70, 153–159.
Fojtik, P., Malátová, I., Bečková, V., Pfeiferová, V., 2013. A case of occupational internal contamination with ^{241}Am. Radiat. Prot. Dosim. 156, 190–197.
Fry, F. A., 1976. Long-term retention of americium-241 following accidental inhalation. Health Phys. 31, 13–20.
Gregoratto, D., Bailey, M.R., Marsh, J.W., 2011. Particle clearance in the alveolar–interstitial region of the human lungs: model validation. Radiat. Prot. Dosim. 144, 353–356.
Guilmette, R. A., 2011, personal communication.
Guilmette, R. A., Cohen, N., Wrenn, M. E., 1980. Distribution and retention of ^{241}Am in the baboon. Radiat. Res. 81, 100–119.
Hamilton, J. G. 1948. The metabolic properties of the fission products and actinide elements. Rev. Mod. Phys. 20, 718–728.
Harrison, J. D., 1995 . Ingested radionuclides. In Radiation and Gut. Potten C.S. and Hendry J.H (Eds). Elsevier: Amsterdam.253–289.
Harrison, J. D., 1983. The gastrointestinal absorption of plutonium, americium and curium. Radiat. Prot. Dosim. 5, 19–35.
Harrison, J. D., 1991. The gastrointestinal absorption of the actinide elements. Science Total Environ. 100, 43–60.
Harrison, J. D., Stather, J. W., Smith, H., Stradling, G. N., 1981. The influence of environmental factors on the gastrointestinal absorption of plutonium and americium. Actinides in man and animals. Proceeding of the snowbird actinide workshop October 15-17, 1979, 323-337.
Harrison, J. D., Naylor, J. P., Stather, J. W., 1994. The gastrointestinal absorption of plutonium and americium in rats and guinea pigs after ingestion of dusts from the former nuclear weapons site of Maralinga: implications for human exposure. Sci. Total Environ. 143, 211–220.
Heid, K. R., Robinson, B., 1985. The U.S. Transuranium Registry report on the ^{241}Am content of a whole body. Part II: Estimate of the initial systemic burden. Health Phys. 49, 569–575.
Herring, G. M., Vaughan, J., Williamson, M., 1962. Preliminary report on the site of localization and possible binding agent for yttrium, americium and plutonium in cortical bone. Health Phys. 8, 717–724.
Howard, B. J., Beresford, N. A., Barnett, C. L., Fesenko, S., 2009. Gastrointestinal fractional absorption of radionuclides in adult domestic ruminants. J. Environ. Radioact. 100 (12), 1069-1078.
Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1986. Transfer of environmental plutonium and americium across the human gut. Science Total Environ. 53, 89–109.
Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1990. Transfer of environmental plutonium and americium across the human gut: A second study. Science Total Environ. 90, 273–282.
ICRP, 1959. Permissible dose for internal radiation, ICRP Publication 2. Pergamon Press, Oxford.
ICRP, 1972. The metabolism of compounds of plutonium and other actinides. ICRP Publication 19. Pergamon Press, Oxford.

ICRP, 1979. Limits for intakes of radionuclides by workers, ICRP Publication 30, Part 1. Ann. ICRP 2(3/4).

ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48, Ann. ICRP 16(2/3).

ICRP, 1989. Age-dependent doses to members of the public from intake of radionuclides: Part1. ICRP Publication 56. Ann. ICRP 20(2).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).

ICRP, 1994a. Human respiratory tract model for radiological protection. ICRP Publication 66. Ann. ICRP 24 (1-3).

ICRP, 1994b. Dose coefficients for intakes of radionuclides by workers. ICRP Publication 68. Ann. ICRP 24(4).

ICRP, 1995. Age-dependent doses to members of the public from intake of radionuclides: Part 4. Inhalation dose coefficients, ICRP Publication 71. Ann. ICRP 25(3/4).

ICRP, 1997. Individual monitoring for internal exposure of workers – Replacement of ICRP Publication 54. ICRP Publication 78. Ann. ICRP 27(3/4).

ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. ICRP Supporting Guidance 3. Ann. ICRP 32(1/2).

ICRP, 2006. Human alimentary tract model for radiological protection. ICRP publication 100. Ann. ICRP 36(1/2).

Il'in, L. A., Popov, B. A., Zalikin, G. A., et al., 1975. Metabolism and acceleration of the elimination of americium-241 from the organism after inhalation of the isotope. Radiobiology [English translation of Russian journal "Radiobiologiya"]; ERDA-tr-51, 15, 86–90.

James, A. C., Stather, J. W., Strong, J. C., et al., 1978. The translocation of americium-241 from hamster lung after its inhalation as the dioxide. National Radiological Protection Board Annual Research and Development Report 1977, NRPB/R&D2, 41–42. National Radiological Protection Board, Chilton, UK.

Jeanmaire, L., Ballada, J., 1970. Etude de deux cas de contamination par ^{241}Am. In: Proceedings of the International Radiation Protection Association Congress, Brighton, England, May 3–8, 1970, 229–244.

Kathren, R. L., Filby, R. H., Dagle, G. R., 1996a. Plutonium and americium in the tissues of two whole body donors, USTUR cases 0262 and 0769: Final radiochemical results. USTUR annual report for October 1, 1995 through September 30, 1996, 119–121.

Kathren, R. L., McInroy, J. F., 1992. Implications of postmortem human tissue analysis on biokinetic models for actinides. J. Radioanal. Nucl. Chem. 156, 413–424.

Kathren, R. L., McInroy, J. F., Reichert, M. M., Swint, M. J., 1988. Partitioning of Pu-238, Pu-239 and Am-241 in skeleton and liver of U.S. Transuranium Registry autopsy cases. Health Phys. 54, 181–188.

Kathren, R. L., Pham, M. V., Ronald, E. P., 1997. Actinide concentrations in tissue donations from routine autopsy donations to the USTUR. USTUR annual report for October 1, 1996 through September 30, 1997, 99–249.

Kathren, R. L., Russel, J. J., Filby, R. H., 1996b. ^{238}Pu, ^{239}Pu and ^{241}Am in the tissues of USTUR case 0259, a whole body donor with an acute accidental exposure to 238Pu: final radiochemical results. USTUR annual report for October 1, 1995 through September 30, 1996, 82–84.

11078 Kathren, R. L., Lynch, T. P., Traub, R. J., 2003. Six-year follow-up of an acute ^{241}Am
11079 inhalation intake. Health Phys. 84, 576–581.
11080 Khokhryakov, V. F., Suslova, K. G., Tsevelyova, I. A., Aladova, E. E., Filipy, R. E. 1998,
11081 Classification of alpha-active workplace aerosols based on coefficient of
11082 transportability as measured by the dialysis method. J. Radoioanal. Nucl. Chem. 234,
11083 209–212.
11084 Lafuma, J., Nénot, J.C., Morin, M., et al., 1974. Respiratory carcinogenesis in rats after
11085 inhalation of radioactive aerosols of actinides and lanthanides in various physico-
11086 chemical forms. In: Experimental Lung Cancer: Carcinogenesis and Bioassays. (Eds.
11087 Karbe, E. and Park, J. F.) 443–453. Springer-Verlag, Berlin.
11088 Leggett, R. W., 1992. A retention-excretion model for americium in humans. Health Phys. 62,
11089 288–310.
11090 Lloyd, R. D., Atherton, D. R., Mays, C. W., McFarland, S. S., Williams, J. L., 1974. The early
11091 excretion, retention and distribution of injected curium citrate in beagles. Health Phys.
11092 27, 61–67.
11093 Lloyd, R. D., Mays, C. W., Taylor, G. N., Atherton, D. R., 1970. Americium-241 studies in
11094 beagles. Health Phys. 18, 149–156.
11095 Lloyd, R. D., Mays, C. W., Jee, W. S. S., Taylor, G. N., 1972. Skeletal distribution of ^{241}Am
11096 and ^{239}Pu in beagles: Can they be compared. In: Research in radiobiology. University
11097 of Utah. COO-119-246, 249–255.
11098 Luciani, A., Polig, E., Lloyd, R.D., Miller, S.C., 2006. Americium in the beagle dog:
11099 Biokinetic and dosimetric model. Health Phys. 90, 459–470.
11100 Lynch, T. P., Kathren, R. L., Dagle, G. E., McInroy, J. F., 1989. Comparative skeletal
11101 distribution of Am and Pu in man, monkey, and baboon. Health Phys. 57, 81–88.
11102 Lyubchanskiy, E.R., Nifatov, A.P., 1972. Americium-241 metabolism after inhalation. In:
11103 Biological Effects of Radiation from External and Internal Sources, Document No
11104 AEC–tr–7457, 412–426.
11105 Malátová, I., Bečková, V., Vrba, T., 2007. Evaluation of committed effective doses from
11106 internal contamination of ^{241}Am using experimentally determined parameters of the
11107 contaminant. Radiat. Prot. Dosim. 127, 521–525.
11108 Malátová, I., Foltánová, Š, Becková, V., et al., 2003. Assessment of occupational doses from
11109 internal contamination with ^{241}Am. Radiat. Prot. Dosim. 105, 325–328.
11110 Malátová, I., Vrba, T., Becková, V., Pospíšilová, H. 2010. Twelve years of follow up of cases
11111 with old ^{241}Am internal contamination. Health Phys. 99, 495–502.
11112 McClellan, R. O., Casey, H. W., Bustad, L. K., 1962. Transfer of some transuranic elements
11113 to milk. Health Phys. 8, 689–694.
11114 McClellan, R.O., 1972. Progress in studies with transuranic elements at the Lovelace
11115 Foundation. Health Phys, 22, 815–822.
11116 McInroy, J. F., Kathren, R. L., Swint, M. J., 1989. Distribution of plutonium and americium
11117 in whole bodies donated to the United States Transuranium Registry. Radiat. Prot.
11118 Dosim. 26, 151–158.
11119 McInroy, J. F., Boyd, H. A., Eutsler, B. C., Romero, D., 1985. The U.S. Transuranium
11120 Registry report on the ^{241}Am content of a whole body. Part IV: Preparation and
11121 analysis of the tissues and bones. Health Phys. 49, 587–621.
11122 McInroy, J. F., Kathren, R. L., Toohey, R. E., Swint, M. J., Breitenstein Jr., B. D., 1995.
11123 Postmortem tissue contents of 241Am in a person with a massive acute exposure.
11124 Health Phys. 69, 318–323.

Ménétrier, F., Taylor, D. M., Comte, A., 2008. The biokinetics and radiotoxicology of curium: A comparison with americium. Appl. Radiat. Isot. 66, 632–647.

Mewhinney, J. A., Griffith, W. C., 1982. Models of Am metabolism in beagles and humans. Health Phys. 42, 629–644.

Mewhinney, J. A., Griffith, W. C., 1983. A tissue distribution model for assessment of human inhalation exposures to $^{241}AmO_2$. Health Phys. 44, Suppl. 1, 537–544.

Mewhinney, J. A., Muggenburg, B. A., 1985. Comparison of retention of ^{241}Am in immature, young adult and aged dogs and in monkeys after inhalation of $^{241}AmO_2$. Inhalation Toxicology Research Institute Annual Report 1984–1985, LMF–114, 348–353. Lovelace Biomedical & Environmental Research Institute, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Mewhinney, J. A., Griffith, W. C., Muggenburg, B. A., 1978. Biomathematical models for ^{241}Am inhaled as $^{241}AmO_2$ by the beagle dog. Inhalation Toxicology Research Institute Annual Report 1977–1978, LF–60, 43–47. Lovelace Biomedical & Environmental Research Institute, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Mewhinney, J. A., Griffith, W. C., Muggenburg, B. A., 1982. The influence of aerosol size on retention and translocation of ^{241}Am following inhalation of $^{241}AmO_2$ by beagles. Health Phys. 42, 611–627.

Mewhinney, J. A., Hobbs, C. H., Mo, T., 1976. Toxicity of inhaled polydisperse or monodisperse aerosols of $^{241}AmO_2$ in Syrian hamsters III. Inhalation Toxicology Research Institute Annual Report 1975–1976, LF–56, 251–258. Lovelace Biomedical & Environmental Research Institute, Albuquerque, New Mexico. Available from National Technical Information Service, Springfield, Virginia.

Morgan, A., Holmes, A., Pratley, F.W., 1990. Solubility in the rat lung of actinides associated with estuarine silt from West Cumbria. J. Radiol. Prot. 10, 135–142.

Moskalev, Y. I., 1977. Problems of the radiobiology of americium-241. DOE tr-190, , translated from the Russian book "Problemy Radiobiologii Ameritsiya 241", Atomizdat.

Nénot, J. C., Masse, R., Morin, M., Lafuma, J., 1972. An experimental comparative study of the behaviour of ^{237}Np, ^{238}Pu, ^{239}Pu, ^{241}Am and ^{242}Cm in bone. Health Phys. 22, 657–665.

Nénot, J. C., Morin, M., Lafuma, J., 1971. Experimental study of skeletal decontamination following inhalation of americium nitrate [Etude Expérimentale de la décontamination du squelette après inhalation de nitrate d'américium.] Health Phys. 21, 395–400.

Newton, D., Taylor, B. T., Eakins, J. D., 1983. Differential clearance of plutonium and americium oxides from the human lung. Health Phys. 44, 431–439.

Paquet, F., Stather, J. W., 1997. Americium. In: Toxiques Nucléaires (Ed. by P.Galle), 247–279. Paris, Masson.

Popplewell, D. S., Ham, G. J., 1989. Distribution of plutonium and americium in tissues from a human autopsy case. J. Radiol. Prot. 9, 159–164.

Priest, N. D., Howells, G., Green, D., Haines, J. W., 1983. Pattern of uptake of americium-241 by the rat skeleton and its subsequent redistribution and retention: implications for human dosimetry and toxicology. Human Toxicology 2, 101–120.

Ramounet, B., Matton, S., Guezingar-Liebard, F., et al., 2000. Comparative biokinetics of plutonium and americium after inhalation of PuO_2 and mixed oxides $(U, Pu)O_2$ in rat. Int. J. Radiat. Biol. 76, 215–222.

11172 Ramounet-Le Gall B., Fritsch P., Abram M.C., et al., 2002. Mesure de paramètres spécifiques
11173 pour le calcul de dose après inhalation d'aérosols renfermant des éléments
11174 transuraniens. Can. J. Physiol. Pharmacol. 80, 727–732.
11175 Rateau-Matton S., Ansoborlo E., Hodgson A., 2004. Comparative absorption parameters of
11176 Pu and Am from PuO2 and mixed oxide aerosols measured after *in vitro* dissolution
11177 test and inhalation in rats. Int. J. Radiat. Biol. 80, 777–785.
11178 Robinson, B., Heid, K.R., Aldridge, T.L., Glenn, R.D., 1983. 1976 Hanford americium
11179 exposure incident: Organ burden and radiation dose estimates. Health Phys. 45, 911–
11180 921.
11181 Robinson, B., Heid, K.R., Aldridge, T.L., Glenn, R.D., 1983. 1976 Hanford americium
11182 exposure incident: Organ burden and radiation dose estimates. Health Phys. 45, 911–
11183 921.
11184 Rosen, J. C., Cohen, N., Wrenn, M. E., 1972. Short term metabolism of Am 241 in the adult
11185 baboon. Health Phys. 22, 621–626.
11186 Rosen, J. C., Gur, D., Pan, S. F., Wald, N., Brodsky, A., 1980. Long-term removal of Am-241
11187 using Ca DTPA. Health Phys. 39. 601–609.
11188 Rundo, J., Keane, A. T., May, H. A., 1971. Measurement of americium-241 in a 10-year old
11189 boy. In: Symposium on the Assessment of Radioactive Organ and Body Burdens.
11190 Proceedings of a Symposium held in Stockholm, November 2–26, 1971, Document
11191 No IAEA/SM–150/32. International Atomic Energy Agency, Vienna.
11192 Sanders, C. L., Mahaffey, J. A., 1983. Inhalation carcinogenesis of high-fired $^{241}AmO_2$ in rats.
11193 Radiat. Res. 94, 66–80.
11194 Sanders, S. M. Jnr., 1974. Excretion of ^{241}Am and ^{244}Cm following two cases of accidental
11195 inhalation. Health Phys. 27, 359–365.
11196 Scott, K. G., Copp, D. H., Axelrod, D. J., Hamilton, J. G., 1948. The metabolism of
11197 americium in the rat. J. Biol. Chem. 175, 691–703.
11198 Sérandour, A. L., Fritsch, P., 2008. Pulmonary retention of actinides after dissolution of PuO2
11199 aerosols: interest in modelling DTPA decorporation. Radioprotection 43, 239–253.
11200 SFMT, 2011. French Society of Occupational Medicine. Good practice recommendations:
11201 medical monitoring of occupational internal exposure to radionuclides in nuclear
11202 installations.
11203 Sokolova, A. B., Suslova, K. G., Khokhryakov, V. F., et al., 2013. Development of an
11204 inhalation intake model for ^{241}Am based on Mayak Production Association worker
11205 data. Health Phys. 105, 21–30.
11206 Sokolova, A. B., Suslova, K. G., Efimov, A. V., Miller, S. C., 2014. Use of *in vivo* counting
11207 measurements to estimate internal doses from ^{241}Am in workers from the Mayak
11208 Production Association. Health Phys. 107, 135–142.
11209 Sokolova, A. B., Suslova, K. G., Khokhryakov, V. F., et al., 2013. Development of an
11210 inhalation intake model for ^{241}Am based on Mayak Production Association worker
11211 data. Health Phys. 105, 21–30.
11212 Stanley, J. A., Eidson, A. F., Mewhinney, J. A., 1982. Distribution, retention and dosimetry of
11213 plutonium and americium in the rat, dog and monkey after inhalation of an industrial-
11214 mixed uranium and plutonium oxide aerosol. Health Phys. 43, 521–530.
11215 Stather, J. W., James, A. C., Brightwell, J., Rodwell, P., 1979. The clearance of plutonium
11216 and americium from the respiratory system of rodents after the inhalation of oxide
11217 aerosols of these actinides either alone or in combination with other metals.
11218 Proceedings of the Symposium on Biological Implications of Radionuclides Released

from Nuclear Industries. March 26-30, 1979. Vienna, Austria. International Atomic Energy Agency, 3-25.

Stather, J. W., Harrison, J. D., Rodwell, P., David, A. J., 1979. The gastrointestinal absorption of plutonium and americium in the hamster. Phys. Med. Biol. 24, 396–407.

Stather, J. W., Priest, N. D., 1977. The pulmonary clearance and the comparative metabolism of plutonium-238, plutonium-239, americium-241 and curium-242 in the rat. NRPB Annual Research and Development Report for 1976. NRPB R&D 1, 46–48. (Chilton, HMSO).

Stevens, W., Atherton, D. R., Bates, D., et al., 1977. Retention and distribution of AmIII-241 in neonatal beagles. Health Phys. 33, 553–559.

Stradling, G. N., Ham, G. J., Smith, H., Breadmore, S. E., 1978. The mobility of americium dioxide in the rat. Radiat. Res., 76, 549–560.

Stradling, G. N., Hodgson, S. A., Hodgson, A., et al., 1998. Dose coefficients and assessment of intake after inhalation of contaminated dusts from Palomares. Radiat. Prot. Dosim. 79, 179–182.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1987. Studies on the metabolic behaviour of industrial actinide-bearing aerosols after deposition in the rat lung: An experimental basis for interpreting chest monitoring data and assessing limits on intake for workers. Human Toxicol., 6, 365–375.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1989. Assessment of intake of an actinide-bearing dust formed from the pond storage of spent magnox fuel. Radiat. Prot. Dosim. 26, 201–206.

Stradling, G. N., Stather, J. W., Gray, S. A., et al., 1992. Radiological implications of inhaled ^{239}Pu and ^{241}Am in dusts at the former nuclear test site in Maralinga. Health Phys. 63, 541–650.

Sullivan, M. F, Crosby, A. L., 1975. Absorption of uranium-233, neptunium-237, plutonium-238, americium-241, curium-244 and einsteinium-253 from the gastrointestinal tract of newborn and adults rats. Battelle; BNWL-1950 Pt1 UC-48; BNWL-1950 Pt1 UC-48.

Sullivan, M. F, Miller, B. M., Ruemmler, P. S., 1985. Further studies on the influence of chemical for and dose on absorptions on Np,Pu,Am and Cm from the gastrointestinal tracts of adult an neonatal rodents. Health Phys. 48, 61–73.

Sullivan, M. F., 1980. Absorption of actinide elements from the gastrointestinal tract of rats, guinea pigs and dogs. Health Phys. 38, 159–171.

Suslova, K. G., Sokolova, A. B., Efimov, A. V., Miller, S. C., 2013. Accumulation, organ distribution, and excretion kinetics of ^{241}Am in Mayak Production Association workers. Health Phys. 104, 313–324.

Sutton, W. W., Patzer, R. G., Mullen, A. A., Hahn, P. B., Potter, G. D., 1978. Metabolism of americium-241 in dairy animals. In: Selected environmental plutonium research reports of the Nevada Applied Ecology Group, ed. by M. G. White and P. B. Dunaway. Report NVO-192, 19–43.

Taya, A., Mewhinney, J. A., Guilmette, R. A., 1994. Subcellular distribution of ^{241}Am in Beagle lungs after inhalation of $^{241}Am(NO_3)_3$. In Inhaled Particles VII. Proceedings of International Symposium organised by the British Occupational Hygiene Society, Edinburgh, 16-22 September 1991, (Eds. Dodgson J, McCallum RI), Pergamon Press, Oxford, United Kingdom. Ann. Occup. Hyg. 38, Suppl. 1, 265–268.

11264 Taya, A., Hotz, G., Mauser, R. Seidel, A., 1988. Transport of intratracheally injected ^{241}Pu
11265 and ^{241}Am hydroxide polymers in rat lung: Biochemical and electron microscopic
11266 autoradiographic studies. Ann. Occup. Hyg. 32, 987–996.
11267 Taylor, D. M., 1984. The retention of plutonium and americium in liver: an interspecies
11268 comparison. voir biblio 1, 431–434.
11269 Thomas, R. G., McClellan, R. O., Thomas, R. L., et al., 1972. Metabolism, dosimetry and
11270 biological effects of inhaled ^{241}Am in beagle dogs. Health Phys. 22, 863–871.
11271 Toohey, R. E., Essling, M. A., 1980. Measurements of ^{241}Am *in vivo* at long times after
11272 inhalation. Health Phys. 38, 139–145.
11273 Truckenbrodt, R., Ruhm, W., Nosske, D., Konig, K., 2000. Application of recent ICRP
11274 models to estimate intake and dose from *in vivo* and excretion measurements of a
11275 single ^{241}Am inhalation case. Radiat. Prot. Dosim., 89, 287–293.
11276 Tseveleva, I. A., Yerokhin, R. A., 1969. Behavior of americium 241 in the body of rats under
11277 intraperitoneal and intratracheal administration. Translated from Radioactive Isotopes
11278 and the Body, (Ed. Moskalev, Y.) Document No AEC–tr–7195, 161–167, US Atomic
11279 Energy Commission.
11280 Turner, G. A., Taylor, D. M., 1968. The binding of plutonium to serum proteins *in vitro*.
11281 Radiat. Res. 36, 22–30.
11282 Vasilenko, E. K., Khokhryakov, V. F., Miller, S. C., et al., 2007. Mayak worker dosimetry
11283 study: an overview. Health Phys. 93, 190–206.
11284 Wernli, C., Eikenberg, J., Marzocchi, O., et al., 2015. 30-year follow-up of a Pu/Am
11285 inhalation case. Radiat. Prot. Dosim. 164, 57–64.
11286 Whalen, R. P., Davies, S., 1972. Americium contamination incident in a New York State
11287 Health Department laboratory. Radiation and Data Reports, 249–253.
11288 Wrenn, McD. E., Rosen, J. C., Cohen, N., 1972. *In vivo* measurement of americium 24 in
11289 man. In: Assessment of radioactive contamination in man, Proceedings of a
11290 symposium organized by IAEA and WHO, Stockholm, 22-26 November 1971; IAEA
11291 SM 150/38; Vienna: International Atomic Energy Agency, 595–621.
11292 Zalikin, G. A., Moskalev, Y. I., Petrovich, I. K., 1968. Distribution and biological effects of
11293 americium-241 metabolism following inhalation and intratracheal administration.
11294 Radiobiologiya 8, 65–71. English translation AEC-tr-6950.
11295 Zalikin, G. A., Popov, B. A., 1977. Kinetics of americium-241 metabolism following
11296 inhalation and intratracheal administration. Translated from Radiobiologiya, 17, 152–
11297 156. Document No ERDA–tr–285/1, 188–192.
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24. CURIUM (Z=96)

24.1. Chemical Forms in the Workplace

(946) Curium is an actinide element which mainly occurs in oxidation state III. Lanthanides such as Eu(III) or Gd(III), and Am(III) are good chemical analogues of Cm(III). Curium may be encountered in industry in a variety of chemical and physical forms, including oxides, (Cm_2O_3, CmO_2), chlorides, oxalates, citrates, nitrates, and may be found together with plutonium compounds including mixed oxide reactor fuel (MOX). Curium-244 is the major isotope of curium found in nuclear reactors and irradiated fuel.

Table 24.1. Isotopes of curium addressed in this report.

Isotope	Physical half-life	Decay mode
Cm-238	2.4 h	EC, A
Cm-239	2.9 h	EC, B+
Cm-240	27 d	A, SF
Cm-241	32.8 d	EC, A
Cm-242[a]	162.8 d	A, SF
Cm-243[a]	29.1 y	A, EC
Cm-244[a]	18.10 y	A, SF
Cm-245	8.5E+3 y	A, SF
Cm-246	4.76E+3 y	A, SF
Cm-247	1.56E+7 y	A
Cm-248	3.48E+5 y	A, SF
Cm-249	64.15 m	B-
Cm-250	8.3E+3 y	A, B-, SF
Cm-251	16.8 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

24.2. Routes of Intake

24.2.1. Inhalation

Absorption Types and parameter values

(947) Some limited information was found on the behaviour of inhaled curium in man. Information on absorption from the respiratory tract is available from experimental studies of curium, mostly as oxides of variable stoichiometry, and for a few as chloride, nitrate and citrate. The few reported incidents of occupational curium intakes in man have clearly shown high rates of curium urinary excretion soon after intake, and studies in animals have shown that clearance from lung to blood is very significant and relatively fast (Bair, 1976; Métivier, 1988). Curium retention in lung is lower than that of plutonium, and closer to that of americium (Stather and Priest, 1977).

(948) Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values: the revised Human Respiratory Tract Model (ICRP, 2014), the Human Alimentary Tract Model (ICRP, 2006), the human systemic model for Am and Cm (ICRP, 1993), the Cm model for the dog of Guilmette and Mewhinney (1989), the rat model for particle transport in the respiratory tract of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002) and the function describing the whole body retention of injected Cm in rats from Ménétrier et al. (2008). Unless specific data indicated otherwise, in analyses carried out here, s_r, f_b, and s_b were fixed at the values assessed for curium below: $s_r = 0.4\ d^{-1}$, $f_b = 0.02$, and $s_b = 0\ d^{-1}$. However, as described in the general actinide section, absorption parameter values based on plutonium ($s_r = 0.4\ d^{-1}$; $f_b = 0.002$; $s_b = 0\ d^{-1}$) are applied in this document to the transplutonium elements for radiation protection purposes. Absorption parameter values and Types, and associated f_A values for particulate forms of curium, are given in Table 24.7.

Curium oxide

(949) McClellan et al. (1972) followed the biokinetics of ^{244}Cm in dogs for 256 d after inhalation of $^{244}CmO_{1.73}$ or $^{244}CmCl_3$ in a CsCl vector (see below). Curium was rapidly absorbed into body fluids, at a similar rate for both chemical forms, and translocated to skeleton and liver. By 16 d, lung retention was about 16% of the Initial Lung Deposit (ILD). At 64 d post-inhalation, about 11% ILD of the oxide was retained in lungs. These results were in agreement with the urinary excretion data obtained after accidental human exposure (Bernard and Poston, 1976). Analysis here of the oxide data gave $f_b = 0.03$, $s_b = 0$, $f_r = 0.8$, $s_r = 0.4\ d^{-1}$ and $s_s = 0.02\ d^{-1}$. This is consistent with assignment to Type M but close to Type F behaviour.

(950) Sanders (1974) described two cases of occupational exposure to ^{244}Cm. The second case was an accidental inhalation of mixed oxides of ^{244}Cm (75% of activity) and ^{241}Am (25% of activity) by a worker. The worker was monitored by chest measurement, urine and fecal analyses for up to 410 d, and treated with DTPA. The isotopic ratio appeared to remain constant with time in faeces and presumably in lung. According to the author and based on a model of ICRP (1959), 37% of the intake was deposited in the lung. In the first 7 d post inhalation, 1.5% ILD was transported to the rest of body, 90% ILD was excreted in faeces and 8% ILD remained in lungs. The remaining lung activity was cleared with a 28-d half-time (T_b), 96% to the rest of body, 4% to faeces. Analysis here gave $f_r = 0.03$ and $s_s = 0.02\ d^{-1}$, consistent with assignment to Type M.

(951) Kanapilly et al. (1975) evaluated the *in vitro* dissolution of Cm oxides. ^{244}Cm oxides labeled with ^{243}Cm were prepared by heat treatment at three different temperatures to yield different oxidation states of Cm (Table 24.2). Dissolution was followed for 11 d in a standard synthetic ultra-filtrate (SUF) and four other solvents. Almost identical dissolution behaviour of the three oxides in all solvents suggested that Cm(IV) was rapidly reduced to Cm(III) which is the only stable oxidation state of Cm in aqueous systems. In SUF, the Cm oxides were nearly insoluble. The addition of DTPA and, much more, the removal of phosphate made them rapidly soluble. Rapid dissolution of Cm oxides was also observed in a slightly acidic NaCl solution. Analysis here of the dissolution of the three oxides in the five solvents gave the parameter values shown in Table 24.2. The large range of solubility depending on the solvent makes it difficult to draw general conclusions. In another study of dissolution in SUF with DTPA, Cm oxides aged for 4 weeks were observed to dissolve much faster (75% in 18 hours) than oxides that were less than 2 d old, suggesting physicochemical changes during aging. Kanapilly and

LaBauve (1976) performed further studies that indicated a moderate increase of solubility from CmO_2 to $CmO_{1.7}$ then to $CmO_{1.5}$. They also observed a slow dissolution of Cm oxides in dog serum or in NaCl + Tris at pH 7.3, at a rate similar to that observed in SUF. An injection study of Cm oxides in the muscle of hamsters was performed. A comparison with the outcome of the injection study and with the inhalation study of McClellan et al. (1972) suggested that *in vivo* dissolution was faster than in SUF but slower than in SUF + DTPA.

Table 24.2. Absorption parameter values for Cm oxides derived from Kanapilly et al. (1975).

treatment temperature (°C)	assumed oxide form	solvent	f_r	s_r (d^{-1})	s_s (d^{-1})
400	CmO_2	SUF	0.03	1	0.002
700	$CmO_{1.73}$	SUF	0.04	0.8	nd [b]
1300	$CmO_{1.5}$	SUF	0.06	1	0.002
400	CmO_2	SUF without phosphate	1	12	nd [b]
700	$CmO_{1.73}$	SUF without phosphate	1	14	nd [b]
1300	$CmO_{1.5}$	SUF without phosphate	1	12	nd [b]
400	CmO_2	SUF and DTPA	0.4 [a]	4 [a]	nd [a,b]
700	$CmO_{1.73}$	SUF and DTPA	0.1 [a]	nd [a,b]	nd [a,b]
1300	$CmO_{1.5}$	SUF and DTPA	0.9	14	nd [b]
400	CmO_2	0.15 M NaCl, pH 4	0.9	nd [b]	nd [b]
700	$CmO_{1.73}$	0.15 M NaCl, pH 4	0.9	nd [b]	nd [b]
1300	$CmO_{1.5}$	0.15 M NaCl, pH 4	0.7	nd [b]	nd [b]
400	CmO_2	SUF without phosphate and cysteine	0.8	3	nd [b]
700	$CmO_{1.73}$	SUF without phosphate and cysteine	0.9	5	nd [b]
1300	$CmO_{1.5}$	SUF without phosphate and cysteine	0.9	7	nd [b]

[a] The dissolution rate increases over time and would be more consistent with the alternative dissolution model involving s_p, s_{pt} and s_t (ICRP, 2015)
[b] nd, not determined

(952) Craig et al. (1975, 1976) studied the distribution of ^{244}Cm in dogs for 270 d after a single inhalation exposure to a $^{244}CmO_x$ oxide at two levels of initial body burden: medium (2.6 kBq with AMAD = 0.52 µm) and high (15.4 kBq with AMAD = 0.47 µm). Urine and faeces were analysed as well as tissue distribution after sacrifice. The results were compared with those obtained after inhalation of Am and Pu oxide. Both Am and Cm were significantly more rapidly translocated to liver, skeleton and muscle than Pu. Cm moved out of the lung twice as fast as Am initially, but its distribution in tissues changed little after 30 d. At 270 d post exposure, Cm and Am distribution was similar. Analysis here gave f_r =0.7 and s_s = 0.007 d^{-1} for the medium exposure level, f_r = 0.7 and s_s = 0.004 d^{-1} for the high level of exposure, the other

parameters being fixed at the default values s_r = 0.4 d^{-1} and f_b = 0.02. Both experiments are consistent with assignment to Type M.

(953) Sanders and Mahaffey (1978) studied the health effects of ^{244}Cm oxide inhalation in rats. Cm was prepared as $^{244}CmO_x$ with x between 1.71 and 2. Five groups of animals were exposed to increasing levels of ^{244}Cm (Table 24.3) and followed up to 900 d with histopathology and radiochemistry of the lung, thoracic lymph nodes, skeleton and liver of the necropsied rats. About 75% ILD was cleared from the lung with T_b 0.5 d, ~25% with T_b 12 d, and ~2% with T_b about 1 year. Analysis here of the data for the five groups of rats gave the values of absorption parameters shown in Table 24.3. All are consistent with assignment to Type M.

Table 24.3. Aerosol characteristics and absorption parameter values for inhaled $^{244}CmO_x$ derived from Sanders and Mahaffey (1978).

initial alveolar deposit (kBq)	AMAD (µm)	f_b	f_r	s_s (d^{-1})
0.02	0.68	0.06	0.8	nd[a]
0.16	1.3	0.05	0.4	0.04
1.8	0.93	0.01	0.6	0.01
17	0.66	0.01	0.7	0.008
67	0.66	nd[a]	0.6	0.02

[a] nd : not determined

(954) Stradling et al. (1979) investigated the transfer of Cm from the rat lungs to other tissues and its excretion after administration of the dioxide as suspensions of variable particle size, with or without previous aging in water. Suspensions of $^{244}CmO_2$ were prepared by sedimentation of particles less than about 2 µm in water and fractionation into size ranges by ultrafiltration either within a day or after 12 weeks in water. The suspensions, or a Cm citrate control, were administered to rats by pulmonary instillation. Cm content was then measured in excreta, lung and other tissues from 1 d to 1 month post-exposure. The transfer rate of ^{244}Cm from lungs to blood was fairly rapid and similar for all suspensions, less than ~10% ILD remaining after 60 d. Analysis here of the data for the different suspensions gave the values of absorption parameters shown in Table 24.4. All are consistent with assignment to Type M.

Table 24.4. Particle characteristics and absorption parameter values for instilled CmO_2, derived from Stradling et al. (1979). By default, f_b = 0.02 and s_b = 0 are assumed.

age of CmO_2 suspension	particle size range (µm)	f_r	s_r (d^{-1})	s_s (d^{-1})
1 day	about 0.001	0.5	2	0.03
	< 0.025	0.6	1	0.03
	0.22 – 1.2	0.3	0.2	0.01
12 weeks	< 0.025	0.5	1	0.03
	0.22 – 1.2	0.5	1	0.02

(955) Guilmette et al. (1984) determined the biokinetics of ^{244}Cm in rats up to 32 d after inhalation of monodisperse $^{244}Cm_2O_3$ aerosols (0.7, 1.3 or 2.6 µm AMAD) heat-treated at 1150°C. The clearance of Cm from the lung was observed to be somewhat more rapid but

similar to PuO_2 and FAP, with T_b 8, 9 and 12 days for the 0.7 µm, 1.3 µm and 2.6 µm particles respectively, with only a small fraction of inhaled Cm translocated to skeleton and liver. At 32 days after exposure, 56-70% of body Cm was in lung, 5-10% in liver and 14-30% in skeleton. For 2.6 µm particles, 2% ILD was measured in tracheobronchial lymph nodes. The analysis here of the data for the 0.7, 1.3 and 2.6 µm groups gave f_r = 0.2, 0.1 and 0.1 respectively and s_s = 0.06, 0.06 and 0.04 d^{-1} respectively (assuming f_b = 0.02 and s_r = 0.4 d^{-1}), indicating Type M for all particle sizes.

(956) Rhoads et al. (1986) followed the biokinetics in rats of ^{239}Pu and ^{244}Cm for 120 d after inhalation individually or as a mixed oxide. Cm was cleared from lung more rapidly than Pu: ~50% with T_b 3.9 d and ~40% with T_b 31 d. However, Cm remained in the lungs longer when administered as a mixed oxide: ~69% with T_b 5.3 d and ~32% with T_b 76 d. The authors noted that the translocation of Cm to extrapulmonary tissues was greatly reduced by incorporation in the PuO_2 matrix. However, the cumulative urinary excretion was significantly higher at 7 and 120 d after inhalation of the mixed oxide than after inhalation of Cm oxide only. Overall, the data appeared to be inconsistent with the systemic model of Ménétrier et al. (2008). Therefore, a systemic model based on the injection data of Durbin et al. (1973) was applied here to the analysis of these data. This gave f_r =0.6, s_r = 0.2 d^{-1} and s_s = 0.007 d^{-1} for Cm oxide; f_r = 0.2, s_r = 2 d^{-1} and s_s = 0.002 d^{-1} for Cm in the mixed oxide. This is consistent with assignment of both forms to Type M.

(957) Guilmette and Kanapilly (1988) studied the tissue distribution of $^{244}Cm_2O_3$ (1.4 µm AMAD) and $^{244}Cm(NO_3)_3$ inhaled by dogs and observed broadly similar kinetics except for a more rapid translocation of Cm from the lung to liver and bone during the first 10-20 d after exposure to nitrate compared to oxide. The dogs were sacrificed from 4 hours to 2 years after exposure for measurement of lung, liver, skeleton, kidneys, spleen, tracheobronchial and mediastinal lymph nodes, and other tissues, along with measurement of excretion in urine and faeces. For the oxide, 78% ILD was cleared from the lung with T_b 7.6 d, 19% with T_b 99 d and 3% with T_b 760 d. Most of the Cm cleared from the lung was deposited in the liver and skeleton: 1% ILD translocated to the tracheobronchial lymph nodes, and much less to the mediastinal lymph nodes. Guilmette and Mewhinney (1989) showed that models based on the dog studies of Guilmette and Kanapilly (1988) are in fairly good agreement with bioassay measurements in human accidental inhalation cases reported by Parker et al. (1960), Vaane and De Ros (1971), Sanders (1974) and Parkinson et al. (1976). Analysis here of the oxide data gave f_b = 0.02, s_b = 0 d^{-1}, f_r = 0.6, s_r = 0.1 d^{-1} and s_s = 0.007 d^{-1}, consistent with assignment to Type M.

(958) Guilmette and Muggenburg (1992) investigated the efficiency of DTPA treatment after inhalation of $^{244}Cm_2O_3$ (0.9 µm AMAD) by dogs. Urinary and fecal excretions were followed up to 62 d. Before treatment, 1 hour after exposure, about 0.7% ILD had translocated from lung. By 64 d after exposure, Cm was distributed in untreated control animals between lung (40% ILD), liver (26% ILD), bone (15% ILD), tracheobronchial lymph nodes (0.3% ILD) and other soft tissues (4% ILD). Injection or infusion of DTPA reduced the Cm body burden. Cm_2O_3 appeared to dissolve faster than AmO_2 based on more rapid urinary excretion and decrease of whole-body burden in Cm exposed animals compared to Am exposed animals given the same therapy. The analysis here of Cm data for untreated animals gave f_r = 0.2 and s_s = 0.01 d^{-1}, consistent with assignment to type M.

(959) Helfinstine at al. (1992) investigated the *in vitro* dissolution kinetics of Cm sesquioxide ($^{244}Cm_2O_3$). The amount of soluble material was determined over 7 d in a phagolysosomal simulant solvent (PSS) made of HCl aqueous solution with DTPA at a 10-1000

ratio to Cm and pH 4-6, or in cultured dog alveolar macrophages (AM). Little dissolved Cm was observed for the first 3 d. Subsequently, the dissolution rate increased significantly. After normalization to the viable cell number, approximately 45% Cm_2O_3 dissolved in AM over 7 d. In PSS, the dissolution rate increased with decreasing pH and increasing DTPA molarity, yielding up to 73% Cm_2O_3 dissolved over 7 d. The dissolution rate increasing with time cannot be well represented by the simple compartment model involving f_r, s_r and s_s and a better fit to the data was obtained here with the alternative model involving s_p, s_{pt} and s_t. The resulting absorption parameter values are summarised in Table 24.5.

Table 24.5. Absorption parameter values for Cm_2O_3 derived from Helfinstine at al. (1992).

medium			f_r	s_r (d^{-1})	s_p (d^{-1})	s_{pt} (d^{-1})	s_t (d^{-1})
AM culture			1	0.06	0	0.2	0.1
phagolysosomal simulant solvent PSS	DTPA:Cm ratio	pH					
	1000	4	1	0.2	0	0.4	0.4
		5	1	0.1	0	0.3	0.3
		6	1	0.09	0	0.3	0.2
	100	4	1	0.1	0	0.3	0.3
		5	1	0.1	0	0.3	0.3
		6	1	0.09	0	0.3	0.3
	10	4	1	0.09	0	0.3	0.3
		5	1	0.05	0	0.2	0.2
		6	1	0.03	0	0.2	0.1

(960) Lundgren et al. (1997) exposed rats by inhalation to $^{244}Cm_2O_3$ heat-treated at 1150°C (AMAD 0.87 to 1.2 µm) in order to obtain information on the α-particle dose-response. Lung, liver and skeleton burden were measured in serially sacrificed rats and in rats that died spontaneously up to 1120 d post-exposure. The lung retention of ^{244}Cm differed between rats with ILD of less or more than 130 kBq kg^{-1} body weight, with more rapid clearance from lungs of the rats that died early, with acute pulmonary injury probably also causing increased vascular permeability. The retention of ^{244}Cm in the lung of rats with ILD < 130 kBq kg^{-1} was fit by a three-component exponential function: 92.5% with T_b 11 d, 7.2% with T_b 100 d and 0.3% with T_b > 1000 d. For rats with greater ILD, lung retention was represented by 95.7% with T_b 3.1 d and 4.3% with T_b 120 d. The early clearance of ^{244}Cm from the lungs of rats with ILD < 130 kBq kg^{-1} and its translocation to liver were similar to that reported by Guilmette et al. (1984) but half as much of the ILD was translocated to the skeleton. Cm_2O_3 appeared to the authors to be less soluble than other Cm oxides used in other studies. Analysis here of data from rats having ILD < 130 kBq kg^{-1} gave f_b = 0.01, f_r = 0.4, and s_s = 0.007 d^{-1}. This is consistent with assignment to Type M.

(961) Absorption parameter values for curium oxides based on *in vivo* data are available from several studies. Most results are consistent with assignment to Type M. Overall, Cm oxides appear to be more soluble than americium oxide and much more soluble than plutonium oxide. Some values are very different from the default values for Type M. The estimated values

of f_r range from 0.02 to 0.8 (median 0.5), well above the default value for Type M (0.2). Estimated values of s_r range from 0.1 to 14 d^{-1} (median 1.5 d^{-1}), compatible with the specific value for curium (0.4 d^{-1}). Estimated values of s_s range from 0.002 to 0.06 d^{-1} (median 0.01 d^{-1}), above the default value for Type M (0.005 d^{-1}). Inhalation exposure to curium oxide is not unlikely. Specific parameter values of f_r = 0.5 s_r = 0.4 d^{-1} and s_s = 0.01 d^{-1} are used here for curium oxide. It is noted however that the oxidation state, the age of the compound, or the association with plutonium or americium oxide may influence the dissolution kinetics of curium oxide.

Curium nitrate

(962) Nénot et al. (1972) investigated the transfer of actinides to rat bone after intramuscular injection or inhalation. The lung burden and the skeletal burden as well as the urinary excretion of ^{242}Cm were followed for three months after inhalation of ^{242}Cm nitrate. Cm was cleared from lung significantly faster than Pu and slightly faster than Am. Analysis here of the Cm inhalation data gave f_r = 0.7, s_r = 0.2 d^{-1} and s_s = 0.03 d^{-1}. This indicates Type F or Type M behaviour.

(963) Crawley and Goddard (1976) studied the tissue distribution and excretion of ^{241}Am and ^{242}Cm in citrate or nitrate solutions one week after administration to rats by instillation into the nasopharyngeal (NP), tracheobronchial (TB) and pulmonary regions of the respiratory system. At 7 d, 63% initial pulmonary deposit of ^{242}Cm nitrate was in lungs while 20% had been absorbed. Following deposition in the NP or TB region, there was less retention in both lung and extrapulmonary tissues, because of faster mucociliary clearance. The analysis here of the data from Cm nitrate deposited in the pulmonary region gave f_r = 0.2. The limited data available prevented reliable estimates of s_r and s_s.

(964) Stather and Priest (1977) studied the distribution of actinides in rat tissues up to 5 months after pulmonary instillation of the nitrates. After administration of a mixture of ^{241}Am and ^{242}Cm nitrates, similar lung clearance of Am and Cm was observed, with ~70% ILD translocated to extra-pulmonary tissues by one week, 88% by one month and 98% by 5 months. The authors noted the possibility that mixed Am and Cm hydroxide polymers formed in the lungs may be cleared at a rate dependent on the properties of the mixed hydroxide rather than those of Am or Cm in isolation. Analysis here of Cm data gave f_r = 0.5 and s_s = 0.01 d^{-1}, consistent with assignment to Type M.

(965) As discussed above, Guilmette and Kanapilly (1988) studied the tissue distribution of $^{244}Cm_2O_3$ and $^{244}Cm(NO_3)_3$ inhaled by dogs. For the nitrate, 42% ILD was cleared from the lung with T_b 0.63 d, 48% with T_b 24 d and 10% with T_b 365 d. Most of the Cm cleared from the lung was deposited in the liver and skeleton. About 1% ILD translocated to the tracheobronchial lymph nodes, and about 0.1% ILD to the mediastinal lymph nodes. Analysis here of the nitrate data gave f_b = 0.02, f_r = 0.6, s_r = 0.5 d^{-1} and s_s = 0.005 d^{-1}. This is consistent with assignment to Type M.

(966) Absorption parameter values for curium nitrate based on *in vivo* data are available from a few studies. The results are consistent with assignment to Type M but some values are very different from the default values for Type M. The estimated values of f_r range from 0.2 to 0.7 (median 0.5), above the default value for Type M (0.2).The estimated values of s_r are 0.15 and 0.5 d^{-1} from only two studies, similar to the specific value for curium (0.4 d^{-1}). Estimated values of s_s range from 0.005 to 0.03 d^{-1} (median 0.01 d^{-1}) above the default value for Type M (0.005 d^{-1}) and similar to curium oxides. Inhalation exposure to curium nitrate is not unlikely.

The same specific parameter values of f_r = 0.5 s_r = 0.4 $d^{-1}$and s_s = 0.01 d^{-1} are used here for curium nitrate as for curium oxide.

Curium chloride

(967) As described above, McClellan et al. (1972) exposed 24 dogs to aerosols of $^{244}CmCl_3$ in a CsCl vector or $^{244}CmO_{1.73}$ by inhalation. Cm was rapidly absorbed, at a similar rate from both chemical forms, into body fluids and translocated to skeleton and liver. By 16 d, lung retention was ~16% ILD, and at 256 d, ~3% ILD. Analysis here of the chloride data gave f_b = 0.03, f_r = 0.8, s_r = 0.4 d^{-1} and s_s = 0.01 d^{-1}. This is consistent with assignment to Type M but close to Type F behaviour.

(968) The absorption parameter values for curium chloride were derived from a single *in vivo* study. Moreover, inhalation exposure to curium chloride is unlikely. However its absorption kinetics was found to be similar to that of curium oxide. Therefore the same specific parameter values of f_r = 0.5, s_r = 0.4 d^{-1} and s_s = 0.01 d^{-1} are used here for curium chloride as for curium oxide and nitrate.

Curium citrate

(969) Crawley and Goddard (1976) followed the tissue distribution and excretion of ^{241}Am and ^{242}Cm administered either as nitrates or citrates to rats by instillation into the NP, TB and pulmonary regions of the respiratory system at 7 d. At one week after instillation of ^{242}Cm citrate into the pulmonary region, only 8% ILD of ^{242}Cm was retained in lungs while more than 70% ILD had been absorbed to blood, much more than for nitrate (~20% ILD, see above). This is consistent with assignment to Type F. Following deposition in the NP or TB region, there was less retention in both lung and extrapulmonary tissues, as a consequence of faster mucociliary clearance. Analysis carried out here of data on citrate deposited in the pulmonary region gave f_r = 1. The limited data available prevented reliable estimates of s_r and s_s, but the results indicate assignment to Type F.

(970) As described above, Stradling et al. (1979) investigated the clearance of CmO_2 from the lungs of rats and used Cm citrate as a control. Analysis here of the citrate data gave f_r = 0.9, s_r = 10 d^{-1}, s_s = 0.03 d^{-1}, consistent with assignment to Type F.

(971) Although absorption parameter values for curium citrate based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for curium citrate are not used here. Instead, it is assigned to Type F. However, the results contributed to the selection of the rapid dissolution rate for curium.

Unspecified compounds

(972) Sanders (1974) described two cases of occupational exposure to ^{244}Cm. In the first case, a worker was exposed to an unknown Cm compound from contaminated waste. *In vivo* measurement indicated a drop of chest activity of 64% from 4.5 h to 4 d after the incident. DTPA treatment was administered; urine samples were collected for 247 d and fecal samples for 73 d. Overall the Cm compound appeared to be relatively soluble. Although the interpretation of the data was complicated by the DTPA treatment, analysis here suggested f_r = 1 and Type F behaviour.

(973) Bernard and Poston (1976) followed four workers who accidently inhaled ^{244}Cm, by urine, faeces and chest measurements for one or two weeks after intake. The excretion kinetics

was found to be broadly consistent with that of dogs exposed to Cm oxide and chloride (McClellan et al., 1972, see above). Analysis here of the measurement results from two of the workers with positive chest counting gave $f_r = 0.8$ and $f_r = 0.3$. The rather steady chest retention of the second worker suggested a value of $s_r = 0.3$ d^{-1}. These values are consistent with assignment to type M.

(974) Parkinson et al. (1976) reported two cases of ^{244}Cm inhalation by workers involved in the same incident. The chemical form was likely to be a mixture of chloride, nitrate and oxide, possibly together with hydrolysis products of the chloride and nitrate. Body ^{244}Cm was measured by chest counting and in faecal and urinary samples collected up to one year after the incident. The inhaled Cm aerosols were observed to be largely soluble. The chest activity was cleared relatively rapidly, as 70% with T_b 2.3 d and 30% with T_b 50 d in the first case; 80% with T_b 1 d and 20% with T_b 50 d in the second case. Analysis here gave f_r =0.9 for both cases, and the early data from the first case suggested $s_r = 0.2$ d^{-1}. This indicates Type F behaviour.

Rapid dissolution rate for curium

(975) All chemical forms of curium appeared at least relatively soluble after inhalation. In 14 relevant studies of Cm compounds, sufficient early retention data were available to allow an estimate of the rapid dissolution rate s_r. The results of analyses here (obtained by fitting models to the experimental data) are summarised in Table 24.6: values of s_r range from 0.1 to 10 d^{-1} with a median of 0.4 d^{-1}. Consequently a default value of $s_r = 0.4$ d^{-1} is proposed for the rapid dissolution rate of curium compounds, in analysing experimental data.

Table 24.6. Case-specific absorption parameter values estimated here for soluble compounds in in vivo studies reporting early retention data.

Inhaled particulate materials	Animal species	Absorption parameter values		References
		f_r	s_r (d^{-1})	
citrate	rat	0.9	10	Stradling et al. (1979)
chloride	dog	0.8	0.4	McClellan et al. (1972)
nitrate	rat	0.7	0.2	Nénot et al. (1972)
	dog	0.6	0.5	Guilmette and Kanapilly (1988)
oxide, Cm_2O_3	dog	0.6	0.1	Guilmette and Kanapilly (1988)
oxide, $CmO_{1.73}$	dog	0.8	0.4	McClellan et al. (1972)
oxide, CmO_2	rat	0.5	2	Stradling et al. (1979)
		0.6	1	
		0.3	0.2	
		0.5	1	

		0.5	1	
oxide	rat	0.6	0.2	Rhoads et al. (1986)
unspecified	human	0.3	0.3	Bernard and Poston (1976)
		0.9	0.2	Parkinson et al. (1976)
Median		0.6	0.40	
Geometric mean		0.6	0.5	
Min - max		0.3 – 0.9	0.1 - 10	

Extent of binding of curium to the respiratory tract

(976) Studies of curium deposited in the respiratory tract in most chemical forms showed rapid or moderately rapid dissolution of most of the ILD. However, the studies of longer duration (>250 d) all show lung retention of a small amount: 0.3 – 4% ILD.

(977) McClellan et al. (1972) observed that about 3 – 3.5% ILD was still retained in dog lungs 256 d after inhalation. Sanders and Mahaffey (1978) observed that 0.2% to 1.8% ILD was retained in rat lungs after about 800 d. Similarly, Guilmette and Kanapilly (1988) observed that about 2% ILD was present in dog lung at 2 years after exposure. Lafuma et al. (1974) concluded from autoradiographic studies that Cm nitrate was widely dispersed in the rat lung at 20 d post-exposure, generating mostly single α tracks and very few particle-like clusters. Sanders and Mahaffey (1978) came to the same conclusion from autoradiographs of rat lung taken immediately after inhalation exposure, and up to 2 years later. Lundgren et al. (1997) observed in a rat life-span study that a small fraction of the ILD (about 0.3%) was retained for an indefinite time and considered that it was probably solubilised curium bound to connective tissue in the lungs, as observed in dogs exposed to Am nitrate (Taya et al. 1994).

(978) Based on these considerations, the bound fraction for curium is assessed to be f_b = 0.02. Since there is no indication of a non-zero clearance rate of the bound fraction, this is considered to be $s_b = 0\ d^{-1}$. There is no evidence of long-term retention of curium deposited in relatively soluble form in the ET, BB or bb regions. Such a small long-term bound state in the alveolar region results in an additional contribution to the committed equivalent dose coefficient for the lungs from inhaled ^{244}Cm of about 270%, about 30%, about 1% for Absorption Types F, M, S respectively, and about 90% for Cm oxide, nitrate and chloride.

(979) Nevertheless, as described in the general actinide section, absorption parameter values for the bound state based on plutonium are applied in this document to the transplutonium elements for radiation protection purposes. Thus, a bound fraction f_b = 0.002 and a rate of uptake $s_b = 0\ d^{-1}$, are applied throughout the respiratory tract except in the ET_1 region.

Table 24.7. Absorption parameter values for inhaled and ingested curium.

Inhaled particulate materials	Absorption parameter values[a]		Absorption from the alimentary

	f_r	s_r (d^{-1})	s_s (d^{-1})	tract, f_A [b]
Specific parameter values[c]				
Curium oxide, nitrate and chloride	0.5	0.4	0.01	3×10^{-4}
Default parameter values[d,e]				
Absorption Type / Assigned forms				
F — Citrate	1	0.4	–	5×10^{-4}
M[e]	0.2	0.4	0.005	1×10^{-4}
S	0.01	0.4	1×10^{-4}	5×10^{-6}
Ingested material[f]				
All compounds				5×10^{-4}

a It is assumed that for curium a bound fraction $f_b = 0.002$ with $s_b = 0\ d^{-1}$ is applied throughout the respiratory tract except in the ET_1 region.The values of s_r for Type F M and S forms of curium (0.4 d^{-1}) are element-specific.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of curium (5×10^{-4}).

c See text for summary of information on which parameter values are based, and on ranges of parameter values observed in different studies. For curium oxide and nitrate, specific parameter values are used for dissolution in the lungs, but a default value of f_A (footnote b).

d Materials (e.g. curium citrate) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values or because specific parameter values would not be significantly different from the default (see text).

e Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

f Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction fA for the secreted activity is the reference fA ($=5 \times 10^{-4}$) for ingestion of the radionuclide.

24.2.2. Ingestion

(980) Popplewell et al (1991) measured the absorption of ^{242}Cm as a citrate in five adult male volunteers by comparing urinary excretion after oral and intravenous administration. The solutions were ingested with a mid-day meal. A mean absorption value of 2×10^{-4} was obtained for Cm(III) with a range of 10^{-4} to 3×10^{-4}.

(981) Curium absorption has been measured in adult rats and guinea pigs. Values for rats were in the range $2\text{-}3 \times 10^{-4}$ for ^{244}Cm nitrate (Sullivan, 1980; Sullivan et al., 1985) $3\text{-}7 \times 10^{-4}$ for ^{244}Cm citrate (Semenov et al., 1973; Sullivan et al., 1985) and $3\text{-}12 \times 10^{-4}$ for ^{244}Cm oxide (Sullivan, 1980). Absorption of curium nitrate was increased by a factor 3 to 6 by fasting and oxidizing agents such as ferric iron and quinhydrone (Sullivan et al., 1986). In guinea pigs given ^{242}Cm citrate, absorption was about 10^{-4} (Naylor et al., 1991).

(982) In *Publication 30* (ICRP, 1979), an absorption value of 5×10^{-4} was recommended by analogy with Am. In *Publication 48* (ICRP, 1986), a general value of 1×10^{-3} for actinides was used. However, in this report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all actinides other than U.

(983) An f_A value of 5×10^{-4} is adopted here for all chemical forms of Cm.

24.2.3. Systemic distribution, retention and excretion of curium

24.2.3.1. Data

(984) In five healthy human subjects administered ^{242}Cm by intravenous injection, urinary excretion accounted for 4.5-6% of the injected amount during the first day and 7-10% during the first week after injection (Popplewell et al., 1991). Similar urinary excretion rates during these time periods were observed in baboons (Lo Sasso et al., 1981) and beagles (Lloyd et al., 1974) injected with curium isotopes.

(985) The rate of urinary excretion of ^{244}Cm was determined over periods of about five months in two workers who were exposed at different times to acidic solutions of $^{244}Cm(NO_3)_3$, one by puncture wound and the other by acid burn of the skin (Parkinson et al., 1980). The two subjects showed similar relative urinary excretion rates during this period. The rate of decline of urinary curium during the first week after exposure was similar to that determined in the human injection study by Popplewell et al. (1991).

(986) Data from the animal studies indicate that the initial distribution and rate of excretion of curium conform to the general pattern determined for other actinide elements, excluding uranium. That is, a substantial portion of the injected or absorbed curium deposits in the liver and skeleton, and biological removal from the body is relatively slow. In beagles receiving ^{243,244}Cm citrate by intravenous injection, about 35% of injected curium was found in the liver and about 53% in non-liver tissues, mainly skeleton, at 1 wk after injection (Lloyd et al., 1974). In beagles exposed to aerosols of $^{244}CmCl_3$ or $^{244}CmO_{1.73}$, the liver and skeleton contained approximately 30% and 45%, respectively, of the initial lung burden at 256 days after inhalation (McClellan et al., 1972). These data suggest relatively long retention of curium in the liver and skeleton. In another study of beagles exposed by inhalation to $^{244}CmO_X$, the liver contained about 44% and the skeleton about 33% of systemic ^{244}Cm at 270 d after inhalation (Craig et al., 1976). In baboons receiving ^{243,244}Cm citrate by intravenous injection, about 20% of injected curium deposited in the liver and 60% in the skeleton (Lo Sasso et al., 1981).

(987) Data on laboratory animals indicate that curium is tenaciously retained in the skeleton. The rate of loss of curium from the liver is species dependent, with half-times of a few days in rats (Durbin, 1973) and a few weeks in baboons (Lo Sasso et al., 1981) but apparently much longer retention in the liver in dogs (McClellan et al., 1972; Guilmette and Mewhinny, 1989). Based on comparative human and animal data on other actinide or lanthanide elements, it seems reasonable to assume that the pattern of retention of curium in the human liver is broadly similar to that in dogs.

(988) Results of experimental studies on rats and other animal species indicate that the biological behavior of curium is similar to that of Am. In an investigation of the transport of different actinides in the blood of rats, Turner and Taylor (1968) observed virtually identical rates of circulatory clearance of ^{244}Cm and ^{241}Am during the first day after intravenous injection of ^{244}Cm nitrate, ^{241}Am nitrate, or ^{241}Am citrate. In rats receiving intramuscular injection of relatively soluble forms of ^{241}Am and ^{242}Cm, similar initial distributions and nearly identical

patterns of excretion of these radionuclides over a period of several months were observed (Scott et al., 1948, 1949; Durbin et al., 1969; Durbin, 1973). In rats injected with ^{241}Am citrate or ^{242}Cm citrate, the concentration of ^{242}Cm at 6 d after administration was virtually the same as that of ^{241}Am in all measured tissues (skeleton, liver, spleen, kidneys, lung, thyroid, adrenals, ovaries), but chelation therapy appeared to be slightly more effective for ^{242}Cm than ^{241}Am (Seidel and Volf, 1972). Stather and Priest (1977) observed similar tissue distributions of ^{241}Am and ^{242}Cm in adult rats at 1 wk, 1 mo, and 5 mo after pulmonary intubation of these radionuclides as nitrates, but ^{242}Cm appeared to be lost from the body at a slightly higher rate than ^{241}Am at 1-5 mo after administration. Crawley and Goddard (1976) found virtually identical systemic distribution and retention of americium and curium in rats during the first week after intubation of these elements into each of three regions of the lung. Nenot et al. (1972) observed similar behavior of ^{241}Am and ^{242}Cm in rats after administration by inhalation or intramuscular injection of these radionuclides as nitrates, with regard to cumulative urinary excretion, levels of uptake and retention by bone, and sites of binding in bone. In a study of comparative retention of bone-seeking radionuclides in rats, Taylor (1983) found that uptake and long-term retention of ^{244}Cm in bone was similar to that of ^{241}Am.

(989) Results of a series of studies at the University of Utah (Lloyd et al., 1970, 1974; Atherton et al., 1973; Bruenger et al., 1976) indicate that the biokinetics of $^{243/244}$Cm in beagles is similar but not identical to that of ^{241}Am over the first 3 wk after intravenous injection, the most important differences being that the observed liver-to-skeleton concentration ratio and urinary-to-fecal excretion ratio were both higher for ^{241}Am than $^{243/244}$Cm. By contrast, data of Craig et al. (1976) indicate that the time-dependent division of ^{244}Cm between liver and skeleton in beagles is roughly the same as that of ^{241}Am at 10-270 d after inhalation of $^{241}AmO_2$ or $^{244}CmO_x$ aerosols. In an investigation of the biological behavior of inhaled ^{244}Cm compounds in beagles, Guilmette and Mewhinney (1989) found that a biokinetic model for Am developed earlier from data on inhaled $^{241}AmO_2$ in beagles (Mewhinney and Griffith, 1983) applied nearly equally well to ^{244}Cm with regard to the behavior of absorbed activity.

(990) To summarise, results of a variety of experimental studies on laboratory animals indicate that the chemically similar elements americium and curium are also close physiological analogues. Although quantitative differences in the biokinetics of systemic americium and curium have been observed in some studies, such differences generally have not been statistically significant and in most cases are contradicted by results of separate investigations. In this report, the systemic biokinetic model adopted for americium is also applied to curium.

24.2.3.2. Biokinetic model

(991) The biokinetic model for systemic curium applied in this report is described in Section 18.2.3.

24.2.3.3. Treatment of progeny

(992) The treatment of radioactive progeny of curium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

24.3. Individual monitoring

^{242}Cm

(993) Measurements of ^{242}Cm concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main technique used for *in vitro* bioassay is alpha spectrometry.

Table 24.8. Monitoring techniques for ^{242}Cm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{242}Cm	Urine Bioassay	α spectrometry	0.2 mBq/L	0.05 mBq/L
^{242}Cm	Faecal Bioassay	α spectrometry	0.2 mBq/24h	

^{243}Cm

(994) Measurements of ^{243}Cm concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main technique used for *in vitro* bioassay is alpha spectrometry. *In vivo* lung measurement of ^{243}Cm may allow evaluating the intake of radionuclide if the measurement system is sensitive enough. The main technique for *in vivo* measurement is gamma spectrometry.

Table 24.9. Monitoring techniques for ^{243}Cm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{243}Cm	Urine Bioassay	α spectrometry	0.2 mBq/L	0.05 mBq/L
^{243}Cm	Faecal Bioassay	α spectrometry	0.2 mBq/24h	0.05 mBq/24h
^{243}Cm	Lung Measurement[a]	γ-ray spectrometry	27 Bq	

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

^{244}Cm

(995) Measurements of ^{244}Cm concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main techniques used for *in vitro* bioassay are alpha spectrometry and ICP-MS; which is the more sensitive and preferable technique to be applied.

Table 24.10. Monitoring techniques for ^{244}Cm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{244}Cm	Urine Bioassay	α spectrometry	0.3 mBq/L	0.05 mBq/L
^{244}Cm	Urine Bioassay	ICP-MS[a]	$0.1x10^{-15}$ g/L	$1x10^{-15}$ g/L
^{244}Cm	Faecal Bioassay	α spectrometry	2 mBq/24h	0.5 mBq/24h

[a] Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

^{248}Cm

(996) Measurement of ^{248}Cm concentrations in urine is used to determine intakes of the radionuclide for routine monitoring. The main technique used for urinalysis urinalysis is alpha spectrometry.

Table 24.11. Monitoring techniques for ^{248}Cm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{248}Cm	Urine Bioassay	α spectrometry	0.2 mBq/L
^{248}Cm	Faecal Bioassay	α spectrometry	0.2 mBq/24h

24.4. Dosimetric data for curium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Atherton, D. R., Stevens, W., Bruenger, F. W., 1973. Early retention and distribution of curium in soft tissues and blood of the beagle. University of Utah College of Medicine. COO-119-248, 178–185.

Bair, 1976. Recent animal studies on the deposition, retention and translocation of plutonium and other transuranic compounds. (Pu, Am, Cm). In: Diagnosis and Treatment of Incorporated Radionuclides. Proceedings of a Seminar held by the International Atomic Energy Agency and the World Health Organization, December 8–12, 1975, Vienna, 51–83. International Atomic Energy Agency, Vienna, Austria.

Bernard, S. R., Poston, J. W., 1976 Estimation of dose commitment from an accidental intake of ^{244}Cm. In: Oak Ridge National Laboratory Annual Report, ORNL–5171, HP division.

Bruenger, F. W., Stevens, W., Atherton, D. R., Grube, B. J., 1976. The subcellular distribution of some actinide elements in the beagle liver. In: The health effects of plutonium and radium, ed. by W. S. S. Jee. Salt Lake City: The J. W. Press, 211–221.

Craig, D. K., Cannon, W. C., Catt, D. L., et al., 1975. Distribution of ^{241}Am and ^{244}Cm in dogs after inhalation of the oxides. Pacific Northwest Laboratory Annual Report for 1974 to the USAEC Division of Biomedical and Environmental Research. BNWL-1950, Part 1, Biomedical Sciences. 17–18. Richland, Washington. Available from National Technical Information Service, Springfield, Virginia.

Craig, D. K., Cannon, W. C., Catt, D. L., et al., 1976. Distribution of ^{241}Am and ^{244}Cm in dogs after inhalation of the oxides. Pacific Northwest Laboratory Annual Report for 1975 to the ERDA Division of Biomedical and Environmental Research. BNWL–2000 Part 1, Biomedical Sciences. 23–35. Richland, Washington. Available from National Technical Information Service, Springfield, Virginia.

Crawley, F. E. H., Goddard, E. A., 1976. The translocation of 241-americium and 242-curium from the respiratory system of the rat. Health Phys. 30, 191–197.

Durbin, P. W., 1973. Metabolism and biological effects of the transplutonium elements. In: Uranium, plutonium, and transplutonium elements, ed. by Hodge, H. C., Stannard, J. N. J., Hursh, B., Handbook of experimental pharmacology 36Berlin: Springer-Verlag, 739–896.

Durbin, P. W., Jeung, N., Williams, M. H., 1969. Dynamics of Am-241 in the skeleton of the rat: A study of the relationship between behavior of bone-seeking elements and bone-growth status. In: Delayed effects of bone-seeking radionuclides, ed. by C. W. Mays; W. S. S. Jee; R. D. Lloyd; B. J. Stover; J. H. Dougherty, G. N. Taylor. Salt Lake City: University of Utah Press; 137–156.

Guilmette, R. A., Kanapilly, G. M., 1988. Biokinetics and dosimetry of inhaled Cm aerosols in beagles: Effect of aerosol chemical form. Health Phys. 55, 911–925.

Guilmette, R. A., Kanapilly, G. M., Lundgren, D. L., Eidson, A. F., 1984. Biokinetics of inhaled ^{244}Cm oxide in the rat: Effect of heat treatment at 1150°C. Health Phys. 46, 845–858.

Guilmette, R. A., Mewhinney, J. A., 1989. A biokinetic model of inhaled curium compounds

in dogs: Application to human exposure data. Health Phys. 57, Suppl. 1, 187–198.
Guilmette, R. A., Muggenburg, B. A., 1992. Effectiveness of continuously infused DTPA therapy in reducing the radiation dose from inhaled $^{244}Cm_2O_3$ aerosols. Health Phys. 62, 311–318.
Helfinstine, S. Y., Guilmette, R. A., Schlapper, G. A., 1992. *In vitro* dissolution of curium oxide using a phagolysosomal simulant solvent system. Environmental Health Perspectives 97, 131–137.
ICRP, 1959. Permissible dose for internal radiation. ICRP Publication 2. Pergamon Press, Oxford. Press.
ICRP, 1979. Limits on intakes of radionuclides for workers. ICRP Publication 30, Pt.1. Pergamon Press, Oxford. Ann. ICRP 2(3/4).
ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Pergamon Press, Oxford. Ann. ICRP 16(2/3).
ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides. Pt.2. ICRP Publication 67. Pergamon Press, Oxford. Ann. ICRP 23(3/4).
ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. ICRP Supporting Guidance 3, Ann. ICRP 32(1/2).
ICRP, 2006. Human alimentary tract model for radiological protection. ICRP Publication 100. Ann. ICRP 36(1/2).
ICRP, 2015. Occupational intakes of radionuclides, Part 1. ICRP Publication 130. Ann. ICRP 44(2).
Kanapilly, G. M., LaBauve, R. J., 1976. Monodisperse aerosols of ^{244}Cm oxides: preparation and evaluation of dissolution properties. Lovelace Biomedical and Environmental Research Institute, Albuquerque, New Mexico, ITRI: annual report 1975-1976, report LF-56, 28–32.
Kanapilly, G. M., Peterson, P. K., Raabe, O. G., 1975. Aerosols of ^{244}Cm oxides: preparation and evaluation of *in vitro* dissolution. Lovelace Biomedical and Environmental Research Institute, Albuquerque, New Mexico. ITRI: annual report 1974-1975, report LF-52, 16–20.
Lafuma, J., Nénot, J. C., Morin, M., et al., 1974. Respiratory carcinogenesis in rats after inhalation of radioactive aerosols of actinides and lanthanides in various physico-chemical forms. In: Experimental Lung Cancer: Carcinogenesis and Bioassays. (Eds. Karbe, E. and Park, J. F.), 443–453. Springer-Verlag, Berlin.
Lloyd, R. D., Atherton, D. R., Mays, C. W., McFarland, S. S., Williams, J. L., 1974. The early excretion, retention and distribution of injected curium citrate in beagles. Health Phys. 27, 61–67.
Lloyd, R. D., Mays, C. W., Taylor, G. N., Atherton, D. R., 1970. Americium-241 studies in beagles. Health Phys. 18, 149–156.
Lo Sasso, T., Cohen, N., Wrenn, M. E., 1981. Distribution and retention of $^{243,244}Cm$ in the adult baboon. Radiat. Res. 85, 173–183.
Lundgren, D. L., Hahn, F. F., Carlton, W. W., et al., 1997. Dose responses from inhaled monodisperse aerosols of $^{244}Cm_2O_3$ in the lung, liver and skeleton of F344 rats and comparison with $^{239}PuO_2$, Radiat. Res. 147, 598–612.
McClellan, R. O., Boyd, H. A., Gallegos, A. F., Thomas, R. G., 1972. Retention and distribution of ^{244}Cm following inhalation of $^{244}CmCl_3$ and $^{244}CmO_{1.73}$ by beagle dogs. Health Phys. 22, 877–885.

Ménétrier, F., Taylor, D. M., Comte, A., 2008. The biokinetics and radiotoxicology of curium: A comparison with americium. Appl. Radiat. Isot. 66, 632–647.

Métivier, H. J., 1988. Transuranium elements. In: Handbook on Toxicity of Inorganic Compounds. (Eds. Seiler, H., Sigel, H. and Sigel, A.) M. Dekker, New York.

Mewhinney, J. A., Griffith, W. C., 1983. A tissue distribution model for assessment of human inhalation exposures to $^{241}AmO_2$. Health Phys. 44, 537–544.

Naylor, G. P. L., Bonas, H. E., Haines, J. W., et al., 1991. The gastrointestinal absorption and tissue distribution of alpha-emitting actinide isotopes and polonium-210. In: Occupational Radiation Protection. Proc. British Nuclear Energy Society meeting, Guernsey. 291–296.

Nenot, J. C., Masse, R., Morin, M., Lafuma, J., 1972. An experimental comparative study of the behaviour of Np-237, Pu-238, Pu-239, Am-241 and Cm-242 in bone. Health Phys. 22, 657–665.

Parker, H. G., Thaxter, M. D., Biggs, M. W., 1960. Current status of curium inhalation exposures in humans. University of California, Lawrence Radiation Laboratory Report UCRL-9361, Berkeley, California.

Parkinson, W. W., Henley, L. C., Goans, R. E., Good, W. M., 1976. Evaluation of two cases of ^{244}Cm Inhalation, In: Proceedings of the 9th Midyear Topical Symposium of the Health Physics Society, on Operational Health Physics, Denver, Co. CONF–760202–19, 252.

Popplewell, D. S., Harrison, J. D., Ham, G. J., 1991. The gastrointestinal absorption of neptunium and curium in humans. Health Phys. 60, 797–805.

Rhoads, K., Killand, B. W., Mahaffey, J. A., Sanders, C. L., 1986. Lung clearance and translocation of ^{239}Pu and ^{244}Cm in rats following inhalation individually or as a mixed oxide. Health Phys. 51, 633–640.

Sanders C. L., Mahaffey, J. A., 1978. Inhalation carcinogenesis of high-fired $^{244}CmO_2$ in rats. Radiat. Res. 76, 384–401.

Sanders, S. M., 1974. Excretion of ^{241}Am and ^{244}Cm following two cases of accidental inhalation. Health Phys. 27, 359–365.

Scott, K. G., Axelrod, D. J., Hamilton, J. G., 1949. The metabolism of curium in the rat. J. Biol. Chem. 177, 325–335.

Scott, K. G., Copp, D. H., Axelrod, D. J., Hamilton, J. G., 1948. The metabolism of americium in the rat. J. Biol. Chem. 175, 691–705.

Seidel, A., Volf, V., 1972. Removal of internally deposited transuranium elements by Zn-DTPA. Health Phys. 22, 779–783.

Semenov, A. I., Moskalev, Y. I., Zalikin, G. A. 1973. Influence of age on the absorption of ^{244}Cm from the rat gastrointestinal tract. Radiobiologiya 13, 155.

Stather, J. W., Priest, N. D., 1977. The pulmonary clearance and the comparative metabolism of plutonium-238, plutonium-239, americium-241, and curium-242 in the rat. NRPB-R&D-1. National Radiological Protection Board. Chilton, Didcot, England; 46-48.

Stradling, G. N., Cooper, J. R., Smith, H., Ham, S. E., 1979. The mobility of curium-244 dioxide in the bronchially intubated rat. Int. J. Radiat. Biol. 36, 19–32.

Sullivan, M. F., Ruemmler, P. S., Ryan, J. L., Buschbom, R. L., 1986. Influence of oxidizing or reducing agents on gastrointestinal absorption of U, Pu, Am, Cm and Pm by rats. Health Phys. 50, 223–232.

Sullivan, M. F., Miller, B. M., Ruemmler, P. S., Ryan, J. L., 1985. Further studies on the influence of chemical form and dose on absorptions of Np, Pu, Am and Cm from the gastrointestinal tracts of adult and neonatal rodents. Health Phys. 48, 61–73.

Sullivan, M. F., 1980. Absorption of actinide elements from the gastrointestinal tract of rats, guinea pigs and dogs. Health Phys. 38, 159–171.

Taya, A., Mewhinney, J. A., Guilmette, R. A., 1994. Subcellular distribution of ^{241}Am in Beagle lungs after inhalation of $^{241}Am(NO_3)_3$. In Inhaled Particles VII. Proceedings of International Symposium organised by the British Occupational Hygiene Society, Edinburgh, 16-22 September 1991, (Eds. Dodgson J, McCallum RI), Pergamon Press, Oxford, United Kingdom. Ann. Occup. Hyg. 38, Suppl. 1, 265–268.

Taylor, D. M., 1983. The comparative retention of bone-seeking radionuclides in the skeletons of rats. Health Phys. 45, 768–772.

Turner, G. A., Taylor, D. M., 1968. The transport of plutonium, americium and curium in the blood of rats. Phys. Med. Biol. 13, 535–546.

Vaane, J. P., De Ras, E. M. M., 1971. Analysis of a case of internal contamination with ^{242}Cm. Health Phys. 21, 821–826.

25. BERKELIUM (Z=97)

25.1. Chemical Forms in the Workplace

(997) Berkelium is an actinide which occurs mainly in oxidation state III and IV. Lanthanides such as Gd(III) or Eu(III) and Am(III) are good chemical analogues of Bk (III). Berkelium has no significant industrial use and may be encountered in a number of chemical forms, including oxides (Bk_2O_3, BkO_2), chlorides and nitrates.

(998) Berkelium-249 is synthesised by irradiation of curium in dedicated high-flux neutron reactors, and ^{247}Bk results from the irradiation of ^{244}Cm with high-energy alpha particles.

Table 25.1. Isotopes of berkelium addressed in this report.

Isotope	Physical half-life	Decay mode
Bk-245	4.94 d	EC, A
Bk-246	1.80 d	EC
Bk-247	1.38E+3 y	A
Bk-248m	23.7 h	B-, EC
Bk-249[a]	330 d	B-, A
Bk-250	3.212 h	B-
Bk-251	55.6 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

25.2. Routes of Intake

25.2.1. Inhalation

Absorption Types and parameter values

(999) Limited information is available on the biokinetics of inhaled berkelium in an occupational contamination case.

(1000) Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values: the revised Human Respiratory Tract Model (ICRP, 2015), the Human Alimentary Tract Model (ICRP, 2006), the human systemic model for berkelium described in *Publication 30* (ICRP, 1988). The bound state parameters were fixed at default values, $f_b = 0.002$, $s_b = 0\ d^{-1}$ as explained below.

(1001) As described in the general actinide section, absorption parameter values based on plutonium ($s_r = 0.4\ d^{-1}$; $f_b = 0.002$; $s_b = 0\ d^{-1}$) are applied in this document to the transplutonium elements for radiation protection purposes. Absorption parameter values and Types, and associated f_A values for particulate forms of berkelium, are given in Table 25.2.

Berkelium oxide

(1002) Rundo and Sedlet (1973) reported a case of accidental inhalation exposure to a mixture of ^{249}Cf and ^{249}Bk, which became airborne when ignited on a tantalum disc, and so

probably consisted of oxides. (See also the californium section in this report.) Berkelium-249 is principally a beta emitter and was not directly measured in the body. Its biokinetics was studied by excretion analysis over the first year after intake. Except for an initially rapid clearance in faeces, the urinary and faecal excretion rate of both radionuclides increased with time for 2-3 months after intake and then declined. The non-monotonic pattern of urinary excretion presumably reflects an increasing rate of dissolution of the inhaled aerosol in the lungs that can be described by the dissolution model shown in Fig. 6(b) of OIR Part 1 (ICRP, 2014). Analysis here gave $s_p = 0$, $s_{pt} = 0.001$ d^{-1} and $s_t = 0.06$ d^{-1}. Considering, for simplicity, only absorption in the absence of particle transport, these parameter values would indicate a long-term half-time of about 700 d. In the absence of particle transport, 98% ILD and 85% ILD of berkelium oxide would be retained in lungs at 30 d and 180 d respectively after intake. This suggests assignment to absorption Type S but very close to the criterion for Type M.

(1003) Absorption parameter values for berkelium oxide based on *in vivo* data are available from only one study. Berkelium oxide appears to be less soluble than californium oxide. Inhalation exposure to it is unlikely. Therefore specific parameter values for berkelium oxide are not used here. Instead, it is assigned to Type S.

Rapid dissolution rate for berkelium

(1004) The study of inhaled berkelium oxide indicates that its early absorption is slow. However, information is too limited to assess element specific parameter values. As described in the general actinide section, the value based on plutonium ($s_r = 0.4$ d^{-1}) is applied in this document to the transplutonium elements for radiation protection purposes. Because it is lower than the general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S forms of berkelium.

Extent of binding of berkelium to the respiratory tract

(1005) There is no specific information on berkelium binding to the respiratory tract. As described in the general actinide section, absorption parameter values for the bound state based on plutonium are applied in this document to the transplutonium elements. Thus, a bound fraction $f_b = 0.002$ and a rate of uptake $s_b = 0$ d^{-1}, are applied throughout the respiratory tract except in the ET_1 region.

Table 25.2. Absorption parameter values for inhaled and ingested berkelium.

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A[b]
Absorption Type	Assigned forms				
F		1	0.4	–	5×10^{-4}
M[c]		0.2	0.4	0.005	1×10^{-4}
S	berkelium oxide	0.01	0.4	1×10^{-4}	5×10^{-6}
Ingested material[d]					
All compounds					5×10^{-4}

a It is assumed that for berkelium a bound fraction f_b = 0.002 with s_b = 0 d^{-1} is applied throughout the respiratory tract except in the ET_1 region. The values of s_r for Type F, M and S forms of berkelium (0.4 d^{-1}, respectively) are element-specific.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of berkelium ($5x10^{-4}$).

c Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, *e.g.* if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

d Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A (=5 x 10^{-4}) for ingestion of the radionuclide.

25.2.2. Ingestion

(1006) An early study by Hungate (1972) indicated that fractional absorption of intragastrically administered ^{248}Bk chloride in the rat is about 1 x 10^{-4}.

(1007) In *Publication 30* Part 4 (ICRP, 1988) and *Publication 48* (1986) an absorption value of $1x10^{-3}$ for berkelium was used. However, in this report available data provided a sufficient basis for the use of a general value of 5 x 10^{-4} for all actinides other than U.

(1008) An f_A value of 5 x 10^{-4} is adopted here for all chemical forms of berkelium.

25.2.3. Systemic distribution, retention and excretion of berkelium

25.2.3.1. Data

(1009) The biokinetics of Bk has been studied in rats (Hungate et al., 1972; Zalikin et al., 1984; Zalikin and Nismov, 1988), beagles (Taylor et al., 1972), and to a limited extent in accidentally exposed human subjects (Rundo and Sedlet, 1973). The data for human subjects reveal little about the systemic behavior of Bk. Comparative data for Bk and Es in laboratory animals indicate that these elements have broadly similar biokinetics, but Bk has a lower rate of urinary excretion, lower deposition in the skeleton, greater deposition in the liver, and perhaps greater deposition in the kidneys than Es.

(1010) Following intravenous administration of ^{249}Bk and ^{253}Es to rats, about 8% of injected ^{249}Bk was excreted in urine during the first day, compared with about 35% of injected ^{253}Es (Hungate et al., 1972). The urinary excretion rate of Bk declined more slowly than that of Es. After the first day or two, the rate of faecal excretion of ^{249}Bk exceeded its urinary excretion rate. Total excretion of ^{249}Bk over the first 3 wk amounted to roughly 20% of the injected amount. The liver content of ^{249}Bk decreased from about 23% at 4 h to 3% at 21 d. During the same period the skeletal content, estimated as 20 times the content of one femur, increased from about 30% to 38% of the injected amount. Equilibrium levels in bone appeared to be achieved more slowly for Bk than for Es, possibly due to differences in initial binding of the two elements to blood components.

(1011) Taylor et al. (1972) found that the microscopic distributions of ^{249}Bk and ^{249}Cf in the soft tissues of beagles at 1-3 wk following intravenous administration of a citrate solution were similar to the distribution of ^{241}Am. Relatively high concentrations of these radionuclides were found in the hepatic cells of liver, glomeruli of kidneys, interfollicular region of the thyroid, the cartilaginous tissues of the lung, and the media of the smaller arterioles of most organs. With the exception of the liver, most of the sites of deposition in soft tissues were extracellular and associated with connective tissue.

(1012) Smith (1972) concluded from studies of decorporation of internally deposited transuranics in rats that berkelium, einsteinium, and californium are similar in their *in vivo* solubility characteristics, translocation rates in the body, and response to chelation therapy following deposition in liver, kidneys, bone, and muscle.

(1013) Following intraperitoneal administration of ^{249}Bk nitrate to rats, activity cleared slowly from blood and deposited primarily in the skeleton (up to ~40%) and liver (~18%) (Zalikin et al., 1984). Activity concentrations initially decreased in the order adrenal glands > liver > spleen > kidneys > osseous tissues. Over the first 30 d, about 18% of the administered amount was excreted in urine and 10% was excreted in faeces. Following per os or intravenous administration of ^{249}Bk to rats, the preponderance of the amount entering blood deposited in the skeleton and liver (Zalikin and Nisimov, 1988).

25.2.3.2. Biokinetic model

(1014) The biokinetic model for systemic berkelium applied in this report is described in Section 18.2.3.

25.2.3.3. Treatment of progeny

(1015) The treatment of radioactive progeny of berkelium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

25.3. Individual monitoring

^{249}Bk

(1016) Measurements of ^{249}Bk concentrations in urine and faeces are used to determine intakes of the nuclide. The main technique used for urinalysis is alpha spectrometry.

Table 25.3. Monitoring techniques for ^{249}Bk.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{249}Bk	Urine Bioassay	α spectrometry	1mBq L^{-1}	
^{249}Bk	Fecal Bioassay	α spectrometry	1 mBq $24h^{-1}$	

25.4. Dosimetric data for berkelium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Campbell, J. E., Robajdek, E. S., Anthony, D. S., 1956. The metabolism of 227Ac and its daughters 227Th and 223Ra by rats. Rad. Res. 4, 294–302.

Hungate, F. P., Ballou, J. E., Mahlum, D. D., et al., 1972. Preliminary data on 253Es and

249Bk metabolism in rats. Health Phys. 22, 653–656.
Hunt, G. J., Leonard, D. R. P., Lovett, M. B. 1990. Transfer of environmental plutonium and americium across the human gut: A second study. Sci. Total Environ. 90, 273–282.
Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1986. Transfer of environmental plutonium and americium across the human gut. Sci. Total Environ. 53, 89–109.
Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1989. Transfer of environmental plutonium and americium across the human gut. Radiol. Prot. Bull. 106, 7–11.
ICRP, 1988. Limits for intakes by workers. ICRP Publication 30, Part 4. Ann. ICRP 19(4).
ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6(2/3).
ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).
ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).
ICRP, 2006. Human alimentary tract model for radiological protection. ICRP Publication 100. Ann. ICRP 36(1/2).
ICRP 2015. Occupational intakes of radionuclides, Part 1. ICRP Publication 130. Ann. ICRP 44(2).
Popplewell, D. S., Ham, G. J., 1989. Distribution of plutonium and americium in tissues from a human autopsy case. J. Radiol. Prot. 9, 159–164.
Popplewell, D. S., Harrison, J. D., Ham, G. J., 1991. The gastrointestinal absorption of neptunium and curium in humans. Health Phys. 60, 797–805.
Rundo, J., Sedlet, J., 1973. Retention and elimination of berkelium-249-californium-249 following acute accidental inhalation. In: Proceedings of the 3rd International Congress of the International Radiation Protection Association. Washington, D.C. September 9-14, IRPA CONF-730907-P1.
Smith, V. H., 1972. Therapeutic removal of internally deposited transuranium element. Health Phys. 22, 765–778.
Taylor, G. N., Jee, W. S. S., Mays, C. W., et al., 1972. Microscopic distribution of californium-249 and berkelium-249 in the soft tissues of beagles. Health Phys. 22, 691–693.
Zalikin, G. A., Moskalev, Y. I., Nisimov, V. G., 1984. Berkelium-249 metabolism in the body of animals. Radiobiologiia 24, 122–125.
Zalikin, G. A., Nisimov, P. G., 1988. Absorption of ^{249}Bk from the gastrointestinal tract of rats. Radiobiologiia 28, 845–847.

26. CALIFORNIUM (Z=98)

26.1. Chemical Forms in the Workplace

(1017) Californium is an actinide element, which occurs mainly in oxidation state III. Lanthanides such as Gd(III) or Eu(III) and Am(III) are good chemical analogues of Cf (III). Californium may be encountered in a number of chemical forms, including oxides, chlorides citrates and nitrates.

(1018) Californium-249 is formed from the beta decay of ^{249}Bk and most other californium isotopes are made by subjecting berkelium to intense neutron radiation in a nuclear reactor. Californium-252 has a number of specialised applications as a strong neutron emitter.

Table 26.1. Isotopes of californium addressed in this report.

Isotope	Physical half-life	Decay mode
Cf-244	19.4 m	A
Cf-246	35.7 h	A, SF
Cf-247	3.11 h	EC, A
Cf-248	334 d	A, SF
Cf-249[a]	351 y	A, SF
Cf-250	13.08 d	A, SF
Cf-251	900 y	A
Cf-252[a]	2.645 y	A, SF
Cf-253	17.81 d	B-, A
Cf-254	60.5 d	A, SF
Cf-255	85 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

26.2. Routes of Intake

26.2.1. Inhalation

Absorption Types and parameter values

(1019) Limited information on absorption of californium from the respiratory tract is available from a rat inhalation study of the chloride and two occupational exposure cases involving oxide forms.

(1020) Reference biokinetic models were used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values: the revised Human Respiratory Tract Model (ICRP, 2015), the Human Alimentary Tract Model (ICRP, 2006), the human systemic model for Cf described in this document, the rat model for particle transport in

the respiratory tract of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002). A simple systemic model for Cf in the rat was developed here from the injection data reported by Graham et al. (1978), Durbin (1973) and Mewhinney et al. (1971). Unless stated otherwise, the following parameters were fixed at default values, f_b = 0.002, s_b = 0 (see above), and s_r = 1 d^{-1} (based on californium chloride as explained below).

(1021) As described in the general actinide section, absorption parameter values based on plutonium (s_r = 0.4 d^{-1}; f_b = 0.002; s_b = 0) are applied in this document to the transplutonium elements.

(1022) Absorption parameter values and Types, and associated f_A values for particulate forms of californium, are given in Table 26.2.

Californium chloride

(1023) Graham et al. (1978) studied the tissue distribution of ^{252}Cf for 32 d after intratracheal instillation of the chloride into rats. Lung retention was described by 47.8% of the initial lung deposit (ILD) being cleared with a half-time (T_b) of 10 h, 38.4% ILD with T_b 2.6 d and 13.8% ILD with T_b 18.4 d. Early measurement data were available to determine a value of s_r. Analysis here gave f_r = 0.6, s_r = 1 d^{-1} and s_s = 0.05 d^{-1}, consistent with assignment to Type F.

(1024) The absorption parameter values for californium chloride were derived from a single *in vivo* study. Moreover, inhalation exposure to it is unlikely. Although specific parameter values for californium chloride based on *in vivo* data are available, they are not adopted here. Instead, californium chloride is assigned to Type F. However, the data are used as the basis of the default rapid dissolution rate for californium.

Californium oxide

(1025) Rundo and Sedlet (1973) reported a case of accidental inhalation exposure to a mixture of ^{249}Cf and ^{249}Bk, which became airborne when ignited on a tantalum disc, and so probably consisted of oxides. The biokinetics of inhaled ^{249}Cf was studied by external measurements and excretion analysis over the first year after intake. Half-times of retention in the chest of 25 d (17% ILD) and 1210 d (83% ILD) were reported. Except for an initially rapid clearance in faeces, the urinary and faecal excretion rate of both radionuclides increased with time for 2-3 months after intake and then declined. The non-monotonic pattern of urinary excretion presumably reflects an increasing rate of dissolution of the inhaled aerosol in the lungs that can be described by the dissolution model shown in Fig. 6(b) of OIR Part 1 (ICRP, 2015). Analysis here gave s_p = 0.00041 d^{-1}, s_{pt} = 0.0035 d^{-1} and s_t = 0.031 d^{-1}. Considering, for simplicity, only absorption in the absence of particle transport, these parameter values would indicate a long-term half-time of about 180 d, much less than the 1210 d observed by the authors. This greater chest retention might be explained by the contribution of systemic organs to the *in vivo* measurements. In the absence of particle transport, 95% ILD and 56% ILD of californium would be retained in lungs at 30 d and 180 d respectively after intake, which is consistent with assignment to absorption Type M.

(1026) Poda and Hall (1975) described the follow-up of two workers over 36 and 75 d respectively after inhalation of $^{252}Cf_2O_3$. Both subjects were treated with DTPA and a cathartic. Their body content was below the detection limit of *in vivo* measurement after 3 d. Fecal excretion was sampled over a month after the incident and decreased rapidly after 3 d. Rapid renal excretion of Cf was observed for the initial 24-hr period. After that, the urine data could be described by a sum of two exponentials with T_b 0.8 d and 10 d, or <1 d and 12 d,

12246 respectively, for the two subjects. Analysis here gave f_r = 0.5 and 0.1; and s_s = 0.006 d^{-1} and
12247 0.08 d^{-1}, respectively, for the two subjects, indicating Type M and Type F respectively. In this
12248 analysis s_r was not estimated but fixed at 1 d^{-1} because the early data were complicated by the
12249 decorporation treatment.
12250 (1027) Absorption parameter values for californium oxides based on *in vivo* data are
12251 available from two studies. Overall, Cf oxides appear to be more soluble than plutonium oxide,
12252 with most results consistent with assignment to Type M, However, considerable variability is
12253 observed. In particular, an increasing dissolution rate was observed by Rundo and Sedlet (1973)
12254 but not by Poda and Hall (1975). Although specific parameter values for californium oxide
12255 based on *in vivo* data are available, they are not adopted here. Instead, californium oxide is
12256 assigned to Type M.
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12258 ***Rapid dissolution rate for californium***

12259 (1028) The value of s_r estimated for californium chloride above, 1 d^{-1}, is applied here to all
12260 Type F forms of californium, in analysing experimental data. However, as described in the
12261 general actinide section, the value based on plutonium (s_r = 0.4 d^{-1}) is applied in this document
12262 to the transplutonium elements for radiation protection purposes. Because it is lower than the
12263 general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S
12264 forms of californium.
12265
12266 ***Extent of binding of californium to the respiratory tract***
12267 (1029) There is no specific information on californium binding to the respiratory tract. As
12268 described in the general actinide section, absorption parameter values for the bound state based
12269 on plutonium are applied in this document to the transplutonium elements. Thus, a bound
12270 fraction f_b = 0.002 and a rate of uptake s_b = 0 d^{-1}, are applied throughout the respiratory tract
12271 except in the ET_1 region.
12272

12273 Table 26.2. Absorption parameter values for inhaled and ingested californium.

Inhaled particulate materials		Absorption parameter values[a]			Absorption from the alimentary tract, f_A
		f_r	s_r (d^{-1})	s_s (d^{-1})	
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Chloride	1	0.4	–	5×10^{-4}
M[d]	Oxide	0.2	0.4	0.005	1×10^{-4}
S		0.01	0.4	1×10^{-4}	5×10^{-6}
Ingested material[e]					
All compounds					5×10^{-4}

a It is assumed that for californium a bound fraction $f_b = 0.002$ with $s_b = 0$ d^{-1} is applied throughout the respiratory tract except in the ET_1 region. The values of s_r for Type F, M and S forms of californium (0.4 d^{-1}) are element-specific.

b Materials (e.g. californium chloride) are generally listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

c For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type and the f_A value for ingested soluble forms of californium (5×10^{-4}).

d Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

e Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A (=5×10^{-4}) for ingestion of the radionuclide.

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26.2.2. Ingestion

12290 (1030) Animal data on the absorption of Cf were reviewed in *Publication 30* (ICRP, 1979).

12291 (1031) Results for absorption of californium nitrate $Cf(NO_3)_3$ after gavage administration to
12292 adult rats ranged from about 1.2×10^{-3} and 5.9×10^{-4} (Sullivan and Crosby, 1974; Sullivan
12293 1980). In *Publication* 30 (ICRP, 1979), an absorption value of 5×10^{-4} was recommended. In
12294 *Publication 48* (1986), a general value of 1×10^{-3} for actinides was used. However, in this
12295 report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all
12296 actinides other than U.

12297 (1032) An f_A value of 5×10^{-4} is adopted here for all chemical forms of Cf.

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26.2.3. Systemic distribution, retention and excretion of californium

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26.2.3.1. Data

12303 (1033) The biokinetics of inhaled californium has been studied by external measurement and
12304 bioassay in a few accidentally exposed workers. The results provide useful information on the
12305

lung retention and total body retention of the inhaled material but are difficult to interpret in terms of the systemic biokinetics of californium. Results of two studies are summarised below.

(1034) A chemist accidentally inhaled a mixture of ^{249}Cf and its parent, ^{249}Bk (Rundo and Sedlet, 1973). The inhaled material was ignited before intake and was presumably highly insoluble. The biokinetics of inhaled ^{249}Cf was studied by external measurements and excretion analysis over the first year after intake. Except for an initially rapid clearance in faeces, the urinary and faecal excretion rate of both radionuclides increased with time for 2-3 months after intake and then declined (Fig. 26.1). The non-monotonic pattern of urinary excretion presumably reflects an increasing rate of dissolution of the inhaled aerosol in the lungs.

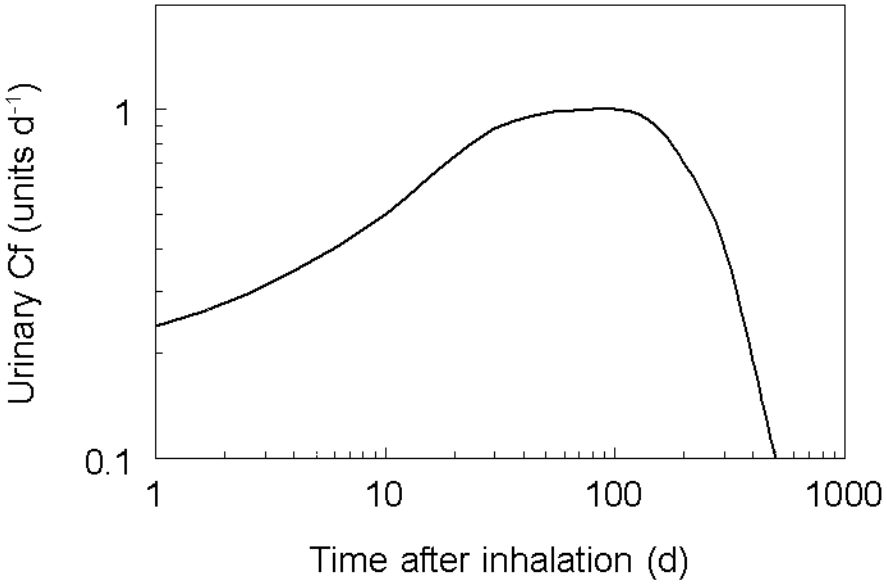

Fig. 26.1. Observed pattern of urinary excretion of ^{249}Cf by a chemist following inhalation of a form with initially low solubility in the lungs (based on data of Rundo and Sedlet, 1973).

(1035) A chemist and an analyst inhaled ^{252}Cf while attempting to reprocess a medical source (Poda and Hall, 1975). Approximately 1 μg of $^{252}Cf_2O_3$ was released when the inner capsule was accidentally cut during removal of the outer capsule. Both subjects left the work area when an air monitor sounded. Both were treated with chelates. Rapid renal excretion of Cf was observed for the first 24-hour period in each subject but may have been strongly affected by DTPA treatment. DTPA treatments on days 4 and 18 did not appear to affect the excretion rate. Urinary excretion patterns for the two subjects are shown in Fig. 26.2, where excretion has been normalised to the percentage of the first day's excretion for each subject.

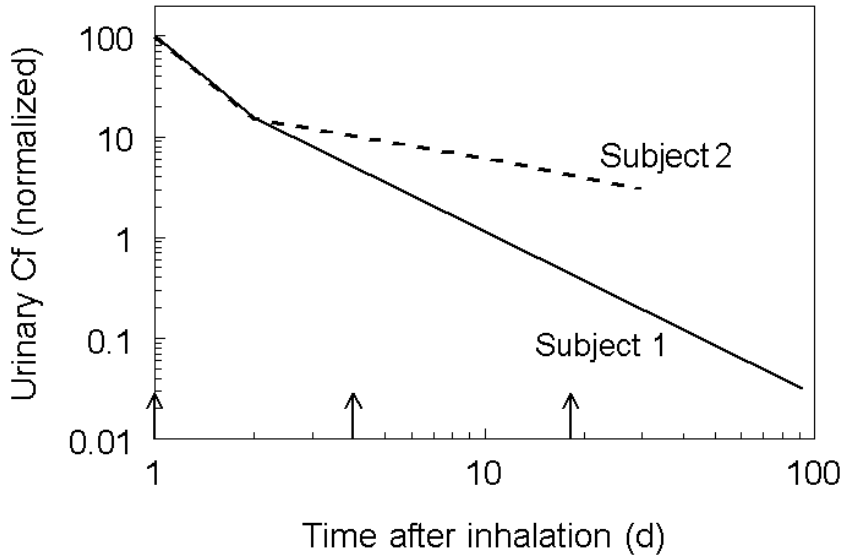

Fig. 26.2. Observed patterns of urinary excretion of ^{252}Cf following acute inhalation. DTPA administered on Days 1, 4, and 18 (arrows). Data normalised to individual's Day 1 excretion (percent).

(1036) The biological behavior of californium has been studied in different animal species including mice, rats, Chinese and Syrian hamsters, and beagles (Parker et al., 1962; Mewhinney et al., 1971, 1972; Lloyd et al., 1972, 1976; Smith, 1972; Atherton and Lloyd, 1972; Bruenger et al., 1972; Stevens and Bruenger, 1972; Taylor et al., 1972; Durbin, 1973; Graham et al., 1978). Its behavior is qualitatively similar to that of other transuranium elements. That is, much of the absorbed or injected californium deposits in the skeleton and liver; the skeletal deposit is almost entirely on bone surfaces; and most of the activity reaching the systemic circulation is tenaciously retained in the body.

(1037) Among the frequently studied transuranics, americium appears to be its closest physiological analogue. The microscopic distribution of californium in soft tissues of beagles 1-3 wk after intravenous injection of a citrate solution was found to be similar to that of americium (Taylor et al., 1972). The gross distribution of californium in the skeleton, expressed as the percentage of skeletal californium in a given bone, is similar to that of americium (Lloyd et al., 1972). The microscopic distribution of californium in the skeleton is also similar to that of americium in rats, with heaviest deposits on the trabeculae of the primary spongiosa and on epiphyseal and metaphyseal trabeculae (Durbin, 1973).

(1038) Species differences in the biokinetics of californium have been observed. For example, Mewhinney et al. (1972) found significant differences in the behavior of ^{252}Cf in rats and Chinese hamsters over 64 d following intraperitoneal injection of the citrate complex, including lower uptake of activity by the liver and kidneys and higher uptake by the skeleton in rats and much faster removal from the liver in rats (Table 26.3). The behavior of californium in beagles receiving ^{249}Cf or ^{252}Cf by intravenous injection (Lloyd et al., 1972) was broadly similar to that in the hamster with regard to uptake and retention in major repositories. The

faecal to urinary excretion ratio was much higher in rats than in dogs, probably due to a higher rate of biliary secretion of californium by rats.

Table 26.3. Early distribution of ^{252}Cf injected as citrate into hamsters, rats, and dogs (Mewhinney et al., 1972; Lloyd et al., 1972; Durbin, 1973).

	% injected activity at 7-8 d		
Tissue or excreta	Hamster	Rat	Dog
Kidney	2.9	1.2	0.9
Liver	25.6	3.5	19.2
Skeleton	25.3	65.7	44.1
Whole body	66.3	69.3	78.3
Urine	--	7.8	15.1
Faeces	--	11.0	6.9

(1039) Measurements on rats and mice indicate a biological half-time for the whole body on the order of 2 y (400-1000 d). This reflects primarily skeletal retention in these animals because the removal half-time from the liver is short and other soft tissues do not retain much californium. In dogs or hamsters, whole-body retention of californium reflects tenacious retention of in both the liver and skeleton. For the beagle, half-times of 8.5 y and 4.2 y have been estimated for the whole body and liver, respectively.

(1040) Observed species differences in the retention time of californium in the liver is consistent with a pattern seen for other transuranic elements. That is, certain mammalian species show rapid removal of transuranics from the liver, while others show extremely slow removal. For example, rats, tree shrews (small mammals, closely related to primates, native to the tropical forests of Southeast Asia), macaque monkeys, and baboons show rapid loss of plutonium from the liver, with half-times of 4-200 d, while another set of adult animals with an overlapping range of body weights, including hamsters, dogs, pigs, and humans, show tenacious retention of plutonium in the liver, with half-times measured in years or decades (Taylor, 1984).

(1041) In the skeleton, californium appears to be deposited most heavily about the trabeculae of the primary spongiosa and on epiphyseal and metaphyseal trabeculae. In soft tissues of dogs, relatively high concentrations are found in the hepatic cells of the liver, the glomeruli of the kidney, the interfollicular region of the thyroid, the cartilaginous tissues of the lung, and in the smaller arterioles of most organs. Scattered clusters of activity were found in the renal papillae and the submucosa of the bronchioles. Except for deposition in hepatic cells, most of the deposition sites in soft tissues were extracellular, associated with connective tissue.

26.2.3.2. Biokinetic model

(1042) The biokinetic model for systemic californium applied in this report is described in Section 18.2.3.

26.2.3.3. Treatment of progeny

(1043) The treatment of radioactive progeny of californium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

26.3. Individual monitoring

^{249}Cf

(1044) Measurement of ^{249}Cf concentrations in urine is used to determine intakes of the radionuclide for routine monitoring. The main technique used for *in vitro* bioassay is alpha spectrometry. *In vivo* lung measurement of ^{249}Cf may be used as additional technique for special investigation.

The main technique for *in vivo* measurement is gamma spectrometry.

Table 26.4. Monitoring techniques for ^{249}Cf.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{249}Cf	Urine Bioassay	α spectrometry	0.2 mBq/L
^{249}Cf	Faecal Bioassay	α spectrometry	0.2 mBq/24h
^{249}Cf	Lung measurement[a]	γ-ray spectrometry	800 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

^{252}Cf

(1045) Measurements of ^{252}Cf concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. The main technique used for *in vitro* bioassay is alpha spectrometry.

Table 26.5. Monitoring techniques for ^{252}Cf.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{252}Cf	Urine Bioassay	α spectrometry	0.2 mBq/L	0.05 mBq/L
^{252}Cf	Faecal Bioassay	α spectrometry	0.2 mBq/24h	

26.4. Dosimetric data for californium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Atherton, D. R., Lloyd, R. D., 1972. The distribution and retention of 249Cf in beagle soft tissue. Health Phys. 22, 675–677.

Bruenger, F. W., Atherton, D. R., Stevens, W., 1972. Intracellular distribution of ^{249}Cf in canine liver. Health Phys. 22, 685–689.

12427 Durbin, P. W., 1973. Metabolism and Biological Effects of the Transuranium Elements. In:
12428 Uranium, Plutonium and Transplutonic Elements. Eds. H. C. Hodge, J. N. Stannard
12429 and J. B. Hursh. Handbook of Experimental Pharmacology. (Berlin, Springer-Verlag),
12430 739–896.
12431 Graham, B. W., Ziemer, P. L., Landolt, R. R., Shaw, S. M., 1978. The metabolism of $^{252}CfCl_3$
12432 in the rat and the effect of *in vivo* DTPA chelation therapy. Health Phys. 34, 635–641.
12433 ICRP, 1979. Limits for intakes by workers. ICRP Publication 30, Part 1. Oxford: Pergamon
12434 Press.
12435 ICRP, 1988. Limits for intakes by workers. ICRP Publication 30, Part 4. Ann. ICRP 19(4).
12436 ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part
12437 2. ICRP Publication 67. Ann. ICRP 23(3/4).
12438 ICRP, 1994. Dose coefficients for intakes of radionuclides by workers. ICRP Publication 68.
12439 Ann. ICRP 24(4).
12440 ICRP, 1996. Age-dependent doses to members of the public from intake of radionuclides:
12441 Part 5 Compilation of ingestion and inhalation dose coefficients. ICRP Publication 72.
12442 Ann. ICRP 26(1).
12443 ICRP, 1997. Individual monitoring for internal exposure of workers. ICRP Publication 78.
12444 Ann. ICRP 27(3/4).
12445 ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model.
12446 ICRP Supporting Guidance 3. Ann. ICRP 32(1/2).
12447 ICRP, 2006. Human alimentary tract model for radiological protection. ICRP Publication 100.
12448 Ann. ICRP 36(1/2).
12449 ICRP, 2015. Occupational intakes of radionuclides, Part 1. ICRP Publication 130. Ann. ICRP
12450 44(2).
12451 Leggett, R. W., 2001. Consistent biokinetic models for the actinide elements. Rad. Prot. Env.
12452 24, 616–622.
12453 Lloyd, R. D., Mays, C. W., McFarland, S. S., Atherton, D. R., Williams, J. L., 1976.
12454 Californium studies in beagles. Radiat. Res. 65, 462–473.
12455 Lloyd, R. D., Mays, C. W., Taylor, G. N., Williams, J. L., 1972. Californium excretion and
12456 retention by beagles injected with ^{249}Cf or ^{252}Cf. Health Phys. 22, 667–673.
12457 Mewhinney, J. A., Brooks, A. L., McClellan, R. O., 1972. Comparison of the retention and
12458 distribution of injected ^{252}Cf in rats and chinese hamsters. Health Phys. 22, 695–700.
12459 Mewhinney, J. A., Ziemer, P. L., Landolt, R. R., 1971. Retention and distribution of injected
12460 californium-252 in the rat. Health Phys. 21, 860–862.
12461 Parker, H. G., de Low-Beer, A., Isaac, E. L., 1962. Comparison of retention and organ
12462 distribution of Am-241 and Cf-252 in mice: The effect of *in vivo* DTPA chelation.
12463 Health Phys. 8, 679–684.
12464 Poda, G. A., Hall, R. M., 1975. Two californium-252 inhalation cases. Health Phys. 29, 407–
12465 409.
12466 Rundo, J., Sedlet, J., 1973. Retention and elimination of berkelium-249-californium-249
12467 following acute accidental inhalation. In: Proceedings of the 3rd International
12468 Congress of the International Radiation Protection Association. Washington, D.C.
12469 September 9-14, 1973. IRPA CONF-730907-P1.
12470 Smith, V. H., 1972. Therapeutic removal of internally deposited transuranium elements.
12471 Health Phys. 22, 765–778.
12472 Stevens, W., Bruenger, F. W., 1972. Interaction of ^{249}Cf and ^{252}Cf with constituents of dog
12473 and human blood. Health Phys. 22, 679–683.

12474 Taylor, D. M., 1984. The Retention of Plutonium and Americium in Liver: An Interspecies
12475 Comparison. In: Radiation - Risk - Protection, Compacts Volume I, ed. by A. Kaul, R.
12476 Neider, J. Pensko, F.-E. Stieve, H. Brunner. 6th International Congress Organized by
12477 the Fachverband für Strahlenschutz e.v. Berlin (West) May 7-12, 1984, IRPA, 431–
12478 434.
12479 Taylor, G. N., Jee, W. S. S., Mays, C. W., et al., 1972. Microscopic distribution of
12480 californium-249 and berkelium-249 in the soft tissues of beagles. Health Phys. 22,
12481 691–693.
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27. EINSTEINIUM (Z=99)

27.1. Chemical Forms in the Workplace

(1046) Einsteinium is a rare element, which occurs mainly in oxidation state III. Lanthanides such as Gd(III) or Eu(III) and Am(III) are good chemical analogues of Es (III). Einsteinium has no significant industrial use and may be encountered in a number of chemical forms, including oxides (Es_2O_3, EsO_2), chlorides and nitrates.

(1047) Einsteinium-253 is synthesised by irradiation of curium in dedicated high-flux neutron reactors, and some heavier einsteinium isotopes can result by bombarding ^{249}Bk with high-energy alpha particles.

Table 27.1. Isotopes of einsteinium addressed in this report.

Isotope	Physical half-life	Decay mode
Es-249	102.2 m	EC, B+, A
Es-250	8.6 h	EC
Es-250m	2.22 h	EC, B+
Es-251	33 h	EC, A
Es-253	20.47 d	A, SF
Es-254[a]	275.7 d	A, B-, SF
Es-254m	39.3 h	B-, A, EC, SF
Es-255	39.8 d	B-, A, SF
Es-256	25.4 m	B-

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

27.2. Routes of Intake

27.2.1. Inhalation

Absorption Types and parameter values

(1048) No information was found on the behaviour of inhaled einsteinium (Es) in man. Information on absorption from the respiratory tract is available from experimental studies of einsteinium chloride and nitrate.

(1049) A reference biokinetic model was used here (i.e. by the Task Group) for the analysis of the data and the determination of absorption parameter values: the rat model for particle transport in the respiratory tract of the Guide for the Practical Application of the ICRP Human Respiratory Tract Model (ICRP, 2002). A simple systemic model for Es in rodents was developed here from the injection data reported by Hungate et al. (1972) and Parker at al. (1972). Unless stated otherwise, the following parameters were fixed at default values, f_b = 0.002, s_b = 0 (see below), and $s_r = 3\ d^{-1}$ (based on einsteinium chloride as explained below).

(1050) As described in the general actinide section, absorption parameter values based on plutonium ($s_r = 0.4\ d^{-1}$; $f_b = 0.002$; $s_b = 0$) are applied in this document to the transplutonium elements.

(1051) Absorption parameter values and Types, and associated f_A values for particulate forms of Es, are given in Table 27.2.

Einsteinium chloride ($EsCl_3$)

(1052) Ballou et al. (1975) measured the tissue distribution of ^{253}Es in rats for 42 d after intratracheal instillation of the chloride. Clearance from the lung followed two biological half-times of 1.3 d and 16 d, involving about the same amount of material. Early measurement data were available to determine a value of s_r, which was used as the basis of the rapid dissolution rate for einsteinium, and applied in the analysis of the other studies below, for which there were insufficient early data. Analysis here gave f_r = 0.7, s_r = 3 d^{-1} and s_s =0.03 d^{-1}. This is consistent with assignment to Type F.

(1053) Hungate et al. (1972) studied the tissue distribution of ^{253}Es in rats for 20 d after intratracheal instillation of either $EsCl_3$ or $Es(OH)_3$. It was not possible to assess absorption parameter values from the $Es(OH)_3$ data since they appeared to be inconsistent with the systemic kinetics observed after intravenous injection: the authors suspected lung damage from the alkaline solution. For Es administered as the chloride, after 20 d, 60% Initial Lung Deposit (ILD) was retained in the body: about 10% ILD remained in the lung. Analysis here gave f_r = 0.5 and s_s = 0.07 d^{-1}. This is consistent with assignment to Type F.

(1054) Although absorption parameter values for einsteinium chloride based on *in vivo* data were derived, inhalation exposure to it is unlikely. Therefore specific parameter values for einsteinium chloride are not used here. Instead, it is assigned to Type F. However, the data are used as the basis of the rapid dissolution rate for einsteinium.

Einsteinium nitrate ($Es(NO_3)_3$)

(1055) Ballou et al. (1979) studied the tissue distribution of ^{253}Es in rats for 100 d after inhalation as the nitrate $^{253}Es(NO_3)_3$. Lung retention could be described by two exponential functions with biological half-times of 1.1 d and 19.5 d, accounting for 65% ILD and 35% ILD, respectively. Analysis here gave f_r = 0.7 and s_s =0.02 d^{-1}. This is consistent with assignment to Type M.

(1056) Absorption parameter values for einsteinium nitrate based on *in vivo* data were derived from a single study. Moreover, inhalation exposure to it is unlikely. Therefore specific parameter values for einsteinium nitrate are not used here. Instead, it is assigned to Type M.

Rapid dissolution rate for einsteinium

(1057) The value of s_r estimated for chloride above, 3 d^{-1}, is applied here to all Type F forms of einsteinium, in analysing experimental data. However, as described in the general actinide section, the value based on plutonium (s_r = 0.4 d^{-1}) is applied in this document to the transplutonium elements for radiation protection purposes. Because it is lower than the general default value of 3 d^{-1} for Type M and S materials, it is also applied to Type M and S forms of einsteinium.

Extent of binding of einsteinium to the respiratory tract

(1058) There is no specific information on einsteinium binding to the respiratory tract. As described in the general actinide section, absorption parameter values for the bound state based on plutonium are applied in this document to the other transplutonium elements. Thus, a bound

fraction f_b = 0.002 and a rate of uptake s_b = 0 d^{-1}, are applied throughout the respiratory tract except in the ET_1 region.

Table 27.2. Absorption parameter values for inhaled and ingested einsteinium.

Inhaled particulate materials		Absorption parameter values[a]			Absorption from the alimentary tract, f_A[b]
		f_r	s_r (d^{-1})	s_s (d^{-1})	
Default parameter values					
Absorption Type	Assigned forms				
F	einsteinium chloride	1	0.4	–	5×10^{-4}
M[c]	einsteinium nitrate	0.2	0.4	0.005	1×10^{-4}
S		0.01	0.4	1×10^{-4}	5×10^{-6}
Ingested material[d]					
All compounds					5×10^{-4}

a It is assumed that for einsteinium a bound fraction f_b = 0.002 with s_b = 0 d^{-1} is applied throughout the respiratory tract except in the ET_1 region. The value of s_r for Type F, M and S forms of einsteinium (0.4 d^{-1}) is element-specific.

b For inhaled material deposited in the respiratory tract and subsequently cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of einsteinium (5×10^{-4}).

c Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

d Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A (=5×10^{-4}) for ingestion of the radionuclide.

27.2.2. Ingestion

(1059) An early study by Hungate (1972) indicated that einsteinium and americium are both absorbed from the gastrointestinal tract of the rat to a similar extent. Sullivan and Crosby (1975) reported an absorption of 1.4×10^{-4} for nitrates of einsteinium in the adult rat.

(1060) In *Publication 30* Part 4 (ICRP, 1988) and *Publication 48* (ICRP, 1986) an absorption value of 1×10^{-3} for einsteinium was therefore used. However, in this report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all actinides other than U.

(1061) An f_A value of 5×10^{-4} is adopted here for all chemical forms of einsteinium.

27.2.3. Systemic distribution, retention and excretion of einsteinium

27.2.3.1. Data

(1062) The biokinetics of Es has been studied in mice (Parker et al., 1972), rats (Hungate et al., 1972; Ballou et al., 1975, 1979), miniature swine (McClanahan and Ragan, 1984) and beagles (Lloyd et al., 1975). Comparative data for Am, Cf, and Es indicate that skeletal

deposition increases in the order Am < Cf < Es. The initial urinary excretion rate is much greater, and the initial fecal excretion rate is much lower, for Es than for Cf or Am.

(1063) The systemic behavior of ^{253}Es was studied up to about 8 wk following its intravenous injection as citrate to six young adult beagle dogs (Lloyd et al., 1975). Excluding two dogs with possibly anomalous initial urinary losses, mean losses in urine and faeces over the first three weeks represented about 18% and 7%, respectively, of the administered amount. The skeleton and liver were the main sites of deposition of injected activity, with the skeleton containing about 30-50% and the liver about 10-13% of the administered activity between 7 and 55 d after administration. The investigators compared the behavior of Es in dogs with that of Pu, Am, Cm, and Cf determined earlier at the same laboratory and concluded that Es most closely resembled Cf in its tissue distribution, retention, and excretion.

(1064) The biokinetics and adverse effects of ^{253}Es were studied in rats following various routes of administration of different compounds (Hungate et al., 1972). Following intravenous administration of the chloride, about 35% of the injected amount was excreted in urine during the first day. During the next 20 d the urinary and fecal excretion rates were about the same. Total excretion over 21 d amounted to almost 50% of the injected amount. Bone was the primary site of deposition. There was no indication of a change in the bone content from 4 h to 83 d post injection. The liver content declined from about 18% at 4 h to 1.6% at 21 d. The behavior of ^{253}Es administered as the hydroxide was much different: about 80% of the administered activity was lost from the body within 4 h, and less than 1% remained after 20 d. The authors suggested that the much different results for the hydroxide could be related to damaging effects of the alkaline solution in the lung. The systemic behavior of ^{253}Es observed in later studies at the same laboratory involving intratracheal administration of $^{253}EsCl_3$ or inhalation of $^{253}Es(NO_3)_3$ (Ballou et al., 1975, 1979) seem reasonably consistent with the results obtained by Hungate et al. for ^{253}Es injected as the chloride.

(1065) Parker et al. (1972) studied the distribution, retention, and excretion of ^{253}Es in mice following intramuscular injection and compared the results with previous findings by the same group for americium and californium in mice. Over the first 4 d approximately 30% and 1.4% of the administered ^{253}Es was excreted in urine and faeces, respectively. At 4 d, the liver contained about 7% of the administered ^{253}Es and the skeleton plus carcass contained about 45%. At that time the liver deposition of Es was about the same as the value determined earlier for Cf and about 30% of the value for Am; skeletal retention was somewhat greater for Es than for Cf or Am; urinary excretion of Es was about 5 times that of Cf or Am; and faecal excretion of Es was an order of magnitude lower than that of Cf or Am.

(1066) At 1 d after intravenous administration of ^{253}Es as the chloride to juvenile miniature swine, the skeleton and liver contained roughly 60-70% and 15%, respectively, of the injected amount (McClanahan and Ragan, 1984). The skeletal content appeared to decrease little if any over the following 70 d, while the liver content decreased by roughly 50%. Over the first 7 d, about 2.4% of the administered amount was removed in urine and 3.3% was removed in faeces.

27.2.3.2. Biokinetic model

(1067) The biokinetic model for systemic einsteinium applied in this report is described in Section 18.2.3.

27.2.3.3. Treatment of progeny

(1068) The treatment of radioactive progeny of einsteinium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

27.3. Individual monitoring

^{254}Es

(1069) Measurements of ^{254}Es concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. *In vivo* lung measurement of ^{254}Es may allow evaluating the intake of radionuclide if the measurement system is sensitive enough. The main measurement technique is gamma spectrometry.

Table 27.3. Monitoring techniques for ^{254}Es.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{254}Es	Urine Bioassay	γ-ray spectrometry	4 Bq/L
^{254}Es	Faecal Bioassay	γ-ray spectrometry	4 Bq/24h
^{254}Es	Lung measurement[a]	γ-ray spectrometry	3 Bq

[a] Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

27.4. Dosimetric data for einsteinium

Dosimetric data will be provided in the final version of the document.

References

Ballou, J. E., Dagle, G. E., Gies, R. A., Smith, L. G., 1979. Late effects of inhaled $^{253}Es(No_3)_3$ in rats. Health Phys. 37, 301–309.

Ballou, J. E., Dagle, G. E., Morrow, W. G., 1975. The long-term effects of intratracheally instilled $^{253}EsCl_3$ in rats. Health Phys. 29, 267–272.

Hungate, F. P., Ballou, J. E., Mahlum, D. D., et al., 1972. Preliminary data on ^{253}Es and ^{249}Bk metabolism in rats. Health Phys. 22, 653–656.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1990. Transfer of environmental plutonium and americium across the human gut: A second study. Sci. Total Environ. 90, 273–282.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1986. Transfer of environmental plutonium and americium across the human gut. Sci. Total Environ. 53, 89–109.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1989. Transfer of environmental plutonium and americium across the human gut. Radiol. Prot. Bull. 106, 7–11.

ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6(2/3).

ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).

Popplewell, D. S., Ham, G. J., 1989. Distribution of plutonium and americium in tissues from a human autopsy case. J. Radiol. Prot. 9, 159–164.

ICRP, 2002. Guide for the practical application of the ICRP Human Respiratory Tract Model. ICRP Supporting Guidance 3. Ann. ICRP 32(1/2).

Lloyd, R. D., Dockum, J. G., Atherton, D. R., Mays, C. W., Williams, J. L., 1975. The early retention, excretion, and distribution of injected einsteinium citrate in beagles. Health Phys. 28, 585–589.

McClanahan, B. J., Ragan, H. A., 1984. Distribution of ^{253}Es in juvenile miniature swine. Health Phys. 47, 472–475.

Parker, H. G., Wright, S. R., Low-Beer, A. G., Yaeger, D. J., 1972. The metabolism of ^{253}Es in mice. Health Phys. 22, 647–651.

Popplewell, D. S., Harrison, J. D., Ham, G. J., 1991. The gastrointestinal absorption of neptunium and curium in humans. Health Phys. 60, 797–805.

Sullivan M. F., Crosby A. L., 1975. Absorption of uranium-233, neptunium-237, plutonium-238, americium-241, curium-244 and einsteinium-253 from the gastrointestinal tract of newborn and adult rats. BNWL-1950 PT 1, Pacific Northwest Laboratory Annual Report for 1974, Battelle, Richland, Washington, USA, 105–108.

28. FERMIUM (Z=100)

28.1. Chemical Forms in the Workplace

(1070) Fermium is an actinide which occurs mainly in oxidation state III. Am(III) and lanthanides such as Gd(III) or Eu(III) are good chemical analogues of Fm (III). Fermium has no significant industrial use and may be encountered in a number of chemical forms, including oxides (Fm_2O_3, FmO_2), chlorides and nitrates.

(1071) Fermium-257 is synthesised by irradiation of curium in dedicated high-flux neutron reactors.

Table 28.1. Isotopes of fermium addressed in this report.

Isotope	Physical half-life	Decay mode
Fm-251	5.30 h	EC, B+, A
Fm-252	25.39 h	AS, F
Fm-253	3.00 d	EC, A
Fm-254	3.240 h	AS, F
Fm-255	20.07 h	A, SF
Fm-256	157.6 m	A, SF
Fm-257[a]	100.5 d	A, SF

[a]Dose coefficients and bioassay data for this radionuclide are given in the printed copy of this report. Data for other radionuclides listed in this table are given in the accompanying electronic annexes.

28.2. Routes of Intake

28.2.1. Inhalation

Absorption Types and parameter values

(1072) No reports were found of experimental studies on the behaviour of fermium (Fm) following deposition in the respiratory tract, nor of its retention in the lung following accidental intake.

(1073) As described in the general actinide section, absorption parameter values based on plutonium (s_r = 0.4 d^{-1}, f_b = 0.002; s_b = 0 d^{-1}) are applied in this document to the transplutonium elements. Absorption parameter values and Types, and associated f_A values for particulate forms of fermium, are given in Table 28.2.

Table 28.2. Absorption parameter values for inhaled and ingested fermium.

Inhaled particulate materials		Absorption parameter values[a]			Absorption from the alimentary tract, f_A[b]
Absorption Type	Assigned forms	f_r	s_r (d^{-1})	s_s (d^{-1})	

F	1	0.4	–	5×10^{-4}
M[c]	0.2	0.4	0.005	1×10^{-4}
S	0.01	0.4	1×10^{-4}	5×10^{-6}

Ingested material[d]	
All compounds	5×10^{-4}

a It is assumed that for fermium a bound fraction $f_b = 0.002$ with $s_b = 0\ d^{-1}$ is applied throughout the respiratory tract except in the ET_1 region. The value of s_r for Type F, M and S forms of fermium $0.4\ d^{-1}$) is element-specific.

b For inhaled material deposited in the respiratory tract and subsequent cleared by particle transport to the alimentary tract, the default f_A values for inhaled materials are applied: *i.e.*, the product of f_r for the absorption Type (or specific value where given) and the f_A value for ingested soluble forms of fermium (5×10^{-4}).

c Default Type M is recommended for use in the absence of specific information on which the exposure material can be assigned to an Absorption Type, e.g. if the form is unknown, or if the form is known but there is no information available on the absorption of that form from the respiratory tract.

d Activity transferred from systemic compartments into segments of the alimentary tract is assumed to be subject to reabsorption to blood. The default absorption fraction f_A for the secreted activity is the reference f_A ($=5 \times 10^{-4}$) for ingestion of the radionuclide.

28.2.2. Ingestion

(1074) There are no data available on the uptake of fermium from the gastrointestinal tract. By analogy with americium, an absorption value of 1×10^{-3} for fermium was therefore used in *Publication 30* Part 4 (ICRP, 1988) and *Publication 48* (ICRP, 1986). However, in this report available data provided a sufficient basis for the use of a general value of 5×10^{-4} for all actinides other than U.

(1075) An f_A value of 5×10^{-4} is adopted here for all chemical forms of fermium.

28.2.3. Systemic distribution, retention and excretion of fermium

28.2.3.1. Data

(1076) No biokinetic data were found for Fm.

28.2.3.2. Biokinetic model

(1077) The biokinetic model for systemic einsteinium is applied in this report to fermium (see Section 18.2.3).

28.2.3.3. Treatment of progeny

(1078) The treatment of radioactive progeny of fermium produced in systemic compartments or absorbed to blood after production in the respiratory or gastrointestinal tract is described in Section 18.2.4.

28.3. Individual monitoring

^{257}Fm

(1079) Measurements of ^{257}Fm concentrations in urine and faeces are used to determine intakes of the radionuclide for routine monitoring. *In vivo* lung measurement of ^{257}Fm may allow evaluating the intake of radionuclide if the measurement system is sensitive enough. The main measurement technique is gamma spectrometry.

Table 28.3. Monitoring techniques for ^{257}Fm.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit
^{257}Fm	Urine Bioassay	γ-ray spectrometry	40 Bq/L
^{257}Fm	Faecal Bioassay	γ-ray spectrometry	40 Bq/24h
^{257}Fm	Lung measurement[a]	γ-ray spectrometry	30 Bq

a Measurement system comprised of two Broad Energy Germanium Detectors (BEGe), counting time of 36 minutes and chest wall thickness of 2.54 cm.

28.4. Dosimetric data for fermium

Dosimetric data will be provided in the final version of the document.

REFERENCES

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1990. Transfer of environmental plutonium and americium across the human gut: A second study. Sci. Total Environ. 90, 273–282.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1986. Transfer of environmental plutonium and americium across the human gut. Sci. Total Environ. 53, 89–109.

Hunt, G. J., Leonard, D. R. P., Lovett, M. B., 1989. Transfer of environmental plutonium and americium across the human gut. Radiol. Prot. Bull. 106, 7–11.

ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 3. Ann. ICRP 6(2/3).

ICRP, 1986. The metabolism of plutonium and related elements. ICRP Publication 48. Ann. ICRP 16(2/3).

ICRP, 1993. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. ICRP Publication 67. Ann. ICRP 23(3/4).

Popplewell, D. S., Ham, G. J., 1989. Distribution of plutonium and americium in tissues from a human autopsy case. J. Radiol. Prot. 9, 159–164.

Popplewell, D. S., Harrison, J. D., Ham, G. J., 1991. The gastrointestinal absorption of neptunium and curium in humans. Health Phys. 60, 797–805.