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Occupational Intakes of Radionuclides Part 2

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Abstract- The 2007 Recommendations (*Publication 103*, ICRP, 2007) introduced changes to the radiation and tissue weighting factors used in calculation of effective dose. In addition, *Publication 103* clarified the need for separate calculation of equivalent dose to males and females and sex-averaging in the calculation of effective dose (ICRP, 2007) and adopted the use of reference anatomical computational phantoms, in place of the composite mathematical models that have been used previously.

These substantial changes implied a revision of the dose coefficients for internal exposure, published previously in the *Publication 30* series (ICRP, 1979, 1980, 1981, 1988b). This work was performed by Committee 2 and its Task Groups INDOS and DOCAL.

This report is the second in a series of documents replacing the *Publication 30* series and *Publication 68* (ICRP, 1994b) and providing revised dose coefficients for occupational intakes of radionuclides (OIR) by inhalation and ingestion. It provides data on individual elements and their radioisotopes, including biokinetic data and models, dose coefficients and data for bioassay interpretation. Electronic discs accompanying this series give extensive additional information.

This second report in the series provides the above 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 current version, posted for public consultation, contains only the biokinetic data and the models. The total set of dose coefficients and data for bioassay interpretation will be included in the final version.

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

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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 anatomical computational phantoms, in place of the composite mathematical models that have been used for all previous calculations of organ doses. *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 initially provided in the *Publication 30* series (ICRP, 1979, 1980, 1981, 1988b). This work was performed by Committee 2 and its Task Groups INDOS and DOCAL.

This report is the second in a series of documents replacing the *Publication 30* series and *Publication 68* (ICRP, 1994b) and providing revised dose coefficients for occupational intakes of radionuclides (OIR) by inhalation and ingestion. It provides also radionuclide-specific information for the design and planning of monitoring programmes and retrospective assessment of occupational internal doses, replacing *Publications 54* and *78* (ICRP, 1988a, 1997b).

The first report of this OIR series included chapters describing the control of occupational exposures, biokinetic and dosimetric models, monitoring methods, monitoring programmes and retrospective dose assessment.

The following reports provide data on individual elements and their radioisotopes, including biokinetic data and models, dose coefficients and data for bioassay interpretation. Electronic discs accompanying this series give extensive additional information.

This second report in the series provides the above 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).

Subsequent reports will provide data for the other elements.

The current version, posted for public consultation, contains only the biokinetic data and the models. The total set of dose coefficients and data for bioassay interpretation will be included in the final version.

The membership of the Task Group on Internal Dosimetry (INDOS) at the time of the completion of this report was:

Members:

F Paquet (Chair)	G Etherington	J L Lipsztein
E Ansoborlo	A Giussani	D Melo
M R Bailey	R A Guilmette	
E J A 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 the Task Group on Dose Calculations (DOCAL) at the time of the completion of this report 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 Committee 2 was:

(2009-2013)

H-G Menzel (Chair)	W E Bolch	J D Harrison
F Paquet	M R Bailey	R Cox
N Ishigure	N Petoussi-Henss	M Balonov
G Dietze	R W Leggett	A S Pradhan
D Bartlett	K F Eckerman	J L Lipsztein
V Berkovski	A Endo	J Ma

1. INTRODUCTION

(1) The present report is Part 2 of a report series aimed at providing 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 report series replaces the *Publication 30* series (ICRP, 1979, 1980, 1981, 1988b), *Publications 54*, *68* and *78* (ICRP, 1988a, 1994b, 1997). The revised dose coefficients, dose per unit 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 Part 1 of this report series. In addition, information is provided in this report series on absorption to blood following inhalation and ingestion of different chemical forms of elements and their radioisotopes, in those cases for which it is currently judged that the data are sufficient to make specific recommendations. Revisions have 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) The dose coefficients and dose per unit content values presented in this report series[1] are given for a Reference Worker with an average breathing rate of 1.2 m^3 h^{-1} during an 8 h working day. These data are provided for a range of physico-chemical forms for each radionuclide and for a range of aerosol particle size distributions. 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).

(4) Data are presented 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; and information on the interpretation of individual monitoring data. Each section in the printed documents also includes tables of:

- Dose coefficients (committed effective dose, Sv, per Bq intake) for inhalation of 5 µm AMAD aerosols with the default absorption Types appropriate for the element, for all relevant radioisotopes;
- Principal emissions of selected radioisotopes;
- Measurement techniques, detection limits typically achieved in a practical monitoring programme, and improved detection limits that could be achieved by suitable choice of measurement parameter values, for selected radioisotopes;
- Committed effective dose (Sv) per unit measurement (Bq) for an acute intake by inhalation of a 5 µm AMAD aerosol with the default absorption Types appropriate for the element, for selected radioisotopes;

1 The current version, posted for public consultation, contains only the biokinetic data and the models. The total set of dose coefficients and data for bioassay interpretation will be included in the final version

- Bioassay data (i.e. whole body and/or organ retention, and daily urinary and faecal excretion, Bq per Bq intake), at various times after an acute intake by inhalation of a 5 µm AMAD aerosol with the default absorption Types appropriate for the element;

(5) Bioassay data are also presented graphically.

(6) In cases for which sufficient information is available, lung absorption is specified for different chemical forms and dose coefficients and bioassay data are calculated accordingly.

(7) The full data set of this report is provided on electronic disk. This disk contains in addition to the printed document:

Dose coefficients

- Committed equivalent dose coefficients for organs and tissues, for males and females;
- Dose coefficients for all chemical forms considered;
- Dose coefficients for an inhaled aerosol with particle sizes ranging from an AMTD of 0.001 µm to an AMAD of 20 µm;
- Dose coefficients for intake by ingestion, with the default f_A values appropriate for the element, for all relevant radioisotopes;
- Dose coefficients for radioisotopes not given in the printed reports in this series.

Bioassay data

- Committed effective dose (Sv) per unit measurement (Bq) for an acute intake by inhalation of an aerosol with particle sizes ranging from an AMTD of 0.001 µm to an AMAD of 20 µm;
- Committed effective dose (Sv) per unit measurement (Bq) for an acute intake by ingestion, with default f_A values appropriate for the element;
- Bioassay data (i.e. whole body and/or organ retention, and daily urinary and faecal excretion, Bq per Bq intake), for an acute intake by inhalation of an aerosol with particle sizes ranging from an AMTD of 0.001 µm to an AMAD of 20 µm;
- Similar bioassay data for an acute intake by ingestion
- Figures giving measured activity content per unit dose (Bq Sv^{-1}) in selected body tissues, urine (daily excretion) or faeces (daily excretion), at various times after intake by inhalation or ingestion. These data can also be used to facilitate decisions about the design of monitoring programmes and the extent of the assessment required, as described in Chapter 5 of OIR Part 1.

(8) The list of elements included in this Part 2 is: 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).

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2. HYDROGEN (Z = 1)

2.1. Chemical Forms in the Workplace

(9) Hydrogen is a non-metallic element which occurs mainly in oxidation states –I and I. Hydrogen is able to react chemically with most other elements. Tritium (^{3}H, for convenience the symbol 'T' is often used in this section) is a radioactive isotope of hydrogen. It is found in industry in a variety of chemical forms, including hydrogen gas (elemental tritium), tritiated water, methane, metal tritide, luminizing compounds and tritium-contaminated pump oils. It is also present in a wide variety of organic compounds used in research, including DNA precursors such as [6-^{3}H]-thymidine (Rudran, 1988a; Taylor et al., 1990; Hill and Johnson, 1993). Tritium is an important fuel for controlled nuclear fusion in both magnetic and inertial confinement fusion reactor designs.

Table 2-1. Isotopes of hydrogen addressed in this report

Isotope	Physical half-life	Decay mode
H-3	12.32 y	Beta

2.2. Routes of Intake

2.2.1. Inhalation

(10) Extensive information is available from occupational exposures, and from human volunteer studies with inhaled tritium gas and tritiated water. Information is also available from experimental studies of tritiated organic compounds and particulate forms (mainly metal tritides and luminous compounds), in rats and *in vitro*.

Classification of gases and vapours, absorption Types and parameter values

(11) Absorption parameter values and Types, and associated f_A values for gas and vapour forms of hydrogen (tritium) are given in Table 2-2 and for particulate forms in Table 2-3. Exposures to gas or vapour forms of tritium are more common than exposures to particulate forms, and it is therefore proposed by the Task group that gas/vapour form should be assumed in the absence of information.

(a) Gases and vapours

Tritiated water (HTO)

(12) Pinson and Langham (1957) demonstrated that inhaled HTO is translocated to blood almost completely and instantaneously, and then distributes uniformly throughout the body without changing chemical form. For HTO it is therefore assumed here that there is 100% deposition in the respiratory tract, with instantaneous (Type V) absorption. Note that absorption through skin can add significantly to uptake during unprotected exposure to HTO in the air. Uptake through skin is not included in the inhalation dose coefficient, but employers may wish to take account of it for workplace control. Furthermore, urine bioassay

measurements, which are the basis for most tritium dose assessments, represent the body water concentration from all routes of intake, and therefore do take it into account.

Tritium gas (elemental tritium, HT)

(13) *Publication 30* (ICRP, 1979) identified tritium in the form of hydrogen gas as one of two gases (the other being ^{37}Ar) and for which exposure is dominated by irradiation of the lung (rather than the skin), because the emissions have insufficient energy to reach the basal layer of the skin. However, as described in *Publication 68*, Annex A (ICRP 1994), on the assumption that 0.01% of inhaled HT is absorbed and converted to HTO (see below) the effective dose per unit intake from absorbed HT is several times higher than that due to irradiation of the lung from gas within it. That conclusion remains applicable, and therefore dose coefficients are calculated here for tritium in the form of hydrogen gas, based on its absorption.

(14) Studies in which human volunteers inhaled tritium gas (composed of 93% HT) showed that ~1% of the inhaled HT dissolved in body fluids and tissues, and that ~1% of the dissolved HT (i.e. ~0.01% of the inhaled HT) was subsequently converted to HTO in the gut and the rest exhaled (Peterman et al., 1985a,b). For further information see Section 1.3.4. These results appear to accord with the data of Pinson and Langham (1957). For HT it is therefore assumed here that there is 0.01% effective deposition in the respiratory tract with instantaneous (Type V) absorption and conversion to HTO. It should be noted that in occupational exposure conditions HT in air is always accompanied by HTO vapour, and the latter dominates with regard to human exposure.

Tritiated methane, $CH_{4-x}T_x$

(15) The dosimetric implications of inhaling methane gas were examined by Phipps et al. (1990). They made the conservative assumption that 1% of the methane was metabolized, based on observations by Dougherty et al. (1967) which indicated that approximately 0.3% of methane infused into sheep was converted to carbon dioxide. Carlisle et al. (2005) investigated the extent of oxidation and organic fixation of ^{3}H and ^{14}C following inhalation of ^{3}H-labelled and/or ^{14}C-labelled methane by rats. A pilot study examined retention of activity in skin, liver, brain and carcass at 1 and 24 hours after a 4-hour exposure. It was estimated that uptake was about 0.13% of intake based on retention of ^{3}H in liver and 0.06% of intake based on retention of ^{3}H in the other tissues. About 70% of ^{3}H retained in liver and 10% of ^{3}H retained in other tissues was organically bound. For tritiated methane it is assumed here that there is 0.1% effective deposition in the respiratory tract with instantaneous (Type V) absorption. It is also assumed here that the absorbed tritium follows the systemic model for HTO.

Unspecified organic forms

(16) Volatile organic compounds have a wide range of solubility in body fluids (see Carbon Section). Therefore, in the absence of specific information, the default option for gases and vapours is taken, which is likely to be conservative. For tritium in unspecified organic forms it is assumed here that there is 100% deposition in the respiratory tract (with default regional distribution, Table 2-2) and Type F absorption. It is also assumed here that the absorbed tritium follows the systemic model for (Organically Bound Tritium) OBT.

Unspecified tritium gases and vapours

(17) Other volatile tritiated compounds have a wide range of solubility in body fluids. Therefore, in the absence of specific information, the default option for gases and vapours is

taken. For tritium in unspecified gas and vapour form it is assumed here that there is 100% deposition in the respiratory tract (with default regional distribution, Table 2-2) and Type F absorption. It is also assumed here that the absorbed tritium follows the systemic model for HTO.

(b) Particulate materials (liquid and solid)

(18) Tritium can be released into the work environment in particulate form, and several studies of the dissolution of solid tritiated compounds have been conducted. See the Carbon Section for information on organic compounds, much of which would be applicable to tritium present in such forms. However, dose coefficients and bioassay functions are not given in most cases, because the systemic behaviour of the carbon is specific to the chemical form on intake.

(19) Because of the low energy of the tritium beta emissions, self-absorption within particles can significantly reduce doses, even for particles as small as 1 μm diameter. Kropf et al. (1998) calculated that (for erbium tritide, ErT_{3-x}) the fraction of beta energy that escapes was in the range 0.5–0.1 for particle diameters in the range 1–5 μm.

(20) Cheng et al. (1997), Inkret et al. (2001) and Zhou and Cheng (2003) demonstrated that tritium is released from metal tritides into simulated lung fluids as HTO. It is assumed here that for inhalation of inorganic particulate material, the biokinetics of tritium absorbed into body fluids follows that of HTO.

Tritium-contaminated glass

(21) Cool and Maillie (1983) followed loss of tritium into simulated lung fluid, from fragments of tritium-filled glass microballoons used in laser fusion research, for 150 days. The fraction of total tritium lost during the first 100 days ranged between 16% and 30% for different glass samples. Dissolution kinetics were reported as the fraction lost per day, which decreased from about 2% initially to about 0.04% at 100 days. Average parameter values calculated here were f_r ~0.2, s_r ~0.1 d^{-1} and s_s ~0.0002 d^{-1}, consistent with assignment to Type M. Cool and Maillie (1984) followed the tissue distribution and excretion of tritium for 80 and 180 days respectively following intratracheal instillation into rats of fragments of tritium-labelled glass microballoons. There is insufficient information given for absorption parameter values to be estimated here. However, the authors reported that results obtained *in vivo* were in good agreement with the *in vitro* data obtained from the same type of glass. A large percentage of the tritium present in the glass matrix at the start of the experiments remained with it. The main difference was that generally, a greater proportion of the tritium was associated with the slower phase of tritium dissolution *in vivo* than *in vitro*. The uniform distribution of tritium activity found within the various soft tissues of the body was consistent with the hypothesis that tritium lost from the glass matrix is converted to HTO.

Luminous paint

(22) Balonov et al. (1984, 1995) reported that following intratracheal instillation into rats of "Soviet luminous powder (PS-A)" the lung specific activity showed essentially no decrease within 5 months, and hence should be assigned to ICRP *Publication 30* Class Y. This indicates that such compounds should be assigned to Type M or S.

(23) Results of 5-day *in vitro* studies of the dissolution in bovine serum of samples of commercial luminous paint powder made from tritium-labelled polystyrene (Rudran, 1988a) were described as on average 12% dissolved on the first day, and about 2% of remaining activity on subsequent days, i.e. f_r ~0.12, s_r >1 d^{-1} and s_s ~0.02 d^{-1}, consistent with

assignment to Type M.

Titanium tritide

(24) Balonov et al. (1984, 1995) reported that, following inhalation by rats, titanium tritide (TiT) showed slow lung clearance, and hence should be assigned to ICRP *Publication 30* Class Y. This indicates that TiT should be assigned to Type M or S.

(25) Measurements were made up to 4 months after intratracheal instillation of TiT (1-µm count median diameter, CMD) into rats, and simulation modelling was applied to obtain a time-dependent absorption function (fractional absorption rate) (Cheng et al., 1999). Fitting the HRTM dissolution model to the data gave parameter values: $f_r = 0.6$, $s_r = 0.71$ d^{-1} and $s_s = 0.0002$ d^{-1} with an upper bound on f_A of 0.6 (Cheng, 2009) consistent with assignment to Type M. Results of a 30-day *in vitro* study of the dissolution of the same powder in synthetic serum ultrafiltrate (SUF) (Cheng et al., 1997) were expressed as a two-component exponential retention function, giving $f_r = 0.24$, $s_r = 0.71$ d^{-1}, $s_s = 0.021$ d^{-1}. This dissolution rate is broadly similar to the absorption rate *in vivo*, (initially lower, but higher after a few days), and also consistent with assignment to Type M. Dissolution in the same system of a sample of coarse dust (103-µm CMD) was much slower, but still consistent with assignment to Type M. The results indicated that loss of tritium was related to diffusion and hence increases with the specific surface area of the particles. Although specific parameter values for titanium tritide based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is unlikely. Instead, titanium tritide is assigned to Type M.

Zirconium tritide

(26) Measurements were made up to 6 months after intratracheal instillation of zirconium tritide (0.3-µm CMD) into rats, and simulation modelling was applied to obtain a fractional absorption rate (Zhou and Cheng, 2004). Fitting the HRTM dissolution model to the data gave parameter values: $f_r = 0.0995$, $s_r = 0.058$ d^{-1} and $s_s = 3.9\text{x}10^{-4}$ d^{-1} with an upper bound on f_A of 0.1 (Zhou et al., 2010), consistent with assignment to Type M. Results of 200-day *in vitro* studies of the dissolution in SUF of the same powder (Zhou and Cheng, 2004) were expressed as a two-component exponential retention function, with $f_r = 0.048$, $s_r = 0.016$ d^{-1} and $s_s = 1.8\text{x}10^{-3}$ d^{-1}. This dissolution is somewhat faster than the absorption *in vivo*, but also consistent with assignment to Type M. Although specific parameter values for zirconium tritide based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is unlikely. Instead, zirconium tritide is assigned to Type M.

Carbon tritide

(27) The results of a 110-day *in vitro* study of the dissolution in SUF of carbon tritide (1-µm CMD) samples taken from a test fusion reactor were expressed as a fractional absorption rate (Cheng et al., 2002a). Fitting the HRTM dissolution model to the data gave parameter values: $f_r = 0.035$, $s_r = 0.396$ d^{-1} and $s_s = 3.72\text{x}10^{-4}$ d^{-1} (Cheng 2009), consistent with assignment to Type S.

(28) The results of a 14-day *in vitro* study of the dissolution in serum simulant of "coarse" and "fine" tritium loaded carbon particles taken from another test fusion reactor were expressed as two-component exponential retention functions (Hodgson et al., 2004). For "coarse" particles $f_r = 0.05$, $s_r = 500$ d^{-1} and $s_s = 6.3\text{x}10^{-3}$ d^{-1}, giving assignment to Type M. For "fine" particles $f_r = 0.003$, $s_r = 500$ d^{-1} and $s_s = 3.6\text{x}10^{-4}$ d^{-1}, giving assignment to Type S. Hodgson et al. (2006, 2007) measured dissolution in serum simulant of three samples from two batches of tritium loaded carbon particles from the same reactor for 100 days. Retention of undissolved tritium was expressed as a three-component exponential function. (To take

account of the three components in software that implements the HRTM with only two, dose coefficients were calculated by treating each sample as a mixture of two materials.) For one batch, results for two samples gave assignment to Type M and the third to Type S. For the other batch, results for all three samples gave assignment to Type S.

(29) Specific values are not adopted here (Table 2-3), because only *in vitro* data are available.

Hafnium tritide

(30) Measurements were made up to 6 months after intratracheal instillation of hafnium tritide (1-μm CMD) into rats, and simulation modelling was applied to obtain a fractional absorption rate (Zhou and Cheng, 2003). Fitting the HRTM dissolution model to the data gave parameter values: f_r = 3.07x10^{-4}, s_r = 2.72 d^{-1} and s_s = 1.22x10^{-5} d^{-1} with an upper bound on f_A of 3.07x10^{-4} (Cheng 2009), consistent with assignment to Type S. Results of 200-day *in vitro* studies of the dissolution in SUF of similar powders (Inkret et al., 2001; Cheng et al., 2002b) were expressed as two-component exponential retention functions, with f_r ~1x10^{-3}, s_r ~0.015 d^{-1} and s_s ~2.5x10^{-6} d^{-1}. This dissolution is broadly similar to the absorption *in vivo*, (initially lower, but higher after a few days), and also consistent with assignment to Type S. Although specific parameter values for hafnium tritide based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is unlikely. Instead, hafnium tritide is assigned to Type S.

Rapid dissolution rate for tritium

(31) Although no measurements were found for Type F particulate forms, the evidence of rapid uptake of tritiated gases from the lung indicates a rapid rate of absorption of order 100 d^{-1}. A value of 100 d^{-1} is applied here to all Type F forms of hydrogen.

Extent of binding of tritium to the respiratory tract

(32) The evidence of rapid uptake of tritiated gases from the lung indicates that that there is probably little binding of tritium. It is therefore assumed that for tritium the bound state can be neglected, i.e. f_b = 0.0.

631
632 **Table 2-2. Deposition and absorption for gas and vapour compounds of hydrogen (tritium)[a]**
633

Chemical form/origin	Percentage deposited[b]						Absorption		Systemic model[c]
	Total	ET_1	ET_2	BB	bb	AI	Type	f_A	
Tritiated water (HTO)	100[d]	0	20	10	20	50	V	(f)	HTO
Tritium gas (HT)	0.01[d]	0	0.002	0.001	0.002	0.005	V	(f)	HTO
Tritiated methane ($CH_{4-x}T_x$)	0.1[d]	0	0.02	0.01	0.02	0.05	V	(f)	HTO
Unspecified organic forms	100[e]	0	20	10	20	50	F	1.0	OBT
Unspecified[a]	100[e]	0	20	10	20	50	F	1.0	HTO

634 [a] For tritium in unspecified gas or vapour form, the default option for gases and vapours is recommended:
635 100% total deposition in the respiratory tract; default distribution between regions (footnote e) and Type F
636 absorption.
637 [b] *Percentage deposited* refers to how much of the material in the inhaled air remains behind after exhalation.
638 Almost all inhaled gas molecules contact airway surfaces, but usually return to the air unless they dissolve
639 in, or react with, the surface lining. In the case of tritium gas and methane, a small fraction is absorbed into
640 body fluids and of that, a fraction is metabolised and the rest subsequently exhaled.
641 [c] HTO = Systemic model for tritiated water, Section 3. OBT = Systemic model for organically bound tritium,
642 which is recommended for prospective use only, and not for interpretation of bioassay data, Section 3.
643 [d] Since instantaneous absorption to blood is assumed, calculations can be performed assuming direct injection
644 into blood, and the regional deposition does not need to be considered. However, for completeness, the
645 default distribution is assumed (footnote e).
646 [e] Default distribution between regions (20% ET_2, 10% BB, 20% bb and 50% AI).
647 [f] Not applicable for absorption Type V, because all activity deposited in the respiratory tract is
648 instantaneously absorbed.
649

Table 2-3. Absorption parameter values for inhaled particulate forms of tritium and for ingested tritium[a].

Inhaled particulate materials		Absorption parameter values[b] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[c,d]					
Absorption Type	Assigned forms				
F	—	1	100	-	1
M	Glass fragments; luminous paint; titanium tritide; zirconium tritide; all unspecified compounds[e]	0.2	3	0.005	0.2
S	Carbon tritide; hafnium tritide	0.01	3	$1x10^{-4}$	0.01
Ingested materials					
Soluble forms (as assigned to Type F for inhalation)		–	–	–	1
Relatively insoluble forms (Types M and S)		–	–	–	0.1

[a] Following uptake to body fluids, the systemic model for tritiated water is used, Section 3

[b] It is assumed that for tritium the bound state can be neglected, i.e. f_b = 0.0. The value of s_r for Type F forms of hydrogen (100 d^{-1}) is element-specific. The values for Types M and S (3 d^{-1}) are the general default values.

[c] Materials (e.g. "Glass fragments") are listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

[d] 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 and the f_A value for ingested soluble forms of tritium (1.0).

[e] Default Type M is recommended for use in the absence of specific information, i.e. 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.

2.2.2. Ingestion

Tritiated water (HTO)

(33) Investigations in humans have shown that hydrogen in the form of deuterium oxide or tritiated water is rapidly and virtually completely absorbed from the gastrointestinal tract (Pinson and Langham, 1957; Etnier et al., 1984; Travis et al., 1984).

Organic compounds

(34) Studies using rodents indicate that about 90% of ingested [^{3}H]-thymidine is catabolized into [^{3}H]–thymine in the small intestine and that both compounds pass across the gut by simple diffusion (Lambert and Clifton, 1968). Balonov et al. (1993) showed that 10-20 % of [^{3}H]-thymidine and 60-100% of [^{3}H]-deoxycytidine are absorbed from the GI tract of rats. For other forms of organic tritium compound, including biochemical substrates absorption of the intact molecule is variable according to the authors; it ranges from about 50% for some few specific compounds (Takeda, 1982, 1991; Rochalska and Szot, 1977) to almost 100% for most compounds including [^{3}H]-Cortisol, [^{3}H]-Glucose and [^{3}H]-amino acids (Balonov et al., 1993; Taylor, 2008).

(35) Although absorption of organic tritium compounds is likely to vary substantially, it is conservatively assumed here, as in ICRP *Publications 30* (1979) and 56 (1989), that

absorption is complete unless specific information is available to indicate otherwise; that is, the default assumption for all organic tritium compounds is that f_A= 1.

Insoluble compounds

(36) Insoluble compounds such as metal tritides and luminous compounds are not directly absorbed from the gastro-intestinal tract. *In vitro* experiments showed that these substances, when in contact with water, gradually release 0.5-5% of the activity which passes into solution in the form of oxide and low molecular organic compounds (Balonov et al., 1984). This fraction may then be absorbed and cause a systemic burden.

(37) After oral administration of a suspension containing titanium tritide (TiT) particles to rats, the HTO concentration in body water slightly increased during the 1-1.5 days of the residence of TiT in the gastrointestinal tract. Total absorption in these conditions was less than 0.1 (Balonov et al., 1984).

(38) Following oral administration of [^{3}H]-labeled luminous compounds to rats, less than 5 % of the administered activity was absorbed as HTO after dissolution (Balonov et al., 1984). Measurements of absorption in cats showed that absorption of tritium from luminous paints depended on the plastic substrate involved, with values of 0.007 for polystyrene, about 0.03 for silicone rubber and 0.8 for polyester (Wawerna, 1973; Hill and Johnson, 1993).

f_A values for ingestion

(39) For both tritiated water and organic compounds, an f_A of 1 is adopted in this report, although it is recognized that absorption may be substantially less than complete in the case of some organic compounds. For metal tritides and luminous paints, the available data indicate that an f_A value of $1x10^{-1}$ is generally more appropriate.

2.2.3. Systemic Distribution, Retention and Excretion

2.2.3.1. Summary of the database

Tritiated water

(40) Tritiated water (HTO) mixes rapidly with total body water after its entry into blood (Pinson and Langham, 1957; Moore, 1962; Balonov et al., 1974). In human subjects the blood tritium concentration stabilized within about an hour after intravenous injection of HTO (Moore, 1962; Balonov et al., 1974). Human studies using deuterium or HTO have confirmed that equilibration of HTO throughout the body water pool is essentially complete within an hour after intake (Balonov et al., 1974; Davies et al., 2001; La Forgia and Withers, 2002).

(41) A portion of tritium reaching blood as HTO becomes organically bound in the body. Organically bound tritium (OBT) generally has a lower rate of turnover than HTO in body water. The extent of organic binding of tritium reaching blood as HTO and the turnover time of OBT in a given tissue depend on the types of organic molecules that incorporate the tritium atoms (Smith, 1986; Taylor, 1989; Taylor et al., 1990; Konig, 1990). In general, the binding of tritium is greater, but the retention time of bound tritium is shorter, in metabolically active tissues such as liver and intestine than in skin, brain, and other tissues where metabolic activity is less pronounced (Smith, 1986).

(42) Measurements on laboratory animals indicate that 1-5% of HTO entering blood becomes incorporated into organic components of tissues (Takeda and Kassida, 1979; Diabaté and Strack, 1993). On the basis of kinetic analysis of urinary excretion data for human subjects following acute intake of HTO (Snyder et al., 1968; Sanders and Reinig,

1968; Lambert et al., 1971; Balonov et al., 1974, 1984; Rudran, 1988b; Trivedi et al., 1997; Trivedi et al., 2000) it is estimated that 0.5-20% of the absorbed tritium may bind to organic components of tissues. Estimates for most subjects fall in the range 0.5-3%.

(43) Data from relatively long-term studies of laboratory animals and human subjects exposed to HTO indicate that whole-body retention can be described reasonably well as a sum of three exponential terms (Sanders and Reinig, 1968; NCRP, 1979; Taylor, 2003). These terms presumably represent HTO in body water, tritium incorporated into organic compounds within the tissues, and tritium incorporated into structural tissues. Human data indicate that the removal half-time of HTO in body water ranges from 4-18 days, with an average of about 10 days (Butler and Leroy, 1965). Estimated half-times for the second and third compartments typically are about 30-40 d and a few hundred days, respectively, but depend on the starting and ending times of the observation period and subjective distinctions between intermediate and long-term components of retention. Estimated biological half-times of different components of tritium retention data based on studies of human subjects exposed to HTO are summarized in Table 2-4.

Table 2-4. Reported biological half-times[a] for urinary excretion of tritium by humans exposed to tritiated water, tritium gas, or other inorganic forms of tritium

Study	Number of subjects	Reported biological half-time (d)		
		Early	Intermediate	Late
Fallot et al., 1957	20	8.5	-	-
Pinson and Langham, 1957	9	11.3	-	-
Foy and Schneiden, 1960	10	7.5	-	-
Richmond et al., 1962	5	9.5	-	-
Wylie et al., 1963	7	8.5	-	-
Butler and Leroy, 1965	310	9.5	-	-
Osborne, 1966	30	10.5	-	-
Snyder et al., 1968	1	8.7	34	-
Sanders and Reinig, 1968	1	6.1	23	344
Minder, 1969	1	~11	30	139-230
Lambert et al., 1971	1	9.1	36	-
Moghissi et al., 1971, 1972	3	-	21-26	280-550
Henry, 1972	1	7.5	63	-
Balonov et al., 1974	5	12	39-76	-
Rudran, 1988	8	6.0	31-51	87-226
Trivedi et al., 1997	8	8.4	58-104	-

[a] Values listed for groups of subjects are means except where ranges of values are indicated.

Organic compounds of tritium

(44) Tritium taken into the body in organic form may be oxidized and enter the body water as HTO or may be incorporated into the organic constituents of the body without first being converted to HTO. Soluble organic compounds of tritium entering the blood are incorporated into body tissues to an extent that depends on the specific chemical compound and the metabolic activity of the individual tissues. Tritium attached to oxygen, sulphur, nitrogen or phosphorus is in general readily exchangeable with the hydrogen of the body water pool. Tritium bound to carbon normally will be released through enzyme-mediated breakdown of the molecule in which the carbon atom is situated (Smith, 1986). The rate of such breakdown may be rapid for small molecules but slow for carbon-bound tritium incorporated into structural proteins such as collagen, or the phospholipids of some nerve

cells.

(45) Animal studies comparing the incorporation of tritium into OBT in body tissues after intakes of HTO and OBT have shown that 3-30 times more OBT is present after intakes of OBT than after intakes of HTO (Rochalska and Szot, 1977; Kirchman et al., 1977; Pietrzak-Flis, 1978; Mewissen et al., 1979; Takeda, 1982, 1991; Takeda et al., 1985; Komatsu et al., 1990; Rodgers, 1992). In rats fed HTO, tritiated amino acids, or tritiated DNA/RNA precursors for 22 days, the greatest concentrations of OBT were found after exposure to amino acids with intermediate concentrations found after exposure to DNA/RNA precursors (Takeda, 1991). In rats fed tritiated food or HTO for 5 days, incorporation into OBT was 3 times greater for brain and 15–17 times greater for liver and small intestine after ingestion of tritiated food (Rochalska and Szot, 1977). In mice administered HTO or tritium-labeled amino acids in diet for 56 days, the longer-term component of retention, attributable to OBT in tissues, accounted for about 50% of total body activity after administration of amino acids and about 15% after administration of HTO (Rodgers, 1992).

(46) There is little information on the biokinetics of many of the tritiated organic compounds that may be encountered in the workplace. Available information indicates that tritium retention in the human or animal body after intake of ^{3}H-labeled substances may vary greatly from one substance to another (Etnier et al., 1984; Rodgers, 1992; Richardson and Dunford, 2003a; Taylor, 2008). Dietary components that provide energy (e.g. fats and carbohydrates) are oxidized to HTO within hours of intake, and their hydrogen atoms follow the clearance of HTO.

(47) Hunt et al. (2009) estimated total-body retention half-times of tritium in the range 4-11 d in five volunteers who ate fish taken from waters containing elevated levels of OBT discharged from a facility where tritium was handled. There was no indication of a significant long-term component of retention of tritium.

(48) On the basis of a review of the biokinetics of 11 xenobiotic tritiated organic compounds, Taylor (2008) estimated that the clearance half-time was less than 40 d in all cases. Some organic compounds may be incorporated directly into structural components and retained for much longer times.

Elemental tritium

(49) About 1-2% of inhaled tritium gas (HT) is dissolved in the blood and body fluids and the rest is exhaled rapidly (Pinson and Langham, 1957; Peterman et al., 1985b). Experimental studies by Pinson and Langham (1957) showed that rats and man slowly oxidize the retained HT to HTO. The rate of oxidation in the rat was about 50 times faster than in man. Conversion from HT to HTO presumably results from microbial action in the large intestine, since mammalian tissues do not contain the hydrogenase enzyme necessary for the conversion of HT to HTO (Ichimasa et al., 1988).

(50) Pinson and Langham (1957) found that equivalent rates of appearance of tritium in body fluids of man following inhalation of HT and HTO occurred when the specific activity of HT in ambient air was about 15,000 times that of HTO. This indicates that about 0.007% of the inhaled HT ultimately was converted *in vivo* to HTO. Peterman et al. (1985a) repeated the experiments of Pinson and Langham (1957) with a larger group of human subjects and obtained reasonably consistent results.

Some other studied forms of tritium

(51) Results of *in vitro* studies by Cheng et al. (1997), Inkret et al. (2001), and Zhou and Cheng (2003) indicate that tritium is released from metal tritides into simulated lung fluids as HTO.

(52) Eakins et al. (1975) studied the rate of urinary excretion of tritium in human volunteers whose skin had been exposed by contact with tritium-gas contaminated surfaces. Over the first several days the main form of tritium in urine was OBT, which was excreted in a biphasic pattern with half-times of ~0.2 days (range, 0.1-0.3 d) and 1.7 d (range, 1.1-1.9 d). The concentration of HTO in urine declined with a half-time of ~10 days. At the peak of OBT excretion, which occurred about 24 hours after the exposure, the concentration of OBT was more than 100 times greater than that of HTO. Similar results were observed for exposures to different areas of the skin and from various contaminated metal and glass surfaces. From experimental studies with similarly exposed rats, the distribution of OBT is known to be non-uniform, with the maximum concentration in the skin at the point of contact (Trivedi, 1993).

(53) Trivedi (1995) studied the percutaneous absorption and systemic biokinetics of tritium-gas contaminated pump oil in male hairless rats. Skin-contact exposure with the pump oil resulted in uptake of OBT and HTO to blood. The systemic biokinetics indicated that absorbed tritium was mainly in the form of OBT, most of which was transferred from the skin with a half-time of 1.7 d. A second, long-term component of retention of OBT with a half-life of 27.6 d accounted for <3% of the tritium retained in the skin. HTO in the skin also showed two components of retention, with half-times of 3.7 and 18.1 d. A significant level of OBT was excreted shortly after exposure. Elevated levels of tritium were found in the liver and kidneys. Overall, about 60% of the activity applied to skin was excreted in faeces, mostly as OBT, and about.4% was excreted in urine. The remaining ~36% may have been removed gradually from the skin to the environment. The exposed skin was estimated to receive the highest dose of any tissue, primarily due to retention of OBT at the point of contact with the contaminated pump oil.

2.2.3.2. Biokinetic models for systemic tritium

(54) A number of biokinetic models for tritium have been published, primarily for tritium as HTO or for generic OBT. The following short summary describes the most recent ICRP models for HTO and OBT and selected models appearing in the open literature in recent years.

(55) ICRP *Publication 56* (1989) recommended a two-component model for predicting the behavior of tritium that enters the human body as HTO. It is assumed in that model that 97% of the tritium is eliminated with a biological half-time of 10 days and 3% becomes organically bound and is eliminated with a biological half time of 40 days.

(56) The authors of ICRP *Publication 56* (1989) interpreted the available data as indicating that 9-45% of ingested OBT is incorporated into organic constituents of tissues and that on average about 9 times more OBT is present in body tissues after intakes of OBT than after intakes of HTO. *ICRP Publication 56* recommended a default model for unknown tritiated organic compounds in the environment in which it is assumed that 50% of the OBT entering the systemic circulation enters into bonds with carbon and is cleared with the same half-time as carbon, assumed in that document to be 40 d. The remaining 50% is assumed to be rapidly metabolized to HTO and removed from the body with a biological half-time of 10 days.

(57) Taylor (2003) reevaluated data on tritium excretion by human subjects exposed to

HTO in an effort to develop a biokinetic model for HTO that could be used for protection planning and interpretation of bioassay data collected at early, intermediate, or late times after exposure. He proposed a three-component exponential model with half-times of 10 days (99%), 40 days (0.98%) and 350 days (0.02%).

(58) Richardson and Dunford (2003a, 2003b) designed a generic, physiologically based biokinetic model framework for hydrogen, carbon, nitrogen, and oxygen, with the goal of predicting the biokinetics of each of these elements following ingestion on the basis of the metabolic reactions of the principal nutrients: carbohydrates, fats, and proteins. A relatively simple form of the model consists of compartments representing the principal nutrients. A more complex form includes compartments representing retention of carbohydrates as glycogen, fats as adipose tissue, and proteins in bone and soft tissues. Parameter values for hydrogen were developed, and ingestion dose coefficients were derived for dietary intake of organically bound tritium.

(59) Galeriu and coworkers (Galeriu et al., 2009; Galeriu and Melintescu, 2010) proposed a physiologically based biokinetic model for dietary tritium in the mammalian body based on organ specific metabolic rates. The model was first developed for non-human mammals (Galeriu et al., 2009) and tested against experimental data on laboratory and farm animals. Parameter values for a modified model structure were later developed for reference persons living in a temperate climate (Galeriu and Melintescu, 2010). The model for humans included compartments representing blood plasma, red blood cells, body water, brain, viscera, muscle, adipose tissue, residual tissue, stomach content, small intestine content, and large intestine content. Dose coefficients were developed for ingestion of tritiated water or organically bound tritium.

Model for tritiated water used in this report

(60) The model for HTO adopted in the present report is a recycling model that includes compartments representing blood, extravascular body water that exchanges rapidly with blood, and organically bound tritium with intermediate and slow turnover rates. The model structure, which is broadly similar to a number of previously proposed structures for HTO (NCRP, 1979; Saito, 1992; Hill and Johnson, 1993), is shown in Figure 2-1. Parameter values for intake of tritiated water are given in Table 2-5. Excretion is from the blood compartment only. The transfer coefficient from Blood to Excreta is set to yield an initial removal half-time from the body of 10 d. The transfer coefficients from compartments OBT-1 and OBT-2 back to Extravascular HTO correspond to half-times of 40 d and 1 y, respectively; the net retention half-times in these compartments are slightly longer than 40 d and 1 y due to recycling of activity. Specific excretion pathways are not shown in Figure 2-1, but the following division is assumed on the basis of reference data for water balance (ICRP *Publication 89*, 2002): urine, 55%; faeces, 4%; exhalation, 12%; and loss through skin (sweat plus insensible loss), 29%.

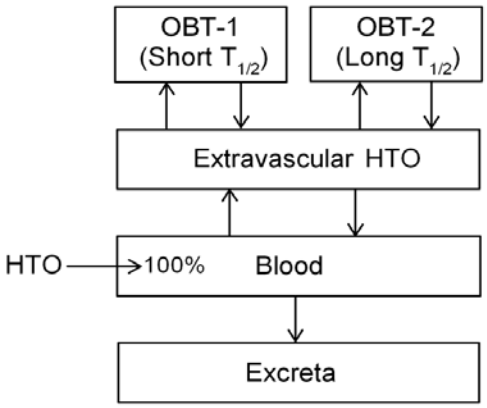

Figure 2-1. Structure of the model for tritium entering the systemic circulation as HTO. Transfer from blood to excreta (or excretion pathways) is divided as follows: 55% to urinary bladder contents; 4% to upper colon; 12% exhaled with no retention in lungs; 29% removed through the skin (sweat plus insensible loss) with no retention in skin.

Table 2-5. Transfer coefficients (d^{-1}) in the systemic model for tritiated water

Path		Transfer coefficient
From	To	(d^{-1})
Blood	Extravascular HTO	400
Extravascular HTO	OBT-1	0.0006
Extravascular HTO	OBT-2	0.00008
Blood	Excreta[a]	0.7
Extravascular HTO	Blood	44
OBT-1	Extravascular HTO	0.01733
OBT-2	Extravascular HTO	0.0019

[a] 55% to UB contents, 4% to colon contents, 12% exhaled, and 29% lost through skin.

(61) Model predictions of the blood content of tritium as a function of time after intravenous injection of HTO are compared in Figure 2-2 with estimates based on data of Moore (1962) and Balonov et al. (1974) for human subjects. The data of Moore (1962) were reported as concentrations of tritium in blood plasma. Derived estimates of tritium in whole blood are based on the assumptions that plasma water represents two-thirds of blood water and red blood cell water equilibrates with plasma water during the first few minutes after injection. The data of Balonov et al. (1974) were reported as relative concentrations over time in whole blood normalized to 1.0 at equilibrium, with equilibrium assumed to be reached within a few hours after injection. These data were converted to percentages of injected tritium by assuming that blood contains 10% of total-body HTO at equilibrium, based on the estimate that blood water represents 10% of total-body water.

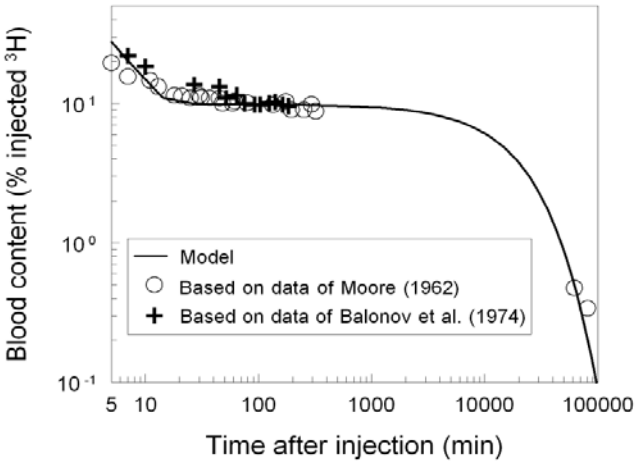

Figure 2-2. Observations and model predictions of blood content of tritium blood following intravenous injection of HTO

(62) Model predictions of urinary excretion of tritium as a function of time after acute intake of HTO are compared in Figure 2-3 with data for individual human subjects of five different long-term studies. Four of the subjects were accidentally exposed to HTO in the workplace (Snyder et al., 1968; Sanders and Reinig, 1968; Rudran, 1988; Trivedi et al., 1997). The fifth subject ingested HTO as part of a controlled biokinetic study (Balonov et al., 1974). In two of the cases of accidental exposure, an effort was made to accelerate the removal of tritium from the body at early times after intake, either by administration of an oral diuretic (Sanders and Reinig, 1968, days 3-35) or by increasing fluid intake (Trivedi et al., 1997, days 1-32). The observations and model predictions shown in Figure 2-3 are normalized to a urine concentration of 1.0 on day 1.

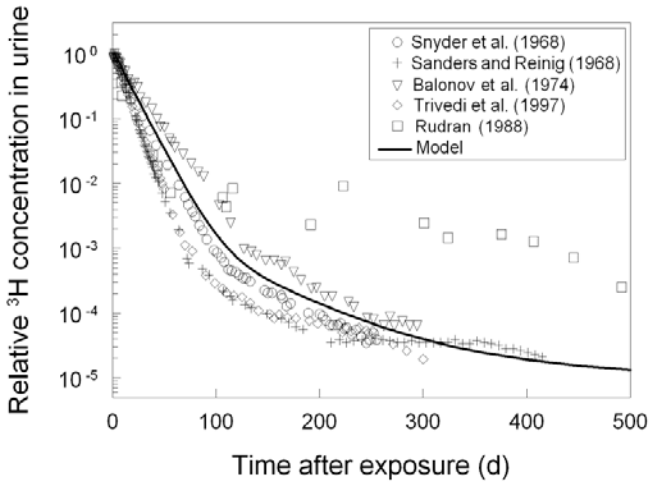

Figure 2-3. Observations and model predictions of urinary excretion of tritium as a function of time after acute intake of HTO by human subjects. Data and model predictions are normalized to a urine concentration of 1.0 on day 1.

Model for OBT used in this report

(63) In view of the wide range of ^{3}H-labelled substances that could be encountered in the workplace and the limited data on their biokinetics, it is not feasible to define specific models for individual organic compounds of tritium. A default model for systemic OBT is adopted in the present report (Figure 2-4). This is a modification of the model for HTO described earlier. It is assumed here that 50% of tritium entering blood as OBT transfers immediately to compartment OBT-1 (the OBT compartment with the shorter half-time) and 50% is converted immediately to HTO within the blood compartment. Tritium entering OBT-1 or Blood follows the HTO model defined in Figure 2-1 and Table 2-5. For application to individual organic tritium compounds the division of absorbed activity between compartment OBT-1 and Blood can be modified as allowed by specific information.

(64) The default model for OBT predicts that OBT would represent about 65-70% of total-body tritium in a worker who is chronically exposed to OBT. The model for HTO adopted in this report predicts that OBT would represent about 5-6% of total body tritium in a worker who is chronically exposed to HTO.

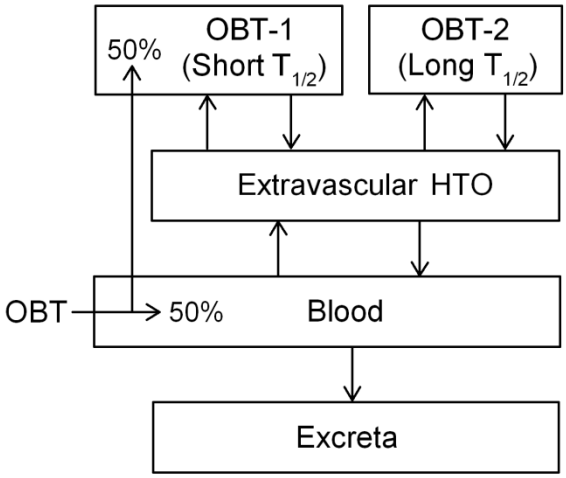

Figure 2-4. The default model for tritium entering the systemic circulation as OBT. Tritium entering OBT-1 or Blood follows the HTO model defined earlier. For application to individual organic tritium compounds the division of absorbed activity between compartment OBT-1 and Blood can be modified as allowed by specific information.

2.3. Individual monitoring

(65) Tritium intakes are generally monitored though measurements of the activity excreted in urine. The most common method of analysis is liquid scintillation counting.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{3}H	Urine Bioassay	Liquid Scintillation Counting	100 Bq/L	5-10 Bq/L

(66) Currently most laboratories do not perform fecal monitoring of tritium in routine. Fecal monitoring of workers exposed to particulate forms of tritium might be desirable. The AEC (Trivedi et al., 1993) has published a method to measure organically bound tritium in faeces, with an MDA of 5Bq/g.

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3. CARBON (Z = 6)

3.1. Chemical Forms in the Workplace

(67) Carbon is a non-metal which occurs mainly in oxidation states II and IV. It may be encountered in industry in a variety of chemical forms, including carbon monoxide, carbon dioxide and methane, as well as in a wide range of organic carbon compounds and particles containing ^{14}C.

(68) Only two isotopes of carbon are of importance for radiation protection, ^{11}C and ^{14}C. Because of its short half-life, and the penetrating 511 keV annihilation radiation it emits, external irradiation from ^{11}C may well be a greater hazard than internal exposure.

Table 3-1. Isotopes of carbon addressed in this report

Isotope	Physical half-life	Decay mode
C-11	20.39 min	EC, Beta+
C-14[a]	5700 y	Beta-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

3.2. Routes of Intake

(69) It is not feasible to provide biokinetic models, dose coefficients and bioassay functions for the very large number of compounds with specific biokinetic behaviour. Hence systemic biokinetic models and dosimetric information are only given for certain forms, although some information is given on other forms. It is the responsibility of employers to assess doses to ensure appropriate protection for forms for which dose coefficients are not provided.

3.2.1. Inhalation

(70) Some information is available on the behaviour of inhaled gases of carbon in man and in experimental animals. Some information is also available on the behaviour of ^{14}C-labelled compounds and particles, mainly in rats, and on forms of carbon labelled with other radionuclides.

(71) Absorption parameter values and Types, and associated f_A values for gas and vapour forms of carbon are given in Table 3-2 and for particulate forms in Table 3-3.

(72) Exposures to both gas/vapour forms and particulate forms of carbon are common, and it is therefore proposed by the Task group that in the absence of information 50% particulate; 50% gas/vapour should be assumed (ICRP, 2002a).

(a) Gases and vapours

Carbon monoxide (CO)

(73) Carbon monoxide at high concentration is a potent asphyxiant, and for that reason its human respiratory physiology has been studied extensively (Lipsett et al., 1994). Carbon monoxide diffuses readily across the membranes of the gas exchange (alveolar-interstitial, AI) region (Crapo et al., 1982). Although CO has only a low solubility in biological fluids,

once absorbed into the pulmonary circulation it binds avidly to haemoglobin molecules within red blood cells. Peterson and Stewart (1970) estimated the biological half-life of CO in the blood to be between 150 and 200 minutes, and these values together with the haemoglobin content of the blood of a reference worker (ICRP, 2002b) can be used to estimate that 0.4 of the inhaled CO becomes bound to haemoglobin (ICRP, 1981). On that basis it is assumed that for carbon monoxide there is effective deposition of 40% of the inhaled activity in the respiratory tract, with instantaneous (Type V) absorption. It is assumed that the ^{14}C-carboxyhaemoglobin formed releases ^{14}C to the bicarbonate pool with a biological half-time of 200 minutes, from where it follows the carbon dioxide/bicarbonate model (Section 3.2.3.).

Carbon dioxide (CO_2)

(74) Release to the environment of blood borne carbon dioxide resulting from tissue carbon metabolism is a central function of the respiratory system, and the transport processes have been documented in detail (Guyton and Hall, 2000). Because of the very high solubility of CO_2 and the associated bicarbonate ion (HCO_3^-) in tissue fluids, CO_2 is transferred 20 times more rapidly than oxygen across the alveolar membrane (Guyton and Hall, 2000). Thus despite the net flow of CO_2 into the alveolar space, inhaled radioactive CO_2 rapidly equilibrates with blood borne CO_2 /HCO_3^-, and is absorbed quantitatively into the circulation. On that basis, for carbon dioxide it is assumed here that there is 100% deposition in the respiratory tract with instantaneous (Type V) absorption. The carbon dioxide/bicarbonate systemic model (Section 3.2.3.) is applied to the absorbed material.

Methane (CH_4)

(75) The dosimetric implications of inhaling methane gas were examined by Phipps et al. (1990). They made the conservative assumption that 1% of the methane was metabolized, based on observations by Dougherty et al. (1967) which indicated that approximately 0.3% of methane infused into sheep was converted to carbon dioxide. Carlisle et al. (2005) investigated the extent of oxidation and organic fixation of ^{3}H and ^{14}C following inhalation of ^{3}H-labelled and/or ^{14}C-labelled methane by rats. A pilot study examined retention of activity in skin, liver, brain and carcass 1 and 24 hours after a 4-hour exposure. It was estimated that uptake was about 0.2% of intake based on retention of ^{14}C in liver and 0.03% of intake based on retention of ^{14}C in the other tissues. Most (82 – 95%) of retained ^{14}C was organically bound. For methane it is therefore assumed here that there is 0.1% deposition in the respiratory tract with instantaneous (Type V) absorption. It is assumed here that 50% of carbon in the absorbed methane follows the systemic model for carbon dioxide and 50% follows the generic systemic model for carbon (Section 3.2.3.).

Benzene (C_6H_6)

(76) Krins et al. (2003) conducted a study of the distribution, retention and excretion of ^{14}C-labelled benzene [^{14}C] C_5H_6, based on existing pharmacokinetic models. They reported that in humans exposed to 55 ppm for 4 hours, about 30% of inhaled benzene is absorbed into blood (Nomiyama and Nomiyama, 1974a, 1974b). Studies on rats, however, showed that retention during exposure is highly dependent on the concentration of benzene the inhaled air (Sabourin et al., 1987). A systemic model for benzene is described in Section 3.2.3. but dose coefficients are not provided.

(77) As part of a programme to study the disposition of selected industrial organic chemicals thought to pose an inhalation health risk to humans, biokinetic studies were conducted on several which might be inhaled in vapour form, including benzene (see above),

dichloropropene, methyl bromide, butadiene, isoprene, butoxyethanol, and isobutene. Brief summaries of relevant information follow, but no systemic model, dose coefficients or bioassay functions are given here for these compounds. Except where noted otherwise, in these studies retention, metabolism and excretion were followed for about 3 days after a 6-hour inhalation exposure of rats to a vapour of the ^{14}C-labelled compound.

Dichloropropene (DCP)

(78) It was estimated that 38% of inhaled DCP was absorbed (Bond et al., 1985a, Dutcher et al., 1985). The results indicated that the absorbed DCP is rapidly metabolised in tissues and the metabolites excreted.

Methyl bromide

(79) It was estimated that 48% of inhaled methyl bromide was absorbed at the lower concentrations used, but the fraction decreased to 27% at the highest concentration (Bond et al., 1985b, Medinsky et al., 1985). The results indicated that the absorbed methyl bromide is rapidly metabolised in tissues (>90% within an hour) and the metabolites excreted: about 20% of the amount in tissues immediately after exposure was retained at 65 hours.

1,3-Butadiene

(80) Interspecies differences were investigated. About 20% of inhaled butadiene was absorbed (and retained at the end of exposure) in rats and mice at the lowest concentrations used, with the fraction decreasing to 2-4% at the highest concentrations (Bond et al., 1986a). Bond et al. (1987) followed the tissue distribution of ^{14}C for 13 d after 3.4-hour inhalation exposures of rats and mice. In both species, about 90% of ^{14}C present in the lungs at the end of exposure cleared with a half-time of several hours, the rest with a half-time of about a week. In monkeys, the fraction absorbed and excreted within 4 days was lower, at about 3%, than in rats and mice exposed to the same concentration (Dahl et al., 1991).

Isoprene (2-Methyl-1,3-butadiene).

(81) In rats, about 20% of inhaled isoprene was absorbed (and retained at the end of exposure) at the lowest concentration used, with the fraction decreasing to about 4% at the highest concentration. Mice showed similar absorption, but less change with concentration (Dahl et al., 1987; Bond et al., 1991).

Butoxyethanol

(82) As part of a wider study of the biokinetics and metabolism of glycol ethers administered by different routes, Sabourin et al. (1992) followed retention and excretion of ^{14}C for 66 hours after 6-hour inhalation exposures of rats to [^{14}C]butoxyethanol. It was estimated that about 20% of inhaled butoxyethanol was absorbed.

Isobutene (2-Methyl-1-propene)

(83) About 8% of inhaled isobutene was absorbed (and retained at the end of exposure) at the lowest concentrations used, with the fraction decreasing to about 2% at the highest concentration (Henderson et al. 1993).

Other organic compounds

(84) The volatility and solubility in body fluids of organic compounds have wide ranges. Therefore, in the absence of specific information, the default option for gases and vapours is taken. As for tritium (Section 1.2.1), for carbon (gas or vapour) in unspecified organic forms

is it is assumed here that there is 100% deposition in the respiratory tract (with default regional distribution, Table 3-2) and Type F absorption.

(b) Particulate materials (liquid and solid)

^{14}C-labelled compounds

(85) Some information is available for ^{14}C-labelled compounds administered to rats. For the ^{14}C-labelled carbon compounds considered in the following sections, the systemic behaviour is specific to each compound. In these cases no systemic model, dose coefficients or bioassay functions are given here.

DTPA (diethylenetriaminepentaacetic acid)

(86) Absorption of DTPA from the respiratory tract has been studied in detail mainly because of the use of DTPA as a decorporation agent for treating intakes of actinides, and interest in its administration by inhalation. Crawley and Haines (1979b) reported rapid lung clearance of ^{14}C following pulmonary instillation of ^{14}C-DTPA into rats, with <1% ILD retained in the lungs at 1 day, and 0.03% ILD retained at 7 days. Dudley et al. (1980a) determined absorption of ^{111}In-DTPA from the nasopharyngeal (NP), tracheobronchial and pulmonary regions of beagle dogs, following instillation, to be 16, 48 and 90% respectively. NP absorption was slightly higher following nasal inhalation (23%) than following nasal instillation (16%). In rats, Dudley et al., (1980b) found NP absorption to be much higher (68%) following nasal inhalation than following instillation (19%). In complementary experiments, Dudley et al. (1980a,b) found absorption from the alimentary tract to be about 8% in dogs and 4% in rats. Stather et al. (1983) followed the biokinetics of ^{14}C for a week after inhalation of ^{14}C-labelled DTPA by two healthy volunteers. Studies were carried out on the same subjects following intravenous injection, and in one case by ingestion, (which indicated that about 3% was absorbed from the alimentary tract). Modelling by the authors gave an estimated rate of absorption from lungs to blood of about 13 d^{-1} (f_r ~1), giving assignment to Type F. A similar absorption rate (~10 d^{-1}) has been obtained with technetium-99m labelled DTPA, which has been extensively used to study pulmonary epithelial permeability in man (See technetium inhalation section).

Potassium cyanide

(87) Carbon-14 labelled potassium cyanide ($K^{14}CN$) is an important precursor in the synthesis of organic compounds. Crawley and Goddard (1977) studied its behaviour following administration to rats by intravenous injection, pulmonary and gastric intubation, and skin absorption. Biokinetics following pulmonary intubation were very similar to those following intravenous injection, showing that the $K^{14}CN$ was completely and rapidly absorbed from the lungs, with f_r ~1.0 and s_r >100 d^{-1}, giving assignment to Type F. (Absorption following gastric intubation was somewhat slower.)

Methanol

(88) Crawley (1977) reported that the behaviour of ^{14}C following administration of ^{14}C-labelled methanol ($^{14}CH_3OH$) to rats by pulmonary intubation was very similar to that following intravenous injection. Details were only given for the latter, but indicated that the ^{14}C-methanol was completely and rapidly absorbed from the lungs, with f_r ~1.0 and s_r >100 d^{-1}, giving assignment to Type F.

Sodium acetate

(89) Crawley and Haines (1978) reported that the behaviour of ^{14}C following administration of ^{14}C-labelled sodium (2-^{14}C) acetate to rats by pulmonary intubation was very similar to that following intravenous injection, but few details were given. By 1 day most tissue levels were below 1% of the injected activity, indicating assignment to Type F.

Nitrobenzene

(90) Crawley and Haines (1979a) reported that following pulmonary intubation of ^{14}C-labelled nitrobenzene into rats, lung clearance was very rapid. Retention could be described by a three-component exponential function with half-lives of 2.5 minutes (99%), 0.75 d (0.7%) and 5 d (0.3%), giving f_r ~0.99 and s_r ~400 d^{-1}, and assignment to Type F.

Other organic compounds

(91) Brown and Schanker (1983) measured the absorption rate of a range of ^{14}C-labelled drugs for up to an hour after inhalation by rats. For lipid-insoluble compounds the half-time (range 1.4 – 35 minutes) tended to increase with molecular mass (range 60 – 300 daltons (Da)). Lipid soluble compounds were more rapidly absorbed (range 0.25 – 6 minutes), with less clear dependence on molecular mass (range 80 – 700 Da).

(92) Bond et al. (1986a and b) summarised studies of the biokinetics, following inhalation by rats, of ^{14}C- or ^{3}H-labelled chemicals selected as representative of different important chemical classes found in atmospheric pollutants: benzo[a]pyrene, aminoanthracene, nitropyrene, and phenanthridone. The chemicals were inhaled in pure form and in some cases associated with carbonaceous (diesel exhaust), organic (coal tar) or inorganic (gallium oxide) particles. Lung retention and excretion of the labels were followed for up to 26 days after inhalation. For all four compounds, in pure form, >99% cleared from the lungs with a half-time <1 day. Association with particles increased lung retention in some cases but not others. For benzo[a]pyrene associated with coal tar a similar fraction (>99%) cleared rapidly, with gallium oxide slightly less (98%), and with diesel soot only 50%. For amino-anthracene associated with coal tar rapid clearance was less (92%). For nitropyrene associated with gallium oxide >99% cleared rapidly and with diesel soot 92%. Bond et al. (1985c) followed lung retention of ^{14}C for 4 days after instillation into the lungs of rats of ^{14}C-labelled anthracene, benz[a]athracene, 1-nitropyrene, 6-nitrobenzo[a]pyrene, and dibenzo[c,g]carbazole. They found that the retention half-time of the small fraction that was retained beyond 2 days increased with the lipophilicity (as measured by the octanol: water partition coefficient) over the range 26 to 63 hours.

(93) Studies were also conducted with azodicarbonamide (ADA). Mewhinney et al. (1987) followed the kinetics of ^{14}C for 102 d after inhalation of ^{14}C-ADA by rats. In complementary experiments 30% of administered ADA was absorbed following gavage and 90% following intratracheal instillation. The lungs contained about 0.5% ILD at 3 d after intratracheal instillation, and there was similar rapid lung clearance after inhalation. Results suggested that ADA was rapidly converted to biurea, most of which was rapidly eliminated in urine.

(94) Henderson et al. (1988) reported that a wide range of inhaled organic compounds with molecular mass less than 300 Da, including those studied by Bond et al. (1985c, 1986a and b) are cleared rapidly (half-time <12 hours) from the lungs of rats. They determined lung retention up to 24 hours after instillation into rat lungs of a series of dyes (easily traced without radiolabels) of varying molecular mass and lipophilicity (which increases with molecular mass). For organic-soluble compounds the fraction of initial lung deposit (ILD) retained in the lungs at 24 hours increased from about 3% for molecular mass of 250 Da to about 90% at 400 Da. However, retention of a compound [1,5-di(2-sulfo-*p*-toluidino)

anthraquinone] of higher molecular mass (576 Da), but containing a polar functional group, was only 21%. The authors concluded that both molecular mass and lipophilicity are important in determining lung retention.

^{14}C-labelled particles

(95) Some information is also available from experimental studies on ^{14}C-labelled particles, for which carbon released in the lungs would reasonably be expected to follow the generic systemic model for carbon (Section 3.2.3.).

Barium carbonate

(96) Crawley and Haines (1979a) followed retention and excretion of ^{14}C following pulmonary intubation of a suspension of barium ^{14}C-labelled carbonate into rats. Lung retention decreased rapidly, from 70% ILD at 6 hours to 0.2% at 8 days, indicating assignment to Type F. Kramer et al. (1996) measured lung retention of ^{14}C for 550 days after accidental inhalation of barium ^{14}C-labelled carbonate by a worker. Most of the activity remaining in the lung at 2 days after the presumed intake (the first *in vivo* measurement), cleared rapidly with an effective half-time of 0.77 days, also indicating assignment to Type F. The carbon dioxide/bicarbonate systemic model (Section 3.2.3.) is applied to the absorbed carbon.

Elemental carbon

(97) Johnson (1989) followed the biokinetics of ^{14}C for 146 days after administration to rats by intratracheal instillation of ^{14}C-bearing material obtained from air filters during re-tubing of a CANDU reactor (Greening, 1989). No ^{14}C above background was detected in urine or liver, indicating negligible dissolution in the lungs (or alimentary tract). After the first few days lung clearance was very slow, with more than 70% of the ILD retained at 146 d, giving assignment to Type S. Oberdörster et al. (2002) reported significant translocation of particles to the liver following inhalation by rats of ultrafine (count median diameter 22 nm) ^{13}C-carbon particles. However, far less translocation to liver was observed by this group in a similar experiment using ^{192}Ir-labelled carbon particles (Kreyling et al., 2009).

Diesel exhaust particles

(98) Lee et al. (1983) followed the biokinetics of ^{14}C for 365 days after inhalation of ^{14}C-labelled diesel exhaust particles by rats and guinea pigs. Lung retention at 180 days was about 15% of the initial lung deposit (ILD) in rats and 80% ILD in guinea pigs, with no ^{14}C detected in other tissues after the first day, indicating Type S behaviour. Similar lung retention in rats was observed in other studies (Chan et al., 1981; Lee et al., 1987).

Carbon particles labelled with isotopes of other elements

(99) Carbon particles may also contain other elements, which may or may not be chemically bound to the particle matrix. For such particles some information may be available from studies with particles labelled with a radioisotope of one of the other elements. For details refer to the Section dealing with the labelling radioelement.

Carbon 'tritide' (Tritium-loaded carbon particles) (Section 1.2.1)

(100) The results of *in vitro* dissolution tests are consistent with assignment to Type S.

Technetium-labelled carbon particles (Section 14.2.1)

(101) The results of human inhalation studies suggest that it is more likely to be Type M or

S than Type F.

Rapid dissolution rate for carbon

(102) Very rapid uptake of carbon (100 d^{-1} or more) has been observed for several chemical forms. A value of 100 d^{-1} is applied here to all Type F forms of carbon.

Extent of binding of carbon to the respiratory tract

(103) The evidence of rapid uptake from the lung of carbon gases and several solid and liquid forms indicates that that there is probably little binding of carbon. It is therefore assumed that for carbon the bound state can be neglected, i.e. $f_b = 0.0$.

Table 3-2. Deposition and absorption for gas and vapour forms of carbon[a]

Chemical form/origin	Percentage deposited[b]						Absorption		Systemic model[c]
	Total	ET_1	ET_2	BB	bb	AI	Type	f_A	
Carbon monoxide (CO)	40[d]	0	8	4	8	20	V	(f)	CO
Carbon dioxide (CO_2)	100[d]	0	20	10	20	50	V	(f)	CO_2
Methane (CH_4)	0.1[d]	0	0.02	0.01	0.02	0.05	V	(f)	Methane
Unspecified organic compounds	100[e]	0	20	10	20	50	F	1.0	C

[a] For carbon in unspecified gas or vapour form, the default option for gases and vapours is recommended: 100% total deposition in the respiratory tract; default distribution between regions (footnote e) and Type F absorption.

[b] *Percentage deposited* refers to how much of the material in the inhaled air remains behind after exhalation. Almost all inhaled gas molecules contact airway surfaces, but usually return to the air unless they dissolve in, or react with, the surface lining. In the case of methane, a small fraction is absorbed into body fluids and of that, a fraction is metabolised and the rest subsequently exhaled.

[c] CO = Systemic model for carbon monoxide; CO_2 = Systemic model for carbon dioxide/bicarbonate; C = Generic systemic model for other ^{14}C compounds (Section 3)].

[d] Since instantaneous absorption to blood is assumed, calculations can be performed assuming direct injection into blood, and the regional deposition does not need to be considered. However, for completeness, the default distribution is assumed (footnote e).

[e] Default distribution between regions (20% ET_2, 10% BB, 20% bb and 50% AI).

[f] Not applicable for absorption Type V, because all activity deposited in the respiratory tract is instantaneously absorbed.

Table 3-3. Absorption parameter values for inhaled particulate forms of carbon and for ingested carbon[a]

Inhaled particulate materials		Absorption parameter values[b] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[c,d]					
Absorption Type	Assigned forms				
F	Barium carbonate[a]	1	100	-	1
M	All unspecified forms[e]	0.2	3	0.005	0.2
S	Elemental carbon, carbon tritide	0.01	3	$1x10^{-4}$	0.01
Ingested materials					
All chemical forms					1

[a] Following uptake into body fluids, the generic systemic model for carbon is used (Section 3), with the exception of barium carbonate, for which the carbon dioxide/bicarbonate systemic model (Section 3) is applied to the absorbed carbon.

[b] It is assumed that for carbon the bound state can be neglected i.e. $f_b = 0$. The value of s_r for Type F forms of carbon (100 d^{-1}) is element-specific. The values for Types M and S (3 d^{-1}) are the general default values.

[c] Materials (e.g. elemental carbon) are listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

[d] 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 and the f_A value for ingested soluble forms of carbon (1.0).

[e] Default Type M is recommended for use in the absence of specific information, i.e. 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.

3.2.2. Ingestion

(104) The uptake of carbon from the gastrointestinal tract is highly dependent on the form in which it is ingested. Absorption is almost complete for carbon administered as [^{14}C]-labelled inorganic compounds such as potassium cyanide (Crawley and Goddard, 1977) or [^{14}C]-labelled organic compounds such as methyl methacrylate (Bratt and Hathway, 1977). Absorption may be much lower for some other organic or inorganic compounds such as polydiethylstilboesterol, octanoic acid, or hydrolysed polyacrylonitrile grafted cellulose (Lai et al., 1978).

(105) ICRP *Publication 30* (1981) recommended that, in the absence of compound-specific information, organic compounds labelled with radioactive isotopes of carbon should be assumed to be completely absorbed from the gastrointestinal tract, and this recommendation is retained here for all chemical forms (i.e. $f_A = 1$).

3.2.3. Systemic Distribution, Retention and Excretion

(106) The biokinetics of systemic radiocarbon depends on the carbon compound taken into the body and presumably the location of the radioactive atom within the molecule (Taylor, 2004). Internally deposited ^{14}C-labelled compounds have shown residence times varying

from a few hours to several months in human volunteers (Stather et al., 1981; Stenström et al., 1996; Taylor, 2004). The distribution of radiocarbon in the body and the fractions of ingested or inhaled activity lost by exhalation, urinary excretion, and faecal excretion also depend on the nature of the carbon compound taken into the body.

(107) Variation in the biokinetics of carbon compounds is illustrated in Table 3-4, which is based on a review of the literature and a biokinetic and dosimetric analysis of the collected data (Taylor 2004, 2007). The relative dose estimates represent the effective dose coefficient derived from the compound-specific information, divided by the effective dose coefficient based on a generic biokinetic model for carbon introduced in ICRP *Publication 30* (1981). That model assumes that internally deposited carbon is uniformly distributed in the body and removed with a half-time of 40 d (ICRP, 1981). The 7-d retention values and relative dose estimates given in Table 3-4 are rough estimates in some cases, and the effective dose estimates are based on tissue weighting factors that have since been replaced (ICRP, 2008). Nevertheless, the data demonstrate the large differences in the biokinetics of different carbon compounds in the body and, as a result, a wide variation in radiation dose per unit intake of carbon compounds for a given mode of intake.

(108) Compound-specific systemic biokinetic models are applied in the present report only for radiocarbon that is assumed to reach the systemic circulation as carbon monoxide, carbon dioxide, bicarbonate, or methane. A common model is applied to carbon dioxide and bicarbonate. A generic systemic model for carbon is applied in this report to unspecified forms of carbon. For example, the generic model is used to develop dose coefficients for inhalation of particulate forms of carbon described as Type F, Type M, or Type S material.

(109) The following section summarizes several published systemic biokinetic models for internally deposited carbon. A later section describes the models used in the present report.

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Table 3-4. Retention of ^{14}C in the human body at 7 d and relative effective dose estimates for intake of various [^{14}C]-labelled compounds, as estimated by Taylor (2004, 2007) on the basis of a review of biokinetic models and data for carbon

^{14}C-labeled compound	Intake mode	Retention at 7d (%)	Relative effective dose[a]	Reference
Testosterone	IV	<20	0.1	Fukushima et al., 1954
Corticosterone	IV	~10	0.05	Migeon et al., 1956
Glycine	IV	~35	0.6	Berlin and Tolbert, 1955
Cholesterol	IV	~ 55	0.5	Hellman et al., 1955
Cortisol	IV	< 10	0.02	Hellman et al., 1954
Estrone – Estradiol-17ß	IV	< 20	0.08	Sandberg and Slaunwhite, 1957
Thymidine	IV	~30	1.1	Thierens et al., 1994
Methanol[b]	IV	<10	0.09	Crawley, 1977
Acetate	IV	<10	0.08	Crawley and Haines, 1979
Alanine	IV	~18	0.3	Simmons et al., 1982
Inulin	IV	< 1	0.01	ICRP, 1987; 1998
Glucose	IV	~35	0.4	Baker et al. 1954, Fine et al. 1962
Potassium cyanide[b]	Intubation	8	0.2	Crawley and Goddard, 1977
Nitrobenzene[b]	Intubation	<6	0.3	Crawley and Haines, 1979
Barium carbonate	Inhalation	~ 80	1.0	Kramer et al., 1996
Carbon monoxide	Inhalation	< 5	0.004	ICRP, 1981;1996
Methane	Inhalation	< 1	0.01	ICRP,1998
Benzene	Inhalation	<1	0.07	Krins et al., 2003
Carbon dioxide	Inhalation	<10	0.01	Leggett, 2004
	Ingestion	<10	0.005	
Urea	Ingestion	<10	0.5	ICRP, 1998
	Ingestion	<10	0.7	Leide-Svegborn et al., 1999
Triolein	Ingestion	~10	3.6	ICRP 1998
	Ingestion	~10	0.5	Gunnarsson, 2002
Glycocholic acid	Ingestion	~35	0.7	Gunnarsson et al., 2003
DTPA	Ingestion	<1	0.05	Stather et al., 1981
	Inhalation		0.4	
Delmopinol	Ingestion	<5	0.05	Eriksson et al., 1998
Dexloxiglumide	Ingestion	< 7	0.4	Webber et al., 2003
Xylose	Ingestion	~15	0.2	Gunnarsson et al., 2003
Colestipol	Ingestion	<1	0.5	Taylor, 2007
Sevelamer	Ingestion	<1	0.5	Taylor, 2007
Levitiracetam	Ingestion	<2	0.02	Taylor, 2007
Ifetroban	Ingestion	<5	0.3	Taylor, 2007

[a] Multiple of effective dose based on ICRP's generic model for carbon introduced in ICRP *Publication 30* (1981).
[b] Estimates based on data for rats.

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3.2.3.1. Examples of published biokinetic models for systemic carbon

Generic models for inhaled or ingested carbon

(110) ICRP *Publication 30* (1981) recommends a generic biokinetic model for application to ^{14}C-labelled compounds for which biokinetic data are not available. It is assumed that inhaled or ingested ^{14}C-labelled compounds are instantly and uniformly distributed throughout all organs and tissues of the body, where they are retained with a biological half-time of 40 d. The half-time of 40 d is based on balance considerations, assuming daily carbon intake of 0.3 kg and a carbon pool of mass 16 kg in Reference Man (ICRP, 1975):

$$T_{1/2} = \ln 2 \times \text{total body carbon / daily carbon intake} = 0.693(16/0.3) \sim 40 \text{ d}.$$

(111) ICRP *Publication 30* (1981) states: "It is considered that this assumption will yield realistic whole body doses for ^{14}C-labelled metabolites and that it will overestimate whole body doses from most other ^{14}C-labelled compounds." This assumption is supported by a review and analysis of the effective doses delivered by a range of ^{14}C-labelled compounds (Taylor, 2004), based on tissue weighting factors recommended in ICRP *Publication 60* (1991).

(112) This generic model was not applied in *Publication 30* to inhaled forms of carbon expected to show significant retention in the lungs and limited absorption to blood.

(113) The same assumptions applied in the generic model of ICRP *Publication 30* (1981) for inhaled or ingested carbon were used in ICRP *Publication 68* (1994b) and *Publication 71* (1995) as the basis for a systemic model for radiocarbon. That is, absorbed carbon was assumed to be uniformly distributed in systemic tissues and removed from the body with a half-time of 40 d. This generic systemic model was used in conjunction with the Human Respiratory Tract Model (ICRP, 1994a) to derive dose coefficients for radiocarbon inhaled as Type F, Type M, or Type S material.

Inhaled carbon monoxide

(114) Inhaled carbon monoxide (CO) diffuses readily across the membranes of the alveolar interstitial region of the lung and enters the pulmonary blood, where it is bound to haemoglobin (ICRP, 1987). It is released from haemoglobin and removed from the body in expired air over a period of hours. In ICRP *Publication 30* (1981) it is assumed that 40% of inhaled CO is instantly absorbed to blood and bound to hemoglobin, and 60% is instantly exhaled. Carbon monoxide bound to haemoglobin is assumed to be uniformly distributed throughout all organs and tissues and retained with a biological half-life of 200 min. As discussed in a later section, essentially the same model is applied in this report to inhaled carbon monoxide.

Inhaled methane

(115) In ICRP *Publication 80* (1998) (in an addendum to ICRP *Publication 72*, 1996) and *Publication 88* (2001) it is assumed that 1% of radiocarbon inhaled as methane is absorbed to blood from the lungs and subsequently metabolized. The conservative assumption is made that one half of the metabolized fraction follows the biokinetics of carbon dioxide and one half follows the biokinetics of organic carbon as described by models applied in that report to these forms of carbon.

Carbon reaching blood as carbon dioxide or bicarbonate

(116) Inhaled carbon dioxide (CO_2) is transferred rapidly across the alveolar membrane into blood (Guyton, 2000). Carbon dioxide is also formed in the body during the metabolism of organic substances. Because most of the absorbed or internally produced CO_2 is converted to bicarbonate after entering blood (Guyton, 2000), data from metabolic studies involving intravenous injection of [^{14}C]bicarbonate provide information on the systemic biokinetics of carbon inhaled as CO_2.

(117) Data for intravenously injected [^{14}C]bicarbonate were used in the development of the model for inhaled CO_2 introduced in ICRP *Publications 30* (1981) and applied in several subsequent ICRP documents on occupational or environmental intake of radionuclides. According to that model, inhaled CO_2 is rapidly and completely absorbed from the lungs and distributed uniformly throughout the body. Retention, R(t), is described by the sum of three exponential terms:

$$R(t) = 0.18 \exp(-0.693t/5) + 0.81 \exp(-0693t/60) + 0.01 \exp(-0.693t/60{,}000), \quad \text{(Eq. 1)}$$

where t is in minutes. The first two terms are based on a two-exponential curve fit to data of Winchell et al. (1970) on retention of ^{14}C in 13 normal human subjects over the first 120 min after intravenous injection with [^{14}C]bicarbonate. The third term was added to represent a small component of relatively long-term retention observed in laboratory animals administered $^{14}CO_2$ by inhalation. The coefficient of the third term, 0.01, is based on the interpretation that the two short-term components of retention identified in the subjects of Winchell and coworkers accounted for at least 99% of the administered activity. The removal half-time associated with the third term (~40 d) is the estimated effective half-time for dietary carbon in a typical adult human, i.e. assuming the body's carbon behaves as a single well-mixed pool.

(118) ICRP *Publication 80* (1998), which addresses doses from radiopharmaceuticals, describes a recycling model for ^{14}C as carbon dioxide or bicarbonate formed in the body after administration of ^{14}C-urea. The model adds bone compartments to a recycling model of Winchell and coworkers (1970) developed from the same [^{14}C]bicarbonate injection data used by the authors of ICRP *Publication 30* to derive the model for inhaled carbon dioxide. The model of *Publication 80* contains a central blood compartment that exchanges carbon with four tissue compartments: a rapid-turnover soft-tissue compartment, a slow-turnover soft-tissue compartment ($T_{1/2}$ ~ 40 d), and two bone compartments representing trabecular and cortical bone. The bone compartments return carbon to blood at the rate of bone turnover. Carbon is lost from the body by transfer from blood to the environment in expired air.

(119) Leggett (2004) proposed a more detailed recycling biokinetic model for systemic radiocarbon taken into the body as carbon dioxide or bicarbonate. Parameter values describing retention and excretion of activity during the first few weeks after administration were based on studies of the fate of radiocarbon in human subjects after intake of labeled bicarbonate or carbon dioxide. Data from laboratory animals given labeled bicarbonate, carbon dioxide, or carbonate were used to model the tissue distribution and the long-term retention of carbon. The model includes a central blood compartment that exchanges carbon with six soft tissue compartments and five bone compartments representing different phases of retention as indicated by the experimental data. In addition to loss of label through exhalation of carbon dioxide, the model depicts small losses in urine and faeces and through skin. The model provides a reasonably close reproduction of reported biokinetic data from studies of human subjects exposed to labeled bicarbonate or carbon dioxide. The model was designed to yield higher total-body retention and bone retention of activity than observed in

laboratory animals exposed to carbon dioxide or bicarbonate in view of the relatively high metabolic rates and bone turnover rates in the studied animal species. A modified version of Leggett's model, described in a later section, is applied in this report to radiocarbon entering blood as carbon dioxide or bicarbonate.

Inhaled benzene

(120) A biokinetic model for radiocarbon inhaled as benzene was proposed by Krins et al. (2003). Transfer coefficients depend on the concentration of benzene in air. It is assumed that inhaled benzene is immediately deposited in a blood pool that exchanges activity with five compartments: adipose tissue, a muscle group, an organ group, bone marrow, and liver. The bone marrow and liver compartments feed a metabolite compartment that circulates the metabolites through the body. The bone marrow and liver compartments are governed by Michaelis-Menten kinetics such that excretion is nearly equally divided between urine and breath at high concentrations of benzene in air and is primarily (~90%) in urine at low concentrations. The water soluble metabolites empty into the urinary bladder after removal from blood by the kidneys.

Dietary carbon

(121) A number of biokinetic models have been proposed for purposes of estimating radiation doses due to ingestion of ^{14}C in food and drink. Relatively detailed models with varying levels of physiological realism have been proposed in recent years by Richardson and Dunford (2003a,b), Whillans (2003), Galeriu et al. (2009) and Manger (2011). A physiologically detailed biokinetic model proposed by Richardson and Dunford (2003a,b) separates dietary carbon into carbohydrates, lipids, and protein. A relatively complex version of the model further divides carbohydrates into glucose and glycogen, lipids into adipose fat and fatty acids, and protein into amino acids and soft tissue proteins. The biokinetics of carbon or other major elements that form the structure of the principal nutrients carbohydrates, fats, and proteins (hydrogen, nitrogen, oxygen) is assumed to be determined primarily by the oxidation of glucose, fatty acids, and amino acids and the formation of water, carbon dioxide, and urea. Carbon-specific transfer coefficients were not presented by Richardson and Dunford. A simpler biokinetic model for carbon proposed by Whillans (2003) also separates dietary carbon into carbohydrates, fat, and protein. Transfer coefficients are based on intakes by Reference Man (ICRP, 1975) and transfer rates suggested by Brown and Chant (1995). A model proposed by Galeriu et al. (2009) uses anatomical compartments and transfer coefficients determined from reference physiological constants such as metabolic rates, body energy densities, and empty body masses. Transfer coefficients were developed for various farm animals. Organ compositions for farm animals were based on reference values for man. Organ masses, energy expenditures, and intakes of organic carbon were taken from the literature on animal metabolism, nutrition, and physiology.

Ingested urea

(122) The urea breath test is a diagnostic method to test for *Helicobacter pylori (Hp)* infection by oral administration of a cocktail of ^{14}C-labelled urea to the patient. A biokinetic model for orally administered ^{14}C-labelled urea is described in ICRP *Publication 80* (1998). For the normal case, ^{14}C-urea is assumed to be completely absorbed by the stomach with a half-life of 5 minutes. In the *Hp* positive case, it is assumed that 65% of the intake is immediately converted into carbon dioxide, and the remaining 35% is absorbed by the stomach as in the normal case. The urea absorbed by the stomach is rapidly distributed in the total body water. Eighty percent of the urea in the total body water is excreted by the kidneys

with a half-time of 6 h, and 20% is rapidly dissociated to ammonia and carbon dioxide and treated according to the biokinetic model for carbon dioxide used in ICRP *Publication 80*.

Ingested triolein (glycerol trioleate)

(123) Gunnarsson et al. (2000) studied the biokinetics of ingested ^{14}C-triolein by performing breath tests on human subjects. The investigators later (Gunnarsson et al., 2003) developed a biokinetic model from the derived data and an ICRP model for ^{14}C-labelled neutral fat (ICRP, 1993). Ingested ^{14}C-triolein rapidly passes through the stomach into the small intestine, where 70% of the ingested material is transported to the liver following hydrolysis. In the liver, 28% of the fat compound is metabolized to $^{14}CO_2$ ($T_{1/2}$ = 1 h) and transported to the bicarbonate pool. The remaining 42% becomes incorporated into adipose tissue (85%) (a_1=57%, $T_{1/2}$ = 2 days; a_2 = 43%, $T_{1/2}$ = 137-620 days), muscle (10%) ($T_{1/2}$ = 2 days), and other organs (5%) ($T_{1/2}$ = 137-620 days), where the triglycerides are oxidized and transferred to the bicarbonate pool (Gunnarsson et al., 2003). The kidney-bladder system receives 25% of the administered activity ($T_{1/2}$ = 4 h). The remaining 5% of the administered activity passes through the gastrointestinal tract and is excreted in faeces.

Ingested glycocholic acid

(124) [1-^{14}C]-Glycocholic acid (GCA) is used to investigate abnormal bacterial overgrowth or reduced resorption of bile acids in the small intestine. Gunnarsson (2002) developed a model for the ingestion of labeled GCA consisting of three main physiological pathways, one involving the conjugated compound, a second involving a liberated glycine moiety, and a third representing activity converted to carbon dioxide. According to the model, the ingested conjugated bile acid is absorbed primarily by the terminal ileum during the enterohepatic cycle and becomes almost exclusively confined to the lumen of the biliary ducts, gut, and liver. The bile acid undergoes enterohepatic circulation roughly six times per day. Approximately 18% of the bile acid is deconjugated during each enterohepatic circulation, resulting in a biological half life of 19 h. For the normal case, 46% of the [1-^{14}C]-glycine is transported rapidly through the intestinal tract [$T_{1/2}$ = 3 h (11%), $T_{1/2}$ = 14 h (89%)], converted to $^{14}CO_2$ by the bacteria in the colon, and transported to the bicarbonate pool to be exhaled. Roughly the same amount (44%) is transported in the blood from the liver and incorporated into tissue proteins, where glycine is metabolized to CO_2 by tissue enzymes and transferred to the bicarbonate pool [$T_{1/2}$ = 6 days (70%) and $T_{1/2}$ = 77 days (30%)]. The distribution of glycine within the tissue proteins is divided according to protein contents in various organs (ICRP, 1975). A small fraction (2.5%) of the ^{14}C is excreted in urine. The rest (7.5%) is excreted in faeces.

Ingested xylose

(125) Xylose is a monosaccharide used for the diagnosis of abnormal intestinal bacterial flora. Gunnarsson (2002) developed a model for the ingestion of D-[U-^{14}C]-xylose. According to the model, ingested xylose is transported from the stomach to the small intestines where a major fraction is absorbed and transported to the plasma and extracellular fluid. It is assumed that 70% of the absorbed xylose is excreted in urine with a half-time of 2.5 h and the remaining 30% is exhaled. Of the exhaled activity, fractions 0.168, 0.232, and 0.6 are removed with half-times 1.1 h, 3 d, and 60 d, respectively. The 3-d half-time is associated with metabolism of xylose in the liver. The 60-d half-time is associated with incorporation of xylose in adipose tissue and metabolism to $^{14}CO_2$.

3.2.3.2. Biokinetic models for systemic carbon used in this report

Inhaled carbon monoxide

(126) The model for inhaled carbon monoxide used in this report is based on deposition fractions and retention half-times applied in ICRP *Publication 30* (1981) and *Publication 71*(1995). It is assumed that 40% of inhaled CO is instantly absorbed to blood and bound to hemoglobin and 60% is instantly exhaled. Carbon monoxide is assumed to be lost from blood to the environment via the lungs with a biological half-time of 200 min (Glass et al., 1968; Peterson and Stewart, 1970).

Carbon reaching blood as carbon dioxide or bicarbonate

(127) A variation of the model of Leggett (2004) described earlier is applied in this report to radiocarbon assumed to reach blood as carbon dioxide or bicarbonate, e.g. as inhaled carbon dioxide or ingested or intravenously injected bicarbonate. The structure of the modified model is shown in Figure 3-1. Parameter values are listed in Table 3-5. The modifications were made to make the model more consistent with the generic modeling scheme used in this report, simplify implementation of the model by reducing the total numbers of compartments and pathways, and improve predictions of the long-term urinary excretion rate by including additional phases of transfer from soft tissues to the urinary excretion pathway. The modified model adds a blood compartment (Blood 2 in Figure 3-1) and some paths of movement of carbon but simplifies the original model overall by eliminating compartments and pathways depicting rapid exchange of activity between blood and peripheral compartments. The eliminated features of the original model are not of much practical importance in radiation protection.

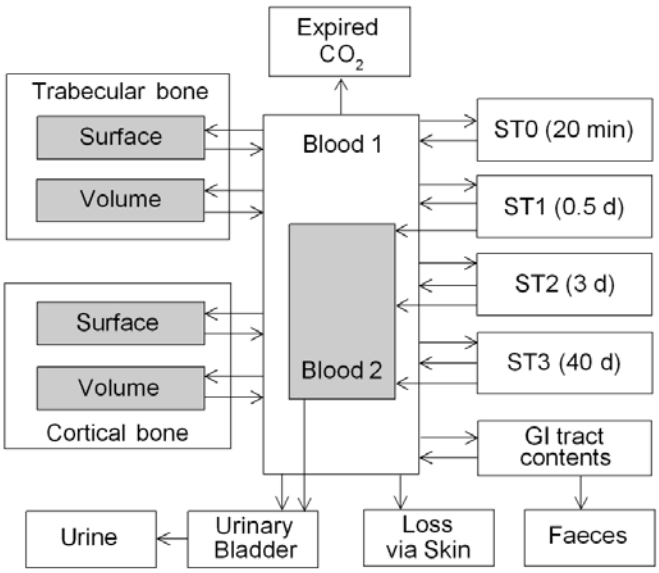

Figure 3-1. Structure of the systemic model used in this report for carbon taken into the body as carbon dioxide or bicarbonate (simplification of a model of Leggett, 2004)

(128) In the model, absorbed carbon is assigned to Blood 1. Activity leaves Blood 1 at the rate 100 d^{-1} ($T_{1/2}$ = 10 min), with 60% of the outflow assigned to ST0, 1.8% to ST1, 0.3% to ST2, 0.44% to ST3, 0.15% to bone surface, 0.01% to bone volume, 36.2% to excreta through exhalation, 0.3% to excreta via skin, 0.65% to the bladder contents, and 0.15% to the right

colon contents. Removal half-times from ST0, ST1, ST2, and ST3 are 20 min, 0.5 d, 3 d, and 40 d, respectively. It is assumes that 4% of outflow from ST1, ST2, and ST3 enters Blood 2 and all other outflow from the four soft tissue compartments returns to Blood 1. Activity transfers from Blood 2 to the urinary bladder contents at the rate 1000 d^{-1} ($T_{1/2}$ = 1 min). Based on estimates of the relative masses of trabecular and cortical bone replaced per unit time in an adult human, 60% of carbon entering bone is assigned to trabecular bone and 40% is assigned to cortical bone. The trabecular and cortical bone surface compartments are assumed to lose carbon to Blood 1 with a half-time of 40 d. The bone volume compartments are assumed to lose carbon to Blood 1 at the rate of bone turnover, which differs for trabecular and cortical bone.

Table 3-5. Transfer coefficients for the systemic model used in this report for radiocarbon assumed to reach blood as carbon dioxide or bicarbonate

From	To	Transfer coefficient (d^{-1})
Blood 1	Excreta (exhalation)	36.2
Blood 1	Excreta (via skin)	0.3
Blood 1	Urinary bladder contents	0.65
Blood 1	Right colon contents	0.15
Blood 1	ST0	60
Blood 1	ST1	1.8
Blood 1	ST2	0.3
Blood 1	ST3	0.44
Blood 1	Trabecular bone surface	0.09
Blood 1	Cortical bone surface	0.06
Blood 1	Trabecular bone volume	0.006
Blood 1	Cortical bone volume	0.004
ST0	Blood 1	49.91
ST1	Blood 1	1.331
ST2	Blood 1	0.2218
ST3	Blood 1	0.01664
ST1	Blood 2	0.05545
ST2	Blood 2	0.009242
ST3	Blood 2	0.0006931
Blood 2	Urinary bladder contents	1000
Trabecular bone surface	Blood 1	0.01733
Cortical bone surface	Blood 1	0.01733
Trabecular bone volume	Blood 1	0.000493
Cortical bone volume	Blood 1	0.0000821

(129) Total-body retention of carbon following acute input of carbon dioxide or bicarbonate into blood based on the present model agrees closely with predictions based on the original model (Leggett, 2004). Also, in agreement with the original model, the present model predicts that exhalation, urinary excretion, faecal excretion, and loss through skin accounts for 96.8%, 2%, 0.4%, and 0.8%, respectively, of the total loss of activity from the body over an extended period. The present model predicts slower accumulation of activity in bone than the original model, but the two models predict similar levels of activity in bone beyond a few days after acute input of activity to blood. For example, the present model predicts that bone contains 0.41% of intake at 1 d, 0.36% at 10 d, and 0.098% at 100 d after intake, compared with predictions of 0.89% at 1 d, 0.38% at 10 d, and 0.096% at 100 d based

on the original model. In view of the uncertainty in the early distribution of radiocarbon in bone, a relatively long residence time of carbon on bone surface (40 d) is assigned in the original model as a dosimetrically cautious measure.

Inhaled methane

(130) The available data indicate that some radioactive carbon-labelled methane is oxidised to carbon dioxide (Dougherty et al., 1967), but a large fraction is organically bound (Carlisle et al., 2005). In ICRP *Publication 80* (1998) (in an addendum to ICRP *Publication 72*, 1996) and in ICRP *Publication 88* (2001) the assumption is made that one half of the metabolised fraction is retained with the half-time of carbon dioxide and one half with that of organic carbon (ICRP *Publication 80*, 1998). That assumption is also made here: 50% of radiocarbon in the absorbed methane enters the blood pool in the carbon dioxide model (Figure 3-1 and Table 3-5) and follows the kinetics described in that model, and 50% enters the blood pool in the generic carbon model (described below) and follows the kinetics described in that model.

Generic model for systemic carbon

(131) For general radiological protection purposes a generic biokinetic is applied in this report to radiocarbon absorbed to blood following intake in forms other than carbon monoxide, carbon dioxide, bicarbonate, or methane. The model is less conservative than the ICRP's previous generic systemic model for carbon, which assigns a 40-d half-time to absorbed radiocarbon, but accounts for the possibility that a dosimetrically significant portion of absorbed radiocarbon may be retained in the body for an extended period. Based on its design and on comparison of dose estimates with biokinetic models for a number of specific forms of carbon, the revised generic model seems more likely to overestimate than underestimate dose per unit intake of ^{14}C in the workplace.

(132) The generic model structure and its connections to the respiratory and alimentary tract models and urinary bladder are shown in Figure 3-2. Baseline transfer coefficients for systemic pathways are listed in Table 3-6.

(133) The revised model is based on consideration of retention times and rates of loss along specific excretion pathways identified in published studies of ^{14}C-labeled carbon compounds. The model was designed with the goal of providing cautious but not unnecessarily conservative estimates of dose per unit intake of unknown forms of radiocarbon, as judged from published biokinetic data for carbon compounds. It was also considered that the model should be adaptable to case-specific information such as measurement of the rates of urinary excretion and exhalation of activity following exposure to a carbon compound in the workplace.

(134) The excretion pathways addressed in the model are urinary and faecal excretion and exhalation. Three systemic compartments are used to represent blood, relatively short-term retention in systemic tissues, and relatively long-term retention in systemic tissues. The short-term compartment represents losses with a half-time of a few days, which typically accounts for most of the loss of the label from the body as indicated by published studies of different carbon compounds. The long-term compartment depicts the longer removal half-times depicted in several models for specific carbon compounds. This long-term retention is generally associated in these models with adipose tissue. The carbon dioxide / bicarbonate model defined in Figure 3-1 and Table 3-5 is included as a submodel that describes the fate of labeled carbon dioxide produced in systemic tissues by metabolism of the initial form of carbon that reaches blood. Carbon dioxide produced in systemic tissues is assumed to move instantly to the compartment Blood 1 in the carbon dioxide model (Figure 3-1).

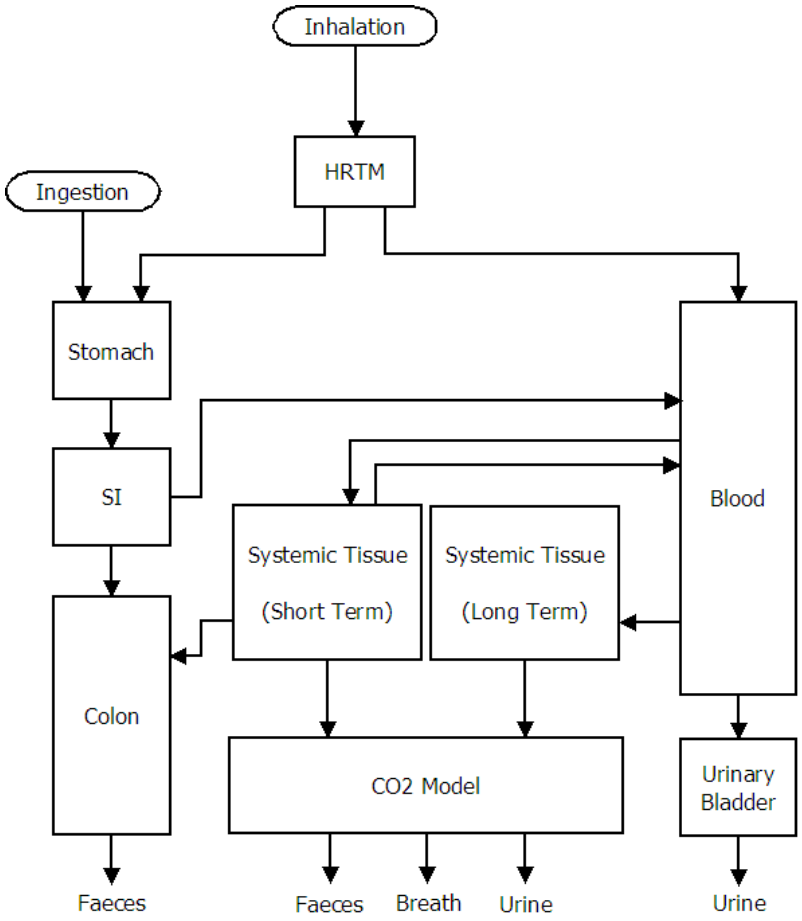

Figure 3-2. Generic structure for radiocarbon labelled substances. SI is small intestine contents, and HRTM is the Human Respiratory Tract Model

Table 3-6. Transfer coefficients for the generic model for systemic carbon

Path	Baseline transfer coefficients (d^{-1})
Blood to Systemic Tissue (Short-Term)	1.27
Blood to Systemic Tissue (Long-Term)	0.276
Blood to Bladder	1.51
Systemic Tissue (Short-Term) to CO_2 Model	0.062
Systemic Tissue (Short-Term) to Blood	0.095
Systemic Tissue (Short-Term) to Colon	0.070
Systemic Tissue (Long-Term) to CO_2 Model	0.0099

(135) For the case of ingested radiocarbon, activity moves through the alimentary tract as described in the Human Alimentary Tract Model and is nearly completely (99%) absorbed to blood from the small intestine contents (SI). Blood loses activity with a half life of 5 hours, with 50% of the outflow assigned to the urinary bladder contents; 40% to the short-term systemic compartment, and 10% to the long-term compartment. The short-term systemic tissue compartment loses activity with a half-life of 3 days. Outflow from this compartment is divided as follows: 40% returns to Blood, 30% is secreted into the colon contents and

subsequently excreted in faeces, and 30% moves to Blood 1 in the carbon dioxide model (Figure 3-1). Carbon entering the long-term retention compartment is assumed to be metabolized slowly to carbon dioxide, which moves to Blood 1 in the carbon dioxide model with a half-time of 70 d.

(136) For the case of inhaled radiocarbon, activity enters the Human Respiratory Tract Model (HRTM) and is absorbed to blood or transported to the alimentary tract over time. Activity moving from the HRTM to blood or to the alimentary tract is treated as described above for the ingestion case.

(137) The baseline transfer coefficients for the systemic pathways (Table 3-6) were determined by fitting central estimates of excretion rates determined in studies involving administration of different carbon compounds. Average fractional excretion along the major excretion pathways was estimated as 0.59 for urine (range, 0.01 – 1.00), 0.24 for exhalation (range, 0 – 0.95), and 0.17 for faeces (range, 0 – 0.99) (Crawley, 1977; Baker et al., 1954; Fine et al., 1962; Berlin and Tolbert, 1955; Hellman et al., 1955; Fukushima et al., 1954; Sandberg and Slaunwhite, 1957; Migeon et al., 1956; Hellman et al., 1954; Thierens et al., 1994; ICRP, 1987; ICRP, 1998; Stather et al., 1981; Crawley and Haines, 1979; Eriksson et al., 1998; Webber et al., 2003). Up to three phases of urinary excretion were determined in different studies, depending in part on the length of the observation period (Fukushima et al., 1954; Berlin and Tolbert, 1955; Hellman et al., 1955; Migeon et al., 1956; Sandberg and Slaunwhite, 1957; Crawley, 1977; ICRP, 1987; Kramer et al., 1996; Eriksson et al., 1998; Webber et al., 2003). The average half-time was 0.43 d (range 0.07-1.0 d) for the fastest phase, 3.3 d (range, 0.29-7.0 d) for the intermediate phase, and 70 d (range 33-620 d). The fast phase typically represented 85% or more and the intermediate component about 5% of total urinary excretion. In the generic model, the fast phase of loss is represented mainly by transfer from blood to the urinary bladder contents, and removal half-times and pathways from the two systemic tissue compartments are used to account for the intermediate and long-term phases of loss inferred from the published data.

(138) The systemic transfer coefficients shown in Table 3-6 were derived by fitting the excretion data using computer software. The same type of fitting procedure could be used to derive case-specific transfer coefficients for the model if reliable bioassay data are available. For example, bioassay data might indicate different fractional excretion of ^{14}C in urine, breath, and faeces, or different phases of urinary excretion from those used to derive the baseline transfer coefficients.

(139) Cumulative activity of intravenously injected ^{14}C in the body based on the generic model was compared with predictions of models described earlier for benzene, glycocholic acid, triolein, urea, and xylose, and with the model for inulin described in ICRP *Publication 53* (1987). These compounds represent some of the longest and some of the shortest retention times that have been determined for carbon compounds. Comparison was also made with the generic systemic model for carbon used in ICRP *Publication 71* (1995). Results of the comparison are shown in Table 3-7.

Table 3-7. For intravenous injection of ^{14}C, comparison of cumulative activity in the body as predicted by the revised generic model and by existing models for various specific carbon compounds

Model[a]	Nuclear transformations expressed as multiple of value predicted by the revised generic model
Revised generic model	1
Benzene	0.05
Glycocholic Acid	1
Inulin (ICRP, 1987)	0.04
Triolein	1
Urea	1
Xylose	2
Generic model in ICRP *Publication 71* (1995)[b]	5

[a] Models described in this report except for inulin.
[b] Assumes uniform distribution in body and biological half-time of 40 d.

3.3. Individual monitoring

(140) ^{14}C intakes are generally monitored though measurements of the activity excreted in urine. The most common method of analysis is liquid scintillation counting. Measurements of activity in exhaled breath may be used for ^{14}C-labeled organic material metabolized to CO_2 but there are no information on MDAs or routine use of the technique.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{14}C	Urine Bioassay	Liquid Scintillation Counting	60 Bq/L	1-5 Bq/L

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4. PHOSPHORUS (Z = 15)

4.1. Chemical Forms in the Workplace

(141) Phosphorus is a non-metal which occurs in numerous oxidation states, with V the most common. It is able to react chemically with many other elements to form organic and inorganic compounds. The most common phosphorus compounds in solution are phosphates, which occur in different forms depending on the pH (e.g. HPO_4^{2-}, PO_4^{3-}). Phosphorus may be encountered in industry in a variety of chemical forms, including the oxide, hydride, halide, phosphate, phosphide and also organophosphorus and organophosphate.

(142) Phosphorus-32 and ^{33}P are routinely used to produce radiolabelled compounds.

Table 4-1. Isotopes of phosphorus addressed in this report

Isotope	Physical half-life	Decay mode
P-32[a]	14.26 d	B-
P-33	25.34 d	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

4.2. Routes of Intake

4.2.1. Inhalation

Absorption Types and parameter values

(143) Information is available from a few experimental studies on the behaviour of inhaled phosphorus. However, most of it relates to phosphates for which the cation, rather than the phosphorus itself was radiolabelled.

(144) Absorption parameter values and Types, and associated *f*A values for particulate forms of phosphorus are given in Table 4-2.

Sodium phosphate

(145) Schiessle (1956, 1957) followed retention of ^{32}P in guinea pigs for 28 days after inhalation of $Na_3(^{32}PO_4)$. Most of the initial lung deposit (ILD) was absorbed over this period, but not very rapidly: there was little transfer to blood at the end of the 25-minute exposure, about 40% ILD remained after 1 day and 9% ILD after 28 days. (The author noted that there was greater uptake to bone compared to liver than after intravenous injection of ^{32}P.) Specific parameter values were estimated by the task group to be: $f_r = 0.8$, $s_r = 1\ d^{-1}$ ($t_{½}$ ~ 17 hours) and $ss = 0.02\ d^{-1}$ ($t_{½}$ ~ 3 d), consistent with assignment to Type F. Although specific parameter values for sodium phosphate based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is so unlikely. Instead, sodium phosphate is assigned to Type F. However, the data are used as the basis of the default rapid dissolution rate for phosphorus.

Phosphates labelled with isotopes of other elements

(146) For details relating to zinc and yttrium refer to the sections dealing with the labelling radioelement. Details are given here for stannic phosphate because inhalation of tin has not been covered elsewhere yet.

Zinc phosphate ($Zn_3(PO_4)_2$) (See section 9.2.1)

(147) The results of a study of inhalation of $^{65}Zn_3(PO_4)_2$ by dogs were consistent with assignment to Type M.

Yttrium phosphate (YPO_4) (See section 11.2.1)

(148) The results of a study of inhalation of $91YPO_4$ by dogs were consistent with assignment to Type M. The authors (Newton et al., 1971) noted that following both inhalation and gavage of $^{91}YPO_4$, the ratio of deposition in the skeleton to that in the liver was lower than following inhalation of other forms of ^{91}Y.

Stannic phosphate

(149) Morrow et al. (1968) followed lung clearance of ^{113}Sn for 7 days after inhalation of $^{113}Sn_3(PO_4)_2$ by dogs and rats, but few details are given. Lung retention in dogs was described by a two-component exponential function with half-times of 2 days (28%: clearance rate 0.35 d^{-1}) and 59 days, (clearance rate 0.012 d^{-1}), giving predicted lung retention at 30 d and 180 d to be 50% and 8% of the initial lung deposit (ILD), and indicating Type M behaviour.

Rapid dissolution rate for phosphorus

(150) The value of s_r estimated for sodium phosphate above, 1 d^{-1}, is applied here to all Type F forms of phosphorus. 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 phosphorus.

Extent of binding of phosphorus to the respiratory tract

(151) Evidence from the sodium phosphate study outlined above suggests that there is probably little binding of phosphorus. It is therefore assumed that for phosphorus the bound state can be neglected, i.e. $f_b = 0.0$.

Table 4-2. Absorption parameter values for inhaled and ingested phosphorus

		Absorption parameter values[a]			Absorption from the alimentary tract, f_A
Inhaled particulate materials		f_r	s_r (d^{-1})	s_s (d^{-1})	
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Sodium phosphate	1	1	–	0.8
M	Yttrium, stannic and zinc phosphates, all unspecified forms[d]	0.2	1	0.005	0.2
S	—	0.01	1	$1x10^{-4}$	0.008
Ingested materials					
All unspecified forms					0.8

[a] It is assumed that for phosphorus the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of phosphorus (1 d^{-1}) are element-specific.
[b] Materials (e.g. sodium phosphate) are 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 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 and the f_A value for ingested soluble forms of phosphorus (0.8).
[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

4.2.2. Ingestion

(152) Phosphorus intake is mainly through the diet in the form of inorganic phosphate and phosphorus-containing biomolecules such as nucleic acids and phospholipids. According to Eakins et al. (1966), fractional absorption of ^{32}P from the gastro-intestinal tract is about 0.75 when it is ingested as phosphate under normal dietary conditions, and is above 0.9 while fasting. The Food and Nutrition Board of the US Institute of Medicine reports absorption values ranging from 0.55 to 0.70 in adults and from 0.65 to 0.90 in infants and children (FNB, 1997).

(153) Animal studies have shown that maximal absorption of phosphate occurs in the ileum for mice and in the duodenum and in the jejunum for rats (Radanovic et al., 2005: Stauber et al., 2005; Marks et al., 2006). Absorption of phosphorus can be reduced by the simultaneous administration of unusually high levels of calcium (FNB, 1997). According to recent findings, the intestinal transport process of inorganic phosphate is known to occur by both a sodium-independent, non saturable process and via an active process mediated by sodium-phosphate cotransporters (Katai et al., 1999a). Studies by Katai et al. (1999b) and by Kirchner et al. (2008) with rats showed that transporter-mediated absorption of inorganic phosphate is inhibited by nicotinamide and fructose, respectively. Intestinal sodium-dependent phosphate absorption was significantly reduced (reduction between 35% and 60%) in mice and rats with simulated inflammable bowel diseases (Chen et al., 2009).

(154) In *Publication 30* (ICRP, 1979), the recommended absorption value was 0.8 for all compounds of the element. This value is used here; that is, $f_A = 0.8$ for all compounds.

4.2.3. Systemic Distribution, Retention and Excretion

4.2.3.1. Summary of the database

(155) Phosphorus represents roughly 1% of the weight of the human body. In adults about 85% of the phosphorus is in bone, 9% is in muscle, and 6% is in remaining tissues and fluids. Most of the phosphorus in blood is contained in the red blood cells (RBC) (Eakins et al., 1966; ICRP, 1975; Parfitt and Kleerekoper, 1980).

(156) Normal dietary intake of phosphorus is about 1.0-1.5 g/d, in the form of inorganic phosphates, lipids, and proteins. Roughly three-fourths of phosphorus ingested as phosphate typically is absorbed to blood. Excretion is primarily in urine as inorganic phosphate (Eakins et al., 1966).

(157) The rate of biological removal of ^{32}P from the body varied widely in human subjects following intravenous injection of $Na_2H^{32}PO_4$ (Erf et al., 1941; Hevesy, 1948; Weijer et al., 1962; Eakins et al., 1966). On average, about one-fourth of the administered amount was excreted in urine and faeces during the first six days, with urinary excretion generally

representing 90% or more of total excretion. Average daily excretion of activity as measured in four human injection studies is summarized in Figure 4-1.

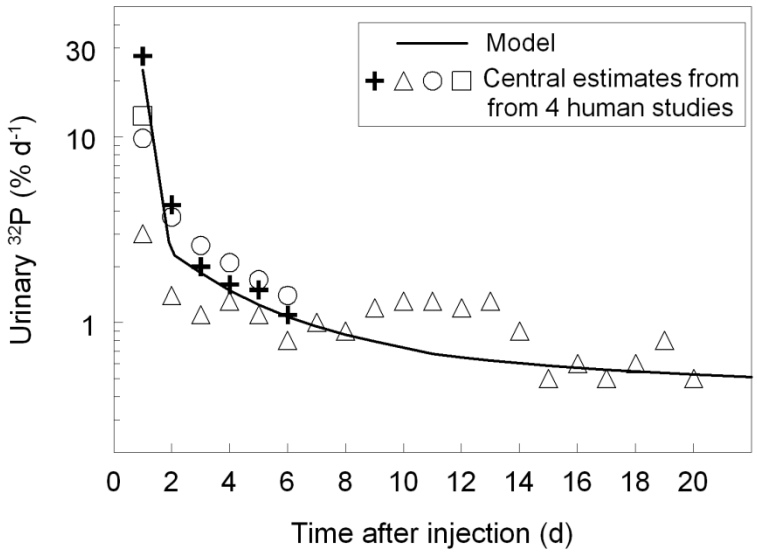

Figure 4-1. Average daily urinary excretion of phosphorus following intravenous injection into human subjects (data summarized by Eakins et al., 1966). The curve shows predictions of the systemic biokinetic for phosphorus used in this report.

(158) Following intravenous injection, labeled phosphorus is distributed throughout the extracellular fluids within a few minutes. Kinetic analysis indicates that the rapidly exchangeable pool is larger than the extracellular pool and thus presumably includes a portion of the intracellular phosphorus. Labeled phosphate is incorporated quickly into organic compounds in the body. The tissue turnover rate of phosphate as measured by the rate of exchange of radio-phosphorus depends on the rate of glycolysis of the tissue and is relatively high in red blood cells, intermediate in liver and heart, and low in resting muscle and nerve tissue (Parfitt and Kleerekoper, 1980).

(159) Within a short time after administration of labeled phosphorus to human subjects or laboratory animals much of the activity accumulates in bone. The behavior of phosphorus in bone resembles that of calcium. Rapid uptake of both elements occurs on all bone surfaces, with considerable variability in the uptake rate between different bones and different surfaces of the same bone. Within a period of hours or days radioisotopes of phosphorus or calcium diffuse throughout bone volume. Both elements can penetrate into the interior of bone crystal. The exchangeable and non-exchangeable fractions of the total bone mineral are approximately the same for phosphorus and calcium (Neuman and Neuman, 1958; Parfitt and Kleerekoper, 1980).

(160) As is the case for calcium, uptake of phosphorus is considerably greater in forming or growing bone than in mature bone. Labeled phosphorus and calcium both show high concentration in forming osteons (Parfitt and Kleerekoper, 1980). In rats injected intraperitoneally with ^{32}P, skeletal uptake decreased with increasing age at injection, from about 90% of the injected amount at age 15 d to about 17% of the injected amount at age 170 d (Bonner, 1948).

(161) Stather (1974) compared the distribution and retention of ^{32}P and the alkaline earths

^{45}Ca, ^{85}Sr, and ^{133}Ba in the mouse skeleton. At 24 h after intraperitoneal injection into 8-week old mice the distribution of the four radionuclides was virtually the same throughout the skeleton, but skeletal content as a percentage of injected activity differed from one radionuclide to another: ^{32}P, 21.6%; ^{45}Ca, 61.5%; ^{85}Sr, 37.3%; and ^{133}Ba, 48.8%. The skeletal burden represented about 37% of total body ^{32}P compared with about 90% of total-body ^{85}Sr.

(162) Bauer and Carlsson (1955) compared the uptake of ^{32}P and ^{45}Ca by bone (tibial shaft) and incisors in adult rats over the first 5 d after simultaneous subcutaneous injection of these radionuclides. The percentage of the administered ^{45}Ca found in bone was consistently about 2.3 times the percentage of administered ^{32}P in the same bone samples at corresponding times after administration. The ratio of uptake of ^{45}Ca and ^{32}P was about the same for incisors as for bone.

4.2.3.2. Biokinetic model for systemic phosphorus

(163) Dyson (1966) proposed the compartment model shown in Figure 4-2 as a sufficiently close description of the biokinetics of phosphorus for radiation protection purposes. The flow rates are given in terms of the movement of stable phosphorus at equilibrium. It is assumed that 1 g of phosphorus is absorbed daily from dietary phosphorus. Presumably, 15% of phosphorus entering plasma is promptly excreted, and the rest is removed to cell fluids (15%), other soft-tissue components (40%), and bone (30%) with a half-time of 0.5 days. Phosphorus is returned to plasma from cell fluids and other soft-tissue components with half-times of 2 d and 19 d, respectively. The removal half-time from bone to plasma is long compared with the radiological half-lives of radioisotopes of phosphorus.

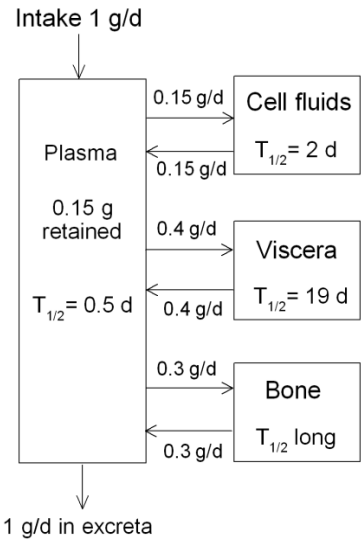

Figure 4-2. Compartmental model of the biokinetics of systemic phosphorus proposed by Dyson (1966). The flow rates are given in terms of daily transfers of stable phosphorus at equilibrium.

(164) The biokinetic model for systemic phosphorus used in ICRP *Publication 30* (1979) and ICRP *Publication 68* (1994) is based on the model proposed by Dyson (1966). As implemented in *Publication 68* (1994), activity leaves blood with a half-time of 0.5 d and is distributed as follows: 15% goes to excretion pathways; 30% goes to mineral bone, and 55% is uniformly distributed in remaining tissues (Other). Other is divided into two

compartments, one receiving 15% of activity leaving blood and having a removal half-time of 2 d, and the second receiving 40% and having a half-time of 19 d. Activity is permanently retained in bone. Activity that is promptly excreted or removed from tissues transfers directly to the urinary bladder contents or right colon contents. A urinary to fecal excretion ratio of 9:1 is assigned. Phosphorous isotopes with half-life less than 15 d are assumed to be uniformly distributed on bone surfaces, and all others are distributed in bone volume.

(165) The systemic model for phosphorus used in this report is broadly similar to the model of Dyson (1966) but describes the movement of phosphorus in more detail. The model istructure is shown in Figure 4-3. Parameter values are listed in Table 4-3.

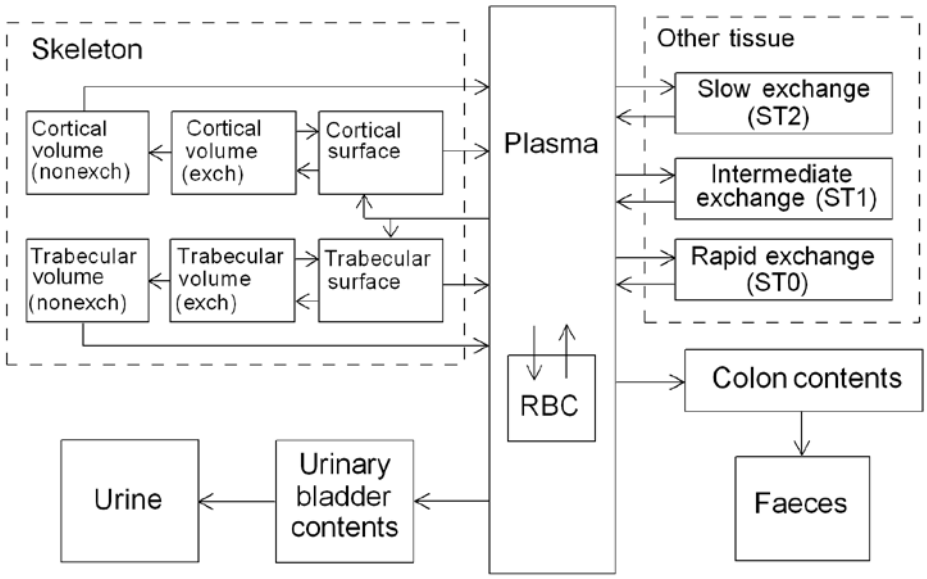

Figure 4-3. Structure of the model for systemic phosphorus. Abbreviations: exch = exchangeable, nonexch = non-exchangeable, RBC = red blood cells.

(166) Phosphorus is assumed to leave blood plasma at the rate 50 d^{-1}, corresponding to a removal half-time of 20 min. The outflow from plasma is divided as follows: 3% goes to red blood cells (RBC), 20% to the urinary bladder contents, 2% to the right colon contents, 20% to bone surfaces, and 55% to soft tissues. The soft tissues are divided into three compartments called ST0, ST1, and ST2, representing fast, intermediate, and slow turnover, respectively. These compartments receive 14.9%, 40%, and 0.1% of outflow from plasma, respectively, and return activity to plasma with half-times of 2 d, 20 d, and 5 y, respectively. The biokinetics of phosphorus in the skeleton is assumed to be identical to that of calcium, including the division of deposited activity between cortical and trabecular bone surfaces. Fractions 0.445 and 0.555 of the deposited amount (8.9% and 11.1% of the amount reaching blood) are assigned to cortical and trabecular surfaces, respectively. The transfer coefficients describing translocation of phosphorus within the skeleton and return from skeletal compartments to blood plasma are taken from the ICRP's systemic model for calcium (ICRP, 1995).

Table 4-3. Transfer coefficients (d^{-1}) in the biokinetic model for systemic phosphorus.

Path[a]		Transfer coefficient (d^{-1})
From	To	
Plasma	Urinary bladder contents	10
Plasma	Right colon contents	1.0
Plasma	Trabecular bone surface	5.55
Plasma	Cortical bone surface	4.45
Plasma	ST0	7.45
Plasma	ST1	20
Plasma	ST2	0.05
Plasma	RBC	1.5
RBC	Plasma	0.13863
STO	Plasma	0.34657
ST1	Plasma	0.034657
ST2	Plasma	0.00038
Cortical bone surface	Plasma	0.578
Cortical bone surface	Exch cortical bone volume	0.116
Trabecular bone surface	Plasma	0.578
Trabecular bone surface	Exch trabecular bone volume	0.116
Exch cortical bone volume	Cortical bone surface	0.002773
Exch cortical bone volume	Nonexch cortical bone volume	0.004159
Exch trabecular bone volume	Trabecular bone surface	0.002773
Exch trabecular bone volume	Nonexch trabecular bone volume	0.004159
Cortical bone volume	Plasma	0.0000821
Trabecular bone volume	Plasma	0.000493

[a] ST0, ST1, and ST2 represent soft tissues with fast, intermediate, and slow turnover, respectively; UB = urinary bladder; RBC = red blood cells; Exch = exchangeable; Nonexch = non-exchangeable.

4.3. Individual monitoring

(167) ^{32}P is a pure beta emitter. Monitoring of individuals is done through urine bioassay techniques, typically liquid scintillation.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{32}P	Urine Bioassay	Liquid scintillation counting	15 Bq/L	0.02Bq/L

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5. SULPHUR (Z = 16)

5.1. Chemical forms in the workplace

(168) Sulphur is a non-metal, which occurs mainly in oxidation states –I, -II, II, IV and VI. It is able to react chemically with many other elements, forming organic and inorganic compounds. The most common sulphur compound in solution is sulphate (SO_4^{2-}). Sulphur-35 is the only isotope of radiological significance that may be encountered in the workplace. It may occur in industry in a number of different chemical forms, including the gases hydrogen sulphide (H_2S), sulphur dioxide (SO_2) and sulphur trioxide (SO_3), fluids or their vapours such as carbon disulphide (CS_2), and solid compounds such as barium sulphate ($BaSO_4$). In research laboratories, it can be present in a wide variety of compounds.

Table 5-1. Isotopes of sulphur addressed in this report

Isotope	Physical half-life	Decay mode
S-35[a]	87.51 d	B-
S-38	170.3 m	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

5.2. Routes of Intake

5.2.1. Inhalation

(169) Some information is available on the behaviour of inhaled gases of sulphur in man and in experimental animals. Most of the information available on inhaled particulate forms of sulphur relates to sulphates.

Classification of gases and vapours, absorption Types and parameter values

(170) Absorption parameter values and Types, and associated f_A values for gas and vapour forms of sulphur are given in Table 5-2 and for particulate forms in Table 5-3.

(171) Exposures to both gas/vapour forms and particulate forms of sulphur are common, and it is therefore proposed here that in the absence of site-specific information 50% particulate; 50% gas/vapour should be assumed (ICRP, 2002).

(a) Gases and vapours

Sulphur dioxide (SO_2)

(172) In two human studies (Speizer and Frank, 1966; Andersen et al., 1974), about 85% of the inhaled SO_2 was deposited; all in the ET airways. In dogs, more than 95% of the inhaled gas was deposited in the ET airways during nose breathing and 50 – 90% during mouth breathing (Frank et al., 1967; 1969). A further study with dogs, in which the trachea was perfused with SO_2, gave 90% deposition in the trachea (Balchum et al., 1960). Studies exposing rabbits to different SO_2 concentrations gave 80% respiratory tract deposition at low concentrations (0.05 ppm), 98% at high concentrations (700 ppm) (Strandberg, 1964) and more than 90% upper airway deposition at concentrations between 100 and 300 ppm (Dalhamn and Strandberg, 1961). Absorption to blood of SO_2 deposited in the respiratory

tract of dogs was consistent with assignment to Type F (Balchum et al., 1960; Frank et al., 1967) For sulphur dioxide it is assumed here that there is 85% deposition in the respiratory tract (with default regional distribution, Table 5-2) and Type F absorption.

Carbon disulphide (CS_2)

(173) Studies have been performed with CS_2 in mice, rats, dogs and man (Bergman et al., 1984; McKenna and DiStefano, 1977; McKee et al., 1943; Teisinger and Souček, 1949). In all cases CS_2 was taken up by the respiratory tract and absorbed into the blood. However, there is no information on the fraction of inhaled vapour deposited, or on the site of deposition. McKenna and DiStefano (1977) observed that CS_2 uptake into blood was characterised by a single exponential with half-life of 19.3 minutes, consistent with assignment to Type F. For carbon disulphide it is assumed here by default that there is 100% deposition in the respiratory tract (with default regional distribution, Table 5-2) and Type F absorption.

Hydrogen sulphide (H_2S)

(174) Patty (1963) reported that H_2S is absorbed through the lung and that H_2S does not appear in exhaled breath, indicating that a large fraction is absorbed. In the absence of any real quantitative data on the fraction of H_2S absorbed, the default option for gases and vapours is taken. For hydrogen sulphide it is assumed here that there is 100% deposition in the respiratory tract (with default regional distribution, Table 5-2) and Type F absorption.

Carbonyl sulphide (COS)

(175) Little has been published on the uptake of COS. Patty (1963) noted that COS decomposes in water to H_2S and CO_2. On this basis it is assumed that the uptake of COS is the same as that of H_2S: in the absence of specific information, the default option for gases and vapours is taken. For carbonyl sulphide it is assumed here that there is 100% deposition in the respiratory tract (with default regional distribution, Table 5-2) and Type F absorption.

(b) Particulate materials

(176) No detailed information is available on the rate of absorption of sulphur following respiratory tract deposition of particulate compounds other than sulphates (see below). However, two cases of accidental exposure of humans to ^{35}S compounds have been reported.

Elemental sulphur

(177) A worker was contaminated internally and externally following the explosion of a glass vial containing elemental ^{35}S dissolved in benzene (Maass et al., 1963). Similar amounts of ^{35}S were excreted in urine and faeces during the first few days, and levels in plasma and urine fell rapidly, suggesting rapid absorption from the lungs, and hence Type F behaviour.

Other compounds

(178) Two workers were contaminated with ^{35}S while segregating waste of unknown chemical composition formed by irradiating KCl targets (Spate et al., 1985). Urine monitoring indicated that in both subjects about 90% cleared with a half-time of about 6 hours and the rest with a half-time of about 6 days. From this it was inferred that the activity dissolved rapidly in the lungs, indicating Type F behaviour.

Sulphates

(179) For details of experiments see the element section for the relevant cation. Those in OIR documents are listed below. However, in the studies of the biokinetics of inhaled (or instilled) sulphates only the cation was radiolabelled, and therefore caution must be used in drawing inferences about the behaviour of the anion. For sulphates that are insoluble in both aqueous media and *in vivo*, for example barium sulphate, it is reasonable to assume that the compound will dissociate slowly, and the behaviour of the sulphate moiety will be broadly similar to that of the metal. However other sulphates such as those of caesium, nickel and thorium are very soluble in aqueous media and *in vivo* would be expected to dissociate into the respective metal and sulphate ions, each of which will follow its specific biokinetic pattern. In particular, following deposition in the lungs of thorium sulphate, like other water-soluble forms of thorium, most of the thorium is retained in particulate form and so is assigned to Type M. However, it is reasonable to assume that the sulphur would be rapidly absorbed (Type F). It should also be noted that solubility in water is not a reliable guide to solubility *in vivo*. When $^{90}SrSO_4$, which is insoluble in water, was inhaled by mice, the ^{90}Sr was rapidly absorbed.

Barium sulphate

(180) Studies of respiratory tract clearance in several species indicate a wide range of absorption rates and $BaSO_4$ is assigned to Type M.

Caesium sulphate

(181) Measurements following accidental human inhalation indicate Type F behaviour.

Radium sulphate

(182) Measurements following accidental human inhalation were difficult to interpret, and no assignment was made.

Strontium sulphate

(183) Measurements following inhalation by mice and dogs indicate Type F behaviour.

Thorium sulphate

(184) Measurements following intratracheal instillation into rats indicate Type M behaviour.

Rapid dissolution rate for sulphur

(185) No reliable estimates have been made of the rapid dissolution rate of sulphur in particulate form. The general default value of 30 d^{-1} is therefore applied to all Type F forms of sulphur.

Extent of binding of sulphur to the respiratory tract

(186) The evidence of rapid uptake of sulphur gases from the lung indicates that that there is probably little binding of sulphur. It is therefore assumed that for sulphur the bound state can be neglected, i.e. $f_b = 0.0$.

Table 5-2. Deposition and absorption for gas and vapour forms of sulphur[a]

	Percentage deposited[b]						Absorption		
Chemical form/origin	Total	ET_1	ET_2	BB	bb	AI	Type	f_A	Systemic model[c]
Sulphur dioxide	85[d]	0	17	8.5	17	42.5	F	1.0	Inorganic
Carbon disulphide	100[d]	0	20	10	20	50	F	1.0	Inorganic
Hydrogen sulphide	100[d]	0	20	10	20	50	F	1.0	Inorganic
Carbonyl sulphide	100[d]	0	20	10	20	50	F	1.0	Inorganic
Other organic	100[d]	0	20	10	20	50	F	1.0	Organic
Unspecified[a]	100[d]	0	20	10	20	50	F	1.0	Inorganic

[a] For sulphur in unspecified gas or vapour form, the default option for gases and vapours is recommended: 100% total deposition in the respiratory tract; default distribution between regions (footnote d) and Type F absorption.

[b] *Percentage deposited* refers to how much of the material in the inhaled air remains behind after exhalation. Almost all inhaled gas molecules contact airway surfaces, but usually return to the air unless they dissolve in, or react with, the surface lining. For the forms of sulphur considered here, it is assumed that most, if not all, of the inhaled sulphur is absorbed into body fluids.

[c] Systemic model for inorganic sulphur, Section 3.3.1; systemic model for organic sulphur, Section 3.3.2.

[d] Default distribution between regions (20% ET_2, 10% BB, 20% bb and 50% AI).

Table 5-3. Absorption parameter values for inhaled particulate forms of sulphur and for ingested sulphur[a].

Inhaled particulate materials		**Absorption parameter values[b]** f_r	s_r (d^{-1})	s_s (d^{-1})	**Absorption from the alimentary tract, f_A**
Default parameter values[c,d]					
Absorption Type	Assigned forms				
F	Caesium, nickel, strontium, thorium sulphates[e]	1	30	-	1
M	Barium sulphates; all unspecified forms[f]	0.2	3	0.005	0.2
S	—	0.01	3	0.0001	0.01
Ingested materials					
Unspecified inorganic and organic forms					1
Elemental sulphur and thiosulphate					0.1

[a] Following uptake into body fluids, the systemic model for inorganic sulphur is used, (see Section 2.3.)

[b] It is assumed that for sulphur the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of sulfur (30, 3 and 3 d^{-1}, respectively) are the general default values.

[c] Materials (e.g. caesium sulphate) are listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

[d] 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 and the f_A value for ingested soluble forms of sulphur (1.0).

[e] In the case of thorium sulphate the thorium is assigned to Type M and the sulphur to Type F.

[f] Default Type M is recommended for use in the absence of specific information, i.e. 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.

5.2.2. Ingestion

(187) Bauer (1976) showed that sulphur ingested as radioactive sulphate (^{35}S) by eight volunteers was completely absorbed in tracer amounts. Volwiler et al. (1955) reported that the fractional absorption of sulphur given as organic compounds to adult men was greater than 0.6. Schulz (1984) reported that orally administered thiosulphate ($S_2O_3^{2-}$) in humans was not absorbed from the gastrointestinal tract, but thiocyanate (CNS^-) was completely absorbed.

(188) Results obtained by Dziewiatkowski (1949) for the excretion of ^{35}S in rats after oral administration as the sulphate or sulphide indicated that absorption was 0.9 or greater. Minski and Vennart (1971) measured the absorption of [^{35}S]-methionine in rats and obtained a mean value of about 0.9. Elemental sulphur was found to be less well absorbed with values in rats of around 0.1 (Dziewiatkowski, 1962).

(189) ICRP *Publication 30* (1980) recommended absorption values of 0.8 for inorganic forms of sulphur and 0.1 for elemental sulphur. In ICRP *Publication 67* (ICRP, 1993) a value of 1 was adopted for dietary intakes. In this report, recommended f_A values are 1 for unspecified inorganic and organic compounds, and $1x10^{-1}$ for elemental sulphur and thiosulphate.

5.2.3. Systemic Distribution, Retention and Excretion

5.2.3.1. Inorganic sulphur

(190) Andrews et al. (1960) measured the rate of disappearance of ^{35}S from blood following its intravenous administration as sulphate (H_2SO_4) to an adult male subject with chondrosarcoma. The measurements indicated two components of biological removal from blood with half-times of 0.35 d (94%) and 5.6 d (6%).

(191) Schulz (1984) showed that after intravenous injection of thiosulphate into humans the compound left plasma with a half-time of ~15 min. Most of the thiosulphate was oxidized to sulphate or incorporated into endogenous sulphur compounds. A small proportion was excreted through the kidneys. Following oral administration of thiocyanate to human subjects, sulphur was virtually completely absorbed into the blood and cleared from the serum with a half-time of ~3 days. The volume of distribution of the CNS^- ion was ~0.25 L/kg. Elimination was mainly renal (Schulz, 1984).

(192) Following intravenous injection of dilute $H_2{}^{35}SO_4$ into 15 normal humans subjects, an average of 4.5% (range, 1.3-8.8%) of the administered activity was excreted in urine within 18 min and about half was excreted within 4-9 h (Walser et al., 1953). In a similar study involving dogs, an average of 3.6% (range, 1-6%) of the administered activity was excreted within 25-30 min after injection. Following prior water loading by stomach tube in another group of dogs, mean urinary excretion in the first 25-30 min increased to 5.6% (range, 3.7-8.2%).

(193) In a study involving intravenous administration of ^{35}S to 21 patients with chondrosarcoma or chordoma, an estimated 70-90% of administered activity was excreted in the urine in the first three days (Woodard et al., 1976). Studies of the blood kinetics in six of these patients indicated a major component with a removal half-time of 0.4-0.7 days. Measurements of activity in tissues obtained from biopsies or autopsies indicated high initial uptake in red bone marrow and epiphyseal cartilage. Uptake in other types of cartilage and in

samples of skin, fibrous tissue, and muscle was relatively low, but subsequent loss from these tissues was slow.

(194) In studies of the behaviour of intravenously injected inorganic ^{35}S in human subjects and laboratory animals, it was found that a significant portion of the ^{35}S accumulated in the cartilage and bone (Denko, 1957; Buck, 1958; Gottschalk, 1959). Activity depositing in these tissues was removed with a biological half-time of several days.

(195) Minski and Vennart studied the biokinetics of ^{35}S in 76 rats following its intravenous administration as the inorganic form $Na_2{}^{35}SO_4$ or the organic form ^{35}S-L-methionine. Following administration of inorganic ^{35}S, the cartilage and marrow had the greatest integrated activity per unit mass, and the soft tissue had the lowest integrated activity. Sulfur-35 was eliminated from the body at a faster rate when administered as sodium sulphate than when administered as methionine. The authors determined the retained fraction of administered activity in several tissues and presented results as tissue-specific retention functions.

(196) Studies in rats showed that after intravenous injection of $^{99m}Tc^{35}S$-sulphur colloid the rates of clearance of ^{99m}Tc and ^{35}S from blood and their accumulation in liver and bone were markedly different. The colloid particles apparently were broken down *in vivo* with the release of sulphur (Frier et al., 1981).

5.2.3.2. Gaseous inorganic compounds

Hydrogen sulphide (H2S)

(197) Hydrogen sulphide entering blood is rapidly oxidized to pharmacologically inert compounds such as thiosulphate and sulphate and excreted in urine (Patty, 1963; Vennart and Ash, 1976).

Carbon disulphide (CS_2)

(198) CS_2 is insoluble in water. Results of several studies (Bergman et al., 1984; McKenna and DiStefano, 1977; McKee et al., 1943; Teisinger and Soucek, 1949) indicate that CS_2 is taken up by fat, reaching equilibrium in humans after 1 to 2 hours under continuous exposure. Some activity from the fat reserves is then metabolized and ultimately excreted in urine. McKee et al. (1943) showed that 85-90% of CS_2 in the body is metabolized and the remaining non-metabolized CS_2 is eliminated unchanged, mostly in the breath. There is extensive metabolic incorporation of S released from CS_2 during biotransformation. Bergman et al. (1984) showed that, after initial concentration in liver and kidneys, ^{35}S labelled metabolites are rapidly eliminated from the body, probably in inorganic form.

Carbonyl sulphide (COS)

(199) COS decomposes in water to form H_2S and CO_2. The ^{35}S moiety of COS is assumed to behave like H_2S when in the bloodstream. The toxic effects of COS after inhalation appear to result from the toxicity of the H_2S produced, supporting the assumption that the ^{35}S label can be treated as though it were H_2S (Vennart and Ash, 1976).

Sulphur dioxide (SO_2)

(200) Sulphur dioxide entering the blood is expected to dissolve and produce sulphite and sulphate ions.

5.2.3.3. Generic model for inorganic sulphur

(201) Data for human subjects indicate that following entry of inorganic forms of sulphur into blood there is a rapid phase of excretion with a half-time of about 0.3 days followed by a slower phase of elimination with a half-time of at least 7 days and possibly as much as 80 days (ICRP, 1980; 1993). Studies of dietary sulphur suggest that two components of retention with half-times of this order are insufficient to explain the total-body content of 140 g of sulphur given for Reference Man, (ICRP, 1975) and that at least one longer-term component of retention must be present.

(202) The biokinetic model for inorganic sulphur used in ICRP *Publication 67* (1993) assumes a removal half-time from blood of 0.25 days. The fraction 0.8 is assumed to be promptly excreted, and fractions 0.15 and 0.05 are assumed to be distributed uniformly throughout the body and removed with biological half-times of 20 and 2000 days, respectively.

(203) The structure of the systemic model for inorganic sulphur used in the present report is shown in Figure 5-1. Transfer coefficients are listed in Table 5-4. Sulphur is assumed to be removed from blood at the rate 2.5 d^{-1}. Deposition fractions in tissue compartments and excretion pathways are based on data from human studies by Woodard et al. (1976), Andrews et al. (1960), Gottschalk et al. (1959), Maass et al. (1963), and Denko and Priest (1957) and rat studies by Dziewiatkowski (1945, 1949, 1953), Denko and Priest (1957), Minski and Vennart (1971), and Singher and Marinelli (1945). The assumed distribution of activity leaving blood is as follows: 72% goes to the urinary bladder contents, 10% to the cartilage, 8% to the right colon contents, 7% to other, and 3% to red marrow. The retention half-times in compartments were set for reasonable consistency with data for human subjects or rats summarized earlier.

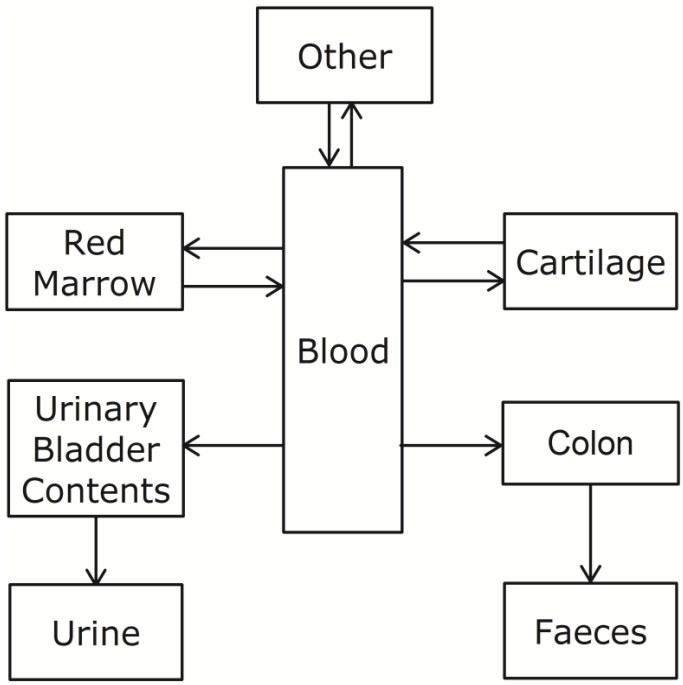

Figure 5-1. Biokinetic model for inorganic sulphur used in this report.

Table 5-4. Transfer coefficients for inorganic sulphur in adults

Compartments	Transfer Coefficient (d^{-1})
Blood to Red Marrow	0.075
Blood to Cartilage	0.25
Blood to Other	0.175
Blood to Urinary Bladder Contents	1.8
Blood to Right Colon Contents	0.2
Red Marrow to Blood	0.3
Cartilage to Blood	0.1
Other to Blood	3.5

5.2.3.4. Organic compounds of sulphur

(204) Minski and Vennart (1971) studied the distribution and retention of ^{35}S in rats following intravenous administration of the organic form ^{35}S-L-methione and the inorganic form $Na_2{}^{35}SO_4$. Sulfur-35 administered in organic form was removed from blood more slowly and distributed in tissues more uniformly than ^{35}S administered in inorganic form. Blood disappearance of ^{35}S administered in organic form was described as a sum of three exponential terms. The cumulative activity in the total body was an order of magnitude higher for ^{35}S administered as methionine than for ^{35}S administered as sodium sulphate. The cartilage and intestines showed the highest cumulative activity per unit mass of tissue following injection of inorganic ^{35}S but relatively low cumulative activity per unit mass compared with several other tissues following its injection as organic ^{35}S. The half-time in blood following administration of the organic form was 40 times larger than that following administration of the inorganic form.

(205) Taking account of these data and dietary intake and the total body content of sulphur in adult humans (ICRP, 1975), Vennart and Ash (1976) proposed that organic sulphur ingested in food should be assumed to be completely absorbed from the gastrointestinal tract, uniformly distributed throughout the body tissues and eliminated with a single biological half-time of 140 days. These assumptions form the basis for the systemic model for organic sulphur adopted in ICRP *Publication 30* (1980) and carried over to ICRP *Publication 67* (1993). In *Publication 67* a urinary to faecal excretion ratio of 9:1 was assigned.

(206) The structure of the systemic model for organic sulphur used in this report is presented in Figure 5-2. Transfer coefficients are listed in Table 5-5. The distribution of activity in the body and the removal half-times from tissues to blood are based on data for rats (Minski and Vennart, 1971). Minski and Vennart described sulphur retention in the blood by a three component exponential – 34% with a half time of 0.16 days, 14% with a half time of 4.1 days and 52% with a half time of 60.5 days. The initial transfer from Blood 1 to the Urinary Bladder occurs with a half time of approximately 0.16 days. Since there is no selective uptake of organic radiosulphur, it was determined that sulphur is deposited in a Soft Tissue compartment and removed with a biological half time of 160 days. Organic sulphur is excreted via three primary pathways: urine, faeces, and hair.

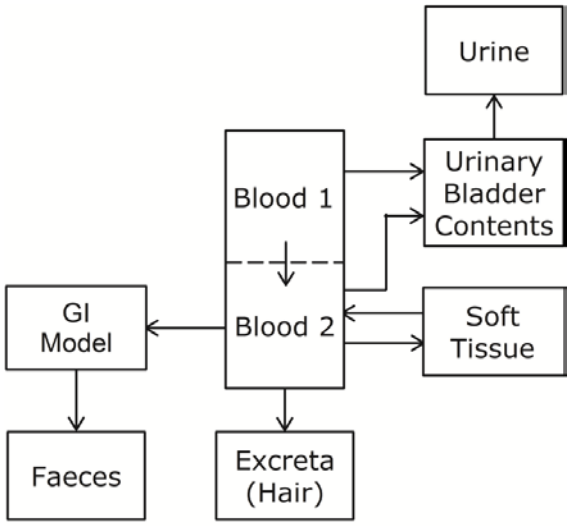

Figure 5-2. Biokinetic model for organic sulphur used in this report.

5.2.3.5. Treatment of radioactive progeny

(207) The only radioactive progeny of a sulphur isotope addressed in this report is ^{38}Cl (T1/2 = 37.24 m), produced by decay of ^{38}S. It is assumed for dosimetric purposes that ^{38}Cl decays at its site of production in the body.

Table 5-5. Transfer coefficients for organic sulphur in adult humans

Compartments	Transfer Coefficient (d^{-1})
Blood 1 to Blood 2	8.3
Blood 1 to Urinary Bladder Contents	4.
Blood 2 to Urinary Bladder Contents	0.0011
Blood 2 to Excreta (Hair)	0.0009
Blood 2 to SI Contents	0.0002
Blood 2 to Soft Tissue	0.0170
Soft Tissue to Blood 2	0.0042

(208) Model predictions of the clearance of intravenously injected organic sulphur from blood are consistent with the clearance pattern determined for rats following intravenous administration of ^{35}S-L-methione (Minski and Vennart, 1971).

Applicability of the ^{35}S-L-methionine model

(209) For general radiological protection purposes, this modified biokinetic model for ^{35}S-L-methionine could be applied with caution to other organic forms of sulphur in the absence of other compound-specific data. However, this model should not be used for the interpretation of bioassay data.

5.2.3.6. Gender-related differences in biokinetics

(210) There are insufficient data either from human or animal studies to define any systematic gender related differences in organ retention functions or excretion for ^{35}S compounds. However, some gender-related differences in the biokinetics of ^{35}S might be

expected following entry of certain types of labelled organic compound.

5.3. Individual monitoring

(211) ^{35}S intakes are generally monitored though measurements of the activity excreted in urine. The most common method of analysis is liquid scintillation counting.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{35}S	Urine Bioassay	Liquid Scintillation Counting	15 Bq/L	1-5 Bq/L

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6. CALCIUM (Z = 20)

6.1. Chemical Forms in the Workplace

(212) Calcium is an alkaline earth element, which mainly occurs in oxidation state II. It is an essential element for life. Chemical forms encountered in industry include oxides, phosphates, nitrates, sulphides, chlorides, carbonates and fluorides. ^{45}Ca and ^{47}Ca are occasionally used in research and in medicine.

Table 6-1. Isotopes of calcium addressed in this report

Isotope	Physical half-life	Decay mode
Ca-41	1.02E+5 y	EC
Ca-45	162.67 d	B-
Ca-47	4.536 d	B-

6.2. Routes of Intake

6.2.1. Inhalation

Absorption Types and parameter values

(213) No information was found on the behaviour of inhaled calcium in man. Information is available from experimental studies of calcium chloride.

(214) Absorption parameter values and Types, and associated f_A values for particulate forms of calcium are given in Table 6-2.

Calcium chloride

(215) Schiessle et al. (1964) followed the retention of ^{45}Ca in the lungs of guinea pigs for 28 days after inhalation of $CaCl_2$. Most of the initial lung deposit was very rapidly absorbed: at 1 day less than 1% of the initial lung deposit remained, consistent with assignment to Type F. Specific parameter values were estimated by the task group to be: $f_r = 0.996$, $s_r = 70\ d^{-1}$ ($t_{½}$ ~ 14 minutes) and $s_s = 0.07\ d^{-1}$ ($t_{½}$ ~ 10 d), consistent with assignment to Type F. Although specific parameter values for calcium chloride based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is so unlikely. Instead, calcium chloride is assigned to Type F. However, the data are used as the basis for the default rapid dissolution rate for calcium. Hence specific parameter values for calcium chloride would be the same as default Type F calcium parameter values.

Rapid dissolution rate for calcium

(216) The value of s_r estimated for $CaCl_2$ above, 70 d^{-1}, is applied here to all Type F forms of calcium.

Table 6-2. Absorption parameter values for inhaled and ingested calcium

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Calcium chloride	1	70	–	0.4
M	All unspecified forms[d]	0.2	3	0.005	0.08
S	—	0.01	3	$1x10^{-4}$	0.004
Ingested materials					
All unspecified forms					0.4

[a] It is assumed that for calcium the bound state can be neglected i.e. $f_b = 0$. The value of s_r for Type F forms of calcium (70 d^{-1}) is element-specific. The values for Types M and S (3 d^{-1}) are the general default values.

[b] Materials (e.g. calcium 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 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 and the f_A value for ingested soluble forms of calcium ($4x10^{-1}$).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

Extent of binding of calcium to the respiratory tract

(217) Evidence from the calcium chloride study outlined above suggests that there is probably little binding of calcium. It is therefore assumed that for calcium the bound state can be neglected, i.e. $f_b = 0.0$.

6.2.2. Ingestion

(218) Calcium is the first member of the alkaline earth metal series and it may exist under physiological conditions partly as a divalent cation and partly as complexes with proteins and other ligands. However, unlike strontium, barium and radium, the other alkaline earth elements, calcium is an essential element and physiological mechanisms facilitate its intestinal absorption.

(219) Calcium absorption has been measured in numerous volunteer studies and in most cases the reported mean absorption values were in the range 0.2 to 0.5 (Samachson, 1963; DeGrazia and Rich, 1964; Lutwak, 1969; Mautalen et al., 1969; Jovanovic, 1978; Cochet et al., 1983; Marchandise et al., 1986; Spencer et al., 1987; Harvey et al., 1988; Heaney et al., 1989, 1999). Greater mean values of 0.6 (Sambrook et al., 1985) and 0.7 (Rumenapf and Schwille, 1987) have also been reported for normal volunteers. These differences may probably be explained by the large inter-individual differences in calcium absorption observed in healthy subjects, with individual values ranging from 0.3 to 0.6 (Barger-Lux and Heaney, 1995) or even from 0.4 to 0.9 (Isaksson et al., 2000). Indeed calcium absorption depends first on the intraluminal concentration of ionized calcium (Schachter et al., 1960) which can be locally reduced by the presence of calcium binding agents such as EDTA or citrate ions (Rumenapf and Schwille, 1987). Additional variability may be associated with

morphological factors since Ca absorption is positively correlated to body size (Davies et al., 2000, Barger-Lux and Heaney, 2005) and to many nutritional factors. It is known that fractional calcium absorption is increased by high intakes of vitamin D, and by a high protein or carbohydrate diet, by calcium deficiency or low calcium intake and by pregnancy or lactation (Allen, 1982; Spencer et al., 1987; Heaney et al., 1989, Cashman and Flynn, 1996; Griffin et al., 2002; Kerstetter et al., 2005, Holloway et al., 2007). On the other hand, caffeine intake or oral supplementation with magnesium decreased calcium absorption in humans (Barger-Lux and Heaney, 1995; De Swart et al., 1998, Heaney 2002).

(220) Calcium absorption is known to occur mainly from the small intestine (ICRP 2006). However, a few percent of calcium may also be absorbed from other sites, such as the colon, which, at 26 hours after ingestion, can absorb as much as 4% of calcium provided to healthy peri-menopausal women (Barger-Lux et al., 1989).

(221) In ICRP *Publication 30* (1980) and ICRP *Publication 71* (1995), an absorption value of 0.3 was recommended. Since absorption appears to be generally greater than 0.3 in normal subjects, an f_A value of 0.4 for all chemical forms is adopted here.

6.2.3. Systemic Distribution, Retention and Excretion

6.2.3.1. Summary of the database

(222) The biokinetics of calcium in the human body has been investigated extensively in physiological and clinical studies and in radiobiological studies comparing the behavior of isotopes of the alkaline earth elements. Reviews and bibliographies can be found in ICRP *Publication 20* (1973), ICRP *Publication 71* (1995), and an article by Leggett (1992). The primary datasets underlying specific parameter values in the model for systemic calcium used in this report are summarized below.

6.2.3.2. Biokinetic model for systemic calcium

(223) The structure of the model for systemic calcium is shown in Figure 6-1. This is a simplified version of the generic model for bone-volume seekers. All soft tissues including the liver and kidneys are included in the three "Other tissue" compartments, ST0, ST1, and ST2 corresponding to rapid, intermediate, and slow exchange of activity with plasma, respectively. These soft tissue compartments are defined on a kinetic basis rather than an anatomical or physiological basis, but ST0 may correspond roughly to interstitial fluids plus some rapidly exchangeable cellular calcium (Heaney 1964, Harrison et al., 1967, Hart and Spencer 1976); ST1 may be a composite of several pools with slower exchange rates, including mitochondrial calcium, cartilage calcium, and exchangeable dystrophic calcium (e.g. arterial plaque and calcified nodes) (Heaney 1964, Borle 1981); and ST2 may be associated with relatively nonexchangeable dystrophic calcium that gradually accumulates in the human body (Heaney 1964).

(224) Blood is treated as a uniformly mixed pool that exchanges calcium with soft tissues and bone surfaces. Calcium is assumed to be lost from the body only by urinary or faecal excretion. Activity going to urine is first transferred from plasma to the urinary bladder contents, and activity going to faeces is first transferred from plasma to the contents of the right colon contents.

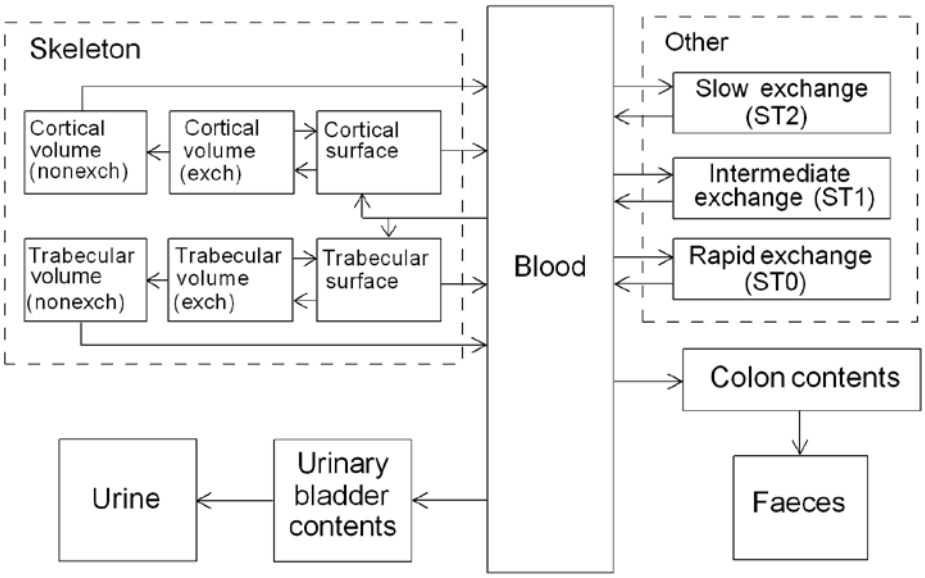

Figure 6-1. Structure of the model for systemic calcium.
Abbreviations: exch = exchangeable, nonexch = non-exchangeable.

Parameter values

(225) The parameter values applied to systemic calcium in the present report are the same as those applied in ICRP *Publication 71* (1995). These values are listed in Table 6-3. The selection of each parameter value is described briefly in the following and explained in more detail by Leggett (1992).

(226) In the following, the "removal half-time" from a compartment refers to the biological half-time that would be observed if there were no recycling to that compartment. This will generally differ from the apparent (or net, or externally viewed) half-time that may be estimated at any given time in the presence of recycling. The "deposition fraction" for a compartment fed by plasma is the fraction of instantaneous outflow from plasma that is transferred to that compartment. For example, the deposition fraction for ST1 is 0.1. This means that ST1 receives 10% of activity leaving plasma over a period of a few seconds.

(227) Kinetic analysis of plasma disappearance curves for normal subjects intravenously injected with radioisotopes of the alkaline earth elements indicates that these elements initially leave plasma at a rate of several hundred plasma volumes per day and equilibrate rapidly with an extravascular pool (presumably consisting largely of interstitial fluids) roughly three times the size of the plasma pool (Heaney, 1964; Harrison et al., 1967; Hart and Spencer, 1976). The present model does not depict the rapid exchange of calcium between plasma and this extravascular pool within the first few minutes after introduction of calcium into blood. However, the model includes a soft-tissue compartment (ST0) that receives more than half of activity leaving plasma, returns activity to plasma with a half-time of a few hours, and contains three times as much activity as plasma at times more than a few hours after introduction of calcium to blood. This compartment is used to account for relatively high concentrations of calcium tracers observed in soft tissues during the first few hours after injection and to help maintain the proper amount of material in plasma. A total transfer rate from plasma of 15 d^{-1} (i.e. a removal half-time of ln(2)/15 d = 0.04621 d) yields reasonable

fits to plasma disappearance curves for calcium or strontium tracers at times beyond 1-2 h after injection into human subjects (Barnes et al., 1961; Heaney ,1964; Heaney et al., 1964; Harrison et al., 1967; Neer et al., 1967; ICRP, 1973; Newton et al., 1990).

(228) It is assumed that 58% of calcium leaving plasma moves to the rapid-turnover soft-tissue compartment ST0; this is the balance after deposition percentages in other compartments are assigned. The corresponding transfer rate from plasma to ST0 is 0.58×15 $d^{-1} = 8.7$ d^{-1}. Based on the assumed relative amounts of calcium in ST0 and plasma, the transfer rate from ST0 to plasma is set at one-third the transfer rate from plasma to ST0, or 2.9 d^{-1}.

(229) Readily exchangeable calcium in soft tissues, meaning calcium that is turned over to a substantial extent in a period of hours or days, is represented in this model as the sum of calcium in compartments ST0 and ST1. The amount of readily exchangeable calcium in soft tissues is approximately 0.35% of total-body calcium in a middle-aged adult human (Heaney, 1964; Borle, 1981). Since plasma contains about 0.03% of total-body calcium in the adult (ICRP, 1975), the threefold larger compartment ST0 is estimated to contain 0.09% and ST1 is estimated to contain about 0.35% - 0.09% = 0.26% of total-body calcium during chronic intake. Parameter values for ST1 are set to reproduce these steady-state conditions while approximating soft-tissue retention data for terminally ill human subjects intravenously injected with ^{45}Ca at times up to 124 d before death (Schulert et al., 1959). This is accomplished by assigning to ST1 a deposition fraction of 0.1 and a removal half-time to plasma of 4 d. The derived transfer rate from plasma to ST1 is 0.1×15 $d^{-1} = 1.5$ d^{-1} and from ST1 to plasma is $\ln(2) / 4$ d = 0.1733 d^{-1}.

(230) Parameter values for Compartment ST2 are set for consistency with estimates of the accumulation of relatively nonexchangeable calcium in adult humans (Heaney, 1964), an estimate of the fraction of total-body calcium in soft tissues under conditions of chronic exposure (Schlenker et al., 1982), and the observed retention of ^{45}Ca in human soft tissues at 3 mo after injection (Schulert et al., 1959). Reasonable agreement with these three values is achieved by assuming that ST2 receives 0.005% of outflow from plasma and that the removal half-time from ST2 to plasma is 5 y. The resulting transfer rate from plasma to ST2 is 0.00005×15 $d^{-1} = 0.00075$ d^{-1}, and the transfer rate from ST1 to plasma is $\ln(2) / (5 \times 365$ d) = 0.00038 d^{-1}.

(231) Data for laboratory animals indicate that fractional deposition on bone surfaces is similar for calcium, strontium, barium, and radium. This is inferred from the similar skeletal contents of these elements in the first few hours after injection (Bligh and Taylor, 1963; Kshirsagar et al., 1966; Domanski et al., 1969, 1980). Use of a common bone-surface deposition fraction for all four elements is consistent with autoradiographic measurements of surface activity in bone samples taken at autopsy from subjects injected with radiocalcium at 0.6 d or longer before death (Riggs et al., 1971, ICRP, 1973); measurements of radiocalcium and radiostrontium in bone samples from subjects injected 3 h or longer before death (Schulert et al., 1959); and external measurements of the buildup of radiocalcium (Anderson et al., 1970; Heard and Chamberlain, 1984) and radiobarium (Korsunskii et al., 1981) after intravenous injection. Based on these data, 25% of calcium, strontium, barium, or radium leaving plasma is assigned to bone surfaces. The transfer rate from plasma to cortical and trabecular surfaces combined is 0.25×15 $d^{-1} = 3.75$ d^{-1}.

(232) The initial distribution between different bones of the skeleton and between the two bone types (cortical and trabecular) appears to be similar for calcium, strontium, barium, and radium (Ellsasser et al., 1969; Wood et al., 1970; Liniecki, 1971; Stather, 1974; Lloyd et al., 1976). Relative deposition of alkaline earth elements on cortical and trabecular bone surfaces is based on the estimated calcium turnover rate of each bone type. This approach agrees with

measurements on laboratory animals (Kshirsagar et al., 1966; Norrdin and Arnold, 1980). As an average over adult ages, deposition on trabecular bone is estimated to be 1.25 times that on cortical bone (Leggett et al., 1982). The transfer rate from plasma to trabecular bone surface is (1.25/2.25) × 3.75 d^{-1} = 2.08 d^{-1} and from plasma to cortical bone surface is (3.75 - 2.08) d^{-1} = 1.67 d^{-1}.

(233) The removal half-time of calcium from bone surfaces to all destinations (plasma and exchangeable bone volume) is estimated as 1 d. This is based on autoradiographic measurements of surface activity in human and canine bone samples taken at times ranging from few hours to a few days after intravenous injection of ^{45}Ca (Riggs et al., 1971, Groer et al., 1972, Groer and Marshall, 1973, ICRP, 1973).

(234) Parameter values for exchangeable bone volume are estimated from whole-body measurements using data for times after bone surfaces and soft tissues have largely cleared of activity but before loss from bone resorption becomes an important consideration. Based on whole-body retention curves for human subjects injected with radioisotopes of calcium, strontium, barium, or radium (Spencer et al., 1960; Bishop et al., 1960; Heaney et al., 1964; Harrison et al., 1967; Maletskos et al., 1969; Phang et al., 1969; Carr et al., 1973; Likhtarev et al., 1975; Malluche et al., 1978; Henrichs et al., 1984; Newton et al., 1990, 1991), the fraction of activity that moves from bone surfaces back to plasma is assumed to be the same for all four elements. Specifically, five-sixths of activity leaving bone surfaces is assumed to return to plasma and one-sixth is assumed to transfer to exchangeable bone volume. The transfer rate from trabecular or cortical bone surface to the corresponding exchangeable bone volume compartment is (1/6) × ln(2)/1 d = 0.116 d^{-1}, and the transfer rate from trabecular or cortical bone surface to plasma is (5/6) × ln(2)/1 d = 0.578 d^{-1}.

(235) Element-specific removal half-times from the exchangeable bone volume compartments are based in part on fits to the intermediate-term retention data indicated above. However, it is also considered that the assigned half-times should increase roughly in proportion to the likelihood of entering nonexchangeable sites in bone mineral, as suggested by data from *in vitro* experiments with hydroxyapatite crystals and whole-body retention patterns for alkaline earth elements in human subjects. A removal half-time of 100 d is assigned to calcium, compared with values of 80 d for strontium, 50 d for barium, and 30 d for radium (Leggett, 1992). Because the data do not allow the derivation of removal half-times as a function of bone type, the same half-time is applied to cortical and trabecular exchangeable bone volume compartments.

(236) Discrimination between alkaline earth elements by bone is accounted for by fractional transfer of activity from exchangeable to nonexchangeable bone volume. It is assumed, in effect, that calcium, strontium, barium, and radium are all equally likely to become temporarily incorporated in bone mineral after injection into plasma but that the likelihood of reaching a non-exchangeable site in bone crystal decreases in the order calcium > strontium > barium > radium. Fractional transfers of calcium, strontium, barium, and radium from exchangeable to nonexchangeable bone volume are set at 0.6, 0.5, 0.3, and 0.2, respectively, for consistency with whole-body and skeletal retention data on these elements (Spencer et al., 1960; Bishop et al., 1960; Heaney et al., 1964; Harrison et al., 1967; Phang et al., 1969; Maletskos et al., 1969; Carr et al., 1973; Likhtarev et al., 1975; Malluche et al., 1978; Henrichs et al., 1984; Newton et al., 1990, 1991) as well as results of in vitro measurements on hydroxyapatite crystals (Neuman, 1964; Stark, 1968). The derived transfer rate from exchangeable trabecular or cortical bone volume to the corresponding nonexchangeable bone volume compartment is 0.6 × ln(2)/100 d = 0.004159 d^{-1} and to the corresponding bone surface compartment is 0.4 × ln(2)/100 d = 0.002773 d^{-1}.

(237) Biological removal from the nonexchangeable bone volume compartments of

cortical and trabecular bone is assumed to result from bone turnover. The average bone turnover rates during adulthood are estimated as 3% y^{-1} and 18% y^{-1} for cortical and trabecular bone, respectively (ICRP, 2002). The corresponding transfer rates from the nonexchangeable bone volume compartments of cortical and trabecular bone to plasma are 0.00008219 d^{-1} and 0.0004932 d^{-1}, respectively. Age-specific rates of bone turnover, including changes with age during adulthood, are provided in the paper by Leggett (1992) for application of the model to specific cases.

(238) Clearance of calcium from plasma to urine and faeces has been studied in human subjects, many of them healthy (Bishop et al., 1960; Spencer et al., 1960; Barnes et al., 1961; Cohn et al., 1963 Heaney et al., 1964; Samachson, 1966; Phang et al., 1969; Carr et al., 1973; Newton et al., 1990). Based on results of these studies, it is assumed that 4% of calcium leaving plasma is transferred to the contents of the urinary bladder contents and subsequently to urine and 3% is transferred to the contents of the right colon and subsequently to faeces. Therefore, the transfer rate from plasma to the urinary bladder contents is $0.04 \times 15\ d^{-1} = 0.6\ d^{-1}$ and from plasma to the contents of the right colon is $0.03 \times 15\ d^{-1} = 0.45\ d^{-1}$.

Table 6-3. Transfer coefficients for systemic calcium

From[a]	To[a]	Transfer coefficient (d^{-1})
Blood	Urinary bladder contents	0.60
Blood	Right colon contents	0.45
Blood	Trabecular bone surface	2.08
Blood	Cortical bone surface	1.67
Blood	ST0	8.70
Blood	ST1	1.50
Blood	ST2	0.00075
Trabecular bone surface	Blood	0.578
Trabecular bone surface	Exch trabecular bone volume	0.116
Cortical bone surface	Blood	0.578
Cortical bone surface	Exch cortical bone volume	0.116
ST0	Blood	2.9
ST1	Blood	0.1733
ST2	Blood	0.00038
Exch trabecular bone volume	Trabecular bone surface	0.002773
Exch trabecular bone volume	Nonexch trabecular bone volume	0.00416
Exch cortical bone volume	Cortical bone surface	0.002773
Exch cortical bone volume	Nonexch cortical bone volume	0.00416
Nonexch cortical bone volume	Blood	0.0000821
Nonexch trabecular bone volume	Blood	0.000493

[a] Exch = exchangeable; Nonexch = non-exchangeable; ST0, ST1, and ST2 are compartments within Other soft tissues with fast, intermediate, and slow turnover, respectively.

6.2.3.3. Treatment of radioactive progeny

Experimental data

(239) The only calcium isotope addressed in this report that decays to another radionuclide is ^{47}Ca ($T_{1/2}$ = 4.54 d), which decays to ^{47}Sc ($T_{1/2}$ = 3.35 d). The biological behavior of ^{47}Sc produced in vivo by decay of ^{47}Ca has been investigated in rats (Taylor, 1966) and mice (Freed et al., 1975).

(240) After intravenous administration of a mixture of ^{47}Ca and ^{47}Sc to rats, the ^{47}Sc introduced as a parent radionuclide accumulated primarily in liver, spleen, kidneys, and bone (Taylor, 1966). There was evidence that ^{47}Sc also translocated to the liver and spleen after its production by decay of ^{47}Ca at other sites in the body. Most of the ^{47}Sc produced in vivo by decay of ^{47}Ca arose in bone due to the high uptake and retention of ^{47}Ca by bone. Nearly all of the ^{47}Sc produced in bone was retained in bone at times greater than a few days after intake, presumably after ^{47}Ca was contained almost entirely in bone volume.

(241) In mice, redistribution of ^{47}Sc produced in the body following intravenous administration of ^{47}Ca accounted for a large part of ^{47}Sc found in soft tissues and blood (Freed et al., 1975). At times greater than 2 d after injection ^{47}Sc was contained largely in bone. It appeared that ^{47}Sc escaped to some extent from its site of production in bone during the early hours after administration of ^{47}Ca, but no preferential loss of ^{47}Sc from bone was observed thereafter. At 1-11 d after injection, loss of ^{47}Sc from bone was slower than that of ^{47}Ca. After 11 d the rate of loss of ^{47}Sc from bone approached that of the parent, suggesting removal of both radionuclides by the process of bone resorption.

General assumptions

(242) It is assumed in this report that ^{47}Sc produced by decay of ^{47}Ca in soft tissues and bone surface is removed to blood with a biological half-time of 3 d and then follows the characteristic model for scandium, i.e. behaves as if injected into blood as a parent radionuclide. The removal half-time of 3 d is the shortest removal half-time of scandium from tissues in the characteristic model for scandium used here. Scandium-47 produced in a bone volume compartment of the calcium model is assumed to be removed to blood at the rate of bone turnover and then to follow the characteristic model for scandium.

Characteristic model for systemic scandium

(243) The structure of the characteristic model for scandium is a modification of the generic model structure for bone-surface-seeking radionuclides. Scandium is treated as a bone-surface seeker based on analogy with its chemical analogue yttrium. The spleen is added to the generic model structure because human and animal data indicate that it is an important repository for scandium. The generic structure is also modified with regard to routes of transfer to and from the marrow compartments, based on indications from animal studies of relatively high transfer from plasma to marrow (Rosoff et al., 1963, 1965; Hara and Freed, 1973; Byrd et al., 1975; Lachine et al., 1976).

(244) Transfer coefficients in the characteristic model for scandium are set for consistency with the following observations of the behavior of scandium isotopes in human subjects and laboratory animals: (1) in human subjects with various illnesses, blood clearance over 3 d, urinary and faecal excretion rates over 15 d, whole body retention over 1.5 y, and activity concentrations in autopsy tissues of subjects dying 5-7 mo after injection (Rosoff et al., 1965); (2) measurements of the time-dependent systemic distribution of activity in rats, mice, and rabbits (Durbin, 1960; Rosoff et al., 1963; Basse-Cathalinat et al., 1968; Hara and Freed, 1973; Byrd et al., 1975; Lachine et al., 1976).

(245) Blood is divided into compartments Blood 1 and Blood 2 representing two components of retention as indicated by data for intravenously injected ^{46}Sc NTA in human subjects (Rosoff et al., 1965). Blood 1 is a central compartment that exchanges activity with Blood 2 and several tissue compartments. Scandium-47 migrating to blood from sites of production is assigned to Blood 1. Blood 2 represents scandium that is firmly bound to plasma proteins.

(246) The total outflow rate from Blood 1 is 3 d^{-1}. Blood 2 receives 15% of outflow from

Blood 1 and loses scandium back to Blood 1 with a half-time of 1.5 d. This half-time is taken from the model for the chemically similar element yttrium.

(247) The liver is divided into two compartments called Liver 1 and Liver 2. Liver 1 receives 20% of outflow from Blood 1. Activity is removed from Liver 1 with a half-time of 3 days, with 50% moving to Blood 1, 25% to Liver 2, and 25% to the SI contents (representing biliary secretion). Faecal excretion of scandium is assumed to arise solely from transfer of scandium from Liver 1 to the SI content based on data of Rosoff et al. (1965) for a human subject. Almost all of the scandium secreted into the small intestine is lost in faeces because of the low rate of absorption of scandium from the small intestine to blood. Activity transfers from Liver 2 to Blood 1 with a half-time of 100 d.

(248) The kidneys are represented as a single compartment that exchanges activity with Blood 1. This compartment receives 3% of outflow from Blood 1 and loses scandium to Blood 1 with a half-time of 20 d. Urinary excretion of scandium is represented as a direct transfer from Blood 1 to Urinary bladder content, without intermediate retention in the kidneys. Urinary bladder content receives 1.8% of outflow from Blood 1.

(249) Trabecular and cortical marrow each receives 5% of outflow from Blood 1. Activity is removed from the marrow compartments to Blood 1 with a half-time of 100 d.

(250) The spleen receives 2% of outflow from Blood 1. The removal half-time from spleen to Blood 1 is 1 y.

(251) Other soft tissues are divided into two compartments representing relatively fast ($T_{1/2}$ = 3 d) and relatively slow ($T_{1/2}$ = 100 d) return of scandium to Blood 1. These compartments receive 20% and 18.2% of outflow from Blood 1, respectively. The deposition fraction in the latter compartment is the balance of outflow from Blood 1 after all other deposition fractions in the model were assigned.

(252) Bone surface receives 10% of outflow from Blood 1. The deposition on bone surface is equally divided between trabecular and cortical surface. The fate of scandium deposited on bone surfaces is described by the generic model for bone-surface-seekers, except that scandium biologically removed from bone is assumed to return to blood rather than to be channeled through bone marrow. Thus, scandium is removed from cortical or trabecular bone surfaces at a rate proportional to (1.5 times) the turnover rate of that bone type. The assumed bone turnover rates are 3% y^{-1} for cortical bone and 18% y^{-1} for trabecular bone. One-third of activity removed from bone surfaces is buried in bone volume and two-thirds transfers to Blood 1. Activity is removed from cortical or trabecular bone volume to Blood 1 at the rate of turnover of that bone type.

6.3. Individual Monitoring

(253) ^{45}Ca is a beta emitter. ^{45}Ca intakes are generally monitored though measurements of the activity excreted in urine. The most common method of analysis is liquid scintillation counting.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{45}Ca	Urine Bioassay	Liquid Scintillation Counting	15 Bq/L	1-5 Bq/L

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7. IRON (Z = 26)

7.1. Chemical Forms in the Workplace

(254) Iron is a transition metal, occurring mainly in oxidation states II and III. Iron is a vital constituent of plant and animal life, and is the key component of haemoglobin. Iron is used in industry in a variety of chemical forms, including oxides (FeO, Fe_2O_3, Fe_3O_4), chlorides, fluorides and bromides.

(255) The main radioactive isotope is ^{59}Fe, which is used as ferrous citrate, chloride or sulphate for diagnostic applications in hospitals. In the nuclear industry, ^{59}Fe is an important neutron activated corrosion product. It is likely to be present as oxides in different parts of the primary circuits of water cooled reactors (Collier et al., 1994).

Table 7-1. Isotopes of iron addressed in this report

Isotope	Physical half-life	Decay mode
Fe-52	8.275 h	EC, B+
Fe-55	2.737 y	EC
Fe-59[a]	44.495 d	B-
Fe-60	1.5E+6 y	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

7.2. Routes of Intake

7.2.1. Inhalation

Absorption Types and parameter values

(256) Extensive information was found on the behaviour of iron inhaled in oxide form in both animals and in man, because it has been used as a test material to study lung clearance. Some information was also found on other forms, such as the chloride.

(257) Absorption parameter values and Types, and associated f_A values for particulate forms of iron are given in Table 7-2.

Iron chloride ($FeCl_3$)

(258) Morrow et al. (1968) followed lung retention of ^{59}Fe for 7 days after inhalation of $^{59}FeCl_3$ by dogs and rats, but few details are given. Lung retention in dogs was represented by a two-component exponential function with half-times of 1.9 days (17%: clearance rate 0.36 d^{-1}) and 85 days (clearance rate 0.0081 d^{-1}), giving predicted lung retention at 30 d and 180 d to be 65% and 19% of the initial lung deposit (ILD), and indicating Type M behaviour.

Iron oxide (Fe_2O_3)

(259) Radiolabelled ferric oxide, Fe_2O_3 has been used as a test material in many studies of the respiratory tract deposition and clearance of inhaled particles, including several human studies of lung retention of duration 2–8 months (See review in ICRP *Publication 66*, Annexe E, Table E.19) (ICRP, 1994). Over this period, retention could be adequately represented by a single exponential function, with a half-time between about 60 and 600 d, but in most cases less than 200 d, indicating Type M behaviour. The results are difficult to interpret as the retention followed was that of the label, which varied, in some cases being ^{51}Cr (Albert et al.,

1967; Morrow et al., 1967a,b; Waite and Ramsden, 1971a, Ramsden and Waite, 1972) and in one case ^{237}Pu (Waite and Ramsden, 1971b, Ramsden and Waite, 1972). As observed in ICRP *Publication 30* (ICRP, 1980) this raises questions about the contributions to retention made by the iron oxide particle matrix itself, and by the chemical form of the label. However, Ramsden and Waite (1972) after careful correction for leaching of the label, estimated a retention half-time for the iron oxide matrix of about 270 d.

(260) Some studies used material labelled with ^{59}Fe itself. Results following inhalation of $^{59}Fe_2O_3$ by rats and dogs showed that lung retention could be fit by a single exponential with a rate of 0.01 d^{-1} (half-time ~70 d) (Gibb and Morrow, 1962; Morrow et al., 1964; Morrow et al., 1968). Calculations by the task group indicate that lung retention at 30 d and 180 d would be 71% and ~13% ILD. Similar experiments performed on rats showed similar results with a clearance rate of 0.011 to 0.013 d^{-1} (Muhle and Bellman, 1986). Other studies where ^{59}Fe-labelled iron oxide particles were periodically inhaled by rats showed that lung retention followed a single exponential function with a rate from 0.008 to 0.011 d^{-1}, depending on the age of the animals (Bellmann et al., 1991).

(261) Studies on the retention of instilled iron oxide particles in human alveolar macrophages (AM) indicated that particles were cleared from the lungs with a rapid-phase clearance rate of 1.4 d^{-1} and long term clearance rate of about 0.006 d^{-1} (Lay et al., 1998). All these results indicate Type M behaviour.

Magnetite (Fe_3O_4)

(262) Ferromagnetic iron oxide particles, Fe_3O_4, have also been used as a test material in studies of the lung retention of inhaled particles, measured using magneto-pneumography (MPG), i.e. measurement of the remanent magnetic field from particles within the chest, after application of a strong magnetic field to it. The results of measurements made in groups of volunteers for up to about a year after inhalation (Cohen et al., 1979; Freedman et al., 1988; Möller, 1991; Stahlhofen and Möller, 1991; Möller et al., 2001; 2004; 2006) are consistent with assignment to Type M. In particular, Möller et al. (2001) measured long-term retention of ferromagnetic iron oxide particles in healthy and diseased subjects. In healthy non-smokers, on average less than 10% ILD cleared from the lungs rapidly (within 2 d). This fraction was somewhat greater (10-20%) in smokers and patients with sarcoidosis, and considerably greater in patients with idiopathic pulmonary fibrosis (IPF) (~30% ILD) and chronic obstructive bronchitis (COB) (~50% ILD). The half-time of the slow phase of lung clearance varied between groups as follows: young (20-39 years) healthy non-smokers 124 ± 66 d; young cigarette smokers 220 ± 74 d; older (40-65 years) healthy non-smokers 162 ± 120 d; older smokers 459 ± 334 d; sarcoidosis patients 275 ± 109 d; IPF patients 756 ± 345 d; COB patients (mostly ex-smokers) 240 ± 74 d. Since lung clearance in healthy subjects was faster than measured in healthy human volunteers with inert particles like Teflon (Philipson et al., 1996), it was concluded that lung clearance was determined by particle dissolution in alveolar macrophages, which was impaired by cigarette smoking and the diseases investigated.

Contaminated dusts ('residues') formed at nuclear power plant (NPP)

(263) The biokinetics of ^{59}Fe were followed for 84 days after intratracheal instillation into rats of a suspension of corrosion 'crud' particles (oxide bearing debris, 5% ^{59}Fe activity) from the primary containment of a water cooled reactor (Collier et al., 1994). Few details are given, but it was assessed here that the results indicate Type S behaviour of the ^{59}Fe present.

Welding fumes

(264) Kalliomäki et al. (1978, 1983a, 1985) used MPG to measure the lung contents of magnetic dusts in groups of welders with similar exposures. A single exponential model was applied to lung retention. Repeated measurements over a 6-year period on welders who worked with mild steel gave a clearance constant of 0.2 y^{-1} ($t_{½}$ ~3.5 y). Results of a cross-sectional study on stainless steel welders gave a $t_{½}$ of 8.5 y. Both indicate Type S behaviour for at least some of the material.

(265) To simulate occupational exposure, rats inhaled fumes from manual metal arc (MMA) or metal inert gas (MIG) welding of stainless steel for 1 hour per working day for 4 weeks (Kalliomäki et al., 1983b,c). Lung contents of iron, chromium, manganese and nickel were measured by neutron activation analysis (NAA) for 106 d after the end of exposure. Retention of exogenous iron (i.e. that derived from the welding fume) was also followed by MPG. For the MMA welding fume, results indicate Type M behaviour for all elements measured except iron measured by NAA (Type S). Clearance was slower following inhalation of MIG welding fumes, indicating Type S for all elements studied except iron measured by MPG (Type M).

(266) Kalliomäki et al. (1986a,b, 1987) followed lung retention of ^{59}Fe, ^{51}Cr and ^{58}Co (as indicators of iron, chromium and nickel respectively) in rats for 106 d after intratracheal instillation of neutron-activated fumes from manual metal arc (MMA) or metal inert gas (MIG) welding of stainless steel (SS), or mild steel (MS) (^{59}Fe only). Results indicate Type S behaviour for the ^{59}Fe present in all fumes studied except MMA (MS) (Type M); Type S behaviour for the chromium and nickel present in MIG (SS) fumes and Type M for these elements in MMA (SS) fumes.

Other compounds

(267) Measurements following inhalation of neutron-activated fly ash by hamsters indicate Type M behaviour for the ^{59}Fe present (Wehner and Wilkerson, 1981). Measurements following inhalation of neutron-activated volcanic ash by rats indicate Type M or S behaviour for the ^{59}Fe present (Wehner et al., 1984).

Rapid dissolution rate for iron

(268) Little experimental information is available except for iron oxide, which is relatively insoluble. Although there is some experimental information for ferric chloride, which is probably absorbed more rapidly, it is insufficient to estimate the rapid dissolution rate. There is therefore no justification for choosing a rate different from the general default value of 30 d^{-1}, which is applied here to all Type F forms of iron.

Extent of binding of iron to the respiratory tract

(269) The only experimental information for iron administered in solution relates to ferric chloride. This indicates Type M behaviour, suggesting that there could be significant binding of iron. However, there is insufficient information to estimate the extent of any bound state. Although it is not clear that the bound state for iron is negligible, it is assumed by default that $f_b = 0$.

Table 7-2. Absorption parameter values for inhaled and ingested iron

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	—	1	100	–	0.1
M	Ferric chloride; ferric oxide; all unspecified forms[d]	0.2	3	0.005	0.02
S	Corrosion products	0.01	3	$1x10^{-4}$	0.001
Ingested materials					
All unspecified forms					0.1

[a] It is assumed that for cobalt a bound fraction f_b = 0.03 with an uptake rate s_b = 0.002 d^{-1} is applied to material deposited in the AI region only. It is assumed that f_b = 0.0 for material deposited in other regions. The values of s_r for Type F, M and S forms of cobalt (1 d^{-1},) are element-specific.

[b] Materials (e.g. cobalt nitrate) are 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 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 and the f_A value for ingested soluble forms of iron (0.1).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

7.2.2. Ingestion

(270) The gastrointestinal absorption of iron has been extensively studied because of its important role in nutrition.

(271) Freiman et al. (1963) reported a mean absorption value of 0.7 for a group of 16 volunteers aged between 27 and 60. Brozovic (1975) reviewed data from radioactive iron uptake studies involving a total of 990 normal human volunteers, and concluded that absorption values of 0.05 - 0.1 are usual. However, individual studies produced mean figures as great as 0.4 for men and 0.6 for women. Some of the variation may be caused by differences in the techniques used to measure absorption, but much of it is caused by dietary and physiological factors as reviewed by Brozovic (1975), Underwood (1977), Morris (1983), Lynch (1984), Cook et al. (1991), Whiting, (1995); Teucher et al. (2004). Human milk and organic acids (ascorbic, lactic, citric…) are enhancers of iron absorption, while dietary fibres (pectins, cellulose…), tannates in tea, polyphenols in coffee and even calcium supplements in diet are potent inhibitors. Similarly, lowered iron status of the individual results in increased iron uptake, as shown by menstruating women and sufferers from anaemia. Uptake is also increased during pregnancy. These latter points, associated to hormonal differences, result in higher iron absorption in females compared to males (Brozovic 1975, Woodhead et al., 1991, Fletcher et al., 1994).

(272) Iron is known to be, in some circumstances, retained in the wall of the small intestine. Study of whole body retention of ^{59}Fe in human volunteers after oral administration

provided evidence of temporary retention of approximately 20% of the ingested ^{59}Fe (Werner et al., 1987, ICRP, 2006). It was suggested that this part of iron was incorporated by macrophages lying under the epithelial layer and then transferred to goblet cells before excreted back in the lumen of the intestine. All these data are consistent with a half-time of intestinal retention of about 3 days (ICRP, 2006).

(273) This iron retention in the intestine wall seems to be dependant of the iron status and to form part of the mechanism operating to regulate iron absorption (Werner et al., 1987).

(274) In *Publication 30* (ICRP, 1980) and *Publication 69* (ICRP, 1995) an absorption value of 0.1 for both males and females was recommended.

(275) In this report it is recommended an f_A value of 0.1 for all chemical forms.

7.2.3. Systemic Distribution, Retention and Excretion

7.2.3.1. Overview of normal iron metabolism

(276) The biokinetics of iron has been investigated extensively in healthy human subjects as well as patients with iron deficiency or overload. The following overview of the physiological functions and normal biokinetics of iron in the human body is based mainly on the authoritative treatise by Bothwell et al., 1979. See also Saito et al., 1964; Green et al., 1968; Munro and Linder, 1978; Trubowitz and Davis, 1982; Barton and Edwards, 2000.

(277) The mass of iron in the human body typically is about 3.5-4.0 g in adult males and 2.0-2.5 g in adult females. The small mass of iron in the body does not reflect its important role in many physiological functions. This small mass usually is sufficient to maintain the normal physiological functions of iron because systemic iron has low rates of entry into the urinary bladder, gastrointestinal contents, and other excretion pathways and is reused repeatedly by the body.

(278) The body's iron content may be divided into two categories: essential (functional) iron and storage iron.

(279) Essential iron is the portion of the body's iron representing integral components of molecules that fulfill well defined physiological functions. For example, iron is an essential component of the oxygen carrying proteins haemoglobin and myoglobin and of numerous haem and non-haem enzymes involved in metabolic processes. The adult human body typically contains 30-40 mg of essential iron per kg of body mass. About 80-85% of this is found in haemoglobin within the red blood cells (RBC), and about 10-12% is found in myoglobin within muscle and other tissues. The remainder is distributed throughout the body tissues as haem enzymes (2-3% of body iron) and non-haem enzymes (3-4% of body iron). Essential iron typically represents about two-thirds of total body iron in adult males and four-fifths or more of total body iron in pre-menopausal adult females.

(280) Storage iron is an iron reserve in the body that assures an adequate supply of iron for normal physiological processes during periods of unusually low intake or rapid loss. It is stored as ferritin and haemosiderin, which hold iron in a relatively non-reactive form. Storage iron is located mainly in two tissues, the reticuloendothelial (RE) system and hepatic parenchyma. In most situations where body iron is increased, storage iron accumulates in both parenchymal and RE cells. The only condition in which selective parenchymal overload occurs is idiopathic hemochromatosis, in which there appears to be an associated defect in the way in which RE cells handle iron, with the result that RE stores are disproportionately small.

(281) Typical iron requirements in males (i.e. uptake to blood from diet) are about 1.2 mg d^{-1}, or 6% of a typical daily intake of 20 mg by an adult male. Iron balance is favorable in the adult male, as reflected by the rarity of nutritional iron deficiency in males. By age 30 y there

is usually a reserve store of iron on the order of 1 g in males.

(282) Iron balance is less favorable in the adult pre-menopausal female due to loss of circulating iron via menstruation. The amount of dietary iron required to replace this loss varies greatly, but the median value is probably about 0.4-0.5 mg/d. The total daily requirement in the female typically is about 1.4 mg, but variation is great. Total-body iron in the adult female typically is about 38 (34- 42) mg/kg. This corresponds to about 2300 mg of total-body iron in a 60-kg female. Essential iron in the adult female is roughly 33 mg/kg. This concentration is 10-20% lower than that in the male, reflecting differences in red cell mass and a larger amount of myoglobin in muscle in the male. The mean hepatic non-haem iron concentration is estimated as 0.1 mg/g liver in women, compared with about 0.27 mg/g liver in men. The average marrow storage iron has been estimated as about 300 mg in adult males and 100 mg in adult females.

(283) Iron is distributed within the body by blood plasma. Nearly all plasma iron is bound to the transport protein transferrin. The removal half-time of transferrin iron from plasma to tissues is about 90 minutes. Most of the transferrin-bound iron leaving plasma enters a circuit starting in the erythroid marrow. A portion enters the extravascular spaces and returns to plasma mainly via the lymphatics. The rest is delivered to the parenchymal tissues, mainly the liver.

(284) The erythroid marrow takes up transferrin iron from plasma for incorporation into haemoglobin. Most of this iron appears in circulating RBC in the next few days and remains there for the life of the cells. The life span of RBC typically is about four months. The portion that does not appear in circulating RBC consists of defective cells or extruded components of developing cells. This portion, called the wastage iron of erythropoiesis, typically represents 20-30% of iron that enters the erythroid marrow. This portion is collected by the body's reticuloendothelial (RE) system, degraded, and returned to plasma.

7.2.3.2. Biokinetic model for systemic iron

(285) The structure of the systemic model for iron used in this report is shown in Figure 7-1. Baseline transfer coefficients are listed in Table 7-3. The model structure and parameter values have been modified slightly from a model developed to compare the normal biokinetics of iron with its biokinetics in persons with hemochromatosis (Leggett et al., 2000). The parameter values were based on data for adult males.

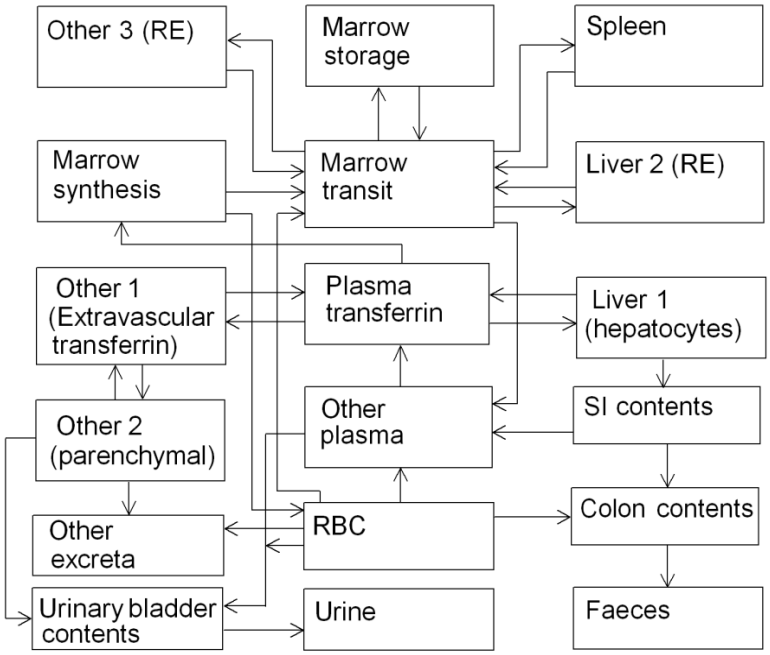

Figure 7-1. Structure of the biokinetic model for systemic iron used in this report.

Table 7-3. Transfer coefficients for systemic iron

From	To	Transfer coefficient (d^{-1})
Other plasma	Plasma transferrin	7.00E+01
Other plasma	Urinary bladder content	1.00E-02
Other plasma	Right colon content	1.00E-01
Plasma transferrin	Marrow synthesis	9.43E+00
Plasma transferrin	Liver parenchyma	5.55E-01
Plasma transferrin	Extravascular transferrin	1.11E+00
RBC	Other plasma	8.33E-04
RBC	Marrow transit	7.29E-03
RBC	Right colon content	2.00E-04
RBC	Urinary bladder content	1.50E-05
Marrow synthesis	RBC	2.43E-01
Marrow synthesis	Marrow transit	1.04E-01
Marrow transit	Other plasma	1.39E+00
Marrow transit	Marrow storage	6.35E-02
Marrow transit	Liver RE	1.06E-02
Marrow transit	Spleen	1.70E-02
Marrow transit	Other RE	6.35E-02
Marrow storage	Marrow transit	3.80E-03
Liver RE	Marrow transit	3.80E-03
Spleen	Marrow transit	3.80E-03
Other RE	Marrow transit	3.80E-03
Liver parenchyma	Plasma transferrin	3.64E-03
Liver parenchyma	Small intestine content	3.70E-04
Extravascular transferrin	Plasma transferrin	8.88E-01
Extravascular transferrin	Other parenchyma	2.22E-01
Other parenchyma	Extravascular transferrin	1.27E-03
Other parenchyma	Excreta	5.70E-04
Other parenchyma	Urinary bladder content	3.00E-05
RBC	Excreta	0.00E+00

(286) Parameter values describing the fate of iron in the first few weeks after entry into blood plasma were based on results of radioiron studies on reasonably healthy male subjects. After the parameter values governing the early kinetics of iron had been set, values controlling long-term retention and excretion were set for consistency with estimated contents of various iron pools in a male of age 50 y, estimated daily losses of iron along various excretion pathways, and the assumption that 0.9 mg of iron is absorbed each day from food. The normal 50-year-old male is assumed to have a total-body iron content of about 3.9 g, and this is assumed to be divided among major iron pools as follows: erythrocytes, 2300 mg; liver hepatocytes, 400 mg; liver RE cells, 50 mg, RE cells of bone marrow, 320 mg; spleen (mainly RE cells), 80 mg; other RE cells, 300 mg; erythroid marrow, 80 mg; plasma transferrin, 2.9 mg; remaining plasma, 0.4 mg; and remainder of the body (including several of the compartments shown in Fig. 1), about 400 mg (Bothwell et al., 1979). The precise total-body and compartmental contents calculated for age 50 years depend to some extent on the age at which the calculation is started and the assumed compartmental contents at that age. The compartment contents given above for a 50-year-old male are based on a starting age of 15 y, with the initial iron content of a given storage pool being 30% of the value indicated above for age 50 years and the initial iron content of any other pool being

80% of the value indicated above for age 50 years.

(287) Iron absorbed from the gastrointestinal or respiratory tract or returning to plasma after degradation of RBC or wastage iron by the RE system enters a compartment in blood plasma called other plasma, which represents plasma iron that is not bound to transferrin. Most of the iron in other plasma transfers to plasma transferrin, but some transfers into the urinary bladder contents. Iron is removed from plasma transferrin with a half-time of 90 min, with about 85% moving to erythroid marrow (marrow synthesis), 5% to the hepatic parenchyma (liver parenchyma 1), and 10% to a compartment representing relatively rapidly exchanging extravascular spaces (extravascular transferrin).

(288) Iron is removed from marrow synthesis with a half-time of 2 d, with 70% transferring to RBC and the remaining 30%, representing ineffective erythropoiesis, transferring to a marrow RE compartment called marrow transit. The removal of aging erythrocytes from the circulation is depicted as a transfer from RBC to marrow transit, representing phagocytosis by RE cells, plus a smaller transfer (about 10% of the total) from RBC to other plasma, representing intravascular breakage of red cells and release of the hemoglobin into the plasma. Most of the iron entering marrow transit is returned to other plasma with a half-time of 12 h. To account for relatively long-term storage of iron throughout the RE system, a small fraction of iron leaving marrow transit is distributed to the RE storage compartments in marrow, liver, spleen, and other tissues called, respectively, marrow storage, liver RE, spleen, and other RE. Iron is removed from these storage sites to marrow transit (and, therefore, largely to other plasma) over a period of months. The use of marrow transit as a central compartment within the RE system is a simplification of the real events, in that destruction of red blood cells (including red cell precursors) actually does not occur entirely in the marrow, and iron entering or leaving RE cells in the liver, spleen, and other extra-skeletal sites is not actually channeled through the marrow.

(289) In addition to the RE system, an important storage site for iron is the hepatic parenchyma, represented in this model (for normal iron kinetics) by the compartment liver parenchyma 1. This compartment receives 5% of the outflow from plasma transferrin. Iron entering liver parenchyma 1 is returned over a period of months to plasma transferrin, except for a small amount, representing biliary secretion, that transfers to the compartment gastrointestinal tract (GI tract).

(290) It is assumed that most (80%) of the iron that transfers from plasma transferrin to extravascular transferrin returns to plasma over the next day or two, but a portion (20%) is taken up by a compartment called other parenchyma 1 representing functional or storage iron not accounted for by explicitly identified tissues and fluids. The compartment other parenchyma 1 also is used to account for losses of iron due to exfoliation of skin, sweating, and losses in urine associated with exfoliation of kidney cells. Iron in other parenchyma 1 that is not lost in excreta returns over a period of months to extravascular transferrin.

(291) In addition to the excretion pathways indicated above, iron is lost from the body in erythrocytes that enter the gut or urinary bladder. According to the model, about two-thirds of iron losses are in faeces and the remainder is in skin, sweat, and urine in normal adult males.

7.2.3.3. Treatment of radioactive progeny

(292) Two isotopes of iron addressed in this report have radioactive progeny that contribute significantly to dose coefficients for the parent radionuclide: ^{52}Fe, with chain members ^{52m}Mn ($T_{1/2}$ = 21.1 min) and ^{52}Mn (5.59 d); and ^{60}Fe, with chain members ^{60m}Co (10.5 min) and ^{60}Co (5.27 y). The models for manganese and cobalt produced in vivo are

modifications of the models applied in this series of reports to these two elements as parent radionuclides. The model for internally deposited cobalt is described in the section on cobalt in the present document. The model for internally deposited manganese will appear in a later part of this series. Both models were amended by the addition of compartments representing the spleen and red marrow, which are represented explicitly in the systemic model for iron. Modifications of the cobalt model were based on biokinetic data for this element developed by Comar et al., 1946; Comar and Davis, 1947; Barnaby et al., 1968; Smith et al., 1971; Hollins and McCullough, 1971; Thomas et al., 1976; Kreyling et al., 1986; and Andre et al., 1989. Modifications of the manganese model were based on results of biokinetic or tissue distribution studies of this element by Fore and Morton, 1952; Koshida et al., 1963; Tipton and Cook, 1963; Furchner et al., 1966; and Dastur et al., 1971.

(293) The compartment in the iron model called Other plasma is identified with the plasma compartment in the manganese model. Manganese produced in tissue compartments in the model for iron is assumed to be transferred to plasma with the following half-times: 1 min for the blood compartment of the iron model that is not included in the manganese model (plasma transferrin), 83.2 d for RBC (based on a mean lifetime of 120 d for RBC), and 2 d for all other iron compartments. Manganese is assumed to leave plasma at the rate 1000 d^{-1}, with 30% going to liver, 5% to kidneys, 5% to pancreas, 1% to right colon contents, 0.2% to urinary bladder contents, 0.5% to bone surface, 0.02% to RBC, 0.1% to brain, 0.3% to spleen, 0.1% to red marrow, and the remaining 57.78% to other soft tissue. The liver is divided into two compartments called Liver 1 and Liver 2. Manganese depositing in the liver is assigned to Liver 1. Manganese is removed from Liver 1 with a half-time of 1 d, with 20% of outflow going to small intestine (SI) contents via biliary secretion and 80% entering Liver 2. Activity transfers from Liver 2 to plasma with a half-time of 2 d. Activity entering the pancreas is removed to plasma with a half-time of 2 d and to SI contents with a half-time of 2 d. The transfer from pancreas to SI contents represents secretion in pancreatic juice. Activity transfers from kidneys to plasma with a half-time of 2 d and from brain to plasma with a half-time of 150 d. The removal half-time from RBC is 83.2 d, as assumed for manganese produced by decay of iron in RBC. Activity depositing on bone surfaces is divided equally between cortical and trabecular surface and leaves bone surface with a half-time of 40 days, with 99% returning to plasma and 1% entering the corresponding bone volume compartment. Activity is removed from cortical or trabecular volume at the reference turnover rate for the specific bone type in adults as given in ICRP *Publication 89* (2002). Other soft tissue is divided into compartments ST0, ST1, and ST2 representing fast, intermediate, and slow turnover of manganese. ST1 receives 14.6% of activity leaving plasma, ST2 receives 4%, and ST0 receives 39.18% (the amount remaining after all other deposition fractions in the model were assigned). Activity is returned from ST0, ST1, and ST2 to plasma with half-times of 30 min, 2 d, and 40 d, respectively.

(294) Cobalt produced in tissue compartments in the model for iron is assumed to be transferred to the central blood compartment in the cobalt model (identified with Other plasma in the iron model) with the following half-times: 1 min for RBC and Plasma transferrin, 2 d for compartments of the liver, 30 d for spleen and compartments of red marrow, and 7 d for all other compartments. The subsequent biokinetics of cobalt entering or produced in the central blood compartment is described by the systemic model for internally deposited cobalt (see the section on cobalt in the present document), with the following modifications for application to cobalt as a daughter of iron. The spleen and red marrow are each added to the model as individual compartments that exchange cobalt with the central blood compartment. These compartments are assumed to receive 0.5% and 1% of outflow from the central blood compartment, respectively. Depositions in the compartments of Other

soft tissue with relatively fast and intermediate turnover rates are reduced from 9% and 5%, respectively, in the original model to 8% and 4.5%, respectively. Cobalt is removed from the spleen and red marrow to the central blood compartment with a half-time of 30 d.

7.2.3.4. Differences with gender

(295) The pre-menopausal adult female typically absorbs a greater portion of dietary iron and has faster turnover of body iron than the adult male due to higher iron requirements. The mass of total body iron typically is 50-100% greater in the adult male due to the combination of a larger body mass and a substantially larger mass of storage iron than the adult female. Despite the higher fractional uptake of iron from diet by females, the mass of storage iron in the pre-menopausal adult female typically is only about one-fourth of that in the adult male due to lower dietary intake of iron by females and substantial losses of iron via menstruation (Bothwell et al., 1979).

7.3. Individual monitoring

(296) ^{59}Fe is a high energy γ emitter. Monitoring of ^{59}Fe is in general accomplished through Whole Body Counting. Urine bioassay monitoring is also used in monitoring for ^{59}Fe.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{59}Fe	Urine Bioassay	γ-ray spectrometry	1 Bq/L	0.1 Bq/L
^{59}Fe	Whole Body Counting	γ-ray spectrometry, in vivo	80 Bq	20 Bq

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8. COBALT (Z = 27)

8.1. Chemical Forms in the Workplace

(297) Cobalt is a transition metal, which occurs mainly in oxidation states II and III. Cobalt may be encountered in industry in a variety of chemical forms, including metal dusts, oxides (CoO, Co_3O_4) and soluble salts such as nitrates and chlorides.

(298) Cobalt-60 is an important activation product produced in nuclear power plants, and could also be present in fragments of irradiated fuel.

(299) Significant quantities of ^{57}Co and ^{60}Co are used as sealed sources in medicine (nuclear medicine, radiotherapy) and in the food industry for sterilization.

Table 8-1. Isotopes of cobalt addressed in this report

Isotope	Physical half-life	Decay mode
Co-55	17.53 h	EC, B+
Co-56	77.23 d	EC, B+
Co-57	271.74 d	EC
Co-58	70.86 d	EC, B+
Co-58m	9.04 h	IT
Co-60	5.271 y	B-
Co-60m	10.467 m	IT, B-
Co-61	1.65 h	B-
Co-62m	13.91 m	B-

8.2. Routes of Intake

8.2.1. Inhalation

Absorption Types and parameter values

(300) Cobalt-60 is relatively easy to measure, and there have been a number of reported studies of its lung retention following accidental inhalation, usually of an oxide. Information is available from experimental studies of cobalt in a variety of forms, including nitrate, chloride, and oxides.

(301) Absorption parameter values and Types, and associated f_A values for particulate forms of cobalt are given in Table 8-2.

Cobalt nitrate ($Co(NO_3)_2$)

(302) Kreyling et al. (1986) followed the biokinetics of ^{57}Co for 1000 days after inhalation of ^{57}Co-labelled $Co(NO_3)_2$ by dogs. Most of the initial lung deposit (ILD) was rapidly cleared from the lungs and excreted from the body, mainly in urine. Lung retention was described by a three-component exponential function with biological half-times of 0.8 days (89%), 27 days (8%) and 400 days (3%). From the results of a complementary gavage experiment with $Co(NO_3)_2$ it was calculated by the task group that fractional absorption from the alimentary tract $f_A = 0.3$. [In carrying out assessments here, the systemic model for cobalt described by Leggett (2008) was used, but to fit the nitrate data, it was necessary to increase the transfer rates from blood to urine and intestine.] Assuming that the cobalt retained in the lungs was bound, rather than particulate (see below), and hence that $f_r = 1$, analysis here gave parameter values of $s_r = 1$ d^{-1}, $f_b = 0.03$ and $s_b = 0.0017$ d^{-1} (giving assignment to Type F). The

estimated value of s_b reflects the biological half-time of the slowest term in the three-exponential representation of lung retention.

(303) Although specific parameter values for cobalt nitrate based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is unlikely. Instead, cobalt nitrate is assigned to Type F. However, the data are used as the basis for the default rapid dissolution rate for cobalt, and with the data on cobalt chloride (see below), are used as the basis for bound state parameter values for cobalt. Hence specific parameter values for cobalt nitrate would be the same as default Type F cobalt parameter values.

Cobalt chloride $CoCl_2$

(304) Morrow et al. (1968) followed lung retention for 7 days after inhalation of $^{58}CoCl_2$ by dogs. Few details are given, but a lung retention half time of 0.01 d was reported, giving f_r ~1, $s_r = 70\ d^{-1}$, and assignment to Type F.

(305) Menzel et al. (1989) followed lung retention for 6 days after inhalation of stable $CoCl_2$ by rats. By that time about 5% of the amount present at the end of exposure remained, but the authors recognised that some clearance took place during exposure. Assuming that the cobalt retained in the lungs was bound, rather than particulate, and hence that $f_r = 1.0$, analysis here gave parameter values of $s_r = 4\ d^{-1}$ and $f_b \leq 0.1$: s_b could not be determined because of the short duration of the measurements.

(306) Kreyling et al. (1987) followed the biokinetics of ^{57}Co for 120 days after intratracheal instillation of $^{57}CoCl_2$ into hamsters, to investigate the retention of cobalt in the lungs and extra-pulmonary airways observed by Kreyling et al. (1986, see above). Additional information on this experiment is provided by Patrick et al. (1994). Most of the ILD cleared rapidly: ~1% ILD was present in the body after one month, with high concentrations of ^{57}Co in tracheal and bronchial cartilage, and 0.15% ILD was present in the lungs after 120 days. From results of a complementary gavage experiment with $CoCl_2$ it was calculated here that $f_A = 0.08$. At one month after administration, the concentration of ^{57}Co in the lungs was about 4 and 40 times the average in the body for gavage and instillation respectively. Thus there was some systemic uptake into the lungs following gavage. However, assuming a similar fraction was transferred from blood to lungs after instillation, it would account for only a small fraction of that retained in lungs in the instillation experiment. Assuming that the cobalt retained in the lungs was bound, rather than particulate, and hence $f_r = 1$, analysis here gave parameter values of $s_r = 1.4\ d^{-1}$, $f_b = 0.015$ and $s_b = 0.015\ d^{-1}$.

(307) Patrick et al. (1994) conducted an interspecies comparison of the lung clearance of ionic cobalt, primarily to determine whether differences in absorption of ^{57}Co following inhalation of $^{57}Co_3O_4$ (Bailey et al., 1989; Kreyling et al., 1991, see below) could be explained by differences in binding of dissolved cobalt. To complement the studies by Kreyling et al. (1986, 1987) in dogs and hamsters (see above), the biokinetics of ^{57}Co were followed for 100 days after intratracheal instillation of $^{57}CoCl_2$ into guinea pigs, rats (two strains), and a baboon. Autoradiography of the tracheas of rats and a guinea pig 30 days after instillation of $^{57}CoCl_2$ into the lungs showed that the ^{57}Co was mainly concentrated in cartilage rings. For one strain of rat, data are available to show that the proportion of ^{57}Co retained in the lungs at 21 days after systemic injection was 1.2% of the total body content (Patrick et al., 1989), compared to 20% at 30 days after $^{57}CoCl_2$ was instilled into the lungs. This indicates that while some of the ^{57}Co retained in the lungs was from the systemic circulation, most came directly from deposition in the lungs. Assuming that the cobalt retained in the lungs was bound, rather than particulate, and hence $f_r = 1$, analysis here gave values of s_r in the range 0.6–0.9 d^{-1}, and the following parameter values for the bound state:

	f_b	s_b (d^{-1})
Guinea pig	0.06	0.013
HMT rat	0.03	0.009
F-344 rat	0.016	0.012

(308) Although specific parameter values for cobalt chloride based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is unlikely. Instead, cobalt chloride is assigned to Type F. Estimates of the default rapid dissolution rate cover a wide range (from ~1 to 70 d^{-1}), but the lower values, which are based on more detailed information, are similar to the default rapid dissolution rate chosen for cobalt (see below). The data are used, with data on cobalt nitrate (see above), as the basis for bound state parameter values for cobalt. Hence specific parameter values for cobalt nitrate would be similar to default Type F cobalt parameter values.

Cobalt oxide

(309) Barnes et al. (1976) followed the biokinetics of ^{60}Co in dogs for 128 days after inhalation of cobaltosic oxide (Co_3O_4), and for 64 days after inhalation of cobaltous oxide (CoO). The oxides were produced from Co nitrate aerosol heated at 850°C and 1400°C, respectively before inhalation. Lung clearance of CoO was faster than that of Co_3O_4: after 8 days 10% versus 85% ILD remained in the lungs, and after 64 days 4% versus 60% ILD, indicating Type F and Type M behaviour respectively. For both oxides, there was high fecal excretion of ^{60}Co during the first 3-4 days, which represented material cleared from the upper respiratory tract, while urinary excretion exceeded fecal excretion after 5 days, reflecting the greater importance of dissolution than particle transport as a clearance mechanism. The authors considered it noteworthy that the ^{60}CoO formed at 1400°C was more soluble than the $^{60}Co_3O_4$ formed at 850°C, because generally aerosols formed at higher temperatures are less soluble than aerosols formed at lower temperatures.

(310) Detailed studies have been conducted of the lung clearance kinetics of various physical forms of cobaltosic oxide (Co_3O_4), which has been used extensively as a test material to investigate factors that affect particle dissolution in the lungs (e.g. Kreyling et al., 1986, 1988). Kreyling et al., (1986) also found that cobalt oxide aerosols formed at higher temperatures are more soluble than aerosols formed at lower temperatures: the *in vivo* dissolution / absorption of a mixed cobalt oxide consisting of Co_3O_4 and CoO (formed at 950°C) was significantly faster than for pure Co_3O_4 particles (formed at 800°C) of similar size.

(311) These studies included two direct intercomparisons of clearance in different mammalian species, one of which involved human volunteers, baboon, dog, guinea pig, rat, hamster and mouse (Bailey et al., 1989), and the other baboon, dog and rat (Kreyling et al., 1991). In these numerous experiments, different parameters were varied, including the specific surface area, which influences the dissolution rate of the compound (ranging from 0.6 to 30 $m^2 g^{-1}$), the AMAD (ranging from 0.8 to 3.5 µm), and the initial lung deposit, ILD, (ranging from 1 to 2000 kBq, depending on species).

(312) Generally, lung retention was longer in humans and baboons than in the other species (dogs, guinea pigs, three strains of rats, hamsters, and mice). Absorption from the human lung was consistent with assignment to Type M, since in that study (Bailey et al., 1989) the test material was designed by means of its physical and chemical parameters to be moderately soluble (specific surface area >6 $m^2 g^{-1}$); s_s ranging from 0.0013 to 0.005 d^{-1}. When the test material was selected to be less soluble (specific surface area <6 $m^2 g^{-1}$), absorption in baboons and dogs was consistent with assignment to Type S (Kreyling et al.,

1988; 1991): s_s ranging from 0.0008 to 0.03 d^{-1}. The *in vivo* rate of dissolution / absorption in dogs was linearly related to the specific surface area of the particles ranging from 0.6 to 30 m^2g^{-1} (Kreyling, 1990). Human and baboon data followed the same linear correlation (Kreyling, 1992). The rate-determining step was shown to be intracellular particle dissolution in alveolar macrophages in all species (Kreyling et al., 1990; Kreyling, 1992). The results of two *in vitro* dissolution tests with lung serum simulant (Collier et al., 1992), gave s_s ranging from 0.0002 to 0.0036 d^{-1}.

(313) In more recent studies, $^{57}Co_3O_4$ (inhaled by dogs) was used as a moderately soluble test particle to investigate the effects of chronic exposure to sulphur-related environmental air pollution on respiratory defence mechanisms, including particle dissolution (Kreyling et al., 1992a, 1999; Heyder et al., 2009). It was found that the *in vivo* dissolution rate decreased during exposure to the acidic sulphate component, but increased during exposure to the sulphite component and also during combined exposure to the acidic sulphate component (6 hours daily) and sulphite component (18 hours daily).

(314) Newton and Rundo (1971) followed retention of ^{60}Co in the chest and/or whole body in five men for 0.4 to 11 years after accidental inhalation of the irradiated metal or its oxide. Estimated half-lives for the long-term clearance from the chest of cobalt were up to 17 years. Using the updated HRTM with the new particle transport model for the AI region (Gregoratto et al., 2010), for three subjects (followed for 2.5 – 9 years), good fits to the data were obtained here with absorption type S. For the subject followed for 11 years, analysis here showed that a slow dissolution rate lower than that of Type S was needed to fit the data: the best estimate was $s_s = (0\pm5) \times 10^{-5}$ d^{-1}.

(315) Gupton and Brown (1972) followed retention of ^{60}Co for 4 years in the chest of a man who was exposed to ^{60}Co-oxide by inhalation during a period of ~6 months prior to the initial count, and following which there was no subsequent exposure. Analysis here showed that retention is predicted adequately by assuming absorption type S, but a better fit is obtained with a higher dissolution rate $s_s = (8\pm2) \times 10^{-4}$ d^{-1}.

(316) Beleznay and Osvay (1994) followed whole body retention of ^{60}Co in six workers for about 4 years, starting one day after a short exposure to an aerosol leaking from a hot cell in which a high activity ^{60}Co source was being manipulated. The authors considered that the aerosol was probably composed of metallic cobalt and cobaltic or cobaltosic oxide formed at 300-400°C on the surface of the high activity cobalt wire. Longitudinal profile scans on one subject showed that on the 15th day a major part of the deposited activity was in the chest, but on the 80th day this had decreased considerably, with an increase in systemic activity. The authors interpreted the long-term retention of ^{60}Co in the body as mainly systemic. Analysis here showed agreement with the data for model predictions assuming absorption type M (s_s = 0.005 d^{-1}).

Fused aluminosilicate particles (FAP)

(317) 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 (montmorillonite) 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 cobalt is incorporated into FAP, only a small fraction may be absorbed rapidly. The rest is retained within the particles and is absorbed slowly. Kreyling et al. (1988) followed the lung clearance of ^{57}Co for 3 years after inhalation of ^{57}Co-FAP by dogs and estimated a dissolution rate, s_s, of 0.0005 d^{-1}. Kreyling et al. (1992a) followed the biokinetics of ^{60}Co for 600 days after inhalation of ^{60}Co-FAP by dogs and estimated a dissolution rate of 0.0009 ± 0.0004 d^{-1}. From measurements following

inhalation of ^{57}Co-FAP in rats the long term dissolution rate, s_s, was estimated to be 0.0008 d^{-1}, while an *in vitro* dissolution test gave s_s = 0.00018 d^{-1} (Collier et al., 1988, 1992). Most of these results give assignment to Type S.

Polystyrene (PSL)

(318) As with FAP, it has been demonstrated that when cobalt is incorporated into a polystyrene matrix, most of it is retained within the particles and is absorbed extremely slowly, making it an exceptionally useful material for studying long-term particle transport from the lungs. Kreyling et al. (1992b) estimated a rate of dissolution of <0.00003 d^{-1} for ^{57}Co-labelled polystyrene inhaled by dogs, but few details were given. Kreyling et al. (1999) and Heyder et al. (2009) used ^{58}Co-and ^{60}Co-labelled polystyrene as insoluble test particles to investigate in dogs the effects of chronic exposure to sulphur-related environmental air pollution on respiratory defence mechanisms, including particle clearance from the alveolar region. Kreyling et al. (1999) estimated dissolution rates of 0.00001 ± 0.00002 d^{-1} and 0.00002 ± 0.00002 d^{-1} respectively. All these results give assignment to Type S.

Contaminated dusts ('residues') formed at nuclear power plant (NPP)

(319) Raghavendran et al. (1978) followed retention of ^{60}Co in four workers at the Bhaba Atomic Research Centre for between 400 and 1250 days. Profile scans showed most activity to be in the chest. Retention in the chest was fit by a one- or two-component exponential function, with long-term half-lives in range 500-18,000 days, indicating Type S behaviour.

(320) Hegde et al. (1979) reported information on chest measurements up to about 400 days for five inhalation cases of ^{60}Co in BWR (Boiling Water Reactor) power station workers. Results for four workers were summarised with an average value of 664 days for the biological half-time. Predictions assuming Type S behaviour are in good agreement with the data.

(321) Ramsden (1984) followed two cases of lung retention of ^{60}Co for about 1500 days after inhalation of mixed corrosion oxide products from water reactor circuitry. Analysis here, using the updated HRTM, showed that a slow dissolution rate lower than that of Type S was needed to fit the data: the best estimate was $s_s = (1\pm0.5)\ x10^{-5}\ d^{-1}$.

(322) Davis et al. (2007) and Gregoratto et al. (2010) analysed the results of measurements (urine and faeces during the first two weeks, and whole body to 15 years) of ^{60}Co in seven workers who inhaled particles of unknown form in the same incident at a NPP. The dataset is extraordinary in that a group of workers had a simultaneous, brief single inhalation exposure, and they have been followed for so long. In order to account for the later whole body retention data in each subject it was necessary to assume slower particle transport from the alveolar region, than that assumed in the HRTM (ICRP, 1994). This study is one of those on which the alveolar-interstitial model in the updated HRTM is based (ICRP, 2012). Specific absorption parameter values were fit to the results for each subject by both Davis et al. (2007) and Gregoratto et al. (2010). Most were similar to those for default Type S, but to fit the early urine data, the fractional absorption in the alimentary tract could be no more than about 0.1%, and a slow dissolution rate lower than that of Type S was needed to fit the data: the best estimate was s_s <0.0001 d^{-1}.

(323) The biokinetics of ^{60}Co were followed for 6 months after intratracheal instillation into rats of a complex radionuclide bearing dust (72% ^{60}Co activity) from the ventilation grid of a NPP reactor fuel hall (Stradling et al., 1996, 1997). Absorption parameter values: f_r = 0.30; s_r = 1.5 d^{-1} and s_s = 5 10^{-4} d^{-1} derived by ICRP (2002a, Section E4.4), are consistent with assignment to Type M. However, since several human studies following intakes at NPP indicate Type S behaviour, these specific values do not seem representative and are not

recommended for use in preference to default Type S.

(324) The biokinetics of ^{60}Co were followed for 280 days after intratracheal instillation into rats of a suspension of corrosion 'crud' particles (oxide bearing debris, 60% ^{60}Co activity) from the primary containment of a water cooled reactor (Collier et al., 1994). Few details are given, but it was assessed here that the results are consistent with assignment of the ^{60}Co present to Type S.

(325) Molokanov et al. (2010) reported *in vivo* lung measurements of ^{60}Co up to 200 days, and several urine and faecal data at about 200 days, for four NPP workers who accidentally inhaled a cobalt compound. No early data are available, but the slow clearance and the small amount in the urine indicate that the material was insoluble. A good fit to the data was obtained here with default Type S absorption but with an increased value for the slow absorption rate, $s_s = 0.0003$ d^{-1}.

Other compounds

(326) Clearance studies of cobalt in the rat after inhalation of neutron-activated fly ash (Griffis et al., 1981) or volcanic ash (Wehner et al., 1984) indicated leaching of cobalt out of the particle matrix consistent with assignment to Type M.

(327) Although numerous studies have been carried out on the toxicity of inhaled cobalt-containing alloys, no data are available from them on the clearance kinetics of cobalt. The data obtained from diamond polishers (Van den Oever et al., 1990) or after exposure of rats (Brune and Beltesbrekke, 1980) suggest, however, long-term retention in the lungs indicative of Type M or S behaviour.

Rapid dissolution rate for cobalt

(328) Most of the estimated values of the rapid dissolution rate, s_r, from studies involving inhalation or instillation into the lungs of cobalt nitrate and chloride were in the range 0.6 – 4 d^{-1}. The exception was the value of 70 d^{-1}, based on a reported lung retention half time of 0.01 day following inhalation of $^{58}CoCl_2$ by dogs (Morrow et al., 1968): but few details were given. Based on the other studies, a value of s_r of 1 d^{-1} is applied here to all Type F forms of cobalt. 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 cobalt.

Extent of binding of cobalt to the respiratory tract

(329) Experimental evidence, described in the sections on cobalt nitrate and chloride, consistently shows long term retention of a few percent of the ILD of cobalt deposited in the lungs in soluble form.

(330) Studies of the kinetics of cobalt following inhalation of cobalt nitrate (soluble) and oxides (moderately soluble) by dogs, and following instillation of cobalt chloride into the lungs of hamsters, showed much larger amounts in the tracheo-bronchial (TB) airways than expected for material transiting the TB following clearance by particle transport from the alveolar region (Kreyling et al., 1986, 1987). Furthermore, the relative amount in TB within the lungs increased with the solubility of the material. Cobalt was also found to be distributed in the lungs after intravenous injection of oxide particles (Co_3O_4) in dogs (Kreyling et al., 1986). Measurements showed a decreasing activity in liver with time while increasing in lungs (and other soft tissues and bones). This suggests that it was not particles injected into blood which were directly absorbed by the lungs, but non-particulate Co, released into blood from liver (where particulate matter is incorporated and digested by Kupffer cells) and then absorbed in the lungs.

(331) Studies were conducted to localise further the distribution of the cobalt retained in

the lungs. A study of the detailed location of cobalt in the lungs of dogs at 14 days after instillation of $Co(NO_3)_2$ into one lung lobe showed that the retained cobalt was mainly located in the airway cartilage (Godleski and Kreyling, 1990). Autoradiographs of rats and guinea pigs at 100 days after instillation of $CoCl_2$ (Patrick et al., 1994) showed the highest concentrations of cobalt to be in cartilaginous structures of the trachea and bronchi.

(332) There is therefore strong evidence for a bound state for cobalt, which can be quantified (although the location of the bound cobalt, in cartilaginous structures, is different from that assumed in the HRTM). Based on this evidence, retention and excretion data for cobalt nitrates and chlorides were analysed assuming that the cobalt retained in the lungs was bound, rather than particulate, and hence $f_r = 1.0$. For cobalt chloride instilled into the lungs of rats and guinea pigs, and followed for 100 days, values of f_b averaged 0.03 (range 0.016 to 0.06), and values of s_b averaged 0.011 d^{-1} (range 0.009 to 0.013 d^{-1}). For cobalt nitrate inhaled by dogs and followed for a much longer period (up to 1500 days) the bound fraction was estimated here to be $f_b = 0.03$, clearing at a rate s_b of $=0.0016$ d^{-1}.

(333) On the basis of these results, a bound fraction with $f_b = 0.03$ and a rate of uptake $s_b = 0.002$ d^{-1} is adopted here for cobalt. No experimental evidence was found to show that cobalt in soluble form deposited in the conducting airways is retained in a bound state. There is evidence that much of the cobalt deposited in the lungs in soluble form that is not absorbed rapidly is retained in airway cartilage. However, this is located some distance below the epithelial tissue which forms the designated source region for material bound in the airway regions (BB and bb). Locating the bound activity in the source region within the epithelium could substantially overestimate doses to the BB and bb regions. It is therefore assumed here that these bound state parameter values apply only in the AI region.

Table 8-2. Absorption parameter values for inhaled and ingested cobalt

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Cobalt nitrate, chloride	1	1	–	0.1
M	All unspecified forms[d]	0.2	1	0.005	0.02
S	Cobalt oxide, FAP, PSL	0.01	1	$1x10^{-4}$	0.001
Ingested materials					
All chemical forms					0.1
Insoluble oxides					0.05

[a] It is assumed that for cobalt the bound fraction f_b is 0.03 with an uptake rate s_b = 0.002 d^{-1}. The values of s_r for Type F, M and S forms of cobalt (1 d^{-1},) are element-specific.

[b] Materials (e.g. cobalt nitrate) are 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 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 and the f_A value for ingested soluble forms of cobalt (0.1).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

8.2.2. Ingestion

(334) Human volunteer studies with ^{60}Co chloride (Paley and Sussman, 1963; Smith et al., 1972) showed that when the cobalt was present in trace quantities (less than 1 μg Co), absorption was 0.05 or less but when larger amounts of cobalt were administered (1-12 mg), absorption was 0.1-0.3. A higher value of 0.44 (from 1.2 mg Co) was recorded by Valberg et al. (1969), and this was increased to 0.7 in volunteers suffering from iron deficiency. Similarly, Paley and Sussman (1963) noticed that fasting for 3 hours or longer increased the absorption by a factor 2.

(335) The absorption of Co in forms encountered in the workplace may be considerably lower than these values for relatively soluble inorganic forms. Chevalier and Gonin (1993) estimated the absorption of ^{60}Co ingested as large particles of stellite following their inhalation; large particles deposited in the upper airways are rapidly swallowed and absorption was assumed to take place solely from the gastrointestinal tract. The absorption values obtained for 5 subjects were in the range of about 10^{-3} to 10^{-4}. Bailey et al. (1989) measured the absorption of ^{57}Co as cobaltosic oxide (Co_3O_4), as part of a comparison of the behaviour of inhaled materials in different mammalian species. Estimates of absorption after intragastric administration of oxide particles with geometric mean diameters of 0.8 μm or 1.7 μm were in the range of about 0.01 to 0.05 for mice, hamsters, rats, guinea pigs and baboons. Comparing the behaviour of ^{57}Co nitrate and a mixed oxide containing Co_3O_4 and CoO in dogs, Kreyling et al. (1986) obtained results for urinary excretion of ^{57}Co after intravenous injection and ingestion which suggested absorption of about 0.3 for the nitrate and 0.06 for the oxide. Collier et al (1991) compared whole body retention and urinary excretion of ^{57}Co in rats from 3 weeks to 48 weeks of age after intravenous injection as the nitrate or intragastric administration as Co_3O_4 (1 μm particles). The results suggested absorption in the

range of $4x10^{-3}$ to $4x10^{-2}$ with the greatest values in the youngest animals.

(336) In ICRP *Publication 30* (1979), an f_1 of 0.05 was recommended for oxides, hydroxides and for all other inorganic forms ingested in trace quantities. For inorganic forms other than oxides and hydroxides ingested in the presence of carrier material, a value of 0.3 was recommended, although the ingestion of large masses of soluble material would only be expected in exceptional circumstances. In ICRP *Publication 67* (1993), a value of 0.1 was adopted for dietary intakes by adult members of the public. In this report, an f_A value of 0.1 is adopted for direct ingestion of all chemical forms but insoluble oxides for which an f_A value of 0.05 is recommended.

8.2.3. Systemic Distribution, Retention and Excretion

8.2.3.1. Summary of the database

Data for human subjects

(337) Smith et al. (1972) studied the behavior of cobalt in 11 healthy adult subjects (10 males and one female) after intravenous injection with $^{60}CoCl_2$. More than 90% of the injected amount was removed from plasma during the first 30 min. Over the next 30 h activity in plasma declined with a half-time of about 1 d. The concentration of ^{60}Co in plasma was 1-2 orders of magnitude higher than that in red blood cells, but the investigators suggested that the measurement techniques may have underestimated ^{60}Co in red blood cells. Measurements of urinary and faecal excretion in six of the subjects during the first 2-8 d after administration revealed that activity was eliminated primarily in urine. The ratio of faecal to urinary excretion during the study period averaged about 0.15. Long-term retention in the total body was estimated for three subjects by external measurements. Average retention for two subjects followed over 1000 d could be described reasonably well by a four-exponential function with the following biological half-times and component sizes: 0.5 days (44%); 6 days (32%); 60 days (13%) and 800 days (11%). External measurements on one subject soon after injection indicated that the liver accumulated roughly one-third of the injected amount. External measurements for 8 subjects indicate that the liver contained roughly 20% (10-30%) of the total-body burden at times from a few days up to 1000 d after injection.

(338) Letourneau et al. (1972) used external whole-body measurements to estimate the rate of loss of ^{58}Co from each of 16 male subjects over an approximately one-year period (305-386 d) following intravenous injection of $^{58}CoCl_2$. Estimated retention was slightly lower on average than determined in the study by Smith et al. (1972), although there was overlap in the range of retention data found in the two studies. On average, about 35-40% of the injected activity was lost with a biological half-time of a few hours, 25% with a halftime <2 d, 20% with a half-time of ~8 d, 10-15% with a half-time of ~50 d, and 9% with a half-time of ~600 d. The size of the long-term component ranged from 5-13%, compared with 9-16% in three subjects of Smith et al. (1972) studied for at least 275 d.

(339) Jansen et al. (1996) used positron emission tomography to study the early biokinetics of ^{55}Co in two adult males, ages 26 and 30 y, after intravenously injection with $^{55}CoCl_2$. Whole-body scans were made immediately (~0.5 h), at 24 h, and at 48 h after injection. The liver and urinary bladder were estimated to contain about 50% and 40%, respectively, of the administered activity in the first scan. These values are qualitatively consistent with other human or animal studies in that they indicate rapid transfer of cobalt to the liver and urinary bladder but are higher than estimated in most studies.

(340) Newton and Rundo (1971) studied the behavior of ^{60}Co in five men for periods up to 11 y after accidental inhalation of the irradiated metal or its oxide. They estimated a long-

term clearance half-time on the order of 7 y for systemic cobalt. Measurements on one of the subjects about 3 y after intake established the presence of ^{60}Co in the skeleton. Activity was not detectable in the liver.

(341) Beleznay and Osvay (1994) measured retention of ^{60}Co in six workers from 10-1850 d after they accidentally inhaled ^{60}Co aerosols during manipulation of a high-activity source. A retention component of 25-78 d was interpreted as activity leaving the deep lungs. A long-term component of retention determined in five of the workers followed for extended periods was interpreted as the slowest component of systemic retention of cobalt. The biological half-time of the long-term component varied from ~500 d to ~1200 d and averaged ~900 d.

(342) The collective data for human subjects indicate that the long-term half-time for cobalt taken into the body in inorganic form tends to increase with the length of the observation period: 600 d for observations over 305-386 d (Letourneau et al., 1972); 800 d for observations over for about 1000 d (Smith et al., 1972); 900 d for observations up to 5 y (Beleznay and Osvay, 1994); and 7 y for observations up to 11 y (Newton and Rundo, 1971). This suggests that there is a component of retention with a biological half-time of many years. As described later, animal studies indicate that the skeleton retains a small portion of deposited cobalt for an extended period.

Data on laboratory animals

(343) The biokinetics of cobalt has been studied in mice, rats, hamsters, guinea pigs, dogs, monkeys, and baboons. Differences between species are indicated. For example, Thomas et al. (1976) compared the biokinetics of cobalt in the mouse, rat, monkey, and dog following intravenous, intragastric, and oral administration of $^{60}CoCl_2$. The long-term retention half-time was longer in the mouse (495 d) than in the rat (309 d), monkey (183 d), or dog (180 d). The investigators noted that the pattern was different than normally encountered in retention of trace metals in that larger animals usually have longer retention times.

(344) In dogs exposed by inhalation to ^{60}Co aerosols (Barnes et al., 1976), the kidneys and liver showed much higher concentrations of ^{60}Co than skeleton at early times but the relative concentration in the skeleton increased over a period of months. The contents of liver, skeleton, and kidneys decreased in the order liver > skeleton > kidneys at early times and in the order skeleton > liver > kidneys after 2-4 months. In dogs exposed to ^{57}Co aerosols (Kreyling et al., 1986), the skeleton and muscle each contained several times more activity than liver, and kidneys contained roughly the same amount as liver, at 1-5 y after exposure.

(345) In rats given a single dose of $^{60}CoCl_2$ by gastric intubation, the liver initially was the main repository, but by 2-4 months the main measured repository was skeleton, followed by muscle, liver, and kidney (Smith, al., 1971). In rats chronically exposed to ^{60}Co in drinking water, the liver remained the dominant repository over 170 d, followed by skeleton and muscle (Smith et al., 1971). Retention of ^{60}Co by rats continuously exposed to ^{60}Co in drinking water was consistent with the long-term whole-body retention component derived from single-administration studies (Smith et al., 1971).

(346) At 8 d after ingestion of $^{57}Co_3O_4$ particles by baboons, the skeleton and kidneys contained 0.6-1.1 times and 0.09-0.15 times, respectively, as much activity as the liver. At 6 mo after inhalation of $^{57}Co_3O_4$ by baboons, the skeleton and kidneys contained 0.6-3 and 0.1-0.3 times as much activity as the liver, respectively (Andre et al., 1989).

(347) Animal studies reveal that the systemic biokinetics of cobalt depends on the chemical form injected into blood (Nishimura et al., 1976; Inaba et al., 1982). Nishimura et al., (1976) compared the behavior of intravenously injected $^{60}CoCl_2$ and ^{58}Co-cyanocobalamin in rats. At 21 d after administration of $^{60}CoCl_2$, 26.4% of the body burden was found in the liver and 13.1% in the kidneys, and cumulative excretion was mainly in

urine. At 21 d after intravenous administration of ^{58}Co-cyanocobalamin, the kidneys contained 38.8% of the body burden and the liver contained 14.6%; excretion of ^{58}Co was mainly in faeces; and loss from the body was considerably slower than for inorganic cobalt.

(348) In studies involving various animal species, more than half of ^{57}Co injected as $Co(NO_3)_2$ was excreted in urine in the first 24 h and more than two-thirds was excreted in urine during the first week (Andre et al., 1989; Bailey et al., 1989; Collier et al., 1989; Talbot and Morgan, 1989). Cumulative faecal excretion over the first week accounted for about 4-28% of the injected cobalt. Other animal studies also indicate that urine is the primary route of excretion of injected cobalt (Comar and Davis, 1947; Barnaby et al., 1968; Onkelinx, 1976; Thomas et al., 1976; Gregus and Klaassen, 1986; Kreyling et al., 1986). Excretion of cobalt in bile amounting to 2-7% of the initial systemic burden has been observed in dogs and rats (Sheline et al., 1945; Cikrt and Tichy, 1981; Gregus and Klaasen, 1986).

(349) The distribution of ^{60}Co was examined by autoradiography in tissues of pregnant mice intravenously injected with $^{60}CoCl_2$ (Flodh, 1968). Sacrifice times were 1 h, 4 h, 24 h, 4 d, and 16 d after injection. Except where otherwise indicated, the following description refers to the mother rather than the fetus. At 1 h the concentration of ^{60}Co in blood was only about one-eighth that in liver. Disappearance from blood was gradual after 1 h but largely complete by 24 h. Cartilage showed a high concentration of activity at 1 h. The concentration of ^{60}Co in cartilage increased with time and was 4 times higher than in liver by 4 d. From 24 h onward the cartilage in the trachea and larynx had the highest concentration. Bones of the skull, the periosteum of the vertebrae, and the pelvic bone also accumulated cobalt. The liver showed a high concentration at all times studied. Accumulation was high in the kidneys with a peak at 4 h. Activity was localized mainly in the inner parts of the cortex. After 4 d the kidney concentration was still as high as the liver. Accumulation in the mammary glands was high, about the same concentration as in the liver and kidneys. In the fetus, the radioactivity was localized mainly in the skeleton, with relatively high uptake in hyaline cartilage and cranial bones. According to the investigators, the distribution of inorganic cobalt in the mother was different from that seen in autoradiographic studies involving ^{58}Co-labeled vitamin B_{12}.

(350) In animal studies involving administration of inorganic compounds of radiocobalt, relatively high concentration of cobalt generally have been found in the liver, kidneys, skeleton, and skeletal muscle. The skeleton typically contains more than any other single organ or tissue by a few months after acute intake, indicating tenacious retention of a portion of the deposited activity. Following intraperitoneal, intravenous, or oral administration of $^{60}CoCl_2$ to rats, the skeletal content decreased by a factor of 6-12 between days 1 and 30 and then showed little decline over the next few months (Barnaby et al., 1968; Thomas et al., 1976). Skeletal muscle showed a longer average retention time than most soft tissues including liver and kidneys.

(351) In hamsters, rats, and guinea pigs, liver and kidneys contained about 20-40% and 3-4%, respectively, of the total body activity at 3 wk after intravenous injection of $^{57}Co(NO_3)_2$ (Collier et al., 1989). In rats, liver, skeleton, and muscle each contained about 20-25% and the kidneys contained about 7-8% of the total-body activity over 10-72 d after intraperitoneal injection of $^{58}CoCl_2$ (Hollins and McCullough, 1971). At 386 d after intraperitoneal injection of $^{58}CoCl_2$, the skeleton, liver, and kidneys contained about 65%, 7%, and 2%, respectively, of total-body activity (Hollins and McCullough, 1971).

(352) The systemic distribution of ^{57}Co-labeled cobalt at 100 d after intraperitoneal injection of $CoCl_2$ into rats depended strongly on the administered mass (Edel et al., 1994). After administration of 5 µg of cobalt the highest concentrations of ^{57}Co were found in spleen and pancreas, followed by skull and femur. After administration of 1 mg the skull and femur

showed far higher concentrations than other tissues.

8.2.3.2. Biokinetic model for systemic cobalt

(353) The model structure for systemic cobalt used in this report (Figure 8-1) is the same as the generic model structure for bone-volume-seeking radionuclides except that compartments within blood are not identified explicitly for cobalt. Although cobalt is not considered a bone-seeking radionuclide, that model structure provides a convenient framework in which to model the biokinetics of cobalt for radiation protection purposes.

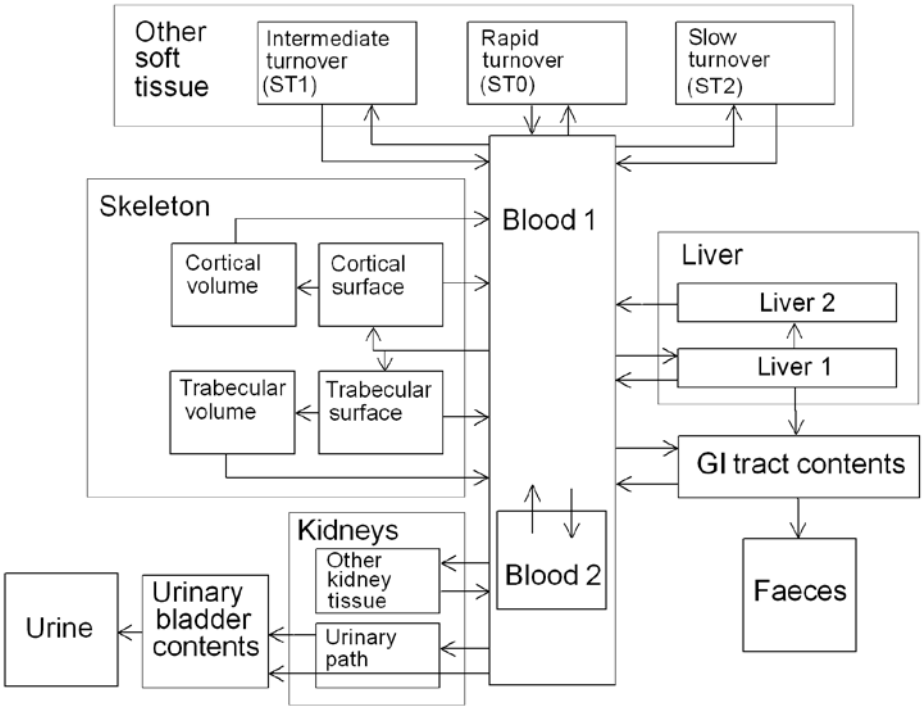

Figure 8-1. Structure of the systemic model for cobalt.

(354) Transfer coefficients (Table 8-3) were based as far as feasible on data from controlled human studies involving administration of inorganic forms of cobalt. Model predictions of total-body retention, including different phases of loss from the body, were required to be consistent with central estimates based on combined data of Smith et al. (1972) and Letourneau et al. (1972) for human subjects injected with $^{60}CoCl_2$ and $^{58}CoCl_2$, respectively. Parameter values for blood were set for consistency with blood retention data of Smith et al. (1972) for subjects injected with $^{60}CoCl_2$. Urinary and faecal excretion rates and uptake and retention by liver were based mainly on measurements by Smith et al. (1972) and Jansen et al. (1996) for subjects injected with $^{60}CoCl_2$ and $^{55}CoCl_2$, respectively. The data for human subjects were supplemented with information on the time-dependent distribution of cobalt among liver, kidneys, skeleton, and other tissues in laboratory animals receiving inorganic forms of radiocobalt by inhalation, ingestion, or injection. For example, the initial distribution of systemic cobalt and the shift with time in its distribution were modeled after general patterns indicated by data on several animal species. Derivations of parameter values describing uptake and retention in specific repositories are summarized below.

Table 8-3. Transfer coefficients (d^{-1}) for systemic cobalt.

Compartments	Transfer Coefficient (d^{-1})
Blood 1 to Liver 1	7.00E+01
Blood 1 to Urinary bladder contents	6.00E+01
Blood 1 to Right colon contents	4.00E+00
Blood 1 to ST0	1.80E+01
Blood 1 to ST1	1.00E+01
Blood 1 to ST2	4.00E+00
Blood 1 to Cortical bone surf	6.00E+00
Blood 1 to Trabecular bone surf	6.00E+00
Blood 1 to Kidneys 1	9.00E+00
Blood 1 to Kidneys 2	1.00E+00
Blood 1 to Blood 2	1.20E+01
Blood 2 to Blood 1	6.93E-01
Liver 1 to SI cont	9.24E-02
Liver 1 to Blood 1	3.47E-01
Liver 1 to Liver 2	2.31E-02
Liver 2 to Blood 1	1.90E-03
ST0 to Blood 1	9.90E-02
ST1 to Blood 1	1.39E-02
ST2 to Blood 1	9.50E-04
Cortical bone surf to Blood 1	8.42E-02
Cortical bone surf to Cortical bone vol	1.49E-02
Trabecular bone surf to Blood 1	8.42E-02
Trabecular bone surf to Trabecular bone vol	1.49E-02
Cortical bone vol to Blood 1	8.21E-05
Trabecular bone vol to Blood 1	4.93E-04
Kidneys 1 to Urinary bladder contents	4.62E-01
Kidneys 2 to Blood 1	1.90E-03

surf = surface, vol = volume, SI = small intestine

Blood

(355) Blood is divided into two compartments called Blood 1 and Blood 2. Cobalt atoms entering blood are assigned to Blood 1, which is a rapid-turnover plasma pool. Blood 2 is a more slowly exchanging pool that contains the preponderance of activity in blood except for a short period soon after acute uptake of radiocobalt. These compartments are used to reproduce observed rates of disappearance of cobalt from blood and are difficult to identify with specific components of blood. The relatively slow loss of a portion of injected cobalt from blood may be associated with retention by certain plasma proteins and red blood cells (RBC), although data of Smith et al. (1972) indicate that RBC contained at most a few percent of the blood content of ^{60}Co during the first 30 h after intravenous injection of $^{60}CoCl_2$ into human subjects.

(356) Activity leaves Blood 1 at the rate 200 d^{-1}, corresponding to a half-time of ~5 min, with 6% of outflow going to Blood 2 and the remaining 94% divided among tissue compartments, urinary bladder contents, and colon contents. Activity moves from Blood 2 back to Blood 1 with a half-time of 1 d.

Liver and faecal excretion

(357) The liver is represented as two compartments, Liver 1 and Liver 2, representing short- and long-term retention, respectively. Liver 1 receives 35% of activity leaving Blood 1. Activity is removed from Liver 1 with a half-time of 1.5 d, with 20% going to the small intestine contents in bile, 5% going to Liver 2, and 75% returning to blood. Activity transfers from Liver 2 to Blood 1 with a half-time of 1 y. Endogenous faecal excretion of cobalt arises from biliary secretion as indicated above, plus secretion from Blood 1 to the right colon. The latter transfer amounts to 2% of cobalt leaving Blood 1.

Kidneys and urinary excretion

(358) The kidneys are divided into two compartments, called Kidneys 1 and Kidneys 2. Kidneys 1 receives cobalt from blood after filtration through the glomerulus, representing 4.5% of outflow from Blood 1, and loses cobalt to the urinary bladder contents with a half-time of 1.5 d. The urinary bladder contents receive an additional 30% of outflow from Blood 1 that is filtered at the glomerulus but not retained in the kidneys. Kidneys 2 is a slow-turnover pool that receives 0.5% of outflow from Blood 1 and returns cobalt to Blood 1 with a half-time of 1 y.

Skeleton

(359) Uptake and retention of cobalt in the total skeleton can be modeled on the basis of data from animal studies, but the distribution of cobalt between cortical and trabecular bone or between bone surfaces and bone volume has not been established. It is assumed that 3% of cobalt atoms leaving Blood 1 deposit on trabecular bone surfaces and 3% deposit on cortical bone surfaces. Cobalt leaves bone surfaces with a half-time of 7 d, with 15% going to the corresponding bone volume compartment and 85% returning to Blood 1. Cobalt is removed from trabecular or cortical bone volume at the rate of bone turnover. Reference values for bone turnover rates are given in ICRP *Publication 89* (2002b).

Other tissues

(360) Remaining soft tissues are divided into three compartments called ST0, ST1, and ST2, with relatively fast, intermediate, and relatively slow turnover, respectively. These compartments receive 9%, 5%, and 2% of outflow from Blood 1 and return cobalt to Blood 1 with half-times 7 d, 50 d, and 2 y, respectively.

(361) The above parameters yield reasonable consistency between model predictions of retention and excretion and observations in controlled human studies. Model predictions are also consistent with the following aspects of the biological behavior of inorganic cobalt indicated by radiocobalt studies on human subjects and laboratory animals:

- The peak content of liver is roughly one-third (model prediction, ~35%) of the intravenously injected amount and occurs during the first hour after injection.
- A high rate of urinary of excretion of cobalt occurs during the first hour or two after absorption or intravenous injection into blood (Apostoli et al., 1994; Jansen et al., 1996).
- The liver contains roughly 20% (model predictions, 15-27%) of the total body burden at times from a few days up to 1000 d after injection.
- The kidneys and liver initially show similar concentrations of cobalt, but the kidney concentration is about twice that of liver at times remote from injection.
- The skeleton contains less cobalt than the liver during the early weeks after injection but gradually becomes the dominant systemic repository for cobalt.

8.2.3.3. Treatment of radioactive progeny

(362) The only cobalt isotopes addressed in this report that have dosimetrically important chain members are ^{58m}Co, which decays to ^{58}Co, and ^{60m}Co, which decays to ^{60}Co. In these cases the biokinetics of the radioactive progeny is presumably identical to that of the parent.

8.3. Individual monitoring

^{57}Co

(363) ^{57}Co is a high energy γ emitter. Monitoring of ^{57}Co is in general accomplished through Whole Body Counting. Urine bioassays are also used in monitoring for ^{57}Co. If needed lung monitoring may be performed.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{57}Co	Urine Bioassay	γ-ray spectrometry	1 Bq/L	0.2 Bq/L
^{57}Co	Whole Body Counting	γ-ray spectrometry	30 Bq	30 Bq
^{57}Co	Lung Counting	γ-ray spectrometry	4-5Bq	4 Bq

^{58}Co

(364) ^{58}Co is a high energy γ emitter. Monitoring of ^{58}Co is in general accomplished through Whole Body Counting. Urine bioassays are also used in monitoring for ^{58}Co. If needed lung monitoring may be performed.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{58}Co	Urine Bioassay	γ-ray spectrometry	0.4 Bq/L	0.03Bq/L
^{58}Co	Whole Body Counting	γ-ray spectrometry	30-40 Bq	9 Bq
^{58}Co	Lung Counting	γ-ray spectrometry		4 Bq

^{60}Co

(365) ^{60}Co is a high energy γ emitter. Monitoring of ^{60}Co is in general accomplished through Whole Body Counting. Urine bioassays are also used in monitoring for ^{60}Co. If needed lung monitoring may be performed.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{60}Co	Urine Bioassay	γ-ray spectrometry	0.4 Bq/L	0.1 Bq/L
^{60}Co	Whole Body Counting (shielded room)	γ-ray spectrometry	30-40 Bq	10 Bq
^{60}Co	Lung Counting	γ-ray spectrometry		8 Bq

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9. ZINC (Z = 30)

9.1. Chemical Forms in the Workplace

(366) Zinc is a transition metal, which occurs mainly in oxidation state II. Zinc may be encountered in industry in a variety of chemical and physical forms, including metal dusts, oxides, phosphates, sulphides or as soluble salts (sulphates, nitrates, chlorides), and chromates.

(367) Zinc-65 is a major activation product in nuclear power plants and could be present in corrosion particles.

Table 9-1. Isotopes of zinc addressed in this report

Isotope	Physical half-life	Decay mode
Zn-62	9.186 h	EC, B+
Zn-63	38.47 m	EC, B+
Zn-65[a]	244.06 d	EC, B+
Zn-69	56.4 m	B-
Zn-69m	13.76 h	IT, B-
Zn-71m	3.96 h	B-
Zn-72	46.5 h	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

9.2. Routes of Intake

9.2.1. Inhalation

Absorption Types and parameter values

(368) Little information was found on the behaviour of inhaled zinc in man, and it is difficult to estimate the contribution of absorption to lung clearance in such cases, because the systemic excretion of zinc is predominantly by the faecal route. Information is available from experimental studies of several compounds of zinc, or associated with corrosion products.

(369) Absorption parameter values and Types, and associated f_A values for particulate forms of zinc are given in Table 9-2.

Zinc oxide

(370) Following inhalation of zinc oxide by rats, Oberdörster et al. (1979) observed a lung retention half-time of about 6 hours, with 7% of the initial lung deposit (ILD) retained at 24 hours. Rosaminth and Breining (1974) administered zinc oxide to rats by instillation five times over 14 days, and less than 2% of the total ILD was retained 7 days later. Hirano et al. (1989) also administered zinc oxide to rats by instillation and observed a lung retention half-time of about 15 hours, with negligible retention after 5 days. The results of all three studies (with stable zinc oxide) are consistent with the assignment to Type F.

Zinc chromate

(371) Following intratracheal instillation of zinc ^{51}Cr-chromate to rats, 25% ILD remained at 30 minutes, and from 30 minutes to 6 days the retention half-time was 1.9 days, consistent

with assignment to Type F (Bragt and van Dura, 1983).

Zinc nitrate

(372) Morrow et al. (1968) followed lung clearance of ^{65}Zn for 70 days after inhalation of $^{65}Zn(NO_3)_2$ by dogs and rats, but few details are given. Lung retention in dogs was described by a two-component exponential function with half-times of 4 days (53%: clearance rate 0.17 d^{-1}) and 120 days (clearance rate 0.0058 d^{-1}), giving lung retention at 30 d to be 40% ILD, consistent with assignment to Type M.

Zinc phosphate

(373) Morrow et al. (1968) followed lung clearance of ^{65}Zn for 65 days after inhalation of $^{65}Zn_3(PO_4)_2$ by dogs and rats, but few details are given. Lung retention in dogs was described by a two-component exponential function with half-times of 7 days (58%: clearance rate 0.099 d^{-1}) and 330 days, (clearance rate 0.0021 d^{-1}), giving lung retention at 30 d to be 42% ILD, consistent with assignment to Type M.

Corrosion Products (contaminated dusts or 'residues' formed at nuclear power plant (NPP)

(374) The biokinetics of ^{65}Zn were followed for 280 days after intratracheal instillation into rats of a suspension of corrosion 'crud' particles (oxide bearing debris, 11% ^{65}Zn activity) from the primary containment of a water cooled reactor (Collier et al., 1994). Few details are given, but it was assessed by the task group that the results are consistent with assignment of the ^{65}Zn present to Type S.

Other compounds

(375) In one case of accidental human exposure to dust from an experimental hole in a reactor, ^{65}Zn was rapidly cleared from the lungs except for a small component that was retained for a period of several months, indicating Type F (Newton and Holmes, 1966). Measurements have also been reported following accidental intakes of ^{65}Zn from metallic zinc (Andrasi and Feher, 1967) and reactor graphite dust (Sedlet and Fairman, 1970), but there is insufficient information to assign the material to absorption Types, since excretion of systemic zinc is predominantly faecal.

Rapid dissolution rate for zinc

(376) There is insufficient experimental information to estimate the rapid dissolution rate for zinc. There is therefore no justification for choosing a rate different from the general default value of 30 d^{-1}, which is applied here to all Type F forms of zinc.

Extent of binding of zinc to the respiratory tract

(377) Evidence from the zinc oxide studies outlined above suggests that there is probably little binding of zinc. It is therefore assumed that for zinc the bound state can be neglected, i.e. $f_b = 0.0$.

Table 9-2. Absorption parameter values for inhaled and ingested zinc

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Oxide, chromate	1	30	-	0.5
M	Nitrate, phosphate, all unspecified compounds[d]	0.2	3	0.005	0.1
S	Corrosion products	0.01	3	$1x10^{-4}$	0.005
Ingested materials					
All forms					0.5

[a] It is assumed that for zinc the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of zinc (30, 3 and 3 d^{-1}, respectively) are the general default values.

[b] Materials (e.g. zinc oxide) are 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 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 and the f_A value for ingested soluble forms of zinc ($5x10^{-1}$).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

9.2.2. Ingestion

(378) Studies in which ^{69m}Zn was administered as chloride to three fed volunteers showed gastrointestinal absorption of zinc of about 0.2 (Molokhia et al., 1980).

(379) Zinc absorption in humans is influenced by numerous factors including fasting, meal composition, the amount of daily dietary zinc and the state of health. Experiments performed on five fasting volunteers showed fractional absorption values ranging from 0.4 to 0.8 (Molokhia et al., 1980). Similar experiments performed on 75 fasting subjects given carrier-free ^{65}Zn, showed similar fractional absorption values, ranging from 0.4 to 0.86 (Aamodt et al., 1981).

(380) When stable or radioactive zinc isotopes were incorporated into meals fed to normal adult subjects, the mean absorption values ranged between 0.05 and 0.5, with a value of about 0.3 being typical (ICRP, 1993). It has been suggested that some foods, such as milk and beef may enhance dietary zinc uptake (Evans and Johnson, 1980; Solomons et al., 1982), while bran and phytate reduce it (Turnland et al., 1984; Sandstrom and Cedarblad, 1980).

(381) Experiments performed with eight healthy subjects showed that when the amount of dietary zinc intake decreased from 15 to 2 $mg.day^{-1}$, this resulted in an increase of fractional zinc absorption from 0.6 to about 0.9 (Istfan et al., 1983). Similarly, studies performed with ^{68}Zn or ^{70}Zn sulfate given to eight fed volunteers together with doses of aqueous zinc decreasing from 30 to 2 mg, showed that fractional absorption values increased from 0.37 to 0.73 (Tran et al., 2004).

(382) Zinc absorption has been reported to be reduced in the elderly (Turnlund et al., 1982) and in the cirrhotic (Mills et al., 1983).

(383) In *Publication 30* (ICRP, 1980), an absorption value of 0.5 was recommended for all forms of Zn. The same value was adopted in *Publication 67* (ICRP, 1993) for dietary intakes. An f_A of 0.5 is also used in this report for all chemical forms.

9.2.3. Systemic Distribution, Retention and Excretion

9.2.3.1. Overview of zinc biokinetics and balance in adult humans

(384) Zinc is an essential trace element required for normal growth, protein production, and function of numerous enzymes in mammals (NAS, 1979; Walravens, 1979; Vallee and Falchuk, 1993; Lowe et al., 2009). Dietary intake of zinc by adults generally is in the range 7-20 mg d^{-1} (Buchet et al., 1983; van Dokkum et al., 1989; Bro et al., 1990; Anke et al., 1991; Becker and Kumpulainen, 1991; Ysart et al., 2000; Hunt and Meacham, 2001; Jaiswal et al., 2002; Conacher, 2003; Noel et al., 2003; Suzuki et al., 2003). Gastrointestinal uptake averages about 30-35% but varies with the level of zinc in diet, timing of intake relative to meals, and other factors (Hambidge et al., 1998; Krebs and Hambidge, 2001; Lowe et al., 2009).

(385) Fecal loss is the primary route of excretion of zinc. Endogenous fecal excretion appears to arise largely from pancreatic secretions into the small intestine contents, with smaller amounts transferred into the gastrointestinal contents in liver bile, saliva, and other secretions (McClain, 1990; Hambidge et al., 1998). Daily excretion in urine typically is about 0.3-0.5 mg (Spencer et al., 1973; Elinder et al., 1978; Wastney et al., 1991; Schuhmacher et al., 1994; Scott and Turnlund, 1994). The amount of zinc lost in sweat under normal conditions appears to be of the same order as losses in urine (Jacob et al., 1981; Johnson et al., 1993).

(386) Following acute entry of labeled zinc into blood, 60% or more of the label rapidly accumulates in the liver (Siegel et al., 1961; Spencer et al., 1965; Aamodt et al., 1979). Relatively high concentrations are also seen in the kidneys and pancreas at early times (Siegel et al., 1961; Spencer et al., 1965). Over a period of weeks the label shifts largely to skeletal muscle and bone, which have low rates of accumulation but long retention of zinc (McKenney et al., 1962; Khristov, 1970; Aamodt et al., 1982).

(387) External measurements ^{65}Zn in human subjects following intravenous or oral administration indicate two main components of systemic retention with half-times on the order of 1-3 wk (15-30%) and 300-450 d (70-85%) (Richmond et al., 1962; Spencer et al., 1965; Aamodt et al., 1982). Biokinetic studies on human subjects have not been sufficiently long to identify small components of retention with extremely long half-times that may arise, for example, from binding of zinc to bone mineral.

(388) The mass of stable zinc in the total body of adult humans is on the order of 2 g (ICRP, 1975; NAS, 1979; Zhu et al., 2010). Muscle contains about 55-65% and bone about 20-30% of the body's zinc.

Summary of the database

Human studies

(389) Siegel et al. (1961) measured ^{65}Zn concentrations in tissue samples taken at autopsy 1-174 d after intravenous injection of ^{65}Zn as chloride into 14 terminal patients with various malignancies. The liver, pancreas, spleen, prostate, seminal vesicles, lung, urinary bladder, and skeletal muscle were sampled. Widely differing concentrations of ^{65}Zn were found in different tissues. The highest levels were found in the liver, in which the concentration reached about 0.05% of the administered activity per gram of tissue in the first few days after administration. This value was about 2-8 times that in the pancreas, which contained the second highest concentrations at early times, and about 10-30 times that in muscle, which

contained the lowest concentrations at early times. Turnover was relatively slow in the liver and relatively fast in the pancreas. The concentration in the pancreas was reduced by about two-thirds within a week, while the concentration in the liver remained high after 81 d.

(390) Richmond et al. (1962) measured uptake, excretion, and whole-body retention of acutely ingested ^{65}Zn in one healthy female subject (A) of age 31 y and three healthy male subjects (B, C, D) of ages 29, 45, and 48 y, respectively. Measurements for Subjects A-D were continued up to 431, 664, 416, and 579 d after intake, respectively. Excretion of absorbed activity was primarily in faeces. Whole-body retention in each subject could be represented as a sum of three exponential terms representing fast, intermediate, and slow turnover. Assuming the term with fast turnover (half-time <30 h) represented fecal excretion of unabsorbed activity, about 20% (range 16-27%) of absorbed activity was lost with a mean biological half-time of 16 d (4.5-26 d) and 80% (73-84%) was lost with a mean half-time of 420 d (387-478 d).

(391) Spencer et al. (1965) investigated the biokinetics of intravenously injected ^{65}Zn in 19 patients, at least 11 of whom had terminal cancers. Whole blood of a subject described as representative contained about 22% of the injected amount at 13 min, 11% at 1 h, 5% at 2 h, 4% at 10 d, and 3% at 40 d. Measurements on three subjects indicate that 75-90% of the activity in total blood was contained in cellular components at 2-29 d after administration of ^{65}Zn. The main pathway of excretion was via the gastrointestinal tract. In two subjects followed over 45 d, cumulative fecal and urinary excretion averaged 19.2% and 2.1%, respectively, of the administered amount. Urinary excretion of activity became extremely low after the first few days, while a small but nearly constant fraction was excreted daily in faeces for an extended period. Whole-body retention measurements made on each of two subjects for approximately 1 y could be closely approximated as a sum of two exponential terms representing fast and slow components of turnover. The biological half-times of the fast component, representing about one-fourth of the injected amount, were 13.1 and 11.8 d in the two subjects. The half-times of the slow components were 334 and 308 d, respectively. In tissue samples obtained at autopsy from 11 subjects dying from metastatic cancers at 1-71 d after administration of ^{65}Zn, the activity concentration was higher in the liver than other tissues over the entire period. The kidney showed the next highest concentration, averaging about half of that in liver, over the entire observation period. Relatively high concentrations were also seen in the pancreas, spleen, and adrenals over the early days or weeks after administration of ^{65}Zn. The concentration in the liver at 71 d was still about one-fourth of that at 1 d. Concentrations of ^{65}Zn in samples of bone and skeletal muscle were relatively low. The activity concentrations in samples from the vertebrae, ribs, and sternum were substantially higher than in samples from the femur of the same subject.

(392) In a case of accidental inhalation of ^{65}Zn, whole-body measurements indicated that 27% of the inhaled activity was retained in the body with a half-time of 18 d and 73% was retained with a half-time of 453 d (Newton and Holmes, 1966). Similar half-times were estimated from time-dependent activity in faeces. A widespread distribution of activity with a relatively high concentration in the liver was apparent throughout the study. An estimated 20-30% of the total daily excretion of ^{65}Zn was in urine.

(393) Hawkins et al. (1976) studied the biokinetics of orally administered ^{65}Zn in nine subjects with skin diseases. The study was motivated by reported findings that some skin diseases respond dramatically to treatment with zinc, and that low plasma zinc concentrations are associated with some skin diseases. Whole blood and plasma concentrations of ^{65}Zn were measured up to 192 d, and whole-body retention was measured externally up to 231 d. Whole-body retention measurements indicated that average absorption of ^{65}Zn from the gut in these subjects exceeded 70%. Whole-body retention R(t) of absorbed activity as a function of

time t (days) in each subject could be represented reasonably well as a sum of two exponential terms: $R(t) = A_1\exp(-0.693t/B_1) + A_2\exp(-0.693t/B_2)$, where the terms represent short- and long-term components of retention, respectively. The coefficients A_1 and A_2 represented on average about 16% and 84% of the absorbed amount, respectively. The biological half-times B_1 and B_2 averaged about 23 d and 399 d, respectively. These results are reasonably consistent with findings of Richmond et al. (1962) for healthy subjects. A subgroup with venous leg ulcers showed a smaller component of long-term retention and a shorter long-term biological half-time than the other subjects. External measurements indicated a high concentration of ^{65}Zn in the liver at early times.

(394) Aamodt and coworkers (Aamodt et al., 1979; Foster et al., 1979) studied the short-term biokinetics of orally or intravenously administered ^{69m}Zn ($T_{1/2}$ = 13.8 h) in 17 subjects with taste or smell dysfunction. Activity was measured over the first five days in total body, urine, faeces, total blood, plasma, and RBC, and externally over the liver and thigh. The biokinetics of zinc did not appear to be affected by the mode of administration. Biological clearance from blood plasma as a function of time t (days) following intravenous administration was described as a four-exponential retention function, $R(t) = 0.79\exp(-176t) + 0.175\exp(-73.4t) + 0.022\exp(-5.87t)+0.013\exp(-0.053t)$. The liver accumulated about 50% of the intravenously injected activity during the first 15 min and reached a peak content of about 60% at 2 h. Activity measured over the thigh increased with a doubling time of about 5.7 d after both oral and intravenous injection. The rate of buildup in the thigh corresponded roughly to the rate of loss from the liver. Activity in RBC increased over the five-day observation period to 6.4% of the injected amount and 2.4% of the ingested amount.

(395) Aamodt et al. (1982) studied the effects of oral zinc loading on the biokinetics of zinc in 50 patients with taste or smell dysfunction for up to 440 d following acute ingestion of ^{65}Zn ($T_{1/2}$ = 244 d). The study was conducted in three phases: (1) all patients were studied for 21 days after oral intake of ^{65}Zn as $ZnCl_2$; (2) from 21 to 290-440 d (mean 336 d), all 50 subjects received placebo for $ZnSO_4$, which was later used for zinc loading; (3) over the next 112-440 d (mean 307 d), 14 patients continued on placebo while 36 ingested high levels of stable zinc (100 mg d^{-1}) as $ZnSO_4$. Prior to zinc loading, retention of absorbed zinc could be represented as a sum of two exponential terms with biological half-times of 18.2 d (32%) and 380 d (68%). Retention during the second (placebo) phase was not significantly different for the 36 subjects subsequently treated with $ZnSO_4$ and the 14 who were continued on placebo through the third phase of the study. Subjects receiving $ZnSO_4$ during the third phase showed accelerated loss of ^{65}Zn (half-time 235 +/- 8 days). Accelerated loss of ^{65}Zn from the thigh, presumably representing mainly loss from muscle, was apparent immediately in these 36 subjects. Accelerated loss from the liver began after a mean delay of 107 days. There was no apparent effect of zinc loading on loss of activity from RBC.

(396) Wastney et al. (1986) studied zinc metabolism in 32 normal subjects after oral (n = 25) or intravenous (n = 7) administration of ^{65}Zn. Activity was measured in blood, urine, faeces, whole body, liver, and thigh over a nine-month period of normal intake of stable zinc (~10 mg d^{-1}) and an additional nine-month period with supplemental zinc intake of 100 mg d^{-1}. Comparison of kinetic data derived during periods of normal and high intake of zinc suggested up to five sites of regulation of zinc concentrations in the body: absorption from the gut, endogenous secretion into the gut, urinary excretion, exchange between plasma and RBC, and release by muscle.

(397) Wastney et al. (1992) assessed changes in zinc metabolism with age based on biokinetic studies of intravenously or orally administered ^{65}Zn in 26 healthy men and 21 healthy women in the age range 20-84 y. The studies covered a nine-month period in with dietary intake of stable zinc was approximately 10 mg/day, followed by a nine-month period

in which intake was approximately 110 mg/day. Zinc-65 kinetics was analyzed by compartmental analysis using measurements of zinc isotopes in plasma, red blood cells, urine, faeces, liver, thigh, and whole body. Significant changes with age in ^{65}Zn kinetics were determined for urinary excretion, exchange between plasma and red blood cells, absorption, and endogenous secretion.

(398) Miller et al. (1994) describe a four-compartment approximation of the model of Wastney et al. (1986). The simplified model consists of a plasma compartment and three satellite compartments representing fast, intermediate, and slow turnover of tissue zinc. The transfer coefficients from plasma to the fast, intermediate, and slow pools and to excretion pathways derived from the collective injection data are 85, 40, 4, and 2.4 d^{-1}, respectively. Removal half-times from the fast, intermediate, and slow pools back to plasma based on the injection data are approximately 112 min, 18 h, and 108 d, respectively. The plasma clearance curve based on these parameter values closely approximates the curve determined in the study by Aamodt and coworkers (Aamodt et al., 1979; Foster et al., 1979) describe above.

(399) Zinc metabolism and balance were studied in 11 healthy men with adequate or low levels of dietary zinc (Johnson et al., 1993). In terms of the mass of zinc excreted daily, urinary zinc decreased with decreasing zinc intake while surface losses, presumably representing mainly losses in sweat, were unaffected by the level of zinc in diet. On average, urinary losses represented 6-7% of dietary zinc during periods of adequate zinc intake and 13-16% during periods of low intake. Fecal excretion represented about two-thirds of dietary zinc during periods of adequate dietary zinc and 39-48% in periods of low intake. Surface losses represented 4-6% of dietary intake during periods of adequate zinc intake and 12-36% during periods of low intake. The estimated surface losses during periods of adequate dietary zinc are reasonably consistent with results of a study by Jacobi et al. (1981) in which an effort was made to collect total-body sweat from 13 male subjects living in a controlled environment for several months.

(400) Lowe et al. (1997) developed a model of the short-term biokinetics of zinc based on stable isotope studies on six healthy women of mean age 30 y. Oral and intravenous tracers enriched in ^{67}Zn and ^{70}Zn, respectively, were administered simultaneously following a seven-day zinc equilibration period involving a controlled diet. Plasma and urine samples were collected over the first 7 d and fecal samples over the first 11 d. A seven-compartment model was developed to describe the kinetics of both tracers as well as that of naturally occurring zinc. The model structure was used to derive the following central estimates from the measurements: fractional absorption from the gastrointestinal tract, 0.28; daily endogenous secretion, 2.8 mg; daily endogenous excretion, 2.0 mg; fractional turnover rate of the plasma pool, 131 d^{-1}; sizes of extravascular compartments representing fast and slow equilibration with plasma, 7.2 mg and 77 mg, respectively; fractional turnover rates of these rapidly and slowly equilibrating pools, 22 d^{-1} and 1.5 d^{-1}, respectively; and size and turnover rate of an extravascular pool with very slow turnover, 1083 mg and 0.014 d^{-1}, respectively. Extrapolation of model predictions to infinity based on average parameter values indicated that cumulative fecal and urinary excretion represented 97.3% and 2.7%, respectively, of the oral tracer and 91.4% and 8.6%, respectively, of the intravenous tracer.

(401) King et al. (2001) used stable zinc tracers to compare the biokinetics of zinc in five men, ages 21-35 y, during normal zinc intake and following acute zinc depletion. The study was divided into two metabolic periods: a 16-d baseline period with dietary zinc of 12.2 mg d^{-1} and a 41-d depletion period with intake of 0.23 mg d^{-1}. Stable isotope tracers of zinc were administered on days 6 or 7 of the baseline period and at the end of the depletion period (day 35). Baseline kinetic data indicated average gastrointestinal absorption of about 26%, a

plasma zinc concentration of 0.71 µg ml^{-1}, fecal excretion of 9.8 mg d^{-1} (about 80% of dietary zinc), urinary excretion of 0.46 mg d^{-1} (about 4% of dietary zinc), and total-body content of about 1600 mg. The modeled rate of transfer of zinc from plasma to other compartments was approximately 144 d^{-1}. After zinc depletion, gastrointestinal absorption was virtually complete, plasma zinc fell on average by 65%, and fecal and urinary excretion fell by 96% and 74%, respectively.

(402) Pinna et al. (2001) studied the effects of low dietary zinc (4.6 mg/d) on the mass of exchangeable zinc pools and its turnover time in seven healthy men confined during a 20-wk clinical study. The estimated mass of exchangeable zinc was maintained when dietary zinc was reduced to roughly one-third the recommended daily allowance over a 10-wk period. Data analysis based on a three-compartment model indicated that the masses of plasma zinc and total exchangeable zinc were 3.25 and 148 mg, respectively, over the different phases of the study. Plasma zinc turned over 5.3 times per hour on average. There was a modest reduction in plasma zinc at 3 wk after the start of the low zinc diet period, but plasma zinc returned to baseline values after 10 wk of zinc restriction.

(403) The concentration of stable zinc in autopsy samples of ribs from Japanese subjects increased with age from early adulthood to age 60 y (Yoshinaga et al., 1989). There was no clear change with age after age 60 y.

(404) Aitken (1976) measured the zinc content of trabecular and cortical bone from 16 male and 12 female cadavers. The mean zinc to calcium ratio was 0.63 µg/mg for trabecular bone and 0.45 µg/mg for cortical bone. There was a significant increase with age in the zinc to calcium ratios of both trabecular and cortical bone.

(405) Alhava et al. (1977) determined the concentration of zinc in cancellous bone of the iliac crest from 66 male and 28 female cadavers. The concentration was statistically related to age despite a large variability in subjects of nearly the same age. The concentration reached a maximum during the fifth decade of life in both men and women. Men who died suddenly had a higher concentration than those with a chronic disease.

(406) Typical (reference) contents of zinc in the total body and specific tissues and fluids of adult humans are listed in Table 9-3. Concentrations in plasma and RBC are based on analyses of samples from living subjects (NAS, 1979; Wastney et al., 1991; Scott and Turnlund, 1994). The other listed concentrations are rounded values based on a review of reported measurements of zinc in tissues collected postmortem, in many cases from subjects who had apparently been in good health up to the time of sudden accidental death (Tipton and Cook, 1963; Tipton and Shafer, 1964; Tipton et al., 1965; Strehlow and Kneip, 1969; Soman et al., 1970; Forssén, 1972; Hamilton et al., 1972; McBean et al., 1972; Evenson and Anderson, 1975; Sumino et al., 1975; Zhu et al., 2010). Median concentrations determined by Tipton and coworkers (Tipton and Cook, 1963; Tipton et al., 1965) for soft tissues other than liver were judged to be typical of reported values and were used in Table 9-3. Central estimates for liver reported by Tipton and coworkers are lower than most reported values and were replaced by the median of reported values from 14 studies of the zinc concentration in adult human liver tissue (see Table 6 of Evenson and Anderson, 1975). The zinc concentration in bone listed in Table 9-3 is based on measurements reported by Tipton and Shafer (1964), Strehlow and Kneip (1969), and Aitken (1976), which together address zinc concentrations in bone tissue sampled from several skeletal sites. Conversions of concentrations to total contents were based on reference masses of tissues and fluids given in ICRP *Publication 89* (2002).

Table 9-3. Reference zinc contents in tissues and total-body of adult humans.

	Concentration (μg/g)	Tissue contents (mg)		Sex-averaged distribution of stable zinc in the body (% per organ or tissue)
		Adult male	Adult female	
Adipose tissue	3	55	67	3.0
Blood plasma	1	3	2.5	0.14
Bone	110	600	440	26
Brain	11	16	14	0.75
Gastrointestinal tract	20	23	22	1.14
Gonads	15	0.5	0.15	0.0164
Heart	30	10	7.5	0.44
Kidneys	50	16	14	0.75
Liver	70	130	100	5.8
Lung	14	7	6	0.33
Muscle	50	1450	870	58
Pancreas	28	4	3.5	0.19
Prostate	83	1.4	--	0.035
Red blood cells	12	29	19	1.2
Skin	6	20	14	0.85
Spleen	18	3	2.5	0.14
Thyroid	30	0.6	0.5	0.028
Urinary bladder	24	1.2	1	0.055
Total-body zinc (mg)	--	2400	11600	2000

Animal studies

(407) The biokinetics of zinc has been studied in different animal species following acute or chronic administration of zinc tracers. Although some species differences are indicated, the animal studies provide insights into aspects of the biokinetics of zinc not clearly defined by kinetic studies on humans such as its skeletal behavior. Species-specific biokinetic models for zinc have been developed from isotopic studies on rats (House et al., 1982; Dunn and Cousins, 1989; House and Wastney, 1997), mice (Wastney and House, 2008), and pigs (Serfass et al., 1996).

(408) Following intravenous injection of ^{65}Zn into mice, the highest activity concentration over the first 7 d was found in the pancreas followed by the liver and kidney (Sheline et al., 1943). As much as 50% of the administered activity was eliminated in faeces during the first 7 d. The rate of elimination in urine was substantially lower than that in faeces.

(409) Following intravenous injection of ^{65}Zn into dogs, about 25% of the administered activity was eliminated in faeces during the first two weeks (Montgomery et al., 1943). Substantially less was lost in urine. The liver contained about 38% of the administered amount at 3 h and about 3.5% at 7 d. A maximum of 0.4% of the administered activity appeared in bile in the first 8 d. As much as 11% of the injected amount was secreted in pancreatic juice in the first 14 d. Activity was also found in large amounts in the juices obtained from an isolated loop of the duodenum.

(410) The concentration of ^{65}Zn was measured in rat tissues over 42 d following intravenous injection (Wakeley et al., 1960). At 1 d after administration the highest concentration was found in pancreas followed by prostate and liver. Thereafter the concentration in prostate was at least twice that in any other tissue. Bone showed the next

highest concentration after the first week. Initial biological half-times for pancreas, liver, kidneys, and muscle were 0.8 d, 1.25 d, 1.7 d, and 40 d, respectively.

(411) Ballou and Thompson (1961) investigated the biokinetics of ^{65}Zn administered to rats by intravenous injection, acute oral intake, or chronic feeding. Following intravenous administration the highest activity concentrations were found in liver, kidneys, and pancreas at early times and in bone at late times. After chronic feeding for 200-400 d the highest concentrations were found in hair, bone, and prostate. The concentration did not reach steady state in these tissues during the feeding studies.

(412) Taylor (1961) measured the retention of ^{65}Zn in the femur, pelvis, and humerus of rats over a period of 630 d following its intravenous injection into 7-wk-old animals. Retention in each bone could be described as a single exponential function. The mean removal half-time was 738 d. Measurements of the specific activities of ^{65}Zn in these three bones and in the ribs at 7 d after injection indicated that the ^{65}Zn was distributed nearly uniformly throughout the zinc content of the skeleton.

(413) Haumont (1961) used histochemical methods to examine the distribution of zinc in bones of young adult dogs and immature rats. High concentrations of zinc were found at sites undergoing calcification. Zinc was detected in the haversian systems of compact bone at the border line between calcified and uncalcified tissue, in the cartilaginous partitions of hypertrophic cells, and in endochondral bone recently deposited in the metaphysis.

(414) Calhoun et al. (1970) observed a significantly increased uptake of ^{65}Zn in healing bones of rats compared with control rats following its intravenous administration. Uptake of ^{65}Zn at the injured site appeared to be correlated with bone formation. No statistically significant difference was found in the uptake of ^{85}Sr or ^{45}Ca in the injured bones and bones of control animals.

(415) Bergman et al. (1972) examined the importance of zinc to cell proliferation in endochondral growth sites of bone in white rats using zinc-deficient feeding and autoradiography. The results of the study suggest that zinc is required in bone formation, especially in the synthesis of the organic matrix.

(416) The time-dependent distribution and excretion of ^{65}Zn was studied in rats following a single subcutaneous, intratracheal, or intraperitoneal administration (Khristov, 1970). The relative contents of tissues as a function of time were similar for all modes of administration. Highest initial activity concentrations were found in the pituitary, pancreas, and liver. At 25 d the highest concentrations were found in pituitary and bone. Excluding activity found at the injection site, total-body retention following subcutaneous injection was approximately 65% at 1 d, 44% at 10 d, and 37% at 25 d post injection. The liver, muscles, and bones contained, respectively, about 24%, 22%, and 32% of the retained activity at 1 d; 7%, 34%, and 31% at 10 d; and 4%, 36%, and 52% at 25 d.

(417) The uptake and distribution of ^{65}Zn were measured in rams at 5, 10, and 20 d after single oral or intravenous injection and in pregnant ewes and a ram 2 wk after the start of daily feeding (McKenney et al., 1962). The liver and kidney cortex initially contained the highest concentrations of activity. After 20 d bone and muscle has substantially higher concentrations than the liver and kidney cortex. The relative concentrations in tissues at 20 d after single intake were independent of the route of administration. After daily feeding the highest concentrations were found in decreasing order in liver, kidney cortex, mammary tissue, pancreas, and spleen.

(418) Richmond et al. (1962) measured uptake and retention of ^{65}Zn after a single oral uptake of $^{65}ZnCl_2$ by dogs, rats, and mice and after intravenous injection of ^{65}Zn into rats and mice. Maximum observation periods were 137, 164, and 540 for mice, rats, and dogs, respectively. Fecal excretion represented the primary mode of elimination in all animals.

Detailed studies of the tissue distribution in rats indicated that rates of loss were similar for tissues other than bone and pelt, which retained zinc more tenaciously than other tissues.

(419) Studies on weanling and 7-week-old mice were conducted to investigate whether bone serves as a reservoir of available zinc (Murray and Messer, 1981). The results indicated that availability of bone zinc depended on the rate of bone resorption but not on zinc status and that the skeleton does not serve as an available reservoir for zinc. Redeposition of zinc in the skeleton following resorption was extensive and independent of the rate of bone mineral deposition. In calcium deficiency there was an increased deposition of zinc, suggesting limited substitution of zinc for calcium in bone mineral.

(420) Feaster et al. (1954) studied the behavior of ^{65}Zn in steers over the first 6 d following acute oral or intravenous administration. Tissue concentrations at 6 d decreased in the order pancreas > liver > pituitary, kidneys, rib sternal end, adrenals > mandible > rib shaft, incisors > whole blood. Accumulation in different bones or portions of bone paralleled their metabolic activity, with highest accumulation in sites with highest blood flow and trabecular bone accumulating more zinc than cortical bone per gram of tissue.

(421) At 7 and 14 d after intravenous injection of ^{65}Zn into young horses the tissue concentrations decreased in the order liver > pancreas > spleen, kidney, heart, lung > rib, femur, skeletal muscle, skin > whole blood, adipose tissue, tibia, metatarsus (Schryver et al., 1980). Tissue samples from the wall of the gastrointestinal tract contained higher concentrations of ^{65}Zn than sampled contents of the tract. Addition of stable zinc to the diet increased the rate of elimination of ^{65}Zn from the body.

(422) House et al. (1982) studied zinc metabolism in male rats by combining nutritional balance methods with an analysis of ^{65}Zn kinetics. Disappearance of zinc from plasma was described by a four-exponential retention function. Measurement of zinc in tissues at different times indicated that plasma zinc exchanged more rapidly with zinc in liver and kidneys than it did with zinc in testes, skeletal muscle, or bone. The total body zinc content was about nine times higher than estimates of exchangeable zinc in the body.

(423) Lowe and coworkers (1991, 1993, 1995) found that intravenously injected zinc isotopes followed similar two-compartment kinetics in rats, dogs, and human subjects over the first few hours after administration. Investigation into the location of the two metabolic pools in the rat indicated that the smaller pool consisted mainly of plasma zinc and the larger pool resided largely within the liver. In normal human subjects the fractional turnover rate of the smaller pool was fivefold faster than that of the larger pool.

(424) House and Wastney (1997) determined zinc kinetics in 15 tissues of rats and analyzed the data using modeling techniques. The study revealed the existence of slow and fast pools of zinc in muscle and bone.

9.2.3.2. Biokinetic model for systemic zinc

(425) The biokinetic model for systemic zinc is taken from a paper by Leggett (2012). The model structure is shown in Figure 9-1. Baseline transfer coefficients for workers are listed in Table 9-4.

(426) The model includes three groups of tissues representing rapid (minutes to hours), intermediate (days), and slow (weeks to years) exchange with plasma, as indicated by a number of studies of the behavior of zinc tracers in human subjects. Rapid exchange occurs between plasma and liver, and between plasma and a soft-tissue compartment called ST0. The kidneys, pancreas, RBC, and a soft-tissue compartment called ST1 have intermediate rates of exchange with plasma. Also, part of the zinc entering the liver moves to a compartment called Liver 2 that returns zinc to plasma with a half-time of a few days.

Muscle, bone, and a soft-tissue compartment called ST2 exchange zinc slowly with plasma. Each of the soft-tissue compartments ST0, ST1, and ST2 is assumed to be uniformly distributed in "Other soft tissues", which represents all soft tissues except liver, kidneys, pancreas, and muscle.

(427) Bone is divided into four compartments: trabecular bone surface, trabecular bone volume, cortical bone surface, and cortical bone volume. Bone surface exchanges zinc slowly with plasma. A small portion (5%) of zinc depositing on bone surface transfers to bone volume, from which it is removed to plasma at the rate of bone remodeling, assumed to be 18% y^{-1} for trabecular bone and 3% y^{-1} for cortical bone (ICRP, 2002).

(428) Systemic zinc is assumed to be removed from the body in faeces, urine, and surface loss representing mainly sweat. Urinary excretion is represented as a transfer from plasma to the urinary bladder contents followed by transfer to urine at the rate 12 d^{-1}, the generic value for adults used in ICRP documents on environmental and occupational exposure (ICRP, 1993). Surface loss is represented as a direct transfer from plasma to the environment. Endogenous fecal excretion of zinc is assumed to arise mainly (80%) from secretion into the gastrointestinal contents in pancreatic juice, represented as a transfer from pancreas to small intestine contents. The remaining endogenous fecal excretion is assumed to be equally divided between biliary secretion, represented as a transfer from liver to small intestine contents, and all other secretions into the alimentary tract combined, represented as a direct transfer from plasma to the small intestine contents.

(429) All secretions into the alimentary tract are assumed to be subject to reabsorption to blood with the same fractional absorption as dietary zinc. Except where otherwise indicated, model predictions given in the following sections are based on absorption of 35% of zinc entering the small intestine contents.

(430) Transfer coefficients between plasma and the liver, kidneys, pancreas, and RBC were set for consistency with observations of accumulation and loss of zinc tracers by these tissues in tracer studies on human subjects (Siegel et al., 1961; Spencer et al., 1965; Aamodt et al., 1979, 1982; Wastney et al., 1986). Transfer coefficients between plasma and other compartments (excluding the generic removal rates from bone volume to plasma, which represent bone turnover rates) were set for reasonable consistency with results of tracer data where available; the typical distribution of stable zinc in adult humans as estimated in Table 9-3, assuming long-term ingestion of zinc at a constant rate; and data for laboratory animals where needed to fill gaps in the database for human subjects.

(431) The total rate of loss of zinc from the body along all excretion pathways combined was set for consistency with observations of whole-body retention of ^{65}Zn in human subjects following acute uptake to blood (Richmond et al., 1962; Spencer et al., 1965; Hawkins et al., 1976; Aamodt et al., 1982). Transfer coefficients describing removal of zinc in faeces, urine, and surface loss were set so that these pathways account for about 80%, 10%, and 10% of total endogenous excretion of zinc, assuming that 35% of endogenous secretion of zinc into the gastrointestinal tract is reabsorbed to blood. The relative quantities of zinc predicted by the model to be excreted in faeces, urine, and surface loss vary to some extent with the assigned gastrointestinal absorption fraction because this affects the level of reabsorption of secreted zinc to blood and hence the amount available for excretion along each pathway.

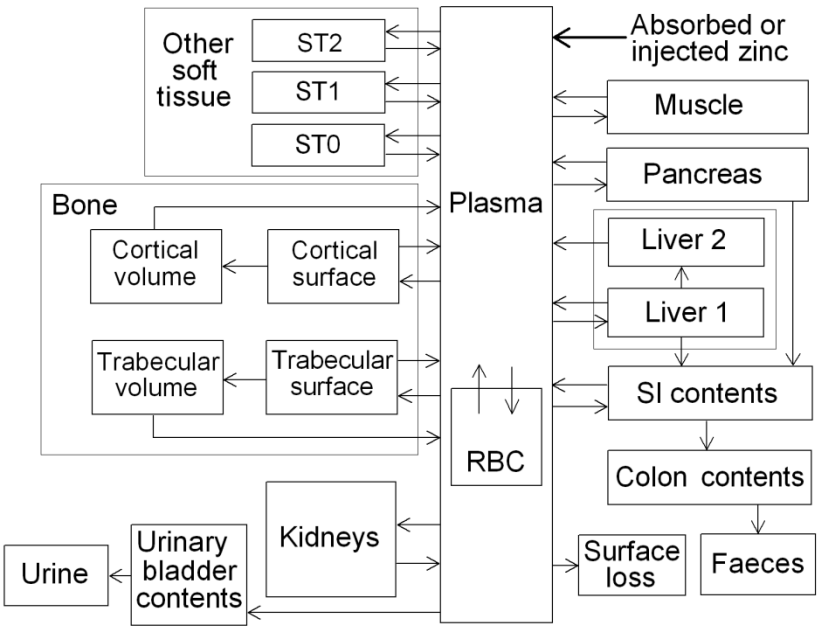

Figure 9-1. Structure of the biokinetic model for systemic zinc. RBC = red blood cells; SI = small intestine; ST0, ST1, and ST2 represent fast, intermediate, and slow turnover, respectively, in soft tissues other than muscle, liver, kidneys, and pancreas.

Table 9-4. Transfer coefficients in the biokinetic model for zinc.

From	To	Transfer coefficient (d^{-1})
Plasma	Liver 1	60
Plasma	Kidneys	4
Plasma	Pancreas	3
Plasma	Muscle	2
Plasma	RBC	1.5
Plasma	ST0	40
Plasma	ST1	30
Plasma	ST2	0.4
Plasma	Urinary bladder contents	0.13
Plasma	Excreta	0.13
Plasma	Small intestine contents	0.2
Plasma	Trabecular bone surface	0.15
Plasma	Cortical bone surface	0.3
Liver 1	Plasma	10
Liver 1	Small intestine contents	0.067
Liver 1	Liver 2	10
Liver 2	Plasma	0.6
Kidneys	Plasma	0.7
Pancreas	Plasma	1.5
Pancreas	Small intestine contents	1.0
Muscle	Plasma	0.005
RBC	Plasma	0.14
ST0	Plasma	10
ST1	Plasma	3
ST2	Plasma	0.01
Trabecular bone surface	Plasma	0.01
Cortical bone surface	Plasma	0.01
Trabecular bone surface	Trabecular bone volume	0.00053
Cortical bone surface	Cortical bone volume	0.00053
Trabecular bone volume	Plasma	0.000493
Cortical bone volume	Plasma	0.0000821

9.2.3.3. Treatment of radioactive progeny

(432) Three isotopes of zinc addressed in this report have progeny that are considered in the derivation of dose coefficients for the parent radionuclide: ^{69m}Zn ($T_{1/2}$ = 13.8 h) decays to ^{69}Zn (56.4 m), ^{62}Zn (9.19 h) decays to ^{62}Cu (9.67 m), and ^{72}Zn (46.5 h) decays to ^{72}Ga (14.1 h). Zinc-69 presumably behaves the same as the parent radionuclide from the time it is produced in the body. Copper-62 produced by decay of ^{62}Zn is assumed to decay at its site of production.

(433) The systemic model for gallium as a daughter of zinc was based on observations of the behavior of gallium in human subjects (Nelson et al., 1972; MIRD, 1973; ICRP, 1981; Priest et al., 1995; Bernstein, 1998), particularly autopsy data for patients administered radio-gallium during terminal illness (Nelson et al., 1972; MIRD, 1973) and results of a biokinetic study of intravenously administered ^{67}Ga in a healthy adult (Priest et al., 1995). The model includes compartments representing blood, liver, kidneys, spleen, pancreas, muscle, trabecular bone surface, trabecular bone marrow, cortical bone surface, and cortical bone marrow, and two compartments representing other soft tissue. Gallium is assumed to leave

blood at the rate 5 d^{-1}, with 20% depositing on bone surface, 10% in marrow, 6% in liver, 8% in kidneys, 4% in muscle, 1% in spleen, 0.1% in pancreas, 3% in right colon contents, 10% in a soft tissue compartment with relatively slow transfer back to blood (half-time of 1 y), and the remainder (37.9%) in a soft tissue compartment with relatively fast transfer back to blood (half-time of 0.5 d). The bone and marrow deposits are assumed to be equally divided between trabecular and cortical bone. Gallium is removed from liver, spleen, pancreas, and muscle to blood with a half-time of 5 d; from kidneys to urinary bladder contents with a half-time of 0.5 d; and from bone surface and marrow to blood with a half-time of 2 d. Blood in the gallium model is identified with the plasma compartment of the zinc model. Gallium produced in compartments of the systemic model for zinc (Figure 9-1) other than plasma are assumed to be transferred to the blood compartment of the gallium model with the following half-times: 1 min for RBC, 5 d for liver compartments, spleen, pancreas and muscle; 0.5 d for kidneys and compartments of other soft tissue; 2 d for bone surface and marrow compartments; and the bone turnover half-time for bone volume compartments.

9.3. Individual monitoring

(434) ^{65}Zn is a γ emitter. Monitoring of ^{65}Zn is in general accomplished through Whole Body Counting or/and urine bioassays.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{65}Zn	Urine Bioassay	γ-ray spectrometry	1 Bq/L	0.1 Bq/L
^{65}Zn	Whole Body Counting	γ-ray spectrometry	80 Bq	20 Bq

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10. STRONTIUM (Z = 38)

10.1. Chemical Forms in the Workplace

(435) Strontium is an alkaline earth element, which mainly occurs in oxidation state II. It is a chemical analogue of calcium. A variety of chemical and physical forms are encountered in industry including, chlorides, sulphates, carbonates and titanate ($SrTiO_3$). ^{85}Sr, ^{89}Sr and ^{90}Sr are the three main fission products which may be encountered in the nuclear industry. Strontium can also be present in fragments of irradiated fuels.

Table 10-1. Isotopes of strontium addressed in this report

Isotope	Physical half-life	Decay mode
Sr-80	106.3 m	EC, B+
Sr-81	22.3 m	EC, B+
Sr-82	25.36 d	EC
Sr-83	32.41 h	EC, B+
Sr-85[a]	64.84 d	EC
Sr-85m	67.63 m	IT, EC, B+
Sr-87m	2.815 h	IT, EC
Sr-89[a]	50.53 d	B-
Sr-90[a]	28.79 y	B-
Sr-91	9.63 h	B-
Sr-92	2.66 h	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

10.2. Routes of Intake

10.2.1. Inhalation

Absorption Types and parameter values

(436) Some information is available on the behaviour of inhaled strontium in man following accidental intakes of several compounds. Information is available from experimental studies of strontium as chloride, sulphate, titanate, irradiated fuel fragments, or in fused aluminosilicate particles (FAP).

(437) Absorption parameter values and Types, and associated f_A values for particulate forms of strontium are given in Table 10-2.

Strontium chloride ($SrCl_2$)

(438) Petkau and Pleskach (1972) measured urinary and fecal excretion of ^{90}Sr for 800 days after a worker's presumed accidental inhalation of strontium chloride, 13 days before the first measurement. The lack of information about the intake, or of measurements during the first week or so after it, limits the conclusions that can be drawn about absorption of the material. The results of measurements made during the first few months suggest that a large fraction (>0.5) was readily soluble, but the later data suggest continuing transfer from the lungs, and hence a low (<0.001 d^{-1}) slow dissolution rate.

(439) Animal experiments have shown that following administration of strontium chloride, most of the strontium is rapidly cleared from the respiratory tract. It was reported that at 12 hours after inhalation of $^{85}SrCl_2$ by dogs, the ^{85}Sr remaining in the lungs was less than 1% of

the total ^{85}Sr in the body (McClellan and Rupprecht, 1967, McClellan et al., 1972), giving f_r ~1. It was calculated by the task group that s_r was greater than 8 d^{-1}. However, it was also noted that a large amount of ^{85}Sr was excreted in faeces in the first few days post exposure, apparently as a result of clearance from the upper respiratory tract, ingestion and only partial gastrointestinal absorption. This shows that in the upper airways the rate of absorption to blood is probably less than the rate of particle transport to the gut (~100 d^{-1}). Morrow et al. (1968) measured a lung retention half time of 0.02 d following inhalation of $^{85}SrCl_2$ by dogs, giving s_r = 35 d^{-1}. Naményi et al. (1986) followed the biokinetics of ^{85}Sr for 45 days after intratracheal instillation of $^{85}SrCl_2$ into rats. Lung retention in healthy control rats was 3.9% of the initial lung deposit (ILD) at 3 hours, from which it was calculated here that s_r = 26 d^{-1}, and about 0.3% ILD at 24 hours. Cuddihy and Ozog (1973) deposited $^{85}SrCl_2$ directly onto the nasal membranes of Syrian hamsters. From the results it was calculated here that f_r = 1 and s_r = 8 d^{-1}. This is somewhat slower than in the other strontium chloride experiments, possibly because of the techniques used, including the anaesthetic, or that clearance from the nasal passage was slower than from the lungs. Similar observations were made for caesium and barium chlorides which were also administered by Cuddihy and Ozog (see caesium and barium inhalation sections).

(440) Based on the results of the experiments outlined above, specific absorption parameter values for strontium chloride were estimated here to be: f_r = 1 and s_r = 30 d^{-1} (consistent with assignment to default Type F). However, although specific parameter values for strontium chloride based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is so unlikely. Instead, strontium chloride is assigned to Type F. However, the data are used as the basis for the default rapid dissolution rate for strontium. Hence specific parameter values for strontium chloride would be the same as default Type F strontium parameter values.

Strontium sulphate ($SrSO_4$)

(441) Following inhalation of $^{90}SrSO_4$ by mice and dogs most of the strontium was rapidly cleared from the lungs, indicating Type F behaviour (Bair, 1961).

Strontium carbonate ($SrCO_3$)

(442) Measurements following accidental inhalation by man of $^{90}SrCO_3$ indicate Type F behaviour (Rundo and Williams, 1961).

Strontium titanate ($SrTiO_3$)

(443) Strontium titanate was shown to be tenaciously retained in the human lungs (Fish et al., 1967) and was assigned to Class Y in ICRP *Publication 30*. *In vitro* dissolution tests performed with various forms of $^{90}SrTiO_3$ from high-level radioactive waste facilities (Anderson et al., 1999) showed that at 181 days, 97% of the strontium remained undissolved, giving assignment to Type S. Absorption parameter values calculated here were f_r = 0.009, s_r = 0.7 d^{-1}, and s_s = 0.00012 d^{-1}. In a parallel *in vivo* study, the biokinetics of strontium and titanium were followed for 30 days after intratracheal instillation of stable $SrTiO_3$ in rats. Uptake of strontium by the skeleton was below the detection limit. Lung retention showed a slow component, accounting for 15% of the instilled material, with a half time of 133 days. It was assessed that 85% of the material deposited in the AI region was retained at 30 d, indicating Type S behaviour. A case of accidental inhalation from a source containing $^{90}SrTiO_3$ was well fitted with the ICRP *Publication 30* strontium model and led the authors to the assumption of a 10-µm AMAD and the assignment of this compound to inhalation Class Y (Navarro and Lopez, 1998). Studies on ingested strontium titanate on rats (see below)

suggest f_A ~0.01. Since specific lung absorption parameter values are available only from in vitro tests, default Type S absorption parameter values and a specific value of f_A =0.01 are used here for strontium titanate.

Irradiated fuel fragments

(444) Measurements following the accidental inhalation of a mixture of fresh fission products, indicate Type M behaviour of the strontium present (Johnson et al., 1983). Results of an *in vitro* study on airborne fission products from the Three Mile Island reactor accident are consistent with assignment to Type F (Kanapilly et al., 1980). An *in vitro* study on aerosols generated during transfer, cutting, storage and shipment of nuclear reactor fuel (Dua et al., 1987) gave absorption parameters f_r = 0.4, s_r = 0.57 d^{-1} and s_s = 0.0045 d^{-1}, consistent with assignment of the strontium present to Type M.

Fused aluminosilicate particles (FAP)

(445) 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 strontium is incorporated into FAP, only a small fraction may be rapidly absorbed, while the remainder is retained within the particles and absorbed slowly. Estimates of the rate of dissolution of Sr-FAP were in the range 0.0005 – 0.002 d^{-1} (Snipes et al., 1972; Kanapilly and Goh, 1973; Bailey et al., 1985a,b), and indicate Type S behaviour.

Polystyrene (PSL)

(446) As with FAP, it has been demonstrated that when strontium is incorporated into a polystyrene matrix, only a small fraction may be absorbed rapidly, while the rest is retained within the particles and is absorbed slowly. Bohning et al. (1982) used ^{85}Sr-PSL to follow lung retention in man for about a year after inhalation. Although absorption to blood of the label was not measured directly, lung retention at 300 days (37% and 64% ILD in smokers and non-smokers, respectively) is consistent with assignment to Type S.

Table 10-2. Absorption parameter values for inhaled and ingested strontium

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Specific parameter values[b]					
Strontium titanate		0.01	3	$1x10^{-4}$	0.01
Default parameter values[c,d]					
Absorption Type	Assigned forms				
F	Strontium chloride, sulphate and carbonate	1	30	–	0.25
M	Fuel fragments, all unspecified forms[e]	0.2	3	0.005	0.05
S	FAP, PSL	0.01	3	$1x10^{-4}$	0.0025
Ingested material					
Strontium titanate					0.01
All other chemical forms					0.25

[a] It is assumed that for strontium the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of strontium (30, 3 and 3 d^{-1}, respectively) are the general default values.

[b] See text for summary of information on which parameter values are based, and on ranges of parameter values observed for individual materials. For strontium titanate Type S default parameter values are used for dissolution in the lungs, but a specific value of f_A.

[c] Materials (e.g. strontium 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] For inhaled material deposited in the respiratory tract and subsequent cleared by particle transport to the alimentary tract, the default fA values for inhaled materials are applied: i.e. the product of fr for the absorption Type and the fA value for ingested soluble forms of strontium (0.25).

[e] Default Type M is recommended for use in the absence of specific information, i.e. 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.

Rapid dissolution rate for strontium

(447) The value of s_r estimated for strontium chloride above, 30 d^{-1}, is applied here to all Type F forms of strontium.

Extent of binding of strontium to the respiratory tract

(448) Evidence from the strontium chloride studies outlined above suggests that there is little binding of strontium. It is therefore assumed that for strontium the bound state can be neglected, i.e. $f_b = 0.0$.

10.2.2. Ingestion

(449) Due to the presence of Sr isotopes in fall-out material and its long-term retention in bone as a Ca analogue, the metabolism of strontium has been the subject of a number of human volunteer studies. Similar fractional absorption values were obtained from studies in which inorganic forms of radiostrontium was administered orally in solution (Spencer et al., 1960; Suguri et al., 1963; Shimmins et al., 1967; Sips et al., 1996) and from experiments where known quantities of radiostrontium incorporated in food were ingested (Fujita et al., 1966; Carr, 1967). In most cases, mean values were between 0.1 and 0.4, averaging about 0.2.

(450) Likhtarev et al. (1975) measured the absorption of ^{85}Sr (chemical form not specified) in nine young adult male volunteers and obtained a mean value of 0.28, with a range of 0.1 – 0.5. LeRoy et al. (1966) measured the absorption of Sr from real and simulated fall-out and after administration of ^{85}Sr chloride. Ten volunteers ingested samples of local fallout, largely comprising silicaceous soil constituents (40-700 μm particles). The estimated absorption averaged 0.03 with a range of 0 - 0.09. For simulated fallout prepared as glass microspheres (30-40 μm), estimated absorption was 0.16 (range 0.06 - 0.25), compared to 0.17 (0.08 - 0.34) after administration as the chloride.

(451) Most of these data have been reanalyzed and summarized in a recent review (Apostoaei, 2002). This author showed that the probability distribution function of f_1 values is well represented by a lognormal curve with a geometric mean of 0.22 and a geometric standard deviation of 1.44.

(452) A number of factors have been found to increase Sr absorption, including fasting, low dietary levels of Ca, Mg and P, milk diets and vitamin D (Gruden, 1984; Moon, 1994; Sips et al., 1996; Bianchi et al., 1999).

(453) Sips et al., (1996) investigated the gastrointestinal absorption of Sr chloride in eight healthy male volunteers under fasting conditions and obtained a mean value of 0.25 (range 0.13-0.41). Spencer et al. (1972) showed that overnight fasting increased absorption from about 0.25 to 0.55. McAughey et al. (1994) also reported an f_1 value of 0.55 (range 0.38 - 0.72) for 4 volunteers after an overnight fast compared with 0.11 in a single volunteer ingesting Sr after breakfast. Höllriegl et al. (2006) and Li et al. (2006) reported absorption of stable Sr on 13 human volunteers after an overnight fast and found f_1 values of about 0.6 (range 0.25-0.97) when Sr was given as chloride, diluted in aqueous solutions.

(454) Similarly, a decrease in the Ca content of the diet from 30-40 to 0-10 mg d^{-1} kg^{-1} increased Sr absorption from an average of 0.2 to 0.4 (Shimmins et al., 1967). By contrast, gender, age at exposure in adult groups (Apostoaei, 2002; Höllriegl et al., 2006) smoking, exercise or use of oral contraceptives in young females (Zitterman et al. 1995) do not seem to change the intestinal absorption of strontium.

(455) Vezzoli et al. (1998) in a study of stable strontium absorption in 47 normocalciuric volunteers (29 men and 18 women) reported no clear evidence of gender on Sr absorption. Results from animal studies are generally similar to those from volunteer studies (Coughtrey and Thorne, 1983), although effects of gender on strontium absorption are controversial. Dahl et al. (2001) reported higher plasma strontium levels in male rats and monkeys, compared to females, and concluded that there were no clear gender differences in the gastrointestinal absorption of strontium. Results for the absorption of Sr administered as the titanate ($SrTiO_3$) to rats show low levels of absorption of about 0.01 (McClellan and Bustad, 1964).

(456) Radioactive strontium has been shown to accumulate in teeth (Neuzil and Dysart, 1984; Kulev et al., 1994; O'Donnell et al., 1997). Most of this deposit comes from gastrointestinal absorption and subsequent systemic distribution but a small part may also be adsorbed directly from the oral cavity onto the dental plaque and enamel during mastication. *Ex vivo* experiments performed with enamel removed from rat teeth and transferred to culture medium containing ^{90}Sr (chemical form not given) showed rapid and large deposition on the enamel surface (White et al., 1980). Similarly, experiments performed with adult participants rinsing their mouths twice a day for 2 weeks with a $SrCl_2$ solution, showed that strontium incorporated into dental plaque and was retained for at least 6 weeks (Spets-Happonen et al. 1998). *In vitro* uptake of strontium directly into plaque-free bovine enamel and, to a lesser extent, human enamel has also been shown after experiments where enamel was agitated for 10 min per day for 7 days in a solution containing 2000 ppm of strontium (Curzon and Spector, 1983). Unfortunately none of these studies provide enough information to derive

robust parameters for Sr adsorption and retention on teeth.

(457) In *Publication 30* (1979), the recommended absorption values were 0.01 for $SrTiO_3$ and 0.3 for all other compounds. In *Publication 67* (1993), a value of 0.3 was recommended for dietary intakes by adults. However, due to the strong link between strontium and calcium absorption and the known discrimination in favour of calcium, a default f_A value of 0.25 is adopted here for all chemical forms but Sr titanate, for which lower f_A value of 0.01 is retained.

10.2.3. Systemic Distribution, Retention and Excretion

10.2.3.1. Summary of the database

(458) Strontium is a chemical and physiological analogue of calcium but has different biokinetics from calcium due to discrimination between these elements by biological membranes and hydroxyapatite crystals of bone. For example, strontium is less effectively absorbed from the intestines and more effectively excreted by the kidney than calcium and is lost from bone at a higher rate than calcium over the first few months after uptake to blood (Bauer et al. 1955, Spencer et al. 1960, Barnes et al. 1961, Cohn et al. 1963, Decker et al. 1964, Harrison et al. 1967).

(459) The biokinetics of strontium has been studied extensively in human subjects and laboratory animals. A large database related to the transfer of ^{90}Sr from food and milk to the human skeleton was developed in the 1950s and 1960s. Interpretation of these environmental data is complicated by the facts that measured skeletal burdens were accumulated over an extended period and depend on assumptions concerning fractional uptake of ^{90}Sr from the gastrointestinal tract. More easily interpreted data are available from controlled studies on human subjects. Data on the behavior of strontium in laboratory animals, particularly dogs, help to clarify the behavior of strontium at early times after intake. Because strontium is a close physiological analogue of calcium, data from controlled studies of calcium in humans provide supporting information for selection of parameter values for strontium, particularly for paths of movement for which comparative information on strontium and calcium transport is available.

(460) Reviews of the biokinetic database for systemic strontium can be found in ICRP *Publication 20* (1973), ICRP *Publication 67* (1993), and an article by Leggett (1992). More recent human studies are described in articles by Shagina et al. (2003) and Li et al. (2008). The primary datasets underlying specific parameter values in the model for systemic strontium used in this report are summarized below.

10.2.3.2. Biokinetic model for systemic strontium

(461) The structure of the model for systemic strontium is shown in Figure 10-1. This is a simplified version of the generic model for bone-volume seekers. All soft tissues including the liver and kidneys are included in the three "Other tissue" compartments, ST0, ST1, and ST2 corresponding to rapid, intermediate, and slow exchange of activity with blood, respectively.

(462) Blood is treated as a uniformly mixed pool that exchanges activity with soft tissues and bone surfaces. Soft tissues are divided into three compartments corresponding to fast, intermediate, and slow return exchange of activity with blood (compartments ST0, ST1, and ST2, respectively). The liver and kidneys are not addressed separately in the model for strontium but are included implicitly in the soft tissue compartments. Bone is divided into cortical and trabecular bone, and each of these bone types is further divided into bone

surfaces and bone volume. Bone volume is viewed as consisting of two pools, one that exchanges with activity in bone surface for a period of weeks or months and a second, non-exchangeable pool from which activity can be removed only by bone restructuring processes. Activity depositing in the skeleton is assigned to bone surface. Over a period of days a portion of the activity on bone surfaces moves to exchangeable bone volume and the rest returns to plasma. Activity leaves exchangeable bone volume over a period of months, with part of the activity moving to bone surfaces and the rest to non-exchangeable bone volume. The rate of removal from non-exchangeable bone volume is assumed to be the rate of bone turnover, with different turnover rates applying to cortical and trabecular bone. Strontium is assumed to be lost from the body only by urinary or fecal excretion.

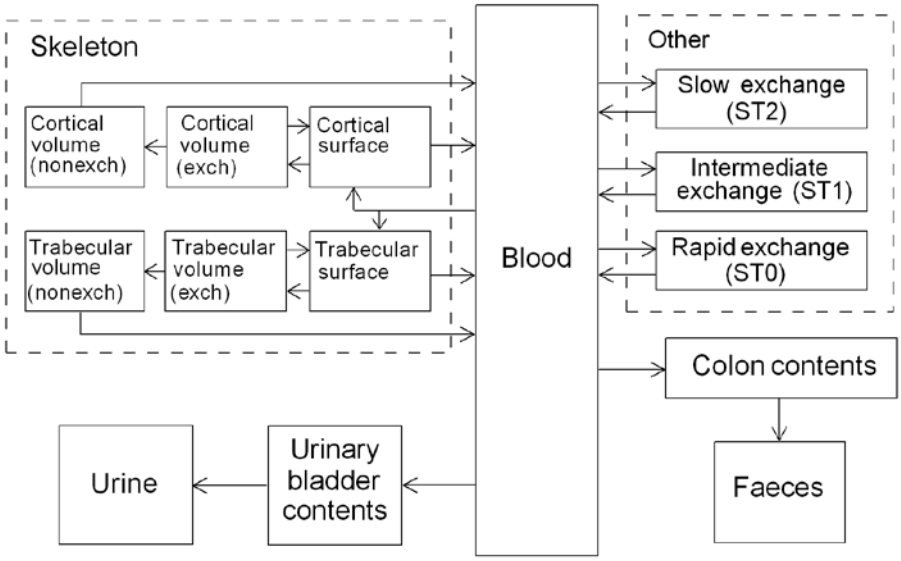

Figure 10-1. Structure of the biokinetic model for systemic strontium.
Abbreviations: exch = exchangeable, nonexch = non-exchangeable.

Parameter values

(463) The systemic biokinetic model for strontium given in ICRP *Publication 67* (1993) is reasonably consistent with later information on the biokinetics of strontium and related elements in adult humans (e.g. Shagina et al., 2003; Li et al., 2008). For example, the model predicts that 2.8-3.2% of total-body ^{90}Sr is eliminated each year at times 25-45 y after acute uptake to blood, compared with average values of 2.7-3.2%, depending on age, in adult males of a Russian population exposed to high levels of ^{90}Sr (Shagina et al., 2003). Average rates of loss for adult females in that population were estimated as 3.2-3.5% up to age 45 y and 4.4-5.8% at higher ages. The model of ICRP *Publication 67* is independent of age and gender after age 25 y.

(464) The parameter values for strontium applied in ICRP *Publication 67* (1993) to an adult member of the public are adopted in this document for application to workers. These values are listed in Table 10-1. The basis for each of the parameter values is summarized below.

(465) Results of controlled studies involving adult humans indicate that whole-body retention, presumably representing primarily skeletal retention, is higher in young adults (<25

y) than in middle-aged or elderly persons (Likhtarev et al., 1975; Leggett, 1992). This is thought to be associated with differences with age in the bone formation rate, which determines the level of deposition of calcium and related elements in bone and which remains elevated until about the middle of the third decade of life. The baseline parameter values for strontium given in this report apply to ages 25 y or greater. Model predictions for younger adult ages can be derived from the age-specific parameter values given in ICRP *Publication 67* (1993), interpolating linearly with age between values provided in that document for ages 15 y and 25 y.

(466) Kinetic analysis of plasma disappearance curves for normal subjects intravenously injected with calcium or strontium tracers indicates that these elements initially leave plasma at a rate of several hundred plasma volumes per day and equilibrate rapidly with an extravascular compartment roughly three times the size of the plasma pool (Heaney, 1964; Harrison et al., 1967; Hart and Spencer, 1976). At times greater than 1-2 h after injection, a transfer rate from plasma of about 15 d^{-1} yields a reasonable fit to plasma disappearance curves for strontium or calcium tracers. The model for strontium used in this report does not depict the extremely rapid removal of activity during the early minutes but assigns a removal rate from plasma of 15 d^{-1}.

Table 10-3. Transfer coefficients for systemic strontium

From[a]	To[a]	Transfer coefficient (d^{-1})
Blood	Urinary bladder contents	1.73
Blood	Right colon contents	0.525
Blood	Trabecular bone surface	2.08
Blood	Cortical bone surface	1.67
Blood	ST0	7.50
Blood	ST1	1.50
Blood	ST2	0.003
Trabecular bone surface	Blood	0.578
Trabecular bone surface	Exch trabecular bone volume	0.116
Cortical bone surface	Blood	0.578
Cortical bone surface	Exch cortical bone volume	0.116
ST0	Blood	2.50
ST1	Blood	0.116
ST2	Blood	0.00038
Exch trabecular bone volume	Trabecular bone surface	0.0043
Exch trabecular bone volume	Nonexch trabecular bone volume	0.0043
Exch cortical bone volume	Cortical bone surface	0.0043
Exch cortical bone volume	Nonexch cortical bone volume	0.0043
Nonexch cortical bone volume	Blood	0.0000821
Nonexch trabecular bone volume	Blood	0.000493

[a] Exch = exchangeable; Nonexch = non-exchangeable; ST0, ST1, and ST2 are compartments within other soft tissues with fast, intermediate, and slow turnover, respectively.

(467) Uptake and retention of radiostrontium in soft tissues and bone have been measured in several seriously ill human subjects (Comar et al., 1957; Schulert et al., 1959). The data indicate that soft tissues initially contain about as much strontium as bone, but the soft-tissue content falls off sharply after a few weeks while the bone content declines only slowly over the first few months.

(468) Soft-tissue contents of ^{85}Sr and ^{45}Ca were measured in postmortem tissues of several human subjects injected with these radionuclides during late stages of terminal illnesses, from a few hours to four months before death (Schulert et al. 1959). The fraction of injected activity remaining in soft tissues after clearance of the rapid-turnover pool was roughly the same for the two radionuclides. It appeared that strontium was removed more slowly than calcium from the intermediate-term pool. No information on the presumably small, long-term retention compartment (ST2) could be gained from this relatively short-term study.

(469) The rates of transfer of strontium between plasma and the soft tissue compartments are set as follows. It is assumed that 50% of strontium leaving plasma moves to the rapid-turnover soft-tissue compartment ST0; this is the balance after deposition percentages in other compartments are assigned. The corresponding transfer rate from plasma to ST0 is $0.50 \times 15\ d^{-1} = 7.5\ d^{-1}$. Based on the assumed relative amounts of strontium in ST0 and plasma, the transfer rate from ST0 to plasma is set at one-third the transfer rate from plasma to ST0, or $2.5\ d^{-1}$. Fractional transfer from plasma to ST1 is assumed to be 0.1, the same as for calcium; the corresponding transfer rate is $0.1 \times 15\ d^{-1} = 1.5\ d^{-1}$). The removal half-time from ST1 to plasma is set at 6 d for strontium (transfer rate = ln(2)/ 6 d = $0.116\ d^{-1}$), compared with 4 d for calcium, to account for the slower decline in soft-tissue activity for strontium than calcium indicated by human injection data. Fractional deposition in the relatively non-exchangeable soft-tissue pool, ST2, is set at 0.0002 (transfer rate = $0.0002 \times 15\ d^{-1} = 0.003\ d^{-1}$) compared with 0.00005 for calcium. This is consistent with the estimate that soft tissues of the adult contain 1% of the body's natural strontium (Schlenker et al., 1982), assuming the removal half-time from ST2 to plasma is the same as that used in the model for calcium (5 y, corresponding to a transfer rate of $0.00038\ d^{-1}$).

(470) Data for laboratory animals indicate that fractional deposition on bone surfaces is similar for calcium, strontium, barium, and radium (Bligh and Taylor, 1963; Kshirsagar et al., 1966; Domanski et al. 1969, 1980). This is consistent with limited data from controlled studies on human subjects, including measurements of radiocalcium and radiostrontium in bone samples from subjects injected 3 h or longer before death (Schulert et al., 1959); and external measurements of the buildup of radiocalcium (Anderson et al., 1970; Heard and Chamberlain, 1984) and radiobarium (Korsunskii et al., 1981) after intravenous injection. Based on these data, 25% of calcium, strontium, barium, or radium leaving plasma is assigned to bone surfaces. The transfer rate from plasma to cortical and trabecular surfaces combined is $0.25 \times 15\ d^{-1} = 3.75\ d^{-1}$.

(471) The initial distribution between cortical and trabecular bone appears to be similar for calcium, strontium, barium, and radium (Ellsasser et al., 1969; Wood et al., 1970; Liniecki, 1971; Stather, 1974; Lloyd et al., 1976). Relative deposition on cortical and trabecular bone surfaces is based on the estimated calcium turnover rate of each bone type. As an average over adult ages, deposition on trabecular bone is estimated to be 1.25 times that on cortical bone (Leggett et al., 1982). The transfer rate from plasma to trabecular bone surface is $(1.25/2.25) \times 3.75\ d^{-1} = 2.08\ d^{-1}$ and from plasma to cortical bone surface is $(3.75 - 2.08)\ d^{-1} = 1.67\ d^{-1}$.

(472) The residence time on human bone surfaces has not been determined with much precision for any of the alkaline earth elements. The removal half-time of 1 d is estimated for all four elements. This value is consistent with autoradiographic measurements of surface activity in human and canine bone samples taken at times ranging from few hours to a few days after intravenous injection of 45Ca (Riggs et al. 1971, Groer et al. 1972, Groer and Marshall 1973, ICRP 1973). It is also reasonably consistent with measurements of the early decline in whole-body retention of intravenously injected radioactive calcium, strontium, barium, and/or radium in human subjects (Spencer et al. 1960; Bishop et al. 1960; Heaney

1964; Harrison et al. 1967; Phang et al. 1969; Carr et al. 1973; Likhtarev et al. 1975; Malluche et al. 1978; Henrichs et al. 1984; Newton et al. 1990, 1991) coupled with measurements of soft-tissue retention as described earlier. A removal half-time of 1 d refers to the half-time that one theoretically would observe if recycling of activity to bone surfaces were eliminated. Given the considerable amount of recycling from plasma to bone surfaces, the corresponding net or apparent half-time would be 3 d or more.

(473) Parameter values for exchangeable bone volume are estimated from whole-body measurements for human subjects using data for times after bone surfaces and soft tissues have largely cleared of activity but before loss from bone resorption becomes an important consideration. Based on analysis of whole-body retention data for human subjects injected with radioisotopes of calcium, strontium, barium, or radium (Spencer et al., 1960; Bishop et al., 1960; Heaney, 1964; Harrison et al., 1967; Maletskos et al., 1969; Phang et al., 1969; Carr et al., 1973; Likhtarev et al., 1975; Malluche et al., 1978; Henrichs et al., 1984; Newton et al., 1990, 1991), the fraction of activity that moves from bone surfaces back to plasma is assumed to be the same for all four elements. Specifically, five-sixths of activity leaving bone surfaces is assumed to return to plasma and one-sixth is assumed to transfer to exchangeable bone volume. The transfer rate from trabecular or cortical bone surface to the corresponding exchangeable bone volume compartment is $(1/6) \times \ln(2)/1\ \text{d} = 0.116\ \text{d}^{-1}$, and the transfer rate from trabecular or cortical bone surface to plasma is $(5/6) \times \ln(2)/1\ \text{d} = 0.578\ \text{d}^{-1}$.

(474) Element-specific removal half-times from the exchangeable bone volume compartments are based in part on fits to the intermediate-term retention data from human injection studies. It is also considered that the assigned half-times should increase roughly in proportion to the likelihood of the element entering nonexchangeable sites in bone mineral, as suggested by data from in vitro experiments with hydroxyapatite crystals and whole-body retention patterns for alkaline earth elements in human subjects. A removal half-time of 80 d is assigned to strontium, compared with 100 d for calcium, 50 d for barium, and 30 d for radium (Leggett, 1992). Because the data do not allow the derivation of removal half-times as a function of bone type, the same half-time is applied to cortical and trabecular exchangeable bone volume compartments.

(475) Discrimination between alkaline earth elements by bone is accounted for by fractional transfer of activity from exchangeable to nonexchangeable bone volume. It is assumed that calcium, strontium, barium, and radium are all equally likely to become temporarily incorporated in bone mineral after injection into plasma but that the likelihood of reaching a non-exchangeable site in bone crystal decreases in the order calcium > strontium > barium > radium. Fractional transfers of calcium, strontium, barium, and radium from exchangeable to nonexchangeable bone volume are set at 0.6, 0.5, 0.3, and 0.2, respectively, for consistency with whole-body and skeletal retention data on these elements (Spencer et al. 1960; Bishop et al., 1960; Heaney et al., 1964; Harrison et al., 1967; Phang et al., 1969; Maletskos et al., 1969; Carr et al., 1973; Likhtarev et al., 1975; Malluche et al., 1978; Henrichs et al., 1984; Newton et al., 1990, 1991) as well as results of in vitro measurements on hydroxyapatite crystals (Neuman, 1964; Stark, 1968). The derived rate of transfer of strontium from exchangeable trabecular or cortical bone volume to the corresponding nonexchangeable bone volume compartment is $0.5 \times \ln(2)/80\ \text{d} = 0.0043\ \text{d}^{-1}$ and to the corresponding bone surface compartment is $0.5 \times \ln(2)/80\ \text{d} = 0.0043\ \text{d}^{-1}$.

(476) Biological removal from the nonexchangeable bone volume compartments of cortical and trabecular bone is assumed to result from bone turnover. The average bone turnover rates during adulthood are estimated as 3% y^{-1} and 18% y^{-1} for cortical and trabecular bone, respectively (ICRP, 2002). The corresponding transfer rates from the nonexchangeable bone volume compartments of cortical and trabecular bone to plasma are

6037 0.0000821 d^{-1} and 0.000493 d^{-1}, respectively. Age-specific rates of bone turnover, including
6038 changes with age during adulthood, are provided in the paper by Leggett (1992) for
6039 application of the model to specific cases.
6040 (477) Clearance of strontium from plasma to urine and faeces has been determined in
6041 several human studies (Spencer et al., 1960; Barnes et al., 1961; Fujita, 1963; Cohn et al.,
6042 1963; Samachson, 1966; Harrison et al., 1967; Wenger and Soucas, 1975; Likhtarev et al.,
6043 1975; Newton et al., 1990). Based on central estimates derived from results of these studies,
6044 it is assumed that 11.5% of strontium leaving plasma is transferred to the contents of the
6045 urinary bladder contents and subsequently to urine and 3.5% is transferred to the contents of
6046 the right colon contents and subsequently to faeces. Therefore, the transfer rate from plasma
6047 to the urinary bladder contents is $0.115 \times 15\ d^{-1} = 1.73\ d^{-1}$ and from plasma to the contents of
6048 the right colon contents is $0.035 \times 15\ d^{-1} = 0.525\ d^{-1}$.
6049
6050 **10.2.3.3. Treatment of radioactive progeny**
6051
6052 (478) Dosimetrically significant radioactive progeny of strontium isotopes considered in
6053 this report include isotopes of rubidium, krypton, and yttrium. Results of animal studies
6054 (Arnold et al., 1955; Lloyd, 1961; Mueller, 1972; Stevenson, 1975) indicate that ^{90}Y
6055 produced by decay of ^{90}Sr in soft tissues tends to migrate from the parent and distribute
6056 similarly to intravenously injected yttrium but shows little if any migration from ^{90}Sr when
6057 produced in bone volume (see the section on yttrium in this report for summaries of reported
6058 data). No information was found on the behavior of rubidium produced in the body by decay
6059 of a strontium parent. The noble gas krypton produced by serial decay of strontium and
6060 rubidium isotopes presumably migrates from these radionuclides over a period of minutes to
6061 hours and escapes from the body to an extent determined by the half-life of the krypton
6062 isotope.
6063 (479) The model used in this report for yttrium as a daughter of strontium is based on the
6064 model for yttrium as a parent described elsewhere in this report, but additional assumptions
6065 are made to address structural differences in the strontium and yttrium models. Yttrium
6066 produced in a compartment of bone is assumed to follow the same kinetics as if deposited in
6067 the compartment as a parent radionuclide. No distinction is made between the exchangeable
6068 and non-exchangeable bone volume compartments of the strontium model when applied to
6069 yttrium, i.e. each compartment is treated simply as the bone volume compartment for the
6070 corresponding bone type in the yttrium model. Yttrium produced in a soft-tissue
6071 compartment of the strontium model (ST0, ST1, or ST2) is assumed to transfer to blood with
6072 a half-time of 3 d (the shortest half-time for Other soft tissue in the model for yttrium as a
6073 parent) and then to follow the kinetics of yttrium as a parent radionuclide.
6074 (480) The model for rubidium as a daughter of strontium is a considerably condensed
6075 version of a proposed model for rubidium as a parent radionuclide (Leggett and Williams,
6076 1988). The model is based on the same principles as the model for cesium, a chemical and
6077 physiological analogue of rubidium, described elsewhere in this report. That is, the
6078 biokinetics of systemic rubidium is predicted on the basis of the distribution of cardiac
6079 output, experimentally determined tissue-specific extraction fractions, and the steady-state
6080 distribution of stable rubidium in the body. The reference division of cardiac output in the
6081 adult male tabulated in ICRP *Publication 89* (2002) is applied here. The present version of
6082 the model depicts blood plasma as a central compartment that exchanges rubidium with red
6083 blood cells (RBC), trabecular bone surface, cortical bone surface, muscle, and a compartment
6084 representing all other soft tissue. Rates of transfer of rubidium from plasma are as follows: 6
6085 d^{-1} to RBC, 255 d^{-1} to muscle, 7 d^{-1} to cortical bone surface, 7 d^{-1} to trabecular bone surface,

855 d^{-1} to other tissue, 3.9 d^{-1} to urinary bladder contents, 1.2 d^{-1} to right colon contents, and 0.1 d^{-1} to excreta (sweat). Transfer rates from RBC or tissues to plasma are as follows: 0.35 d^{-1} from RBC, 1.14 d^{-1} from muscle, 1.68 d^{-1} from bone surface compartments, and 10.3 d^{-1} from other tissue. Rubidium produced by decay of strontium in blood is assigned to plasma. Rubidium produced in exchangeable or non-exchangeable bone volume compartments of the strontium model are transferred to plasma at the rate of bone turnover. Rubidium produced in soft tissue compartments of the strontium model (ST0, ST1, or ST2) are transferred to plasma at the rate 10.3 d^{-1}.

(481) The model for krypton produced by serial decay of strontium and rubidium in systemic compartments is similar to the model applied in this report to radon produced in vivo by decay of a parent radionuclide. Krypton is assumed to follow the bone model for radon introduced in ICRP *Publication 67* (1993) but is assigned a higher rate of removal from soft tissues to blood than is assumed for radon. Specifically, krypton produced in nonexchangeable 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. Krypton produced in a soft-tissue compartment transfers to blood with a half-time of 15 min, compared with an assumed half-time of 30 min for radon produced by radioactive decay in soft tissues. Krypton entering blood is assumed to be removed from the body (exhaled) at the rate 1000 d^{-1}, corresponding to a half-time of 1 min. Partial recycling of krypton to tissues via arterial blood is not depicted explicitly but is considered in the assignment of the effective half-times in tissues. The model is intended to yield a conservative average residence time of krypton atoms in the body assuming introduction into arterial blood and subsequent tissue uptake. It is recognized that the residence time of krypton in the body following production in tissues depends on the distribution of the parent radionuclide.

10.3. Individual Monitoring

^{85}Sr

(482) ^{85}Sr monitoring techniques include in vivo techniques (whole body and if necessary lung counting) as well as urine bioassay.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{85}Sr	Urine Bioassay	γ-ray spectrometry	5 Bq/L	1 Bq/L
^{85}Sr	Whole Body Counting	γ-ray spectrometry	50 Bq	20 Bq
^{85}Sr	Lung Counting	γ-ray spectrometry		5 Bq

^{89}Sr

(483) ^{89}Sr is determined by urine bioassay, by beta counting following chemical separation.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{89}Sr	Urine Bioassay	Beta proportional counting	1 Bq/L	0.05 Bq/L

^{90}Sr

(484) ^{90}Sr intakes are in general estimated by beta counting of urine excreta samples, after chemical separation. ^{90}Sr is determined directly when Liquid Scintillation Counting is used. When beta proportional counter is used ^{90}Sr content is commonly determined based on ^{90}Y content, after a delay of at least seven days to allow for ^{90}Y ingrowth.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{90}Sr	Urine Bioassay	Beta proportional counting	0.4 Bq/L	0.05 Bq/L
^{90}Sr	Urine Bioassay	Liquid Scintillation Counting	0.4 Bq/L	0.1 Bq/L

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11. YTTRIUM (Z = 39)

(485) Yttrium is a rare earth element which occurs mainly in oxidation state III. Lanthanoids are good chemical analogues of yttrium. Yttrium may be encountered in a variety of chemical and physical forms, including oxides (Y_2O_3), hydroxides, chlorides, fluorides, sulphates, nitrates and oxalates.

(486) Yttrium-90 and ^{91}Y are the main fission products which may be encountered in the nuclear industry. ^{90}Y is used in nuclear medicine for the treatment of various cancers with labelled drugs.

Table 11-1. Isotopes of yttrium addressed in this report

Isotope	Physical half-life	Decay mode
Y-84m	39.5 m	EC, B+
Y-85	2.68 h	EC, B+
Y-85m	4.86 h	EC, B+
Y-86	14.74 h	EC, B+
Y-86m	48 m	IT, EC, B+
Y-87	79.8 h	EC, B+
Y-87m	13.37 h	IT, EC, B+
Y-88	106.65 d	EC, B+
Y-90[a]	64.10 h	B-
Y-90m	3.19 h	IT, B-
Y-91	58.51 d	B-
Y-91m	49.71 m	IT
Y-92	3.54 h	B-
Y-93	10.18 h	B-
Y-94	18.7 m	B-
Y-95	10.3 m	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

11.1. Routes of Intake

11.1.1. Inhalation

Absorption Types and parameter values

(487) Information is available from experimental studies of yttrium mainly as chloride or in fused aluminosilicate particles (FAP). Analysis of the results to estimate absorption parameter values is facilitated by the close correspondence of fecal excretion to particle transport from the respiratory tract: absorption of yttrium in the alimentary tract is low, and systemic yttrium is excreted mainly in urine.

(488) Absorption parameter values and Types, and associated f_A values for particulate forms of yttrium are given in Table 11-2.

Yttrium chloride (YCl_3)

(489) Extensive studies have been conducted on the biokinetics of yttrium following deposition of the chloride in the lungs of dogs, guinea pigs, rats, and mice. Most of the studies involved small masses of radiolabelled yttrium, and showed a similar pattern. Initially, most of the excretion was to faeces, indicating that there was little absorption from

the upper respiratory tract. Nevertheless, subsequent clearance of most of the lung deposit was rapid with corresponding systemic uptake: mainly deposition in skeleton and excretion in urine. Similar lung dissolution kinetics were observed in the different species, and the distribution of yttrium absorbed systemically was similar to that observed after intravenous injection.

(490) In a detailed low-level study carried out to complement a lifespan study of the effects of inhaled $^{91}YCl_3$, the biokinetics of ^{91}Y were followed for 270 days after inhalation of $^{91}YCl_3$ (in caesium chloride solution) by dogs (McClellan and Rupprecht, 1967; Muggenburg et al., 1998). On average, about 60% of total-body ^{91}Y cleared during the first few days after administration. It was inferred that ^{91}Y deposited in the upper respiratory tract was mainly cleared by mucociliary transport and subsequent swallowing and fecal excretion. This suggests that the rapid dissolution rate is low compared to particle transport rates from these airways. Nevertheless, there was significant deposition in liver and skeleton immediately after inhalation, with the lung content falling to about 15% of the initial lung deposit (ILD) by 4 days, and to about 2% ILD by 64 days. Studies of the distribution of activity retained in the respiratory tract provide evidence for the formation of particulate material. Autoradiographs were made using tissues from dogs in the life-span study that died in the first few weeks after exposure (McClellan and Rupprecht, 1967). Within the respiratory tract, aggregates of radioactivity were observed on bronchial mucosal surfaces and in recesses of the mucosal lining. Smaller particles were also found in alveolar ducts and alveoli. Some of the material had been phagocytized, absorbed into the lymphatic system, and could be seen in the lymphatic spaces beneath the bronchial epithelium. Large amounts of ^{91}Y were found in bronchial cartilage plates, but attributed to systemic ^{91}Y, with similar deposition in skeletal cartilage. Muggenburg et al. (1998) reported concentrations in a wide range of tissues at 32 days after inhalation. The concentration in tracheo-bronchial lymph nodes was similar to that in liver, and higher than in other soft tissues, suggesting some transfer in particulate form. Modelling conducted by the task group showed a good fit to the data with f_r = 0.94, $s_r = 0.74\ d^{-1}$ and $s_s = 0.013\ d^{-1}$ (consistent with assignment to default Type F). As this is the most comprehensive and longest duration dataset for YCl_3, it probably provides the best estimates of s_r and s_s, and these values were used in analysis of some other datasets below.

(491) Schiessle et al. (1963) followed the biokinetics of ^{91}Y for 180 days after inhalation of $^{91}YCl_3$ (carrier free) by guinea pigs. There are comprehensive measurements at seven time points up to 28 days, but few results at later times. Modelling conducted here gave parameter values: f_r = 0.81, $s_r = 1.07\ d^{-1}$ and $s_s = 0.016\ d^{-1}$ (consistent with assignment to default Type F) in broad agreement with those based on the study by Muggenburg et al. (1998). Schmidtke et al. (1963) followed the biokinetics of ^{91}Y for 56 days after inhalation by guinea pigs of $^{91}YCl_3$ with added stable yttrium. Compared to the behaviour with carrier-free $^{91}YCl_3$ (Schiessle et al., 1963), lung retention and faecal clearance were somewhat higher, and skeletal uptake and urinary excretion lower. Schmidtke et al. (1964) carried out complementary autoradiographic studies on respiratory tract tissues obtained 21 days after inhalation of $^{91}YCl_3$ by guinea pigs. Schmidtke (1964) investigated the effect of DTPA on the biokinetics of ^{91}Y for 8 days after inhalation of $^{91}YCl_3$ (carrier free) by guinea pigs. Unusually, the tissue distribution was measured at several time points during the first day. Modelling conducted here on results from control animals (using a fixed value of $s_s = 0.013\ d^{-1}$, derived above, because of the short duration of measurements in this study) gave parameter values: f_r = 0.83 and $s_r = 1.3\ d^{-1}$ (consistent with assignment to default Type F) in good agreement with those based on the study by Schiessle et al. (1963). Treatment with DTPA caused rapid clearance from the lungs and excretion from the body of ^{91}Y.

(492) Wenzel et al. (1969) followed the biokinetics of ^{88}Y for 32 days after inhalation by rats of $^{88}YCl_3$, either carrier-free with added stable yttrium. Lung retention was higher, and skeletal uptake and urinary excretion lower, in rats exposed to ^{88}Y with stable yttrium than in those that inhaled carrier-free ^{88}Y. Faecal clearance was also higher, suggesting that the additional lung retention was in particulate form, rather than bound. Using fixed values of $s_r = 0.74\ d^{-1}$ and $s_s = 0.013\ d^{-1}$, derived above, modelling conducted here gave values of f_r = 0.94 (consistent with assignment to Type F) for the $^{88}YCl_3$ inhaled in carrier-free form; and f_r = 0.7 (consistent with assignment to Type M) for the $^{88}YCl_3$ inhaled with added stable yttrium.

(493) Bailey et al. (1978) followed the biokinetics of ^{88}Y for 9 days after intratracheal instillation of $^{88}YCl_3$ into rats. By 2 days, about 20% ILD remained in the lungs, 50% ILD had been excreted in faeces, and 30% was deposited in systemic sites or excreted in urine, again suggesting little absorption from the upper airways, but considerable absorption from the deep lung. They also developed a systemic compartment model for ^{88}Y in the rat based on an intravenous injection study. With only two time points, there are insufficient data to define all three dissolution parameter values. Using fixed values of $s_r = 0.74\ d^{-1}$ and $s_s = 0.013\ d^{-1}$, derived above, modelling conducted here showed a good fit to the data with f_r = 0.7 (consistent with assignment to default Type M).

(494) Hirano et al. (1990) followed the lung retention and distribution of yttrium for 162 days after intratracheal instillation into rats of 100 µg of stable yttrium as chloride. The retention half-time of about 170 days is far greater than observed in the studies with $^{88}YCl_3$ or $^{91}YCl_3$ reviewed here. There was also relatively little systemic uptake, but few details are given: the authors concluded that the yttrium was retained in the lungs in an insoluble form. The clearance was considerable slower than would be expected for insoluble particles in rats (ICRP, 2002), suggesting that there was considerable binding of yttrium to lung structures. Yttrium was detected in alveolar and interstitial macrophages and in basement membranes, supporting this inference. However, dose-related inflammatory responses were seen over the range of masses (10 – 200 µg) administered in complementary short-term experiments, and so the kinetics may well differ from those pertaining at tracer levels. Marubashi et al. (1998) reported that 30 days after intratracheal instillation into rats of 50 µg of stable yttrium as chloride, about 67% ILD remained, again, much slower clearance than observed in the radiotracer studies.

(495) Gensicke and Nitschke (1964) showed that treatment with hexametaphosphate increased the clearance of ^{91}Y after inhalation of $^{91}YCl_3$ by mice. There is insufficient information in the paper to enable dissolution parameter values to be derived reliably, but the biokinetics in the controls appears broadly similar to that in the other radiotracer studies outlined above, with activity in the skeleton exceeding that in the lungs by about a week after inhalation.

(496) Based on the results of the experiments outlined above, specific absorption parameter values of f_r = 0.9, $s_r = 1\ d^{-1}$ and $s_s = 0.01\ d^{-1}$ (consistent with assignment to default Type F), and f_A = 0.02 (the default value for ingestion of yttrium) are used here for yttrium chloride.

Yttrium oxide (Y_2O_3)

(497) Newton et al. (1971) measured tissue retention of ^{91}Y at 8 and 64 days after inhalation of $^{91}Y_2O_3$ by dogs. At 8 days, the activity in the skeleton was about 30% of that in the lungs, and at 64 days they were approximately equal. From results of a complementary gavage experiment it was calculated here that fractional absorption from the alimentary tract f_A = 0.0003. Using a fixed value of $s_r = 0.74\ d^{-1}$ derived above for yttrium chloride, modelling

conducted here gave values of f_r = 0.45 and s_s = 0.006 d^{-1}, (consistent with assignment to Type M). Given the relatively sparse information, specific parameter values are not recommended here for yttrium oxide: instead it is assigned to Type M.

Yttrium phosphate (YPO_4)

(498) Newton et al. (1971) measured tissue retention of ^{91}Y at 8 and 64 days after inhalation of $^{91}YPO_4$ by dogs. At 8 days, the activity in the skeleton was about 20% of that in the lungs, and at 64 days 45% of it. [The authors noted that following both inhalation and gavage of $^{91}YPO_4$, the ratio of deposition in the skeleton to that in the liver (~3:1) was lower than following inhalation of other forms of ^{91}Y (~6:1 for chloride, oxide and FAP), but that this observation needed confirmation.] From results of a complementary gavage experiment it was calculated here that fractional absorption from the alimentary tract f_A = 0.0004. Using a fixed value of s_r = 0.74 d^{-1} derived above for yttrium chloride, modelling conducted here gave values of f_r = 0.33 and s_s = 0.002 d^{-1}, (consistent with assignment to Type M). Given the relatively sparse information, specific parameter values are not recommended here for yttrium phosphate: instead it is assigned to Type M.

Fused aluminosilicate particles (FAP)

(499) 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 yttrium is incorporated into FAP, only a small fraction is rapidly absorbed, while the remainder is retained within the particles and absorbed slowly.

(500) In a detailed low-level study carried out to complement a lifespan study of the effects of inhaled ^{91}Y-FAP (Hahn et al., 1994), the biokinetics of ^{91}Y were followed for 320 days after inhalation of ^{91}Y-FAP by dogs (Hobbs et al., 1971). By 8 days after inhalation, 97% of ^{91}Y remaining in the body was in the lungs, with <1% in the skeleton, but by 256 days the latter had increased to about 10%. Using a fixed value of s_r = 0.74 d^{-1} derived above for yttrium chloride, and taking the default assumption for fractional absorption from the alimentary tract (Table 11-2) to be $f_A = 0.002 * f_r$, modelling conducted here gave values of f_r = 0.004 and s_s = 0.0009 d^{-1}, (consistent with assignment to Type S). In a similar low-level study carried out to complement a lifespan study of the effects of inhaled ^{90}Y-FAP (Hahn et al., 1983), the biokinetics of ^{90}Y were followed for 12 days after inhalation of ^{90}Y-FAP by dogs (Hobbs et al., 1970; Barnes et al., 1972). The shorter duration reflects the 64-hour half-life of ^{90}Y. During this period, the activity distribution was similar to seen in the more extensive ^{91}Y-FAP study. Estimates of the rate of dissolution of Y-FAP, following inhalation of ^{88}Y-FAP by rats and men were in the range 0.00015 – 0.0005 d^{-1} (Bailey *et al.*, 1981; 1985), indicating assignment to Type S. Rates of dissolution of ^{91}Y-FAP measured in vitro varied considerably, depending on particle size and conditions, in the range 0.00001 – 0.001 d^{-1} (Kanapilly and Goh, 1973), and indicate Type M or S behaviour.

Rapid dissolution rate for yttrium

(501) Studies with yttrium chloride give values of s_r of about 1 d^{-1}, and this is applied here to all Type F forms of yttrium. 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 yttrium.

Extent of binding of yttrium to the respiratory tract

(502) The results of autoradiographic studies of the distribution of ^{91}Y after

inhalation of $^{91}YCl_3$ suggest that the ^{91}Y retained in the lungs was in particulate form rather than bound to lung structures. It is therefore assumed that for yttrium the bound state can be neglected, i.e. $f_b = 0.0$.

Table 11-2. Absorption parameter values for inhaled and ingested yttrium

Inhaled particulate materials	Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Specific parameter values[b]				
Yttrium chloride	0.9	1	0.01	$1x10^{-4}$
Default parameter values[c,d]				
Absorption Type	Assigned forms			
F		1	1	–	$1x10^{-4}$
M	Oxide, phosphate, all unspecified forms[e]	0.2	1	0.005	$2x10^{-5}$
S	FAP	0.01	1	$1x10^{-4}$	$1x10^{-6}$
Ingested material				
All chemical forms				$1x10^{-4}$

[a] It is assumed that for yttrium the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of yttrium (1 d^{-1}, respectively) 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 yttrium chloride specific parameter values are used for dissolution in the lungs, but the default value of f_A.

[c] Materials (e.g. yttrium-labelled FAP) are listed here where there is sufficient information to assign to a default absorption Type, but not to give specific parameter values (see text).

[d] For inhaled material deposited in the respiratory tract and subsequent cleared by particle transport to the alimentary tract, the default fA values for inhaled materials are applied: i.e. the product of fr for the absorption Type and the fA value for ingested soluble forms of yttrium ($1x10^{-4}$).

[e] Default Type M is recommended for use in the absence of specific information, i.e. 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.

11.1.2. Ingestion

(503) Yttrium absorption has been poorly studied. Studies performed on dogs and goats suggested that yttrium absorption from the gastrointestinal tract is very low (Nold et al., 1960). One other study performed on rats with ^{91}Y used to label solid and liquid food showed that the total recovery of Y in the gastrointestinal tract between 30 min and 12 hours after ingestion was about 98% (Marcus and Langemann, 1962).

(504) Study performed with rats fed daily with ^{90}Y in drinking water showed that, after a 60 days period of ingestion, the skeleton contained less than 0.01% of the total ingested activity (Sullivan et al., 1963). This poor absorbability of yttrium has also been noticed in studies using fowl and has led to designate Y as a non-absorbed reference substance (Sklan et al., 1975).

(505) Recent studies performed in rats (Damment and Pennick, 2007) and in human subjects (Pennick et al., 2006) with lanthanum carbonate can provide a good assessment of yttrium absorption because of their chemical analogies. Results in rats showed that 0.004% of the administered dose was recovered in the urine over a period of 7 days (Damment and

Pennick, 2007), and results in humans showed an absolute bioavailability of lanthanum of about 0.0013 % (Pennick at al., 2006).

(506) In *Publication 30* (ICRP, 1980), an absorption value of $1x10^{-4}$ was recommended. Since no relevant additional data on the gastrointestinal absorption of yttrium is available, an f_A value of $1x10^{-4}$ is adopted here for all chemical forms.

11.1.3. Systemic Distribution, Retention and Excretion

11.1.3.1. Summary of the database

Overview

(507) The biokinetics of systemic yttrium varies with the mode of administration and the administered form and mass, due in part to the tendency of yttrium compounds to form colloids (Lloyd, 1961; Rosoff et al., 1961; Spencer, 1968). Colloidal yttrium deposits largely in the liver, spleen, or bone marrow, with the distribution depending on particle size (Dobson et al., 1948). Yttrium that is absorbed to blood across membranes or intravenously injected in non-colloidal form initially clears with a half-time of 1 h or less (Ekman and Aberg, 1961; Kawin, 1963, Schmidtke, 1964) and transfers mainly to bone surfaces, liver, kidneys, and urinary bladder contents (Hamilton, 1949; Durbin, 1960; Herring et al., 1962; Ando et al., 1989; Muggenburg et al., 1998). A few percent of the absorbed or injected amount clears more slowly from blood, presumably due mainly to attachment to plasma proteins (Rosoff et al., 1958; Hirano and Suzuki, 1996).

(508) Yttrium is tenaciously retained by bone, and a substantial portion of that deposited in soft tissues also shows relatively slow return to blood. After intravenous administration of ^{88}Y as citrate to human subjects, about one-fifth of the injected amount was excreted within a few days, primarily in urine, and the remainder was retained with a projected half-time of years (Etherington et al., 1989a,b).

Data for human subjects

(509) Rosoff et al., (1961) and Spencer (1968) studied the rate of excretion of ^{90}Y in elderly hospital patients after intravenous injection of different forms of yttrium and the effects of chelating agents on the excretion rate. Less than 0.5% of the administered amount was excreted in urine during the first 24 hours after administration of $^{90}YCl_3$. About 5% of the administered activity was excreted in urine during the first day after administration of ^{90}Y as nitrilotriacetate (^{90}Y-NTA), a form thought to prevent the formation of yttrium hydroxy colloids. The chelating agents EDTA and DTPA were found to be effective in removing ^{90}Y from the body if administered in the first day or two after intake of ^{90}Y.

(510) Retention, distribution, and urinary and fecal excretion of yttrium were studied in two healthy adult male volunteers who received ^{88}Y as citrate ($T_{1/2}$ = 107 d) by intravenous injection (Etherington et al., 1989a,b). The behavior of ^{88}Y as determined by *in vivo* measurements and bioassay was similar in the two subjects. An estimated 22% of the injected amount was excreted in the first few days, with urinary excretion accounting for 94% and 93% of the excreted amount in Subjects A and B, respectively, over 5 d and 91% in Subject B over 14 d. The combined retention data for the subjects could be approximated by a two exponential function to time t (days) after injection:

$$R(t) = 0.22 \exp(-0.693\ t / T_1) + 0.78 \exp(0.693\ t / T_2)$$

where the short-term half-time T_1 was about 16 hours and the long-term half-time T_2 was

much longer than the measurement period of about one year. Uptake by the liver was estimated from external measurement as about 12% and 10% for Subjects A and B, respectively. One-fourth or more of the liver content was lost over the first few days or weeks, and the remainder was removed more slowly. In Subject B, at least half the initial deposit was retained in the liver after 6 months. The results of a longitutinal scan on one subject at 22 days were consistent in magnitude and qualitative shape with the estimated bone surface area distribution in the body.

Data for laboratory animals

(511) For comparison with findings summarized above for their two human subjects, Etherington and coworkers (1989a,b) determined the tissue distribution of ^{88}Y in rats intravenously injected with similar ^{88}Y solutions. The findings for rats were broadly consistent with the systemic biokinetics estimated for the human subjects, the main difference being that removal from the liver was faster and the fecal excretion rate was higher in rats. On average, urinary and fecal excretion accounted for 26.1% and 8.4%, respectively, of injected activity after 4 days in rats. The contents of liver, kidneys, gastrointestinal tract, and carcass (including skeleton) accounted for 4.4%, 1.4%, 0.9%, and 58.6%, respectively.

(512) In rats receiving $^{91}YCl_3$ by parenteral injection, 55-65% of the administered amount deposited in the skeleton, and little of this was lost over the next 2-3 months (Hamilton, 1949; Durbin, 1960). At 4 d after administration, the liver contained about 12% of the administered activity, and excreta (primarily urine) accounted for about 26% (Durbin, 1960). Data of Ando et al. (1989) indicate that the liver contained a major portion of the systemic activity between 3 hours and 2 days after intravenous injection of $^{90}YCl_3$ into rats.

(513) Watanabe et al. (2005) studied the effectiveness of $CaNa_3DTPA$ in removing ^{90}Y from the body in rats contaminated with ^{90}Y chloride via a puncture wound. In control animals the concentration of ^{90}Y in bone was on average about 10 times that in liver, 6 times that in kidney, and 60 times that in blood during the first 24 h. At 7 d the concentration in bone was about 39 times that in liver, 17 times that in kidney, and 1900 times that in blood. Prompt treatment of the wound with $CaNa_3DTPA$ was found to be more effective than systemic treatment in minimizing accumulation of ^{90}Y in bone.

(514) A goat receiving ^{91}Y by intravenous injection excreted about 20% of the injected amount in urine and 4% in faeces over the first 10 d (Ekman and Aberg, 1961). The concentration of ^{91}Y in blood serum declined by a factor of ~8 from a few minutes to 3 h after injection and a factor of ~2.5 from 3-24 h after injection. About half of the total 10-d urinary losses occurred on the first day and about one-fourth occurred on the second day. Fecal losses were about 0.7% on day 1, 2% on day 2, and 0.4% on day 3, and declined monotonically thereafter. Examination of cartilage from the trachea and ribs indicated that ^{91}Y may have been bound to chondroitinsulphuric acid.

(515) After brief inhalation of $^{91}YCl_3$ by guinea pigs, about 28% of the deposited activity was absorbed to blood over the first 8 days (Schmidtke, 1964). At that time the skeleton, liver, kidneys, and blood of animals not receiving chelation therapy contained about 65%, 5%, 1%, and 0.15%, respectively, of the absorbed activity. Urinary excretion during the first 8 days accounted for about 22% of the absorbed amount.

(516) The biokinetics, dosimetry, and radiological effects of ^{91}Y have been studied in dogs exposed to different ^{91}Y aerosols (McClellan and Rupprecht, 1967; Barnes et al., 1972; Muggenburg et al., 1998). Detailed systemic data were obtained for dogs exposed to relatively soluble $^{91}YCl_3$ aerosols. A sharp drop in total-body ^{91}Y occurred during the first several days after exposure, presumably due to clearance of activity deposited in the upper respiratory tract by mucociliary transport and subsequent swallowing and fecal excretion.

After about 3 weeks the rate of decline of the body burden approximated the radiological half-life of ^{91}Y. Daily losses in urine and faeces were measured in three dogs through 64 days post exposure. On average about 15% of the initial body burden was removed in urine and about 45-50% in faeces during the first week. Fecal excretion was the dominant route of excretion during the first four days, but beyond two weeks post injection daily urinary excretion was 1.5-4 times greater than daily fecal excretion. Tissue concentrations of ^{91}Y measured in three dogs at 32 d after intake indicated that the skeleton, liver, and kidneys contained roughly 75%, 15%, and 1%, respectively, of the systemic burden. Autoradiographs were made using tissue collected at necropsy of dogs dying in the early postexposure period. In bones, activity was prominent on bone surfaces. The concentration in long bones was higher near the ends than in the shaft. Activity was generally diffuse in the liver and spleen. Absorbed ^{91}Y was found in bronchial cartilage.

(517) In studies on young dogs receiving ^{91}Y by intravenous or intraperitoneal injection, activity depositing in the skeleton was found to concentrate on non-growing, highly calcified surfaces and resorbing surfaces of bone (Jowsey et al., 1958, Herring et al., 1962). No deposition was found in osteoid tissue. It was suggested that the mechanism of binding of yttrium to bone surfaces may be different from that of plutonium or americium despite the general similarities in the skeletal behavior of these elements (Herring et al., 1962).

(518) Weanling rabbits were injected intravenously with ^{91}Y, ^{90}Sr free from ^{90}Y, or ^{90}Sr and ^{90}Y in equilibrium to compare the relative distributions of strontium and yttrium and to determined whether ^{90}Y produced in vivo from decay of ^{90}Sr behaves differently from yttrium introduced as a parent radionuclide (Lloyd, 1961). A qualitative similarity in the two chemically dissimilar radionuclides ^{90}Y and ^{90}Sr was observed in that the tissues containing the highest concentration of ^{90}Sr were also those containing the highest concentration of ^{91}Y (i.e. bone, pituitary, cartilage, and kidney). The distributions of ^{90}Sr and ^{91}Y differed quantitatively. For example, kidney, liver, and spleen concentrated ^{91}Y to a much greater extent than ^{90}Sr. The rate of disappearance of ^{91}Y from the soft tissues was much lower than the rate of disappearance of ^{90}Sr. At 9 days, the ^{91}Y concentration in the liver was 150 times that of ^{90}Sr. When ^{90}Sr was injected there was a secondary uptake of ^{90}Y in the liver, spleen, and kidneys after the initial distribution of ^{90}Sr.

(519) Stevenson (1975) studied the influence of age and gender on the relative behaviors of ^{90}Y and ^{90}Sr in rats over a period of 32 d following administration of solutions with ^{90}Sr and ^{90}Y in equilibrium. The activity ratio ^{90}Y : ^{90}Sr in bone depended to some extent on age and gender but typically was 1.0-1.6 at 1 d, increased by ~30% over the next 3 d, and then declined to near equilibrium levels over the next month. The ratio ^{90}Y : ^{90}Sr in the liver rose from about 10 at 30 min after injection to about 400 by the fourth day. During the same period the ratios for the kidney and spleen rose from about 3 to about 100-150 and the ratio for the heart rose from 1.5 to 14-22. The general conclusion was that the yttrium in blood is initially taken up to a much larger extent than strontium by soft tissues but gradually transfers to the skeleton, resulting in a temporary elevation of the ratio ^{90}Y : ^{90}Sr in bone.

(520) By measuring the relative activities of ^{90}Sr and ^{90}Y in various tissues of a beagle, Arnold et al. (1955) concluded that ^{90}Y does not separate from ^{90}Sr in bone volume. Their conclusion was based mainly on the observation that ^{90}Y did not become more concentrated than ^{90}Sr at sites where migrating ^{90}Y would have tended to accumulate.

(521) Mueller (1972) studied the relative behavior of strontium and yttrium in mice and intraperitoneal injection of ^{90}Sr and ^{90}Y in radioactive equilibrium or ^{90}Sr freshly purified from ^{90}Y. At 7 d after injection of equilibrium activities, the concentration ratio ^{90}Y: ^{90}Sr was about 150 for liver and spleen and near 1 for bone. At 7 d after injection of purified ^{90}Sr, the activity ratio was about 3 for liver and spleen and 0.9 for bone.

11.1.3.2. Biokinetic model for systemic yttrium

(522) The structure of the systemic model for yttrium is shown in Figure 11-1. Transfer coefficients are listed in Table 11-3. The transfer coefficients describing movement of yttrium between bone compartments and removal from bone are default values for bone-surface seekers. Other transfer coefficients in the model are based on deposition fractions and biological half-times summarized below. Deposition fractions and half-times describing uptake and retention by the liver and rates of urinary and faecal excretion were selected for consistency with yttrium injection data for healthy human subjects described earlier. The remaining deposition fractions and half-times were based on animal data described earlier, with preference given to data for large animals.

(523) Blood is divided into compartments Blood 1 and Blood 2 representing fast and slow clearance, respectively. Yttrium leaves Blood 1 at the rate 16.6 d^{-1} corresponding to a biological half-time of 1 h. Outflow from Blood 1 is divide as follows: 3% moves to Blood 2; 15% to the urinary bladder contents; 1% to the small intestine (SI) contents; 40% to bone surfaces, equally divided between trabecular and cortical surfaces; 10% to a fast-turnover liver compartment called Liver 0; 1% to the kidneys; 22% to a fast-turnover soft-tissue compartment called ST0; and 8% to a slow-turnover soft-tissue compartment called ST1. Activity is removed from Liver 0 with a biological half-time of 3 d. Activity leaving Liver 0 is divided among Blood 1, SI contents (representing biliary secretion), and a slow-turnover liver compartment called Liver 1 in the ratio 0.5 : 0.4 : 0.1. Activity is removed from Blood 2 to Blood 1 with a half-time of 1.5 d; from ST0 to Blood 1with a half-time of 3 d; and from Liver 1, Kidneys, and ST1 to Blood 1 with a half-time of 1 y. The fate of yttrium deposited on bone surfaces is described by the generic model for bone-surface-seekers, except that yttrium biologically removed from bone is assumed to return to blood rather than to be channeled through bone marrow. Thus, yttrium is removed from cortical or trabecular bone surfaces at a rate proportional to (1.5 times) the turnover rate of that bone type. The assumed bone turnover rates are 3% y^{-1} for cortical bone and 18% y^{-1} for trabecular bone. One-third of activity removed from bone surfaces is buried in bone volume and two-thirds transfers to Blood 1. Activity is removed from cortical or trabecular bone volume to Blood 1 at the rate of turnover of that bone type.

(524) Model predictions are compared with the human injection data of Etherington et al. (1989a,b) in Figures 11-2 to 11-4. In these two subjects, urinary excretion accounted for 93-94% of the excreted amount over 5 d and 91% over 14 d. Model values are 91% over 5 d and 89% over 14 d.

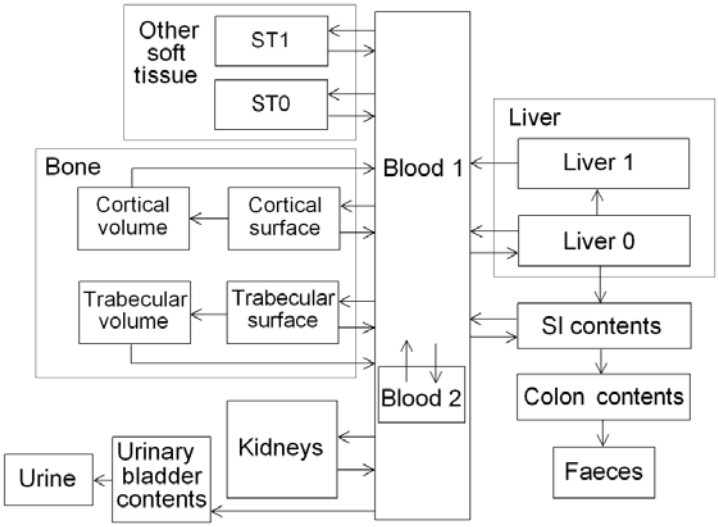

Figure 11-1. Structure of the biokinetic model for systemic yttrium.

Table 11-3. Parameter values in the systemic model for yttrium.

From	To	Transfer coefficient (d^{-1})
Blood 1	Blood 2	0.498
Blood 1	Liver 0	1.66
Blood 1	Kidneys	0.166
Blood 1	ST0	3.652
Blood 1	ST1	1.328
Blood 1	Urinary bladder contents	2.49
Blood 1	SI contents	0.166
Blood 1	Trabecular surface	3.32
Blood 1	Cortical surface	3.32
Blood 2	Blood 1	0.462
Liver 0	SI contents	0.0231
Liver 0	Blood 1	0.0924
Liver 0	Liver 1	0.116
Liver 1	Blood 1	0.0019
Kidneys	Blood 1	0.0019
ST0	Blood 1	0.231
ST1	Blood 1	0.0019
Trabecular surface	Blood 1	0.000493
Trabecular surface	Trabecular volume	0.000247
Trabecular volume	Blood 1	0.000493
Cortical surface	Blood 1	0.0000821
Cortical surface	Cortical volume	0.0000411
Cortical volume	Blood 1	0.0000821

11.1.3.3. Treatment of radioactive progeny

(525) Chain members addressed in the derivation of dose coefficients for internally deposited yttrium isotopes include isotopes of yttrium, strontium, zirconium, and niobium.

An yttrium isotope produced in the body after uptake of an yttrium parent is assumed to have the same systemic biokinetics as the parent. Isotopes of zirconium and niobium produced in systemic compartments after intake of an yttrium parent are assigned the characteristic systemic models for zirconium and niobium, respectively, described elsewhere in this report. The characteristic systemic models for yttrium, zirconium, and niobium all have the same model structure. A zirconium or niobium atom produced in a given compartment by radioactive decay is assumed to behave as if it had entered that compartment as a parent radionuclide. This includes subcompartments of 'Other soft tissue'.

(526) The model for strontium produced in systemic compartments after intake of an yttrium parent is an extension of the characteristic model for strontium described elsewhere in this report. That model is extended by adding individual compartments representing liver and kidneys, which are represented explicitly in the model for yttrium. Each of these compartments is assumed to exchange strontium with blood. Parameter values describing rates of uptake and removal of strontium by liver and kidneys are set for reasonable agreement with postmortem measurements on human subjects injected with ^{85}Sr during late stages of various terminal illnesses (Schulert et al., 1959). The transfer coefficients from blood to liver and kidneys are both set at 0.05 d^{-1}. The transfer coefficient from blood to the intermediate-term soft-tissue compartment in the characteristic model for strontium is reduced from 1.5 d^{-1} to 1.4 d^{-1} to leave the total outflow rate from blood unchanged. The removal half-times from liver and kidneys to blood are set at 6 d and 2 d, respectively. Strontium produced by radioactive decay in compartments of the yttrium model that are not identifiable with compartments of the strontium model is treated as follows. Strontium produced in either of the two blood compartments of the yttrium model is assumed to transfer to the single blood compartment of the strontium model at the rate 1000 d^{-1} (half-time of ~1 min). Strontium produced in either of the two liver compartments of the yttrium model is assumed to transfer to the blood compartment of the strontium model with a half-time of 6 d, which is the removal half-time of strontium from the liver in the extended strontium model described above. Strontium produced in either of the two compartments of 'Other soft tissue' in the yttrium model is assumed to transfer to the blood compartment of the strontium model at the rate 2.5 d^{-1}, which is the shortest removal half-time from the soft-tissue compartments in the characteristic model for strontium.

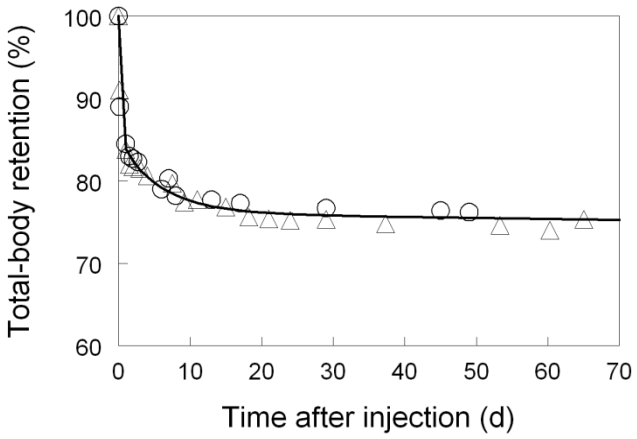

Figure 11-2. Model predictions of total-body retention of intravenously injected yttrium compared with observations of Etherington et al. (1989a,b) for two human subjects intravenously injected with ^{88}Y as citrate.

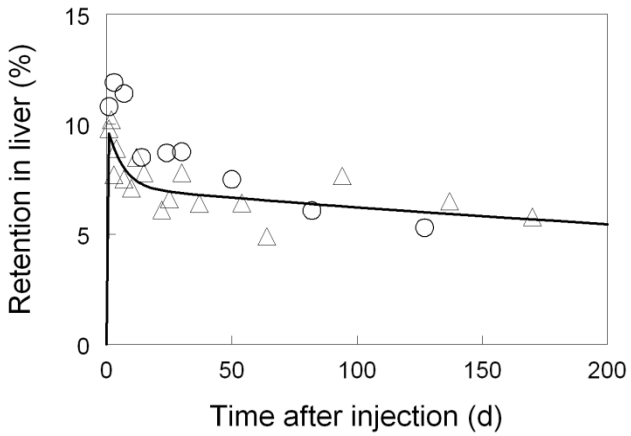

Figure 11-3. Model predictions of liver content of yttrium as a function of time after intravenous injection, compared with observations of Etherington et al. (1989a,b) for two human subjects intravenously injected with ^{88}Y as citrate.

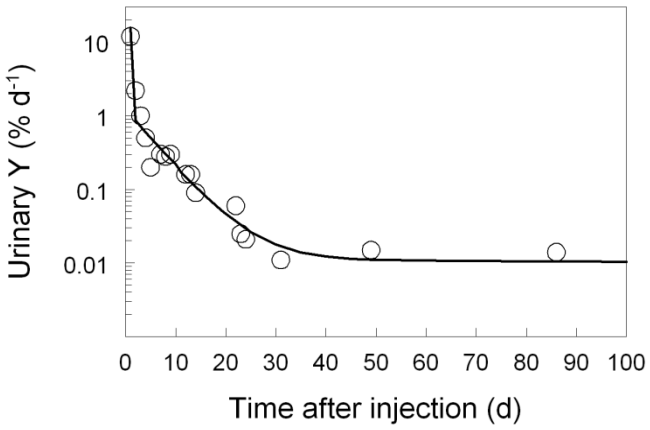

Figure 11-4. Model predictions of urinary excretion of yttrium as a function of time after intravenous injection, compared with observations of Etherington et al. (1989a,b) for two human subjects intravenously injected with ^{88}Y as citrate.

11.2. Individual monitoring

(527) Monitoring of ^{90}Y is generally accomplished by measuring its beta emission in urine, either using liquid scintillation or beta proportional counting.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{90}Y	Urine Bioassay	Liquid Scintillation Counting	1-5 Bq/L	1 Bq/L
^{90}Y	Urine Bioassay	Beta proportional counting	0.4 Bq/L	0.05 Bq

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6966

12. ZIRCONIUM (Z = 40)

12.1. Chemical Forms in the Workplace

(528) Zirconium is a transition metal which mainly occurs in oxidation state IV. It may be encountered in industry in a variety of chemical and physical forms, including oxides, carbonates, oxalates and zircon ($ZrSiO_4$). Zirconium radionuclides such as ^{93}Zr and ^{95}Zr are likely to be encountered in the nuclear industry in the form of activated Zircalloy fuel element cladding, and in acidic fission product solutions. Zirconium could also be present in fragments of irradiated fuel.

Table 12-1. Isotopes of zirconium addressed in this report

Isotope	Physical half-life	Decay mode
Zr-86	16.5 h	EC, B+
Zr-87	1.68 h	EC, B+
Zr-88	83.4 d	EC
Zr-89	78.41 h	EC, B+
Zr-93	1.53E+6 y	B-
Zr-95[a]	64.032 d	B-
Zr-97	16.744 h	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

12.2. Routes of Intake

12.2.1. Inhalation

Absorption Types and parameter values

(529) In all the studies noted below the zirconium isotope followed was ^{95}Zr ($t_{½}$ 64 d), which decays to niobium-95 (^{95}Nb, $t_{½}$ 35 d). In most studies both radionuclides were deposited in the respiratory tract, and the combined activity of the two radionuclides followed. Thus in interpreting the results it has to be assumed that their behaviour was similar. Furthermore, the ^{95}Nb measured was partly that which deposited, and partly that formed from the *in situ* decay of ^{95}Zr. Because of the relatively short half-lives of these radionuclides few studies are of sufficient duration to distinguish Types M and S behaviour based on the ICRP *Publication 71* criteria of lung retention or total absorption up to 180 d after intake.

(530) Some information was found on the behaviour of inhaled zirconium in man, mainly associated with irradiated fuel. Information is available from experimental studies of zirconium as oxalate, oxide, and irradiated uranium dioxide.

(531) Absorption parameter values and Types, and associated f_A values for particulate forms of zirconium are given in Table 12-2.

Zirconium oxalate

(532) Following inhalation by guinea pigs of carrier-free ^{95}Zr-oxalate, the activity in the lungs immediately after the 30-minute exposure, and at 1 and 28 days later was about 24%, 10% and 5% of the “recovered dose”. Amounts in the skeleton at these times were 8%, 15%

and 9% respectively. Similar results were obtained using ^{95}Zr-oxalate with added zirconium oxychloride ($ZrOCl_2$) (Schmidtke et al., 1964; Schiessle et al., 1964). The large uptake in the skeleton at the first measurement suggests a rapid dissolution rate, s_r, of the order of 100 d^{-1}. However, about 10% of the activity deposited in the lungs was not cleared rapidly (f_r ~0.9). The decrease in lung content between 4 and 28 days did not give any obvious increase in activity in the skeleton, and hence no indication of a significant "bound state" from which clearance is only by absorption. The amount retained in the lungs at 28 d suggests assignment to Type M, but is very close to the criterion for assignment to Type F.

(533) Thomas et al. (1971) studied the biokinetics of ^{95}Zr–^{95}Nb following inhalation by mice of aerosols formed by heating droplets of zirconium oxalate solution to various temperatures. *In vitro* dissolution tests were conducted on similar materials by Kanapilly and Goh (1973) and Kanapilly et al. (1973). Immediately after inhalation of the aerosols formed at 100˚C and 250˚C (both zirconium oxalate, but mainly droplets and solid particles respectively) the skeleton contained about 20% of the body content, the lungs 2% and 25% respectively. It was noted that the ratio of ^{95}Nb to ^{95}Zr in the lungs was lower than in the aerosol, indicating a pronounced differential loss of ^{95}Nb. Nevertheless, the results suggest that at the lower temperature most of the material deposited in the lungs was absorbed rapidly: f_r ~0.9 and s_r of the order of 100 d^{-1}. For both materials these results indicate Type F behaviour, as do those of the *in vitro* dissolution tests.

(534) Since rapid absorption is incomplete, the results are difficult to interpret, all the more so because of the radionuclide mixture present. Furthermore, absorption of ^{95}Nb from the lungs following deposition of the oxalate, is also complex (see niobium inhalation section). Hence specific parameter values are not recommended by the task group for zirconium oxalate. The information above suggests assignment to Type F, but also that absorption is slower than for niobium oxalate, for which there is more comprehensive information, which gives assignment to Type M. Zirconium oxalate is therefore also assigned to Type M.

Zirconium oxide and carbonate

(535) As noted above, Thomas et al. (1971) studied the biokinetics of ^{95}Zr–^{95}Nb following inhalation by mice of aerosols formed by heating droplets of zirconium oxalate solution. The aerosols formed at 600˚C ($Zr(CO_3)_2$ and $ZrOCO_3$) and at 1100˚C (ZrO_2 and $ZrOCO_3$) gave very similar results *in vivo* (with no differential loss of niobium). From 10 to 130 d after inhalation the lungs contained more than 90% of the sacrifice body burden (SBB) while the skeleton content increased from 2% SBB at 2 d to 6% SBB at 130 d. These results indicate Type S behaviour. *In vitro* tests on similar materials by Kanapilly and Goh (1973) and Kanapilly et al. (1973) confirmed low dissolution rates, but their duration was too short to distinguish Type M from Type S.

(536) Cuddihy (1978) applied simulation modelling to measurements of ^{95}Nb following inhalation of similar ^{95}Nb-labelled zirconium aerosols (formed at 1000˚C) by dogs to obtain an absorption function (fractional absorption rate):

$$S(t) = 0.00016\ e^{-0.04t} + 0.0001\ d^{-1} \text{ at time } t \text{ (days) after intake,}$$

which can be represented using the HRTM with $f_r = 0.004$, $s_r = 0.04\ d^{-1}$ and $s_s = 0.0001\ d^{-1}$, consistent with assignment to Type S. This assumes that the absorption of ^{95}Nb is a marker for dissolution of the zirconium oxide matrix, and not leaching of the ^{95}Nb from it. *In vivo* measurements following accidental inhalation of what was probably the same material by a person gave a lung retention half time of about 220 days, indicating Type M or S behaviour (Waligora, 1971).

Zirconium tritide

(537) For details see the hydrogen inhalation section. Measurements of tritium following intratracheal instillation of zirconium tritide into rats were consistent with assignment to Type S.

Nuclear weapons fallout

(538) During the early 1960s, measurements were made of ^{95}Zr–^{95}Nb activities in human lungs due to fall-out from atmospheric nuclear weapons tests. Most were made *post mortem* (Schönfeld et al., 1960; Osborne, 1963; Wrenn et al., 1964; Dutailly et al., 1966), but *in vivo* measurements were also made, enabling the variation with time in individual subjects to be determined (Rundo and Newton, 1962; 1965). Several authors compared their measurements with those predicted from measured air concentrations, using a single exponential model (ICRP, 1959). Biological lung retention half-times were estimated to be between about 70 d (Wrenn et al., 1964) and more than 120 d (Rundo and Newton, 1965). Wrenn et al., (1964) noted that little ^{95}Zr–^{95}Nb activity was found in other tissues, and that Wegst et al. (1964) had shown that ^{95}Zr-^{95}Nb activity in the lungs was present in particulate form. Overall this indicates Type M or S behaviour.

Irradiated fuel

(539) Following an accidental release, zirconium could be present in fragments of irradiated fuel, where the matrix is predominantly uranium oxide. The results of a study on one person following accidental inhalation of irradiated fuel indicate Type M behaviour of the zirconium present (Rundo, 1965). In another, measurements of ^{95}Zr-^{95}Nb made on a worker for 6 months following an accidental intake, probably of irradiated fuel (UO_2), indicate Type S behaviour (Thind, 1995).

(540) 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 (49 days for ^{95}Zr-Nb) and different from those expected for systemic retention, indicating that they were trapped in particles and metabolically inert, and thus indicating Type M rather than Type F behaviour.

(541) Tissue distribution and retention of several radionuclides were followed for 3 months after intratracheal instillation of irradiated UO_2 powder into rats (Lang et al., 1994). For ^{95}Zr, the total amounts absorbed by 1 and 3 months were estimated to be about 1% and 3% of the initial lung deposit (ILD) respectively, indicating values of f_r <0.01 and s_s ~0.001 d^{-1}, and assignment to Type S.

(542) The *in vitro* dissolution of samples of particles released from the Chernobyl accident was measured for up to 60 d (Cuddihy et al., 1989). For all radionuclides, including ^{95}Zr-^{95}Nb, 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}, consistent with assignment to Type M.

Other compounds

(543) Measurements of ^{95}Zr–^{95}Nb in the lungs of a person for 5 months following an accidental intake of unspecified material indicate Type M or S behaviour (Cofield, 1963).

Decay products of zirconium formed in the respiratory tract

(544) The general approach to treatment of decay products formed in the respiratory tract is described in Part 1, Section 3.2.3. In summary, it would be expected that the rate at which a

particle dissociates is determined by its matrix, and hence the physico-chemical form of the inhaled material, but that the behaviour of soluble (Type F) material in the respiratory tract would depend on its elemental form, i.e. that of the decay product. Nevertheless, for simplicity, in this series of documents it is assumed that decay products formed in the respiratory tract have the same dissolution parameter values as the parent inhaled.

(545) Of particular importance in the case of zirconium is the formation of ^{95}Nb ($t_{½}$ 35 d) from ^{95}Zr ($t_{½}$ 64 d). Some experimental results were found from which the absorption of ^{95}Nb could be compared directly with that of ^{95}Zr under the same conditions. However, the ^{95}Nb in the respiratory tract would have been partly administered with the ^{95}Zr and partly formed in the respiratory tract by decay of the ^{95}Zr parent.

(546) Thomas et al. (1971) studied the biokinetics of ^{95}Zr–^{95}Nb following inhalation by mice of aerosols formed by heating droplets of zirconium oxalate solution to various temperatures (see above). For the aerosols formed at 100˚C and 250˚C (both zirconium oxalate) the ratio of ^{95}Nb to ^{95}Zr in the lungs was lower than in the aerosol, indicating a pronounced differential loss of ^{95}Nb. The aerosols formed at 600˚C ($Zr(CO_3)_2$ and $ZrOCO_3$) and at 1100˚C (ZrO_2 and $ZrOCO_3$) showed no differential loss of niobium.

(547) 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 (see above and niobium inhalation section). For ^{95}Zr, the estimated total amounts absorbed by 1 and 3 months were ~1% and 3% ILD, whereas for ^{95}Nb they were ~5% and 9% ILD.

(548) Thus there is evidence that for some, especially soluble, forms of zirconium, the niobium daughter is absorbed from the lungs more rapidly than the zirconium parent. However, as there is insufficient information to estimate element-specific rapid dissolution rates for either element, the general default value of 30 d^{-1} is applied to both, and so their dissolution parameter values are the same.

Rapid dissolution rate for zirconium

(549) Evidence from the zirconium oxalate studies outlined above suggests a rapid dissolution rate of the order of 100 d^{-1}, but only of part of the ILD, ($f_r < 1$). There is therefore no justification for choosing a rate different from the general default value of 30 d^{-1}, which is applied here to all Type F forms of zirconium.

Extent of binding of zirconium to the respiratory tract

(550) Evidence from the zirconium oxalate studies outlined above suggests that following the rapid phase of absorption about 10% of the initial lung deposit clears slowly from the lungs. Clearance of this material does not appear to be mainly by absorption to blood, as assumed for material in the “bound state”, and therefore does not give evidence for significant binding of zirconium. Moreover, the results available are difficult to interpret (see above). It is therefore assumed that for zirconium the bound state can be neglected, i.e. f_b = 0.0.

Table 12-2. Absorption parameter values for inhaled and ingested zirconium

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	—	1	30	–	0.002
M	Oxalate; all unspecified forms	0.2	3	0.005	$4x10^{-4}$
S	Carbonate, oxide, tritide	0.01	3	$1x10^{-4}$	$2x10^{-5}$
Ingested material					
All chemical forms					0.002

[a] It is assumed that for zirconium the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of zirconium (30, 3 and 3 d^{-1}, respectively) are the general default values.

[b] Materials (e.g. zirconium oxalate) are 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 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 and the f_A value for ingested soluble forms of zirconium ($2x10^{-3}$).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

12.2.2. Ingestion

(551) Few human data are available on the absorption of zirconium from the gastrointestinal tract. In a study using stable tracer ^{96}Zr-chloride given to a healthy male volunteer, the absorption of zirconium was estimated to be $2.5 \cdot 10^{-3}$ (Veronese et al., 2003a and b). A broader study was conducted with stable tracers in a total of 14 volunteers, to which zirconium was administered in the form of oxalate or citrate (Greiter et al., 2011). The fractional absorption was found to be equal to $(7.4 \pm 1.5) \cdot 10^{-3}$ for oxalate and to $(1.10 \pm 0.23) \cdot 10^{-3}$ for citrate.

(552) These values are similar to those found with animals. Fletcher (1969) reported values ranging from 3.10^{-4} to 2.10^{-3} for the fractional absorption of ^{95}Zr in young adult rats after administration of a number of chemical forms, including the chloride, sulphate and organic complexes with lactate and oxalate. Similar values were reported by Shiraishi and Ichikawara (1972) for Zr oxalate in adult rats, de Bartolo et al. (2000) for Zr sulphate in rabbits and Sirotkin et al. (1970) for Zr chloride in cows. Taylor et al. (1983) obtained values ranging from 1.5 to 8.10^{-4} for the fractional absorption of the chemically similar radionuclide ^{181}Hf in rats and hamsters.

(553) Reference values used previously were 0.002 in ICRP *Publication 30* (1979) and 0.01 for intake from members of the public (ICRP, 1989). However, this latter value was adopted for taking account of the biologically incorporated form of the element present at low concentration in the diet. On the basis of the recent human and animal data, an f_A value of 0.002 is adopted here for all chemical forms.

12.2.3. Systemic Distribution, Retention and Excretion

12.2.3.1. Summary of the database

Human subjects

(554) Mealey (1957) studied the biokinetics of ^{89}Zr ($T_{1/2}$ = 78.4 h) following its intravenous administration as citrate to a comatose subject with brain cancer but with vital signs, electrolyte levels, and renal function within normal limits. Activity cleared slowly from plasma, apparently due to binding of ^{89}Zr to plasma proteins. About 10% of the injected amount (corrected for decay) remained in plasma at 7 d. There was little if any accumulation of ^{89}Zr in red blood cells. Urinary excretion accounted for 2.5% of the administered amount over the first 24 h and 7.6% over 7 d. Intravenously administered ^{89}Zr was also measured in biopsy samples from two patients undergoing neurological surgery. In one of the subjects the ^{89}Zr concentrations in bone (skull) and muscle were 1.2 and 4.8% of injected ^{89}Zr kg^{-1} tissue, respectively, at 90 min after administration. In the other subject, concentrations of ^{89}Zr in bone, muscle, and normal brain tissue were 0.9, 7.6, and 0.8% kg^{-1}, respectively, at 3 h. High accumulation of ^{89}Zr in muscle was also indicated by external measurements on other patients. External measurements on one subject over three successive days indicated a sustained high concentration of activity in muscle but a substantial decrease in the concentrations in the skull and brain during this period.

(555) The biokinetics of zirconium was studied in three healthy subjects (one male and two females in the age range 27-60 y) following oral or intravenous administration of stable zirconium isotopes (Veronese et al., 2003a,b). Clearance of injected zirconium from plasma could be characterized by a relatively fast component representing roughly half of the administered amount, followed by a slower component. The half-time associated with the faster component was estimated as 3.6 h in two subjects and 0.8 h in the third subject. The investigators derived a half-time of about 3 d for the slower component after combining their findings with longer-term measurements of plasma clearance of zirconium reported by Mealey (1957).

(556) Relatively long-term studies of the biokinetics of orally or intravenously administered stable zirconium isotopes were later conducted on seven male and six female subjects in the age range 26-60 y (Greiter et al., 2011). The zirconium isotopes were prepared either in citrate or oxalate solution. Blood plasma and urine were sampled up to 100 d after administration. Mean fractional absorption of zirconium was sevenfold higher after oral intake of zirconium oxalate than after intake of zirconium citrate. The derived urinary excretion data are difficult to interpret in terms of typical excretion rates due to the high variability of the measurements and a relatively high detection limit. Approximately 20% and 40% of the urinary measurements were below the detection limit in the injection and oral tracer studies, respectively. Taken at face value, the data indicate that urinary losses over the first week averaged about 6% of the intravenously injected amount. The investigators' proposed biokinetic model for zirconium with expected transfer coefficients based on results of the study predicts total urinary losses of about 2% at 7 d and 8% at 100 d after intravenous injection.

Laboratory animals

(557) Bone was found to be the main systemic repository for zirconium tracers following their administration by various routes to rats (Durbin, 1960; Fletcher, 1969), guinea pigs (Schiessle et al., 1961), and mice (Bäckström et al., 1967; Thomas et al., 1971; Abou et al., 2011). Autoradiographic studies on rats (Hamilton, 1947) indicated that skeletal zirconium

was confined largely to bone surfaces.

(558) At 4 d after intramuscular administration of ^{95}Zr as citrate to rats, the liver, kidneys, and bone contained approximately 6.6, 4.9, and 35%, respectively, of the administered activity (Durbin, 1960). About 18% of administered activity had been excreted by that time, mainly in faeces. Nearly two-thirds of the administered amount remained in the body after 2-4 mo.

(559) Autoradiographic studies following intravenous administration of ^{95}Nb or ^{95}Zr-^{95}Nb to mice indicated qualitatively similar distributions of activity in the two cases (Bäckström et al., 1967). These distributions were also similar to that observed by the investigators in an earlier study of ^{103}Ru. All of these radionuclides showed an affinity for connective tissue as well as bone. The affinity for bone increased in the order ^{103}Ru < ^{95}Nb < ^{95}Zr-^{95}Nb (Bäckström et al., 1967).

(560) Following intraperitoneal administration of ^{95}Zr citrate to rats, about 60% of the injected amount was retained after 1 mo and about 50% was retained after 3 mo (Richmond et al., 1960). In a similar study on mice conducted by the same investigators (Furchner et al., 1964), nearly half of the injected ^{95}Zr was rapidly lost from the body, and about two-thirds of the administered amount was lost within a few weeks. Measurements up to 420 d after injection indicated that the remaining one-third was removed with a biological half-time of several years.

(561) Fletcher (1969) studied the behavior of ^{95}Zr and ^{95}Nb in rats following oral or intravenous administration of ^{95}Zr-^{95}Nb or pure ^{95}Nb as oxalates. Total-body retention of ^{95}Zr over 80 d was determined by external counting and correction for counts for simultaneously injected ^{95}Nb and ^{95}Nb formed in vivo by radiological decay of ^{95}Zr. The correction was based on the assumption that ^{95}Nb formed in vivo behaves as if it had been injected intravenously at the time of formation. This assumption was consistent with the measured distributions of ^{95}Nb and ^{95}Zr at 80 d. Total-body retention of injected ^{95}Zr was greater in males than females at all measurement times. As an average over both sexes, about 90% of intravenously administered ^{95}Zr was retained in the body after 8 d, 80% was retained after 30 d, and 60% was retained after 80 d. The concentration of ^{95}Zr in tissues following administration of a mixture of ^{95}Zr and ^{95}Nb was determined using physical decay measurements or beta scintillation counting of their distinctive beta emissions. At 8 d an estimated 89-92% of total-body ^{95}Zr was in bone, and the kidneys, spleen, and liver each contained a few tenths of 1% of the administered amount.

(562) The relative behaviours of ^{95}Zr and ^{95}Nb were studied in mice following inhalation of these radionuclides at near-equilibrium conditions in aerosols produced at various temperatures (Thomas et al., 1971). Comparison of the activity ratios ^{95}Nb:^{95}Zr in the aerosols, lung, bone, and liver indicated different systemic biokinetics of these radionuclides. Bone was the main systemic repository for both ^{95}Zr and ^{95}Nb, but ^{95}Zr showed higher accumulation in bone and lower accumulation in liver than ^{95}Nb.

(563) Shiraishi and Ichikawara (1972) studied the gastrointestinal absorption, retention, and distribution of ^{95}Zr-^{95}Nb following a single oral administration to rats of different ages. Similar rates of loss of absorbed activity were seen for all age groups following an initially rapid decline in the total-body content presumably representing removal of unabsorbed activity from the body. At 40 d after administration to adult rats, about 63% of the retained activity was in bone, 3.8% was in the liver, 20% was in muscle, and 2.9% was in the kidneys.

(564) Razumovskii et al. (1966) studied the effects of various complex-forming agents on the biokinetics of ^{95}Zr and ^{95}Nb in rats. At 3 d after intraperitoneal administration of ^{95}Zr-^{95}Nb oxalate to control animals, the liver, spleen, kidneys, and femur contained about 4.2, 0.56, 1.4, and 0.6% of the administered activity, respectively.

(565) Ando and Ando (1986) examined the early distribution of ^{95}Zr in soft tissues of tumor-bearing rats following its intravenous administration as oxalate or nitrate. At 3, 24, and 48 h after administration of either form of ^{95}Zr the liver contained about 3-4%, the kidneys contained about 1-1.5%, and skeletal muscle contained about 13-17% of the administered amount.

(566) Abou et al. (2011) investigated the behavior of ^{89}Zr in mice following its intravenous administration as oxalate, chloride, phosphate, citrate, or desferrioxamine (DFO). Concentrations were determined in blood, liver, kidneys, bone, marrow, muscle, heart, lungs, spleen, and gastrointestinal tissues at 4 h, 8 h, and 6 d. After 6 d the total excretion of ^{89}Zr amounted to about 20% for the chloride or oxalate but only about 5% for the phosphate. Mice injected with the citrate excreted about 30% after 1 d and 35% after 6 d. Virtually all ^{89}Zr administered as DFO was excreted the first day. For administration of ^{89}Zr as phosphate the highest concentrations were found in the liver and spleen at all times. For administration of ^{89}Zr as oxalate, chloride, or citrate, the concentration in bone generally was more than twice that in other tissues at early times and more than 10 times that in other tissues at 6 d. Bone marrow cells showed little activity compared with calcified tissues. The epiphysis, consisting mainly of cartilage, contained most of the bone activity. The authors concluded that weakly bound zirconium is a bone seeker and likely binds to phosphate constituents of mineralized bone and epiphysis.

(567) Results of studies on rats indicate that a substantial portion of ^{95}Nb formed in vivo from decay of systemic ^{95}Zr is free to redistribute. For example, the distribution of ^{95}Nb formed in vivo from decay of ingested or intravenously injected ^{95}Zr it rats was similar to the distribution of administered ^{95}Nb and considerably different from the distribution of ^{95}Zr (Fletcher, 1969). Following oral administration of ^{95}Zr-^{95}Nb to suckling rats, the ratio of ^{95}Zr to ^{95}Nb was 4-5 in bone and close to 1 in other tissues (Shiraishi and Ichikawa, 1972). Measurements of activity in blood and tissues of rats following intraperitoneal injection of ^{95}Zr-^{95}Nb as oxalate indicated preferential accumulation of ^{95}Zr in bone (Rama Sastry et al., 1964).

12.2.3.2. Biokinetic model for systemic zirconium

(568) The systemic model for zirconium used in this report depicts the following general behavior of zirconium. Roughly half of zirconium atoms entering blood transfer to tissues and excretion pathways within a few hours, and the remainder combine with plasma proteins and are cleared much more slowly from blood. More than 95% of zirconium atoms leaving blood deposit in tissues and <5% enter excretion pathways, primarily the urinary bladder contents. Soft tissues initially contain a substantial portion of extravascular zirconium, but bone eventually contains >90% of the systemic burden due to a relatively high deposition fraction and much slower turnover than soft tissues. Zirconium atoms that reach blood have a long residence time in the body due to a low excretion rate and a high level of accumulation in bone.

(569) The structure of the systemic model for zirconium is shown in Figure 11-1. Transfer coefficients are listed in Table 12-3. These values were derived from primary parameter values in the form of deposition fractions and biological half-times. The parameter values were set to yield blood disappearance curves and urinary excretion rates for zirconium consistent with those observed in human subjects, a relatively high zirconium content in soft tissues at early times as observed in human subjects, and a time-dependent systemic distribution of zirconium suggested by animal studies. The comparative biokinetics of zirconium and niobium as observed in animal studies has been taken into account. Niobium

shows qualitatively similar systemic behavior to that of zirconium but a lower rate of transfer to bone, higher urinary clearance, and apparently greater uptake or retention or both by soft tissues than zirconium. It was convenient to derive transfer coefficients for zirconium in soft tissues, in particular, by scaling values developed from more easily interpreted soft-tissue data for niobium, to which the same model structure (Figure 12-1) is applied in this report. Except where there are overriding considerations, the assigned deposition fractions and removal half-times describing uptake and retention of zirconium in soft-tissue compartments are one-half the values used in the model for niobium.

(570) In the systemic model for zirconium, atoms that are absorbed or injected into blood initially enter a blood compartment called Blood 1. Zirconium leaves Blood 1 at the rate 5 d^{-1}, corresponding to a removal half-time of about 3.3 h. Outflow from Blood 1 is divided as follows: 40% goes to a slow-turnover blood pool representing plasma proteins (Blood 2 in Figure 12-1); 40% goes to a soft-tissue pool with relatively fast turnover (ST0); 15% transfers to bone surfaces and is equally divided between cortical and trabecular bone; 1.5% goes to the liver; 0.25% goes to the kidneys; 0.75% transfers to a soft-tissue compartment with relatively slow turnover (ST1); 2% enters the urinary bladder contents; and 0.5% is secreted into the small intestine (SI) contents. The deposition fractions for Blood 2 and ST0 are the same as assumed in the model for niobium; the fraction for bone surfaces is five times greater than for niobium; the fraction for the urinary bladder contents is about one-fifth the value for niobium; and values for other repositories are one-half the values applied to niobium.

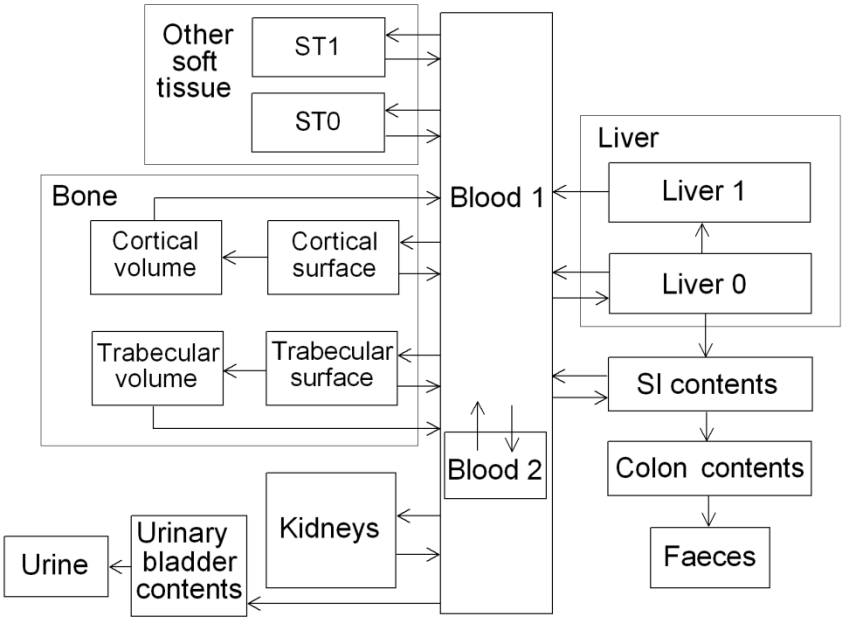

Figure 12-1. Structure of the biokinetic model for systemic zirconium.

Table 12-3. Parameter values in the systemic model for zirconium.

From	To	Transfer coefficient (d^{-1})
Blood 1	Blood 2	2.0
Blood 1	Liver 0	0.075
Blood 1	Kidneys	0.0125
Blood 1	ST0	2.0
Blood 1	ST1	0.0375
Blood 1	Urinary bladder contents	0.1
Blood 1	SI contents	0.025
Blood 1	Trabecular surface	0.375
Blood 1	Cortical surface	0.375
Blood 2	Blood 1	0.462
Liver 0	SI contents	0.116
Liver 0	Blood 1	0.116
Liver 0	Liver 1	0.462
Liver 1	Blood 1	0.01
Kidneys	Blood 1	0.01
ST0	Blood 1	0.462
ST1	Blood 1	0.02
Trabecular surface	Blood 1	0.000493
Trabecular surface	Trabecular volume	0.000247
Trabecular volume	Blood 1	0.000493
Cortical surface	Blood 1	0.0000821
Cortical surface	Cortical volume	0.0000411
Cortical volume	Blood 1	0.0000821

(571) Zirconium is assumed to transfer from Blood 2 back to Blood 1 with a half-time of 1.5 d, from ST0 to Blood 1 with a half-time of 1.5 d, from ST1 to Blood 1 with a half-time of 35 d, and from Kidneys to Blood 1 with a half-time of 70 d. The transfer coefficients derived from these and other half-times given below are rounded values. Zirconium entering the liver is assigned to a compartment called Liver 0. Zirconium is removed from Liver 0 with a half-time of 1 d, with two-thirds going to a long-term retention compartment of liver called Liver 1 and the other one-third equally divided between SI contents (representing biliary secretion) and Blood 1. Zirconium transfers from Liver 1 to blood with a half-time of 70 d. The removal half-times from Blood 2 and ST0 to Blood 1 were set for consistency with the blood retention patterns observed in health human subjects. The removal half-times from other soft-tissue compartments were set to one-half the values for niobium. The fate of zirconium depositing on bone surface is described by the generic model for bone-surface-seeking radionuclides, except that zirconium removed from bone is returned directly to blood rather than channelled through bone marrow.

(572) Model predictions of retention of zirconium in blood are compared in Figure 12-2 with central values for healthy human subjects following intravenous injection with stable isotopes of zirconium (Veronese et al., 2003b; Greiter, 2008). For the case of intravenous injection of zirconium, the model predicts cumulative urinary excretion of about 2.3% of the injected amount over the first 24 h, 5.5% over the first 7 d, and 11% over the first 100 d. These predictions are reasonably consistent with values observed in human subjects following intravenous injection of zirconium tracers (Mealey, 1957; Greiter, 2008, 2011).

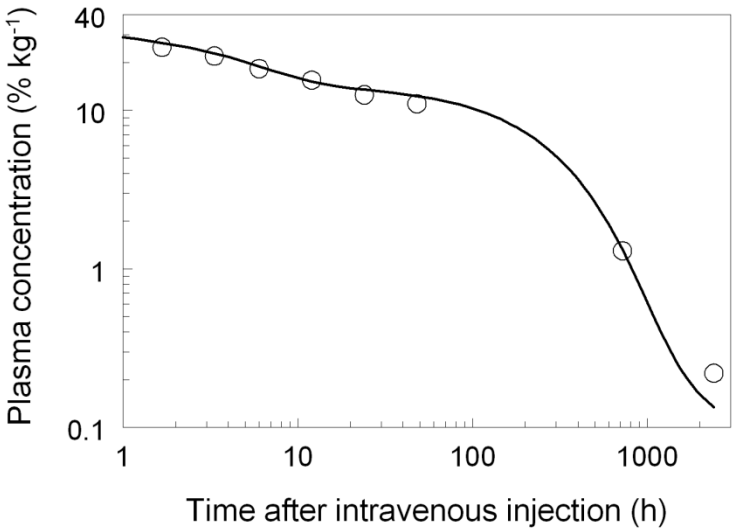

Figure 12-2. Comparison of model predictions of blood retention of zirconium with central values for healthy human subjects following intravenous administration of stable zirconium isotopes (Veronese et al., 2003b; Greiter, 2008).

12.2.3.3. Treatment of radioactive progeny

(573) Chain members addressed in the derivation of dose coefficients for internally deposited zirconium isotopes include isotopes of yttrium, strontium, and niobium. The characteristic systemic models for yttrium, zirconium, and niobium all have the same model structure. An yttrium or niobium atom produced in a given compartment by radioactive decay after intake of a zirconium parent is assumed to behave as if it had entered that compartment as a parent radionuclide. The model for strontium produced in systemic compartments after intake of a zirconium parent is the same as the model for strontium produced after intake of an yttrium parent, as described in the section on yttrium.

12.3. Individual monitoring

(574) ^{95}Zr is a γ emitter. Monitoring of ^{95}Zr is in general accomplished through Whole Body Counting or/and urine bioassays.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{95}Zr	Urine Bioassay	γ-ray spectrometry	5 Bq/L	0.1 Bq/L
^{95}Zr	Lung monitoring	γ-ray spectrometry	19Bq*	
^{95}Zr	Whole Body Counting	γ-ray spectrometry	50 Bq	20 Bq

* Lung monitoring of ^{95}Zr is not generally used in routine monitoring of workers. Monte Carlo program Visual Monte Carlo was used to simulate the photon emission, to calculate the calibration factor for the geometry and radionuclide, and to calculate the minimum detectable activity (MDA) in the lung. (Hunt et al., 2012)

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13. NIOBIUM (Z = 41)

13.1. Chemical Forms in the Workplace

(575) Niobium is a transition metal which occurs mainly in oxidation states III and V. It may be encountered in industry in a variety of chemical and physical forms, including oxides and oxalates. Minerals that contain niobium often contain tantalum and thorium.

(576) Niobium-95 is a high yield fission product, which may be associated with irradiated fuel or corrosion products. Niobium-95 also arises as the decay product of ^{95}Zr, another high yield fission product, which also occurs as a neutron activation product derived from zirconium based fuel cladding. It could also be present in fragments of irradiated fuel.

Table 13-1. Isotopes of niobium addressed in this report

Isotope	Physical half-life	Decay mode
Nb-88	14.5 m	EC, B+
Nb-89	2.03 h	EC, B+
Nb-89m	66 m	EC, B+
Nb-90	14.60 h	EC, B+
Nb-91	680 y	EC, B+
Nb-91m	60.86 d	IT, EC, B+
Nb-92	3.47E+7 y	EC
Nb-92m	10.15 d	EC, B+
Nb-93m	16.13 y	IT
Nb-94	2.03E+4 y	B-
Nb-95[a]	34.991 d	B-
Nb-95m	3.61 d	IT, B-
Nb-96	23.35 h	B-
Nb-97	72.1 m	B-
Nb-98m	51.3 m	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

13.2. Routes of Intake

13.2.1. Inhalation

Absorption Types and parameter values

(577) Cuddihy (1978) reviewed information on the lung clearance of inhaled niobium compounds. He noted that the chemistry of niobium is complex, since it can exist in any oxidation state between I and V. It does not form simple soluble compounds in aqueous solution but tends to hydrolyse and form hydrophilic colloids. Niobium oxalate complexes are stable in acids up to pH 5.5. Niobium oxides, the most common being Nb_2O_5, are sparingly soluble in mineral acids and almost inert in solutions of approximately neutral pH, as are most biological fluids.

(578) In all the studies noted below the niobium isotope followed was ^{95}Nb ($t_{½}$ 35 d), the decay product of ^{95}Zr ($t_{½}$ 64 d). In most studies both radionuclides were deposited in the respiratory tract, and thus the ^{95}Nb followed was partly that which deposited, and partly that formed from the *in situ* decay of ^{95}Zr. In most studies the combined activity of the two radionuclides was measured, and thus in interpreting the results it has to be assumed that their

behaviour is similar. Furthermore, in only a few studies was the inhaled material a pure niobium compound. Because of the relatively short half-lives of these radionuclides, few studies are of sufficient duration to distinguish Types M and S behaviour based on the ICRP *Publication 71* criteria of lung retention or total absorption up to 180 d after intake.

(579) Some information was found on the behaviour of inhaled niobium in man, mainly associated with irradiated fuel. Information is available from experimental studies of niobium as oxalate, oxide, and irradiated uranium dioxide.

(580) Absorption parameter values and Types, and associated f_A values for particulate forms of niobium are given in Table 13-2.

Niobium oxalate

(581) The oxalate has been studied extensively as a form that is relatively soluble in biological fluids (see above). In probably the most detailed study (Cuddihy, 1978) retention was followed in 27 dogs up to 128 days after inhalation of ^{95}Nb-labelled zirconium oxalate by dogs. Cuddihy applied simulation modelling to obtain a time-dependent absorption function (fractional absorption rate):

$$S(t) = 1.7\ e^{-2t} + 0.05\ e^{-0.1t} + 0.004\ d^{-1} \text{ at time } t \text{ (days) after intake,}$$

which shows three phases of absorption. Particle transport was represented by a fractional mechanical clearance rate:

$$M(t) = 0.004\ e^{-0.046t} + 0.001$$

(582) The same function was used to model particle transport of relatively insoluble niobium oxide administered to dogs in the same study (see below). This suggests that "binding" to lung tissues was not a significant factor in the time-dependent absorption. The absorption can be broadly approximated using the HRTM dissolution model with $f_r = 0.6$, $s_r = 1\ d^{-1}$ and $s_s = 0.007\ d^{-1}$, consistent with assignment to Type M. A good fit is obtained by using three dissolution compartments: 0.57 at 2.5 d^{-1}, 0.17 at 0.13 d^{-1} and 0.26 at 0.0041 d^{-1}. [An intake of material with these characteristics could be simulated with software that implements the HRTM by assuming an intake of two materials: 57% with $f_r = 1$ and $s_r = 2.5\ d^{-1}$; and 43% with $f_r = (0.17/0.43)$, $s_r = 0.13\ d^{-1}$ and $s_s = 0.0041\ d^{-1}$.]

(583) In other studies with dogs, rats and mice, the observed behaviour was broadly similar, but variable, indicating assignment to Type F in some and Type M in others. At 30 d after inhalation of ^{95}Nb oxalate by 3 dogs, the lungs contained about 15% of the initial lung deposit (ILD), indicating assignment to Type M (Kanapilly et al., 1969). After inhalation of ^{95}Nb oxalate by rats in one study (Moskalev et al., 1964), ~85% ILD was absorbed within a day (f_r ~0.85 and s_r >10 d^{-1}), and the rest with a half-time of about 10 d, indicating assignment to Type F. In another study (Thomas et al., 1967) ~30% ILD was absorbed within a day (f_r ~0.3 and s_r >10 d^{-1}), and relatively little thereafter, indicating assignment to Type M.

(584) Thomas et al. (1971) studied the biokinetics of ^{95}Zr–^{95}Nb following inhalation by mice of aerosols formed by heating droplets of zirconium oxalate solution to various temperatures. *In vitro* dissolution tests were conducted on similar materials by Kanapilly and Goh (1973) and Kanapilly et al. (1973). Immediately after inhalation of the aerosols formed at 100˚C and 250˚C (both zirconium oxalate, but mainly droplets and solid particles respectively) the skeleton contained about 20% of the body content, the lungs 2% and 25% respectively. This suggests that at the lower temperature most of the material deposited in the

lungs was absorbed rapidly: f_r ~0.9 and s_r of the order of 100 d^{-1}. For both materials niobium was absorbed faster than zirconium, especially that formed at 100˚C. These results indicate Type F behaviour, as do those of the *in vitro* dissolution tests.

(585) Although specific parameter values for niobium oxalate based on *in vivo* data are available, they are not adopted by the task group, because inhalation exposure to it is unlikely, and because a wide range of absorption was reported from different studies. Instead, niobium oxalate is assigned to Type M.

Zirconium oxide and carbonate

(586) As noted above, Thomas et al. (1971) studied the biokinetics of ^{95}Zr–^{95}Nb following inhalation by mice of aerosols formed by heating droplets of zirconium oxalate solution. The aerosols formed at 600˚C ($Zr(CO_3)_2$ and $ZrOCO_3$) and at 1100˚C (ZrO_2 and $ZrOCO_3$) gave very similar results *in vivo*, with no differential loss of niobium. From 10 to 130 d after inhalation the lungs contained more than 90% of the sacrifice body burden (SBB) while the skeleton content increased from 2% SBB at 2 d to 6% SBB at 130 d. These results indicate Type S behaviour. *In vitro* tests on similar materials by Kanapilly and Goh (1973) and Kanapilly et al. (1973) confirmed low dissolution rates, but their duration was too short to distinguish Type M from Type S.

(587) Cuddihy (1978) applied simulation modelling to measurements of ^{95}Nb following inhalation of similar ^{95}Nb-labelled zirconium aerosols (formed at 1000˚C) by dogs to obtain an absorption function (fractional absorption rate):

$$S(t) = 0.00016\ e^{-0.04t} + 0.0001\ d^{-1} \text{ at time } t \text{ (days) after intake,}$$

which can be represented using the HRTM with f_r = 0.004, s_r = 0.04 d^{-1} and s_s = 0.0001 d^{-1}, consistent with assignment to Type S. *In vivo* measurements following accidental inhalation of what was probably the same material by a person gave a lung retention half time of about 220 days, indicating Type M or S behaviour (Waligora, 1971).

(588) Although specific parameter values for niobium oxide based on *in vivo* data are available, they are not adopted here, because inhalation exposure to it is so unlikely. Instead, niobium oxide is assigned to Type S.

Nuclear weapons fallout

(589) During the early 1960s, measurements were made of ^{95}Zr–^{95}Nb activities in human lungs due to fall-out from atmospheric nuclear weapons tests. Most were made *post mortem* (Schönfeld et al., 1960; Osborne, 1963; Wrenn et al., 1964; Dutailly et al., 1966), but *in vivo* measurements were also made, enabling the variation with time in individual subjects to be determined (Rundo and Newton, 1962; 1965). Several authors compared their measurements with those predicted from measured air concentrations, using a single exponential model (ICRP, 1959). Biological lung retention half-times were estimated to be between about 70 d (Wrenn et al., 1964) and more than 120 d (Rundo and Newton, 1965). Wrenn et al., (1964) noted that little ^{95}Zr–^{95}Nb activity was found in other tissues, and that Wegst et al. (1964) had shown that ^{95}Zr-^{95}Nb activity in the lungs was present in particulate form. Overall this indicates Type M or S behaviour.

Irradiated fuel

(590) Following an accidental release, niobium could be present in fragments of irradiated fuel, where the matrix is predominantly uranium oxide. The results of a study on one person following accidental inhalation of irradiated fuel indicate Type M behaviour of the ^{95}Zr–^{95}Nb

present (Rundo, 1965). In another, measurements of ^{95}Zr–^{95}Nb made on a worker for 6 months following an accidental intake, probably of irradiated fuel (UO_2), indicate Type S behaviour (Thind, 1995).

(591) 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 (49 days for ^{95}Zr-Nb) and different from those expected for systemic retention, indicating that they were trapped in particles and metabolically inert, and thus indicating Type M rather than Type F behaviour.

(592) Tissue distribution and retention of several radionuclides were followed for 3 months after intratracheal instillation of irradiated UO_2 powder into rats (Lang et al., 1994). For ^{95}Nb, the total amounts absorbed by 1 and 3 months were estimated to be about 5% and 9% of the initial lung deposit respectively, indicating values of f_r <0.05 and s_s ~0.002 d^{-1}, and assignment to Type M.

(593) The *in vitro* dissolution of samples of particles released from the Chernobyl accident was measured for up to 60 d (Cuddihy et al., 1989). For all radionuclides, including ^{95}Zr-^{95}Nb, 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}, consistent with assignment to Type M.

Other compounds

(594) Measurements of ^{95}Zr–^{95}Nb in the lungs of a person for 5 months following an accidental intake of unspecified material indicate Type M or S behaviour (Cofield, 1963).

Rapid dissolution rate for niobium

(595) As noted above, the oxalate has been studied extensively as a form of niobium that is relatively soluble in biological fluids. The results show rather complex behaviour, with more than one phase of absorption, perhaps reflecting the complex chemistry of niobium. Where measurements have been made soon after administration, there is evidence of very rapid uptake, (s_r ~ 100 d^{-1}) but only of part of the initial lung deposit, (f_r < 1). There is therefore no justification for choosing a rate different from the general default value of 30 d^{-1}, which is applied here to all Type F forms of niobium.

Extent of binding of niobium to the respiratory tract

(596) As described above, the oxalate has been studied extensively as a form of niobium that is relatively soluble in biological fluids. The results show more than one phase of absorption. However, Cuddihy (1978) applied simulation modelling to the results of ^{95}Nb measurements following inhalation by dogs of niobium oxalate and relatively insoluble niobium oxide. The same function was used to model particle transport of both materials, which suggests that “binding” to lung tissues was not a significant factor in the time-dependent absorption of the oxalate, because it is assumed in the HRTM that material in the bound state is not cleared by particle transport, only by absorption to blood. It is therefore assumed that for niobium the bound state can be neglected, i.e. f_b = 0.0.

Table 13-2. Absorption parameter values for inhaled and ingested niobium

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A [c]
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F		1	30		0.01
M	Oxalate, all unspecified forms[d]	0.2	3	0.005	0.002
S	Carbonate, oxide	0.01	3	$1x10^{-4}$	$1x10^{-4}$
Ingested materials					
All forms					0.01

[a] It is assumed that for niobium that the bound state can be neglected, i.e. $f_b = 0.0$. The values of s_r for Type F, M and S forms of niobium (30, 3 and 3 d^{-1}, respectively) are the general default values.

[b] Materials (e.g. niobium oxalate) are 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 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 and the f_A value for ingested soluble forms of niobium (0.01).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

13.2.2. Ingestion

(597) Information on the concentration of stable niobium in human diet and urine has been published by Schroeder and Balassa (1965) but these values were considered to be insufficient for estimating the absorption of niobium from the human gastrointestinal tract (ICRP, 1989).

(598) Data on the absorption of niobium are available from a number of animal studies. A first set of values have been determined by Fletcher (1969), who quoted a range of fractional absorption from 4.10^{-4} to 2.10^{-3} for ^{95}Nb administered to rats in various chemical forms.

(599) Further studies have been then performed on ^{95}Nb given as oxalate. They shown that fractional absorption of ^{95}Nb given to rats varied from about 10^{-3} (Mraz and Eisele, 1977) to 2 to $5x10^{-2}$ (Thomas et al., 1971). These values may vary according to the species as shown by Furchner and Drake (1971), who measured whole body retention of ^{95}Nb given as oxalte, and estimated levels of absorption of about $2x10^{-2}$ in mice and dogs, $8x10^{-3}$ in rats and $9x10^{-3}$ in monkeys. However, these values may overestimate the true absorption because the retention of ^{95}Nb rapidly fell to less than detection limits.

(600) Fasting is known to increase the uptake by the gut. Harrison et al. (1990) measured absorption of $8x10^{-3}$ for ^{95}Nb administered as the citrate to normally fed guinea pigs and $1.4x10^{-2}$ for animals fasted 24h before and 2h after administration. Paquet et al. (1998) investigated the fractional absorption of niobium given to fed rats and obtained values of $1.25x10^{-2}$, $0.37x10^{-2}$ and $0.24x10^{-2}$ for the citrate, oxalate and chloride forms, respectively.

(601) In *Publication 30* (ICRP, 1979), an absorption value of 0.01 was recommended. This value was adopted in *Publication 56* (ICRP, 1989) for dietary intakes and is also adopted here as a default value for all chemical forms ($f_A = 0.01$).

13.2.3. Systemic Distribution, Retention and Excretion

13.2.3.1. Summary of the database

(602) There is little information on the systemic behavior of niobium in humans. Data for laboratory animals indicate broadly similar systemic biokinetics of niobium for different animal species, different routes of exposure, and different chemical forms of niobium taken into the body. Typically, 50% or more of niobium entering blood transfers to tissues and excretion pathways within a few hours, and the remainder clears much more slowly due to binding with plasma proteins. Excretion is mainly in urine. Niobium distributes somewhat uniformly throughout the body but is retained much longer in bone than in other tissues, so that bone eventually contains a large portion of the total-body content. Niobium depositing in bone appears to be retained largely on bone surfaces. Total-body retention generally has been described as a sum of two retention components of roughly equal size. The short-term component typically has a biological half-time of a few days, and the long-term component has a half-time of a few months. Reported biokinetic studies have not been sufficiently long to characterize longer-term components of retention such as may be present in bone.

(603) Hamilton and coworkers (Hamilton, 1948; Durbin et al., 1957; Durbin, 1960) studied the biokinetics of ^{95}Nb in rats following intramuscular injection of relatively soluble niobium compounds. A substantial portion of the absorbed activity apparently combined with plasma proteins and was slowly removed from blood to tissues and excretion pathways. Activity distributed throughout the body and was removed more slowly from bone, kidney, and lymphatic tissue than from other repositories. Activity was excreted mainly in urine over the first 2 wk, but the faecal to urinary excretion ratio increased over time. At 4 d after administration of ^{95}Nb as citrate, the mean contents of bone, liver, kidneys, and blood were 16%, 8.4%, 2.9%, and 7.7% of the administered activity, respectively, and approximately 39% of the administered amount had been excreted by that time. Autoradiographic studies indicated that skeletal ^{95}Nb was located largely on bone surfaces.

(604) The distributions of ^{90}Nb and ^{95}Nb were studied in rats over a 4-d period following their intravenous administration in a solution of oxalic acid (Matthews and Gartside, 1965). Comparison with blood retention of ^{131}I-labeled plasma proteins suggested that a substantial portion of the injected activity combined with plasma proteins. Retention in blood was about 30% of the injected amount at 1 d, 16% at 2 d, 11% at 3 d, and 5% at 4 d after correction for radiological decay. Total-body retention fell to about 65% at 4 d. Bone contained roughly one-fourth of the injected amount at the end of the study, based on extrapolation of data for the femur. The liver content was in the range 4.0-5.4% from 1.2 h to 4 d after injection. Activity in most tissues decreased with time, but activity in the kidneys increased from about 2% after 1.2 h to about 4% at 3-4 d.

(605) Semenov et al. (1966) investigated the distribution of ^{95}Nb in rats following its intravenous or subcutaneous administration as the oxalate. Similar behavior was seen for the two modes of exposure. Niobium in blood combined with plasma proteins, primarily albumin. Little activity was accumulated by red blood cells. Following intravenous injection the blood contained about 17% of the administered activity at 1 d, 2.9% at 4 d, and 0.12% at 64 d; the liver contained about 5-7% during the first day, 9% at 2-8 d, and 2% at 64 d; the kidneys contained about 1-2% during the first day and 2-3% during days 2-64; and the muscles contained 13-24% during the first 8 days, 9% at 16-32 d, and 4% at 64 d. The concentration in bone increased steadily for several days after injection and then remained at about the same level for the remainder of the 64-d study. The concentration in bone was higher than that in most other tissues at 32 and 64 d after injection. About 23% of the

administered amount was excreted in urine and about 10% was excreted in faeces over the first 20 d after intravenous injection. A substantial portion of activity entering the gastrointestinal contents appeared to arise from secretions other than liver bile.

(606) Razumovskii et al. (1966) studied the effects of various complex-forming agents on the biokinetics of ^{95}Zr and ^{95}Nb in rats. At 3 d after intraperitoneal administration of ^{95}Nb oxalate to control animals, the liver, spleen, kidneys, and femur contained about 3.1, 0.62, 0.89, and 0.23% of the administered activity, respectively.

(607) Autoradiographic studies on mice demonstrated high concentrations of ^{95}Nb in bone and connective tissue during the first four days after its intravenous administration as oxalate (Bäckström et al., 1967). The distribution of activity was similar to that observed after intravenous administration of ^{95}Zr-^{95}Nb, but bone appeared to accumulate a smaller portion of the administered activity following injection of pure ^{95}Nb.

(608) Fletcher (1969) studied the behavior of ^{95}Nb in rats following its administration as oxalate. Roughly 30% of intravenously administered activity deposited in the skeleton, 18% in muscle, 2.5% in liver, and 2.5% in kidneys. Total-body retention declined more slowly in males than in females. Retention was about 70% of the injected amount at 8 d, 50% at 40 d, and 40% at 80 d as an average for males and females.

(609) Furchner and Drake (1971) studied retention and excretion of ^{95}Nb after oral and intravenous administration as oxalate to mice, rats, monkeys, and dogs and after intraperitoneal administration as oxalate to mice and rats. The duration of individual studies ranged from 4 d to 192 d. Little difference in retention was seen following intravenous and intraperitoneal administration. Whole-body retention of intravenously injected ^{95}Nb was described as a sum of three exponential terms for mice and rats and a sum of two exponential terms for monkeys and dogs. The cumulative urinary to faecal excretion ratio over the first 3 d was about 9 for mice, 3 for rats and dogs, and 6 for monkeys. Estimated long-term biological half-times were about 100 d for monkeys, 150 d for dogs, 180 d for rats, and 460 d for mice. The long-term half-time represented about half of the administered amount in monkeys, dogs, and rats and about one-fourth of the administered amount in mice. Rats receiving ^{95}Nb by intraperitoneal injection were sacrificed at 1, 4, 7, 14, 23, 35, and 45 d for tissue distribution studies. The percentage of total-body activity in bone in these animals increased from about 16% at 1 d to about 27% at 23 d and remained near 27% thereafter. The muscle, pelt, and liver contained about 33-37%, 17-21%, and 4-5%, respectively, of total-body activity over the entire observation period. The kidney content increased from about 1.5% of total-body activity at 1 d to more than 3% after 35 d.

(610) Niobium-95 oxalate was administered orally or intravenously to sheep and swine 6-18 h after birth or 3 wk after weaning (Mraz and Eisele, 1977). At 3 d after intravenous administration the mean skeletal content was about 67% of the injected amount in newborn sheep compared with 43% in weaned sheep, and 66% in newborn swine compared with 51% in weaned swine. The means contents in the liver, kidneys, and muscle at 3 d varied little if any with age. The liver contained 1.7% of the injected amount in newborn and weaned sheep and 3.4-3.5% in newborn and weaned swine; the kidneys contained 0.7-1.1% in newborns and weanlings of both species; and muscle contained 6.4-7.3% in newborns and weanlings of both species.

(611) Cuddihy (1978) measured the distribution, retention, and excretion of ^{95}Nb in beagle dogs following its inhalation as oxalate or oxide aerosols and used the results to model the respiratory, gastrointestinal, and systemic biokinetics of the inhaled activity. Frequent whole-body measurements were made, and urine and faecal samples were collected daily throughout the study. Dogs were sacrificed for tissue distribution studies at 1 h and 2, 4, 8, 16, 32, 64, and 128 d. An estimated 60% of the initial lung burden was absorbed into the systemic

circulation after inhalation of the oxalate aerosols, compared with <1% after inhalation of the oxide. Daily urinary excretion of ^{95}Nb was 2-3 times greater than daily faecal excretion following early rapid clearance of activity from the upper respiratory tract. As predicted by Cuddihy's model, total-body retention of was 44% at 8 d and 28% at 128 d following acute input of stable niobium to blood. The predicted bone contents at these two times were about 14% and 16%; the liver contents were 9% and 8%; contents of other soft tissues were 17% and 6%; cumulative urinary losses were 45% and 60%; and cumulative faecal losses were 5% and 10%.

(612) Following intravenous administration of ^{95}Nb as oxalate to pregnant rats, there was a slow decrease in the activity concentrations in blood and liver during the first day and a simultaneous increase in kidneys and bone (Schneidereit et al., 1985). Whole-body retention over the first 20 d after injection into dams was described as a sum of two exponential terms with biological half-times of 1.3 d (~30%) and 46 d (~70%). Only a small portion of the injected activity was transferred to the fetus.

(613) The effects of various chelating agents on retention and elimination of ^{95}Nb were tested in mice following its intraperitoneal administration as oxalate (Gachalyi et al., 1987). Total-body retention of ^{95}Nb in control animals was described as a sum of two exponential terms with mean biological half-times of 1.1 d (~50%) and 54 d (~50%). The mean concentrations in liver, kidneys, and bone of control animals were, respectively, 3.9, 0.50, and 2.0% g^{-1} at 4 d and 2.7, 0.54, and 2.4% g^{-1} at 14 d. Desferrioxamine (DFOA) was shown to be an effective chelating agent for ^{95}Nb, particularly when combined with diethylenetriaminepentaacetic acid (DTPA).

(614) Harrison et al. (1990) measured retention of ^{95}Nb following its oral or intraperitoneal administration in a citrate solution to adult and newborn guinea pigs. Whole-body retention following intraperitoneal injection was slightly lower in newborns than in adults, with about 50% of the injected activity excreted by newborns during the first day compared with about 40% in adults. The remaining activity cleared with a half-time of about 30 d in both age groups as estimated from measurements through day 7. Urinary excretion accounted for more than 90% of total losses in adults over the 7-d observation period.

(615) The distribution of ^{95}Nb formed in vivo from decay of ingested or intravenously injected ^{95}Zr in rats was similar to the distribution of administered ^{95}Nb and considerably different from the distribution of ^{95}Zr (Fletcher, 1969). Following oral administration of ^{95}Zr-^{95}Nb to suckling rats, the ratio of ^{95}Zr to ^{95}Nb was 4-5 in bone and ~1 in other tissues (Shiraishi and Ichikawa, 1972). Measurements of activity in blood and tissues of rats following intraperitoneal injection of ^{95}Zr-^{95}Nb as oxalate indicated preferential accumulation of ^{95}Zr in bone (Rama Sastry et al., 1964).

13.2.3.2. Biokinetic model for systemic niobium

(616) The structure of the systemic model for niobium is shown in Figure 13-1. Transfer coefficients are listed in Table 13-3. These transfer coefficients are rounded values derived from the deposition fractions and removal half-times summarized below.

(617) The transfer coefficients were set in part for reasonable consistency with predictions of the systemic model of Cuddihy (1978) of the contents of total body (Figure 13-2), bone, liver, and total soft tissues over the first few months after acute input of niobium to blood. The Cuddihy model was used as a guide for modeling the early behavior of niobium because it was based on detailed measurements of the fate of absorbed niobium in beagle dogs, which have proven to be a useful laboratory model for the behavior of bone seekers; and its predictions are reasonably representative of biokinetic data for niobium from other animal

studies. The present blood retention model was designed for reasonable consistency with observed blood clearance of the related element zirconium in human subjects over the first few days after intravenous injection (Veronese et al., 2003; Greiter, 2008) as well as the blood clearance curve predicted by the Cuddihy model for niobium. Parameter values for the kidneys, which are not addressed explicitly in the Cuddihy model, were set for reasonable agreement with collective data on the kidney contents of ^{95}Nb over the first few months after intravenous or intraperitoneal administration to rats (Semenov et al., 1966; Fletcher, 1969; Furchner and Drake, 1971). The fate of niobium depositing on bone surface is described by the generic bone model for bone-surface-seeking radionuclides used in this report, except that niobium removed from bone is assumed to return to Blood 1 rather than to be channeled through bone marrow.

(618) In the present model, niobium initially entering the systemic circulation is assigned to a compartment called Blood 1. Niobium leaves Blood 1 at the rate 8 d^{-1}, corresponding to a removal half-time of about 2 h. Outflow from Blood 1 is divided as follows: 40% transfers to a slow-turnover blood compartment called Blood 2, representing plasma proteins; 3% transfers to Liver; 0.5% transfers to Kidneys; 3% transfers to bone surfaces and is equally divided between Cortical surface and Trabecular surface; 40% transfers to ST0, a soft-tissue compartment with relatively fast turnover; 1.5% transfers to ST1, a soft-tissue compartment with relatively slow turnover; 11% transfers to Urinary bladder contents; and 1.0% transfers to Small intestine (SI) contents. Activity transfers from Blood 2 back to Blood 1 with a half-time of 0.5 d, from ST0 to Blood 1 with a half-time of 0.5 d, from ST1 to Blood 1 with a half-time of 70 d, and from Kidneys to Blood 1 with a half-time of 140 d. Niobium entering Liver is assigned to a compartment called Liver 0. Niobium is removed from Liver 0 with a half-time of 2 d, with two-thirds going to a long-term retention compartment of liver called Liver 1 and the other one-third equally divided between Blood 1 and SI contents (representing biliary secretion). Relative transfer rates from Blood 1 and Liver 0 into SI contents are set so that biliary secretion accounts for one-third and other endogenous secretions (represented as transfer from Blood 1 to SI contents) account for two-thirds of total faecal excretion. Niobium transfers from Liver 1 to blood with a half-time of 140 d. As indicated earlier, parameter values describing the fate of niobium depositing on bone surface are generic values applied in this report to bone-surface-seeking radionuclides.

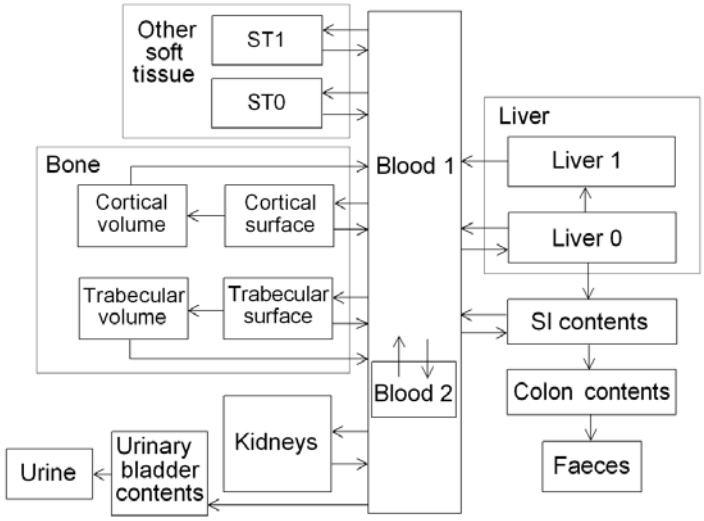


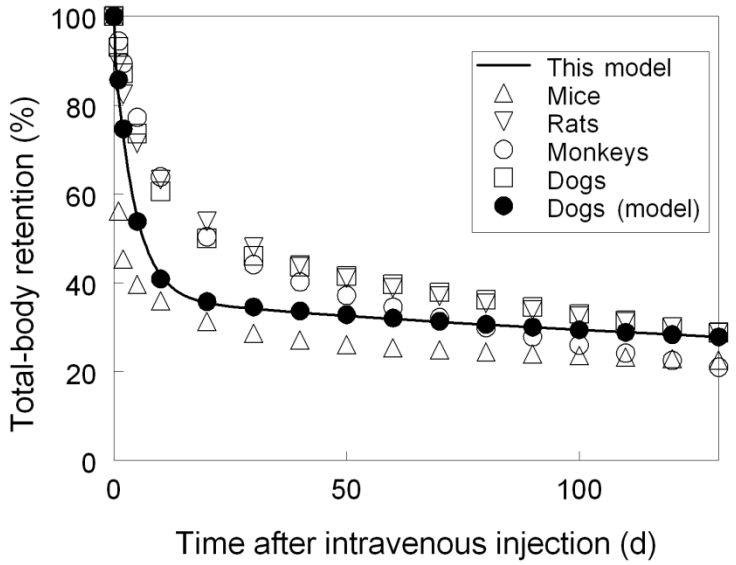
Figure 13-1. Structure of the biokinetic model for systemic niobium.

7913

Table 13-3. Parameter values in the systemic model for niobium.

From	To	Transfer coefficient (d^{-1})
Blood 1	Blood 2	3.2
Blood 1	Liver 0	0.24
Blood 1	Kidneys	0.04
Blood 1	ST0	3.2
Blood 1	ST1	0.12
Blood 1	Urinary bladder contents	0.88
Blood 1	SI contents	0.08
Blood 1	Trabecular surface	0.12
Blood 1	Cortical surface	0.12
Blood 2	Blood 1	1.39
Liver 0	SI contents	0.0578
Liver 0	Blood 1	0.0578
Liver 0	Liver 1	0.231
Liver 1	Blood 1	0.005
Kidneys	Blood 1	0.005
ST0	Blood 1	1.39
ST1	Blood 1	0.01
Trabecular surface	Blood 1	0.000493
Trabecular surface	Trabecular volume	0.000247
Trabecular volume	Blood 1	0.000493
Cortical surface	Blood 1	0.0000821
Cortical surface	Cortical volume	0.0000411
Cortical volume	Blood 1	0.0000821

7914



7915
7916 **Figure 13-2. Total-body retention of niobium after acute uptake to blood.** Values indicated by
7917 closed circles are based on a model developed by Cuddihy (1978) as a fit to inhalation data for dogs.
7918 Values indicated by other symbols are based on curve fits to observations of Furchner and Drake
7919 (1971) for intravenously injected ^{95}Nb.
7920

13.2.3.3. Treatment of radioactive progeny

(619) Chain members addressed in the derivation of dose coefficients for internally deposited niobium isotopes include isotopes of yttrium, zirconium, and niobium. The characteristic systemic models for yttrium, zirconium, and niobium all have the same structure. An atom of any of these elements produced in a compartment by radioactive decay after intake of a niobium parent is assumed to behave as if it had entered that compartment as a parent radionuclide.

13.3. Individual monitoring

(620) Monitoring of ^{95}Nb is in general accomplished through Whole Body Counting or/and urine bioassays.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{95}Nb	Urine Bioassay	γ-ray spectrometry	4 Bq/L	0.5 Bq/L
^{95}Nb	Lung measurement	γ-ray spectrometry	10 Bq*	
^{95}Nb	Whole Body Counting	γ-ray spectrometry	40 Bq	12 Bq

* Lung monitoring of ^{95}Nb is not generally used in routine monitoring of workers. Monte Carlo program Visual Monte Carlo was used to simulate the photon emission, to calculate the calibration factor for the geometry and radionuclide, and to calculate the minimum detectable activity (MDA) in the lung. (Hunt et al., 2012)

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14. MOLYBDENUM (Z = 42)

14.1. Chemicals Forms in the Workplace

(621) Molybdenum is a transition metal which mainly occurs in oxidation states IV and VI. It is an essential element for plants, animals and humans, present in two groups of enzymes, the nitrogenases and the molybdopterins. Molybdenum may be encountered in industry in a variety of chemical and physical forms, including oxides, halides, sulphides, nitrates and ammonium molybdate. In the nuclear industry, ^{99}Mo is a fission product and could be encountered in fragments of irradiated fuel. Large activities of ^{99}Mo are used in ^{99m}Tc generators in nuclear medicine.

Table 14-1. Isotopes of molybdenum addressed in this report

Isotope	Physical half-life	Decay mode
Mo-90	5.56 h	EC, B+
Mo-91	15.49 m	EC, B+
Mo-93	4.0E+3 y	EC
Mo-93m	6.85 h	IT, EC
Mo-99[a]	65.94 h	B-
Mo-101	14.61 m	B-
Mo-102	11.3 m	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

14.2. Routes of Intake

14.2.1. Inhalation

Absorption Types and parameter values

(622) Little information is available on the behaviour of inhaled molybdenum in man following accidental intakes, or from experimental studies in animals.

(623) Absorption parameter values and Types, and associated f_A values for particulate forms of molybdenum are given in Table 14-2.

Ammonium molybdate

(624) Cuddihy et al. (1969) measured the tissue distribution of ^{99}Mo in three dogs at 8 days after inhalation of a solution of ammonium molybdate. About 2% of the sacrifice body burden (SBB) was in the lungs, compared to 79% SBB in systemic organs (liver, skeleton, muscle and kidney), showing that most of the Mo deposited in the lungs had been absorbed, and giving assignment to Type F.

Molybdenum chloride

(625) Cuddihy et al. (1969) measured the tissue distribution of ^{99}Mo in three dogs at 8 days after the inhalation of molybdenum chloride ($MoCl_4$) with 2.5 µm AMAD. About 6% SBB was in the lungs, compared to 68% SBB in systemic organs, giving assignment to Type F.

Molybdenum oxide

(626) Cuddihy et al. (1969) measured the tissue distribution of ^{99}Mo in three dogs at 8 days after the inhalation of molybdenum oxide (MoO_3) with 1.5 µm AMAD. About 46% SBB was in the lungs, compared to 39% SBB in systemic organs, giving assignment to Type M.

Other compounds

(627) Measurements of ^{99}Mo and ^{99m}Tc whole body retention and excretion in urine were made from 1.3 days up to about 10 days after intake of an aerosol released during handling of a ^{99}Mo source (^{99}Mo alkaline solution) by workers at a company manufacturing ^{99m}Tc generators for use in nuclear medicine (Alvarez et al., 1994; Navarro et al., 1995). Navarro et al. showed good agreement between ICRP *Publication 30* model predictions (lung Class D) and measured whole body retention and urinary excretion for two workers representative of Group 1 (workers who were in the facility where the accident happened, and exposed directly to the source aerosol) and Group 2 (workers who were in a nearby laboratory and were contaminated by the aerosols dispersed through the air-conditioning system.) A critical analysis of the data (Giussani et al., 2004) showed different biokinetic behaviours between workers in Group 1 and Group 2. This seems to suggest that the aerosol composition was different in the two environments. Analysis of the data for several workers[2] conducted here confirmed good agreement assuming absorption Type F, and less good for Type M (with a correspondingly lower value of f_A). However, with the first measurement made more than 1 day after intake and a large contribution to systemic uptake from absorption in the alimentary tract, it was not possible to estimate a specific value for s_r from the data.

Rapid dissolution rate for molybdenum

(628) There is insufficient experimental information to estimate the rapid dissolution rate for molybdenum. There is therefore no justification for choosing a rate different from the general default value of 30 d^{-1}, which is applied here to all Type F forms of molybdenum.

Extent of binding of molybdenum to the respiratory tract

(629) Cuddihy et al. (1969) observed that at 8 days after inhalation of ammonium molybdate or molybdenum chloride by dogs, the amounts of ^{99}Mo associated with the nasal turbinates were similar to those in the lungs. This suggests that there could be some binding of molybdenum. However, the experimental information is insufficient to estimate the extent of any bound state, and it is assumed by default that $f_b = 0$.

[2] Data kindly provided by Dr M. A. Lopez, CIEMAT.

Table 14-2. Absorption parameter values for inhaled and ingested molybdenum

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Default parameter values[b,c]					
Absorption Type	Assigned forms				
F	Chloride and ammonium molybdate	1	30	–	0.9
M	Oxide and all unspecified forms[d]	0.2	3	0.005	0.2
S	—	0.01	3	0.0001	0.009
Ingested materials					
Sulphide					0.05
All other forms					0.9

[a] It is assumed that for molybdenum the bound state can be neglected i.e. $f_b = 0$. The values of s_r for Type F, M and S forms of molybdenum (30, 3 and 3 d^{-1}, respectively) are the general default values.

[b] Materials (e.g. molybdenum chloride) are 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 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 and the f_A value for ingested soluble forms of molybdenum (0.9).

[d] Default Type M is recommended for use in the absence of specific information, i.e. 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.

14.2.2. Ingestion

(630) Human investigations with stable isotope have shown that fractional absorption of molybdenum in inorganic form (chloride and ammonium-molibdate) is greater than 0.85 (Turnlund et al. 1995a, 1995b, Giussani et al., 1998a, 2006). These studies also showed that intestinal absorption of molybdenum is usually complete within the first 4 hours after administration (less than two hours if administered in liquid form), indicating that the absorption is only from the upper part of the alimentary tract (Giussani et al., 2006).

(631) A large number of studies have been conducted in ruminants in order to investigate the metabolism of molybdenum after ingestion and the potentially lethally effects of an imbalance between the contents of molybdenum, copper and sulphur in the diet (Huising and Matrone, 1976; Price et al., 1988). Those effects were due to interactions of those elements in the rumen of the animals (production of thiomolybdates) and they were not observed in non-ruminants, except when thiomolybdates were directly administered to them (Mills et al., 1978; Mills, 1985; Chen et al., 1988); therefore, data from studies with ruminants will not be further considered here. Molybdenum is readily absorbed by non-ruminants when ingested as salts of molybdic acid, such as MoO_3 or $CaMoO_4$ (Mills and Davis, 1987). In contrast, the highly insoluble compound molybdenum disulphide is only poorly absorbed (Underwood, 1971). The absorption of Mo is considered to be dependent on its concentration in diet, the amounts of Cu and S present, and the age of the animals (Comar et al., 1949; Nederbragt, 1983).

(632) In *Publication 30* (ICRP, 1979), the recommended absorption values were 0.05 for the sulphide and 0.8 for all other compounds of the element. The value of 1 was adopted in

Publication 67 (ICRP, 1993) for dietary intakes. The f_A values proposed in this report are 0.05 for sulphide and 0.9 for all other compounds.

14.2.3. Biokinetics of systemic molybdenum

14.2.3.1. Summary of the database

Human subjects

(633) In recent years the biokinetics of molybdenum in healthy volunteers was investigated in a series of studies using stable isotopes as tracers.

(634) A study referred to here as the "GSF study" was conducted by the Institute of Radiation Protection of GSF (now Helmholtz Zentrum München) in Munich, Germany, in collaboration with the Department of Physics of the State University of Milano, Italy (Cantone et al., 1995; Giussani et al., 1998, 2006, 2007; Tavola, 2004; Werner et al., 2000). Intestinal absorption, plasma clearance and urinary excretion of molybdenum were studied in a series of investigations on healthy volunteers (6 males and 11 females, age ranging from 27 to 63 y) by simultaneous oral and intravenous administration of two independent tracers. Repeated studies on the same subjects were conducted to investigate whether and how the amount and form of administration affect the biokinetic profiles.

(635) The clearance of molybdenum from blood plasma was rapid in all subjects and could be described with a bi-exponential function with mean characteristic half-times of 30 min (median: 29 min, range 4-70 min) and 6.6 h (median: 4.4 h, range 2.6-30 h). The mean transit time in plasma was calculated to be approximately 150 min, and the average mass of the distribution compartment was evaluated to be in the range 7-19 kg, indicating that molybdenum was at least partially homogeneously distributed between blood plasma and interstitial fluids.

(636) The urinary excretion in the first day after intake ranged between 30% and 80% of the intake, depending on the total mass of molybdenum present in the circulation: the higher the content of circulating molybdenum, the higher the fraction excreted. The excretion process was rapid; most of the molybdenum was excreted in the first eight to twelve hours after administration. It was also shown that administration of elevated dietary molybdenum mobilized molybdenum stored in the body and increased its excretion rate. No significant dependence of the results on age or sex was observed.

(637) Another large study referred to here as the "USDA study" was conducted at the metabolic research unit of the Western Human Nutrition Research Center of the US Department of Agriculture (USDA) , Presidio of San Francisco (Turnlund and Keyes, 2004, Turnlund et al., 1995a, 1995b). In the first set of investigations four healthy male subjects were kept on a low molybdenum diet for 24 days and the metabolic fate of infused molybdenum in plasma was followed. In the second series of investigations four healthy male subjects were kept on a low molybdenum diet for 102 days (depletion regime, daily intake 22 µg Mo), followed by an 18-day repletion period (daily intake approx. 500 µg Mo). A further investigation was structured in five dietary regimes, each with duration of 24 days (dietary intake in each of the five periods: 22, 72, 121, 467 and 1490 µg Mo·d^{-1}, respectively). In all dietary regimes except the depletion regime, the basic diet (containing on average 22 µg Mo·d^{-1}) was supplemented with molybdenum taken from a liquid formula, and the behaviour of systemic molybdenum was studied by injection of the stable isotope ^{97}Mo.

(638) Analyses of the blood plasma samples showed a correlation between daily intake and the plasma level of molybdenum. It was also observed that the intravenous administration of even low amounts of tracer (33 µg of ^{97}Mo) affected the metabolism of endogenous

molybdenum. Initial clearance from plasma was slightly faster than in the GSF studies; the published data could be described with a bi-exponential function with half times of 8 and 40 minutes.

(639) Molybdenum turnover as reflected by urinary excretion was faster with higher dietary molybdenum intakes, similarly to what was observed in the GSF studies. The percentage of oral tracer excreted in the urine over 6 days increased from 18% during the depletion period to 82% at the higher dietary regime. Similarly, the percentage excretion of the infused tracer increased from 33% to 87%. Faecal excretion of systemic molybdenum was negligible, as less than 2% of the infused tracer was excreted over 6 days. The faecal to urinary excretion ratio ranged from 1:20 to 1:62, depending on the total mass of circulating Mo.

(640) Rosoff and Spencer (1964) injected ^{99}Mo (as ammonium molybdate) into four seriously ill human patients and observed fast elimination from blood plasma (less than 4% of the tracer was present one hour after injection), similar to the pattern observed by Turnlund and Keyes (2004). Ten percent of the injected amount was eliminated in urine after 24 hours, and 25% was eliminated in urine after 6 days.

(641) In studies conducted in the 1960's using ^{99}Mo (molybdate) as a liver scanning agent (Sorensen and Archambault, 1963; 1964; Henning et al., 1965), the level of ^{99}Mo in blood after 6 hours was about 1/300 to 1/600 of the original level. In these studies, the whole body retention half-time was reported to be of the order of 20-40 days; however, the estimates were highly uncertain due to the short half-life of ^{99}Mo (2.75 d). Elimination in the urine amounted to 8 % after 6 hours, 20 % after 24 hours, and 30 to 60 % after 2 weeks.

(642) Recently reported concentrations of stable molybdenum in human organs and tissues generally are lower than values reported in older studies, suggesting that improvements in the measuring techniques have led to greater precision and to the elimination of contaminating factors. Most reported values for the molybdenum concentration in whole blood fall between 0.4 $\mu g \cdot L^{-1}$ and 1.2 $\mu g \cdot L^{-1}$, and around 0.6 $\mu g \cdot L^{-1}$ for blood plasma (Iyengar, 1978, Versieck et al., 1988, Vanhoe et al., 1989, 1994, Schramel and Wendler, 1995, Rodushkin et al., 1999, Heitland and Köster, 2006, Yoshida et al., 2006). Blood concentrations appear to be enhanced in people living in regions with higher daily intakes or suffering from particular diseases.

(643) Autopsy determinations of molybdenum in human organs and tissues (Tipton and Cook, 1963, Tipton et al., 1965, Schroeder et al., 1970, Sumino et al., 1975, Iyengar et al., 1978, Coughtrey and Thorne, 1983, Versieck, 1983, Zeisler et al., 1988, Yoo et al., 2002) consistently demonstrate highest concentrations in the liver and kidneys and show that the liver is the most important storage site for molybdenum in the body. Reported concentrations in liver peak around 1 $\mu g \cdot g^{-1}$. Based on the reference organ masses given in ICRP (2002), these values correspond to 1.8 mg Mo in the liver of males (range 0.9-2.7) and 1.4 mg Mo in the liver of females (range 0.7-2.1). Values for kidneys peak around 0.3 $\mu g \cdot g^{-1}$, corresponding to 90 µg (range 60-120) in the kidneys of males and 80 µg (range 55-110) in the kidneys of females (ratio liver:kidneys = 20:1). The preference of molybdenum for liver is confirmed by the findings of the studies with ^{99}Mo in nuclear medicine, with reported uptake by the liver to be as high as 80% of the administered activity (Sorensen and Archambault, 1963; Henning et al., 1965; Colombetti et al., 1974; Shearer et al., 1988).

(644) In previous ICRP reports bone was reported "… to be a major store of molybdenum", based on data presented by Coughtrey and Thorne (1983) and recalculated on the basis of measurements of Mo concentration in bone ashes made by Nusbaum et al. (1965). These values, however, have not been confirmed by any other study (Schroeder et al. 1970, Sumino et al. 1975, Yoo et al., 2002). Furthermore, none of the several studies concerning the distribution of ^{99}Mo administered to patients either as an agent for liver

scanning or accidentally as an impurity in radiopharmaceuticals labelled with ^{99m}Tc did report evidence of accumulation of molybdenum in skeletal tissues (Sorensen and Archambault, 1963, 1964, Henning et al., 1965, Colombetti 1974, Shearer 1988).

Laboratory animals

(645) In dogs, molybdenum translocated from the lung following inhalation of various compounds of the element was deposited mainly in liver, skeleton, muscle and kidney, with liver and kidney containing the highest concentrations (Cuddihy et al., 1969). When ^{99}Mo was intravenously administered as ammonium molybdate to mice, the liver showed the highest uptake with retention of about 26% of the administered activity at 1 h and about 21% at 1 d. The ^{99}Mo content of the kidney was relatively high, accounting for about 3.8% of the administered activity at 1 h and 3.9% at 1 d (Rosoff and Spencer, 1973). When molybdenum was administered to rats as ammonium molybdate, 74% was excreted within 3 h (Ando et al., 1989), and the tissue distribution was similar to that reported for mice.

(646) The marked differences between the ruminants and non-ruminants were clearly shown in the study by Bell et al. (1964) comparing absorption and excretion of molybdenum in swine and cattle. Swine showed fast clearance from blood plasma, fast absorption from the gastro-intestinal tract, and rapid excretion in the urine (50-80 % within 24 hours after administration, depending on the total amount of circulating molybdenum). The results for swine are consistent with those observed in the human stable tracer investigations.

14.2.3.2. Biokinetic model for systemic molybdenum

(647) In ICRP *Publication 30* (1979), on the basis of human data, the whole-body retention R(t) of molybdenum in humans was described by the following equation:

$$R(t)= 0.1\ e^{-0.693t/1} + 0.9\ e^{-0.693t/50}$$

(648) For molybdenum translocated to organs or tissues, fractions of 0.1 and 0.9 were assumed to be retained with half-times of 1 and 50 days, respectively.

(649) In ICRP *Publication 67* (1993), for molybdenum entering the transfer compartment, 10% was assumed to be deposited in the skeleton and to be retained with a biological half-time of 10 000 days. The remaining activity was distributed to liver (25%), kidneys (5%) and all other tissues (60%). A urinary to faecal excretion ratio of 8:1 was assumed for molybdenum that has entered the transfer compartment.

(650) In this publication, a recycling model for molybdenum biokinetics is presented. The definition of the model structure and the procedure for the determination of the model parameters were presented elsewhere (Giussani, 2008) and are here briefly summarized.

(651) The structure of the model consists of:

- Two compartments to describe the available data of molybdenum in blood plasma;
- Liver;
- Kidneys;
- Urinary bladder;
- Generic tissue pool (other tissue).

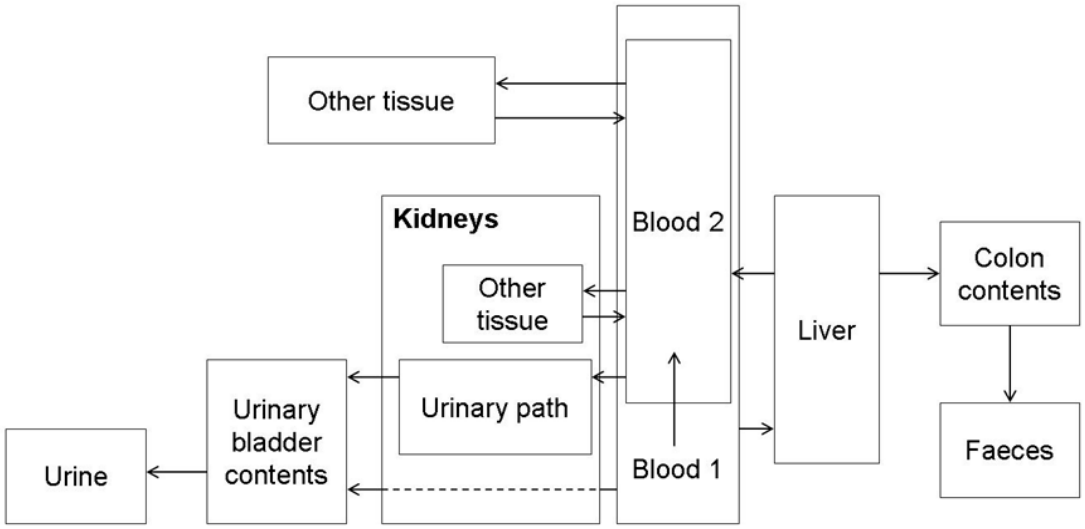


Figure 14-1. The systemic model for molybdenum radionuclides

(652) The presence of a separate compartment for skeleton, as in the previous models, is no longer believed to be justified by the available data, as discussed above. The skeleton is therefore pooled together with the rest of the other tissues in the generic common compartment.

(653) The splitting into two subunits of the compartment associated with the systemic circulation was made in accordance with the results of the analysis presented in (Giussani et al., 2007).

(654) The stable isotope studies showed that the absorption and excretion processes changed for increasing amounts of administered tracers (and consequently of circulating molybdenum). The values of the characteristic parameters given in Table 14-1 were therefore determined by fitting the model predictions to a subset of the available data corresponding to the investigations with molybdenum administration lower than or in the same order of the average daily intake. No allowance was made for age- or sex-dependent parameters, as no indication of such a dependence was evident from the review of data presented in the previous sections.

Table 14-3. Parameter values in the systemic model for molybdenum.

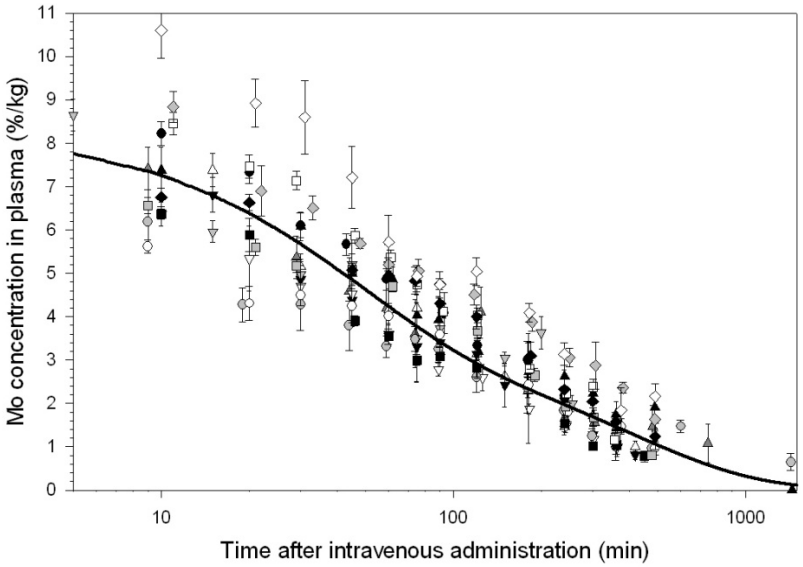
From	To	Transfer coefficient (d^{-1})
Blood 1	Blood 2	12.5
Blood 1	Liver	14.2
Blood 1	Urinary bladder contents	6.5
Blood 2	Urinary path	1.7
Blood 2	Other kidney tissue	0.115
Blood 2	Other tissue	1.73
Liver	Right Colon Contents	0.0048
Liver	Blood 2	0.0122
Other kidney tissue	Blood 2	0.0474
Other tissue	Blood 2	0.0323
Urinary path	Urinary bladder contents	1.40

(655) The Blood 1 compartment receives material from outside (alimentary tract, respiratory tract, wounds), and distributes it to urinary excretion (direct pathway, 19.5%), liver (42.8%) and to Blood 2 (37.7%) with a half-life of 30 min. The second Blood compartment transports material into kidneys (3.2%), into a generic compartment taken to represent all other tissues (48.8%) and into the urine through the renal urinary path (48.0%), with a half-life of 280 min. The total mass of compartments associated to the extracellular fluids (Blood 1+Blood 2) amounts to 12 kg.

(656) The retention half-times of molybdenum in the kidneys and in the other tissues are equal to 14.6 d and 21.5 d, respectively; from these compartments molybdenum is transported back to Blood 2.

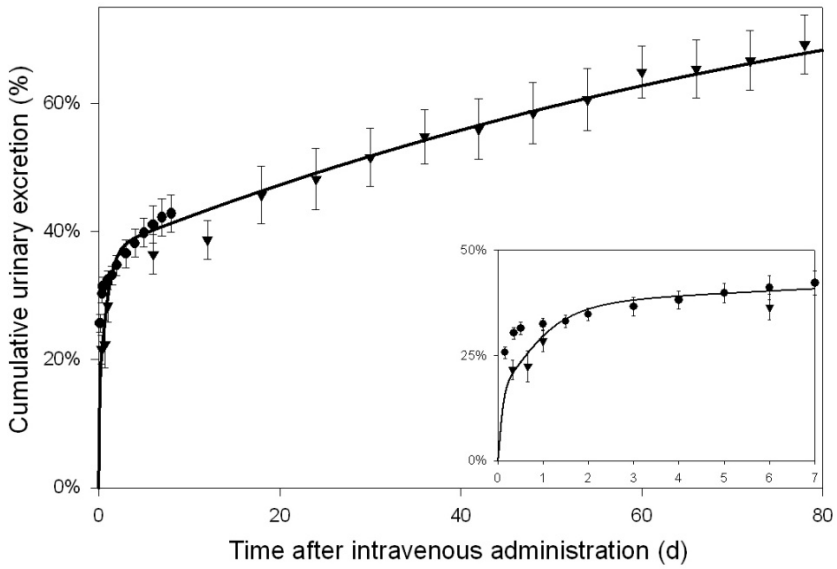
(657) The retention half-time in liver is equal to nearly 41 d; 28% is excreted into the faeces, 72% is transported back to the extracellular fluids (Blood 2). The characteristic half-time for transfer from the urinary pathway into the bladder contents is equal to 0.5 d.

(658) In the following figures the model predictions are compared with the corresponding human data from the stable tracer studies.



8338

8339 **Figure 14-2. Concentration in plasma of injected molybdenum tracer.** Data are from 15
8340 investigations in 6 volunteers (GSF study).



8341

8342 **Figure 14-3. Cumulative urinary excretion of the intravenous tracer.** Dots: data from the GSF
8343 study (one volunteer, error bars: experimental uncertainties) Triangles: data from the USDA study,
8344 depletion conditions (8 volunteers, mean ± SE).
8345

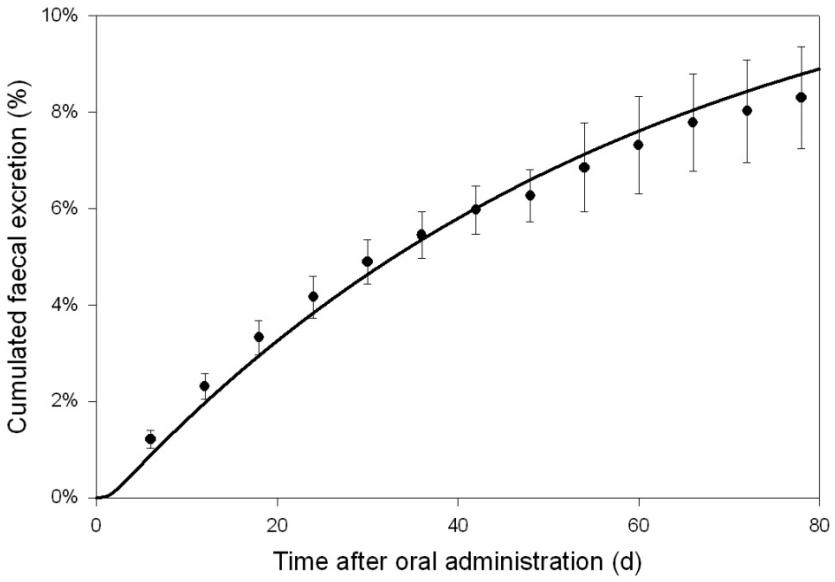


Figure 14-4. Cumulative faecal excretion of the intravenous trac. Dots: data from the USDA study, depletion conditions (8 volunteers, mean er. ± SE).

14.2.3.3. Treatment of radioactive progeny

(659) The radioactive progeny considered in the calculations of dose coefficients for molybdenum isotopes are isotopes of niobium or technetium. The models for niobium and technetium as progeny of systemic molydenium are modifications of the models applied in this series of reports to niobium and technetium, respectively, as parent radionuclides.

(660) External measurements on normal human subjects indicated that ^{99m}Tc produced in the liver by decay of ^{99}Mo following intravenous administration of ^{99}Mo as sodium or ammonium molybdate was retained in the liver for an extended period (Sorensen and Archambault, 1963). By contrast, ^{99m}Tc depositing in the liver after administration as a parent radionuclide was largely removed with a half-time of a few hours (Sorensen and Archambault, 1963). On the basis of these findings, technetium produced in the liver by decay of a molybdenum parent is assigned here to the long-term retention compartment of liver in the characteristic model for technetium described elsewhere in this report. The removal half-time from that compartment to blood is ~22 d. For modeling convenience, the compartment of the molybdenum model called Blood 1 is identified with the central blood compartment of the technetium model. Technetium produced in the compartment Blood 2 of the molybdenum model is assumed to transfer to the central blood compartment of the technetium model at the rate 1000 d^{-1} (half time of 1 min). Technetium produced in any other compartment of the molybdenum model is assumed to transfer to the central blood compartment of the technetium model at the rate 1.39 d^{-1}, the highest rate of transfer to blood from an “other tissue” compartment of the technetium model. After reaching the central blood compartment, technetium is assumed to follow its characteristic model.

(661) No information was found on the behavior of niobium produced in vivo following intake of a molybdenum parent. For modeling convenience, the compartment of the molybdenum model called Blood 1 is identified with the central blood compartment of the characteristic model for niobium. It is assumed that niobium produced in the compartment Blood 2 of the molybdenum model transfers to the central blood compartment of the niobium model at the rate 1000 d^{-1}. Niobium produced in a tissue compartment of the molybdenum

model is assumed to transfer to the central blood compartment of the characteristic model for niobium at the rate 0.433 d^{-1}, the highest rate of transfer to blood from an "other tissue" compartment of the niobium model. After reaching the central blood compartment, niobium is assumed to follow its characteristic systemic model.

14.3. Individual monitoring

(662) Monitoring of ^{99}Mo is in general accomplished through Whole Body Counting or/and urine bioassays.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{99}Mo	Urine Bioassay	γ-ray spectrometry	2 Bq/L	0.01 Bq/L
^{99}Mo	Lung measurement	γ-ray spectrometry		4 Bq
^{99}Mo	Whole Body Counting	γ-ray spectrometry	400 Bq	24 Bq

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15. TECHNETIUM (Z = 43)

15.1. Chemical Forms in the Workplace

(663) Technetium is a transition metal, which occurs mainly in oxidation states IV, VI and VII. Technetate or pertechnetate (TcO_4^-) is the most common technetium ion in solution. Technetium may be encountered in industry in a variety of chemical and physical forms, such as oxides (TcO_2, Tc_2O_7), sulphides, halides and nitrates. Technetium is an artificial element obtained either from uranium fission or after bombarding molybdenum with neutrons. ^{99m}Tc is frequently used in nuclear medicine for a wide variety of diagnostic tests as a label for different pharmaceuticals.

Table 15-1. Isotopes of technetium addressed in this report

Isotope	Physical half-life	Decay mode
Tc-93	2.75 h	EC, B+
Tc-93m	43.5 m	IT, EC, B+
Tc-94	293 m	EC, B+
Tc-94m	52.0 m	EC, B+
Tc-95	20 h	EC
Tc-95m	61 d	EC, B+, IT
Tc-96	4.28 d	EC
Tc-96m	51.5 m	IT, EC, B+
Tc-97	2.6E+6 y	EC
Tc-97m	90.1 d	IT
Tc-98	4.2E+6 y	B-
Tc-99[a]	2.111E+5 y	B-
Tc-99m[a]	6.015 h	IT, B-
Tc-101	14.2 m	B-
Tc-104	18.3 m	B-

[a] Data for these radionuclides are given in the printed copy of this report. Data for other radionuclides are given on accompanying electronic disk.

15.2. Routes of Intake

15.2.1. Inhalation

Absorption Types and parameter values

(664) Most of the experimental information available on the behaviour of technetium following deposition in the respiratory tract relates to pertechnetate, or materials labelled with ^{99m}Tc, especially DTPA. Some information is also available from accidental human intakes.

(665) Absorption parameter values and Types, and associated f_A values for particulate forms of technetium are given in Table 15-2.

Pertechnetate

(666) The absorption of ^{99m}Tc from the lungs following its administration as pertechnetate (TcO_4^-, molecular mass 163 Da) is very rapid. Barrowcliffe et al. (1986) measured retention halftimes of about 10 minutes after intratracheal instillation into rats. Man et al. (1989) measured retention halftimes of 3-4 minutes after inhalation by dogs, several times faster than for ^{99m}Tc-DTPA (see below) inhaled by the same dogs. Following inhalation of sodium

^{99m}Tc-labelled pertechnetate by healthy volunteers, Yeates et al. (1973) and Chopra et al. (1979) measured half-times of absorption of ^{99m}Tc from lungs to blood of about 10 minutes, with less than 2% of the initial lung deposit retained after 2 hours. Chopra et al. (1979) obtained similar results in patients with systemic sclerosis. Rinderknecht et al. (1980) measured retention halftimes in healthy volunteers averaging 13 minutes for inhaled ^{99m}Tc-labelled pertechnetate, significantly faster than for ^{99m}Tc-DTPA (average 44 minutes), with faster clearance in patients with interstitial lung disease and slower clearance in patients with pulmonary alveolar proteinosis. Human studies on ingested pertechnetate (Section 14.2.2) suggest f_A ~0.8. Specific absorption parameter values of f_r = 1, s_r = 100 d^{-1} (consistent with assignment to default Type F) and f_A =0.8 are used here for pertechnetate.

(667) Based on the results of the experiments outlined above, specific absorption parameter values for pertechnetate were estimated here to be: f_r = 1 and s_r = 100 d^{-1} (consistent with assignment to default Type F). However, although specific parameter values for pertechnetate based on *in vivo* data are available, they are not adopted separately here. The data are used as the basis for the default rapid dissolution rate for technetium. Hence specific parameter values for pertechnetate would be the same as default Type F technetium parameter values, and therefore pertechnetate is assigned to Type F instead.

^{99m}Tc-labelled DTPA (diethylenetriaminepentaacetic acid)

(668) ^{99m}Tc-DTPA has been used extensively, as a convenient, radiolabelled, low molecular mass (492 Da) solute to study pulmonary epithelial permeability in man. Following inhalation of ^{99m}Tc-DTPA by healthy non-smokers, lung retention half-times of ^{99m}Tc were reported to be 59 minutes (corresponding to a clearance rate of ~17 d^{-1}) by Jones et al. (1980), 72 minutes (14 d^{-1}) by Braude et al. (1984), 56 minutes (18 d^{-1}) by Nolop et al. (1987a) and 85 minutes (12 d^{-1}) by Silveira et al. (2003). “Baseline” clearance rates were reported to be 1.48% min^{-1} (21 d^{-1}) by Nolop et al. (1987b), 0.7% min^{-1} (10 d^{-1}) by Köhn et al. 1990, 0.83% min^{-1} (12 d^{-1}) by Smith et al. (1992) and 0.69% min^{-1} (10 d^{-1}) by Foster and Stetkiewicz (1996). See also the section on ^{14}C-labelled DTPA (2.2.1). Stather et al. (1983) followed the biokinetics of ^{14}C after administration of ^{14}C-labelled DTPA to healthy volunteers by inhalation, intravenous injection, and ingestion (which indicated that about 3% was absorbed from the alimentary tract). Modelling by the authors gave an estimated rate of absorption from lungs to blood of about 13 d^{-1} (f_r ~1), similar to that obtained for ^{99m}Tc-DTPA, suggesting that it is characteristic of DTPA rather than technetium. Nolop et al. (1987a) obtained similar retention half-times for ^{99m}Tc-DTPA (56 minutes) and ^{113m}In-DTPA (62 minutes), indicating that the results were not affected by dissociation of ^{99m}Tc-DTPA in the lungs. Thin-layer chromatography of ^{99m}Tc in urine, following inhalation of ^{99m}Tc-DTPA, suggested that the ^{99m}Tc-DTPA did not dissociate during its movement from lungs to urine (Köhn et al. 1990).

(669) Jefferies et al. (1984) reported that as premature infants with hyaline-membrane disease recovered, the retention half-time (initially shorter) averaged 56 minutes (18 d^{-1}), similar to that in healthy adults, which suggests no effect of age on absorption of ^{99m}Tc-DTPA from lungs to blood.

(670) The absorption of ^{99m}Tc-DTPA following deposition in different regions of the respiratory tract has been investigated. Chopra et al. (1979) measured retention half-times in healthy non-smokers of 35 minutes (29 d^{-1}) and 65 minutes (15 d^{-1}) for “upper” and “lower” lung fields measured with a gamma camera. (Both fields were peripheral, i.e. predominantly alveolar.) Oberdörster et al. (1986) found absorption to be slower in dogs for ^{99m}Tc-DTPA inhaled with rapid shallow ventilation of large particles to maximise bronchial deposition (1.31% min^{-1}, 19 d^{-1}), than for inhalation with slow deep ventilation of small particles to

maximise alveolar deposition (2.29% min^{-1}, 33 d^{-1}). Wolff et al. (1988) measured similar rates of clearance (~7 d^{-1}) of ^{99m}Tc-DTPA instilled into the nasal passage, trachea, fifth generation airway, and peripheral airway (approximately tenth generation) of dogs. Bennett and Ilowite (1989) found clearance of ^{99m}Tc-DTPA by absorption from the bronchial mucosa to be slower than that from the alveolar region in healthy non-smokers: retention half times were 296 minutes (3.4 d^{-1}) and 107 minutes (9.3 d^{-1}) respectively. Smith et al. (1992) reported clearance of ^{99m}Tc-DTPA to be faster following deep inhalation, to enhance alveolar deposition, than following inhalation with normal tidal breathing.

(671) The absorption of ^{99m}Tc-DTPA from the lungs has been found to be faster in smokers, and in patients with a wide variety of lung diseases. Because of its potential diagnostic use for detecting pathological changes in lung epithelial function, it was extensively studied. However, according to Peterson (1989) in a review, the long list of conditions that produce similar increases in the clearance rate, including severe lung disease, smoking, exposure to ozone, and even increased lung volume, make it insufficiently specific in diagnosis. For example, Jones et al. (1980) found a significantly shorter lung retention half-time of ^{99m}Tc of 20 minutes (50 d^{-1}) in asymptomatic smokers than in non-smokers (59 minutes). Similarly Nolop et al. (1987a) measured "baseline" lung retention half-times of ^{99m}Tc of 25 minutes (40 d^{-1}) in healthy smokers and 56 minutes (18 d^{-1}) in nonsmokers; hyperinflation increased the clearance rate in both groups. Minty et al. (1981) found a rapid, but only partial, increase in retention half-time in smokers who abstained from cigarettes for three weeks

(672) Specific absorption parameter values of $f_r = 1$, $s_r = 10$ d^{-1} (consistent with assignment to default Type F) and $f_A = 0.03$ are used here for ^{99m}Tc-DTPA.

^{99m}Tc-labelled carbon

(673) An aerosol of ultrafine (<100 nm) ^{99m}Tc-labelled carbon particles ("Technegas") has been developed for lung ventilation scans in nuclear medicine. Sodium pertechnetate in saline is vaporised in a graphite crucible at about 2500°C in an argon atmosphere, then diluted with air. The condensation aerosol formed consists of primary particles of about 5-15 nm diameter, forming agglomerates of about 100 nm diameter. Roth et al. (1997) investigated its deposition and clearance following inhalation by healthy volunteers. From total urine collection during 24 hours after inhalation, they assessed that about 9% of the deposited ^{99m}Tc activity dissolved: mostly in the first 6 hours.

(674) To assess to what extent, and how, inhaled particles from "urban combustion" or "soot-like" particulate matter pass into the systemic circulation, volunteers inhaled ultrafine ^{99m}Tc-labelled carbon particles, in most cases produced with a Technegas generator, or a modified version of it (Nemmar et al., 2002; Wiebert et al., 2006; Mills et al. 2006; Möller et al., 2008). Brown et al. (2002), however, used a spark generator (arc between carbon electrodes to which ^{99m}Tc-pertechnetate had been applied). Nemmar et al. (2002) concluded that inhaled ^{99m}Tc-labelled carbon particles pass rapidly into the systemic circulation, based on the estimated liver uptake and the results of thin-layer chromatography (TLC) of blood samples, which indicated that there was one species present corresponding to pertechnetate, and another which they attributed to ^{99m}Tc-labelled carbon particles. The other studies did not support this conclusion. All reported that particle accumulation in the liver was not detectable corresponding to fractions of the ^{99m}Tc-labelled carbon particles deposited in the lungs of <1.5% for Brown et al. (2002) and <0.5% for Möller et al. (2008). Mills et al. (2006) found that (also using TLC) the ^{99m}Tc transferred to blood was associated with pertechnetate rather than with particle-bound ^{99m}Tc.

(675) With regard to dissolution, Nemmar et al. (2002) observed that activity was detected in blood at 1 minute, reached a maximum between 10 and 20 minutes, and remained at this level up to 60 minutes. A considerable fraction of ^{99m}Tc leached from the particles and distributed as pertechnetate, as indicated by accumulation of ^{99m}Tc in the bladder, thyroid and salivary glands. For a representative subject, activity in the bladder reached about 25% of the initial lung activity in 45 minutes. Brown et al. (2000, 2002) measured leaching *in vitro* (0.9% saline) to be ~10-15% in 5 minutes and 15-25% in ~24 hours. Mills et al. (2006) noted that in the presence of even minute amounts of oxygen the Technegas generator produces a mixture of ^{99m}Tc-labelled particles and soluble oxides of ^{99m}Tc-pertechnetate. Wiebert et al. (2006) and Möller et al. (2008) made specific efforts to fix the ^{99m}Tc radiolabel firmly to the carbon particles. Wiebert et al. (2006) reported dissolution *in vitro* (0.9% saline) to be ~3% in 70 hours, compared to 11% in 24 hours for particles produced by the standard Technegas method. Möller et al. (2008) reported dissolution *in vitro* (0.9% saline) to be ~4% in 24 hours. In both studies, urinary excretion of ^{99m}Tc in 24 hours following inhalation by volunteers was about 1% of activity deposited in the lungs.

(676) These results suggest the fraction of ^{99m}Tc leaching rapidly from ^{99m}Tc-labelled carbon particles varies from a few percent to tens of percent, depending on the method of formation. The retention measurements made in the inhalation studies suggest that the remaining material is relatively insoluble, and more likely to be Type M or S than Type F, but the short duration of measurements limits the inferences that can be drawn.

Other particulate forms

(677) The use of ^{99m}Tc-labelled materials such as albumin, erythrocytes, ferric oxide, polystyrene, resin teflon and sulphur colloid, to study mucociliary clearance from the bronchial tree relies on there being relatively little absorption from the lungs to the body fluids over the first day or so after deposition (Isawa et al., 1984; Matthys et al., 1983; Albert et al., 1969; Sutton et al., 1981; Puchelle et al., 1979; Mossberg and Camner, 1980, Man et al. 1989).

Undefined particulate forms

(678) The results of measurements of ^{99}Mo and ^{99m}Tc whole body retention and excretion in urine made from 1.3 days up to about 10 days after intake of an aerosol released during handling of a ^{99}Mo source (^{99}Mo alkaline solution) by workers at a company manufacturing ^{99m}Tc generators for use in nuclear medicine (Alvarez et al., 1994; Navarro et al., 1995) are consistent with assignment to Type F (see section 13.2.1).

Rapid dissolution rate for technetium

(679) Evidence from the pertechetate studies outlined above suggests a rapid dissolution rate of the order of 100 d^{-1}, which is applied here to all Type F forms of technetium.

Extent of binding of technetium to the respiratory tract

(680) Evidence from the experimental studies outlined above suggests that there is probably little binding of technetium. It is therefore assumed that for technetium the bound state can be neglected, i.e. $f_b = 0.0$.

Table 15-2. Absorption parameter values for inhaled and ingested technetium

Inhaled particulate materials		Absorption parameter values[a] f_r	s_r (d^{-1})	s_s (d^{-1})	Absorption from the alimentary tract, f_A
Specific parameter values[b]					
Tc-DTPA		1	10	–	0.03
Default parameter values[c,d]					
Absorption Type	Assigned forms				
F	Pertechnetate	1	100	–	0.9
M	All unspecified forms[e]	0.2	3	0.005	0.2
S	—	0.01	3	0.0001	0.009
Ingested material					
All forms					0.9

[a] It is assumed that for technetium the bound state can be neglected, i.e. $f_b = 0.0$. The values of s_r for Type F of technetium ($100 d^{-1}$) is element specific. The values for types M and S ($3 d^{-1}$) are the general default values.
[b] See text for summary of information on which parameter values are based, and on ranges of parameter values observed for individual materials.
[c] Materials (e.g. pertechnetate) 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] 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 and the f_A value for ingested soluble forms of technetium (0.9).
[e] Default Type M is recommended for use in the absence of specific information, i.e. 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.

15.2.2. Ingestion

(681) Technetium administered as ^{99m}Tc pertechnetate is generally well absorbed by human subjects. Mean absorption values of about 0.9 and 0.95 were obtained by McAfee et al. (1964) and Beasley et al. (1966), respectively, whereas the data presented in Andros et al. (1965) suggest mean absorption fraction of 0.6.

(682) In rats, the fractional absorption seems to range between 0.4 and about 0.9 for pertechnetate (Gerber et al., 1989; Archimbaud et al., 1992, Berthol et al., 2003) and to be equal to about 0.5 for Tc chloride (Hamilton, 1948; Sullivan et al., 1977).

(683) In *Publication 30* (ICRP, 1980), an absorption value of 0.8 was recommended for all compounds of technetium. A lower value of 0.5 was adopted in *Publication 67* (ICRP, 1993) for uptake from food. In this report, an f_A value of 0.9 is used for all chemical forms in the workplace.

15.2.3. Systemic Distribution, Retention and Excretion

15.2.3.1. Summary of the database

Overview

(684) Most biokinetic studies of technetium in human subjects and laboratory animals have involved its administration as the ion pertechnetate (TcO_4^-), the most readily available

chemical form and the starting point for technetium chemistry. The initial distribution of pertechnetate is similar to that of inorganic iodide. Pertechnetate and iodide are both selectively concentrated in the thyroid, salivary glands, and stomach wall. In contrast to iodide, pertechnetate trapped by the thyroid is not organically bound in the thyroid but is largely released back to blood over a period of hours. In normal subjects, 1-2% of intravenously injected pertechnetate is accumulated by the iodide-concentrating mechanism of the thyroid at 1 hr, which is similar to accumulation of radioiodide in the blocked thyroid. Thyroid uptake of both iodide and pertechnetate are increased by an order of magnitude in diffuse toxic goiter. A significant biological difference between the pertechnetate ion and iodide is their markedly different excretion pattern. Iodide is excreted mainly in urine. After intravenous administration, about 25-30% of administered pertechnetate is excreted in urine over the first 24 hr, but thereafter the urinary excretion rate decreases markedly while cumulative faecal excretion increases to 20% or more of the injected amount at 72 h and may eventually exceed cumulative urinary excretion. Most of the absorbed or injected pertechnetate is lost from the body within a few days, but a small percentage is retained for a period of weeks or longer. During chronic intake, relatively high concentrations are found in bone, kidneys, liver, skin, hair, and thyroid.

Data for human subjects

(685) Harper, Lathrop, and coworkers (Harper et al., 1962, Andros et al., 1965) found that intravenously injected $^{99m}TcO_4$ localized within a few minutes in the thyroid, stomach, and salivary glands in human subjects and a variety of laboratory animals. Blood clearance could be described in terms of two approximately equal components with half-times of 8-12 min and 4-8 h. The first component appeared to represent distribution in the extracellular space.

(686) Sorensen and Archambault (1963) developed a liver scanning technique using ^{99}Mo molybdate but based on measurement of gamma radiation emitted by its daughter ^{99m}Tc. Technetium-99m was found to remain in the liver for an extended period after its production by decay of ^{99}Mo already taken up by liver cells. By contrast, ^{99m}Tc depositing in the liver after administration as a parent radionuclide was removed with a half-time of a few hours, in parallel with the decrease in the external counts over the head. About 58% of injected ^{99m}Tc was recovered in urine and 24% was recovered in faeces over the first 3 days after its administration as a parent radionuclide.

(687) McAfee et al. (1964) examined the tissue distribution or excretion of ^{99m}Tc ($T_{1/2}$ = 6.0 h) administered as pertechnetate to 6 healthy male volunteers and 23 patients with suspected brain tumors. The gastrointestinal absorption and tissue distribution of activity resembled that of ^{131}I administered as iodide. Absorbed activity was concentrated in the thyroid, salivary glands, and gastric mucosa. Much of the gastric and salivary secretion was reabsorbed in the small intestine, but in contrast to iodide a substantial fraction accumulated in the colon and was excreted in the faeces. An abdominal scan performed 3 h after intravenous administration revealed high levels of activity within the stomach and duodenal loop and higher levels in the splenic flexure and descending colon. Following either oral or intravenous administration the highest count rates were observed over the stomach and next highest rates over the liver. For both organs the effective (biological plus radiological) removal half-time initially was about 2 h but increased to 5-7 h after the first hour, which is approximately the radiological half-life of ^{99m}Tc. This suggests nearly equilibrium conditions between the rate of secretion into the stomach and removal of the secretion into the small intestine. Activity in the thyroid peaked at 1-2 h after administration, at which time an estimated 3-4% of the administered amount (corrected for radioactive decay) was present within the gland. In contrast to iodide, pertechnetate was not organified by the thyroid but

returned to blood over a period of hours. At 24 hours the thyroid content was estimated as 0.5% of the administered amount. About 20-25% of intravenously injected activity remained in blood after 1 h and about 0.8-5% remained after 24 h. Blood plasma and red blood cells contained on average about 70% and 30%, respectively, of the total blood content at 1 h after intravenous injection. The rate of urinary excretion of activity closely reflected the plasma concentration. Following oral administration to 9 subjects, the average urinary excretion was 25% over the first 24 h, 3% over 24-48 h, and 1% over 48-72 h. Following intravenous administration to 12 subjects, average urinary excretion was 27% at 24 h, 4% over 24-48 h, and 2% over 48-72 h. Total urinary excretion by individual subjects was in the range 15-50% over 24 h and 15-58% over 72 h. Total faecal excretion over 72 h was 30-55% after oral administration and 10-45% after intravenous administration. Recovery of activity from the colon was incomplete despite administration of laxatives. Total loss in urine plus faeces over 72 h averaged 50% (range, 28-68%) following intravenous administration and 70% (39-88%) following oral administration.

(688) Andros et al. (1965) studied the biokinetics of ^{99m}Tc over the first 72 h following its oral or intravenous administration as pertechnetate to 86 patients including 57 euthyroid subjects. Following intravenous administration the thyroid accumulated up to 2% of the administered amount at 1 h. The serum contained on average about 0.00045%/ml at 24 h, indicating that roughly 2% of the dosage was in blood at that time assuming equal concentrations in plasma and red blood cell water. The concentration ratios saliva : plasma and gastric juice : plasma averaged 37.5 (range, 11.5-66) and 17.5 (11-28.5), respectively. In seven subjects, average urinary excretion was 35.7% of the intravenously administered amount after 24 h, 6.2% at 24-48 h, and 4.8% at 48-72 h, giving a total of 46.7%. Average faecal excretion in 6 of these subjects was 8.8% after 72 h. In a normal young adult female, total urinary and faecal excretion at 72 h after intravenous injection accounted for 33.1% and 28.2%, respectively, of the administered amount. The average total-body biological half-time for all subjects based on all excretion data was 53 h.

(689) Beasley et al. (1966) used ^{95m}Tc ($T_{1/2}$ = 60 d) and ^{96}Tc (4.3 d) to study the relatively long-term biokinetics of technetium in 8 normal human volunteers (ages 22-43 y) following its oral or intravenous administration as pertechnetate. The distribution and total-body retention of activity were monitored externally, and samples of plasma, urine, faeces, sweat, tears, and intestinal mucosa were analyzed. By 10 min after intravenous injection the activity had begun to localize in the bladder. At 2 h activity was found in relatively high concentrations in the salivary and thyroid glands, stomach, liver, and urinary bladder. The specific activity of the saliva was high, approaching 95% of dosage per liter of saliva at 2-3 h. For several days after oral or intravenous administration the saliva contained 10-30 times the Tc concentration in plasma. Technetium was not concentrated in lacrimal or sweat glands, but the concentration in nasal secretions was high. There was no indication of localization in the liver or kidneys at 3 d in a subject who received technetium orally. Biopsies of the stomach, duodenum, and rectal mucosa were performed on selected subjects at 2, 7, and 19 d. No appreciable activity was observed in the rectal mucosa, but concentrations in stomach and duodenum were 40-100 times plasma concentrations at comparable times. On average, about 28% of the injected activity was excreted in urine and about 2-3% was excreted in faeces during the first 24 h. Thereafter the urinary excretion rate declined rapidly, and faecal excretion soon became the dominant excretion pathway. Cumulative urinary and faecal excetion averaged about 35% and 55%, respectively, of the injected amount after 8 d. Biological retention R (%) in the total body could be described as a sum of three exponential terms, $R(t)=76.7\exp(-0.693t/1.6)+19\exp(-0.693t/3.7)+4.3\exp(-0.693t/22)$, where t is in days.

(690) Harden and coworkers (1967, 1968, 1969) investigated the uptake of ^{99m}Tc

pertechnetate by the stomach wall and salivary glands and its secretion in saliva and gastric juice following its intravenous administration to human subjects. In 10 subjects with no evidence of diseases of the alimentary tract the mean uptake by the stomach at 20 min was 3.0 +/- 0.4% of the administered activity, and uptake at 1 h was in the range 2.4-11.4%. (Harden et al., 1967). In seven male volunteers the average concentration ratio ^{99m}Tc in saliva : ^{99m}Tc in plasma at 40-70 min after administration was 27.3. The average concentration ratio ^{99m}Tc in gastric juice : ^{99m}Tc in plasma over that time was 11.0. Clearance of $^{99m}TcO_4$ was about half that of ^{132}I in both saliva and gastric juice.

(691) Atkins and Richards (1968) studied thyroidal uptake of ^{99m}Tc pertechnetate in 143 patients who were hospitalized for reasons other than thyroid disease. Uptake of ^{99m}Tc and ^{131}I by the thyroid were positively correlated. Uptake of ^{99m}Tc in 120 euthyroid subjects averaged about 2% and exceeded 5% in only one subject. Fifteen hyperthryoid subjects had ^{99m}Tc uptake in the range 3.5-28.5%.

(692) Mean thyroid uptake of intravenously injected $^{99m}TcO_4$ in 18 normal volunteers was estimated as 1.6 +/- 0.7% (SD) (Goolden et al., 1971). Uptake in 20 patients with thyrotoxicosis ranged from 0.8% to 22%.

(693) Thyroid uptake of ^{99m}Tc pertechnetate was measured 20 min after administration of a tracer dose in seven normal controls and 52 patients with thyroid disease (McGill et al., 1971). The mean uptake was 0·96 ± 0·17% in normal subjects, 2·87 ± 0·39% in patients with non-toxic goiter, 16·7 ± 1·9% in thyrotoxic patients, and 1·94±0·27% in hypothyroid patients.

(694) One hundred patients with clinically suspected Meckel's diverticulum were studied with pertechnetate scintigraphy of the abdomen (Berquist et al., 1976). The investigators noted that intestinal radioactivity seen in a scan could be either in the gut wall or in the lumen. They found no technetium in the mucosa of the small or large intestine at 30 min after administration and only small amounts at later times.

(695) Hays (1973) studied the biokinetics of $^{99m}TcO_4$ after its administration to 15 normal subjects by oral, subcutaneous, or intravenous routes. Absorption from the gut was highly variable. As observed earlier by Andros et al. (1965) and Beasley et al. (1966), $^{99m}TcO_4$ showed substantial pooling in the gut and subsequent faecal excretion after all modes of intake. This is in contrast to radioiodide, which shows substantial pooling in the stomach due to secretion by the salivary glands and gastric mucosa but is nearly completely reabsorbed to blood after passing into the small intestine.

(696) Hays and Berman (1977) investigated the biokinetics of ^{99m}Tc pertechnetate during the first 8 h of its continuous intravenous infusion into normal volunteers. A group of 9 subjects was studied during hours 0-4, and another group of 10 subjects was studied during hours 4-8. One gram of sodium iodide was administered intravenously to the second group at 6.5 h. Plasma, salivary, and urinary activities were assayed, and external measurements were made over the neck, thigh, and right upper abdomen. The investigators found that pertechnetate was initially distributed much like iodide and that the administration of iodide markedly reduced transport of pertechnetate into the thyroid, saliva, stomach, and small intestine. In contrast to the systemic behavior of iodide, the large intestine appeared to play an important role in the retention and excretion of pertechnetate. The investigators developed biokinetic model for pertechnetate from the results of their study, analogy with iodide biokinetics, and data from previous biokinetic studies of pertechnetate. The model depicts three main subsystems that determine the fate of systemic pertechnetate: the thyroid trap; technetium distributed throughout the body, represented by plasma and two extravascular compartments; and four compartments within the gastrointestinal tract representing the salivary glands, stomach plus upper small intestine, and two lower intestinal pools. One of

the latter compartments is identified with the bowel wall on the basis of external measurements.

Data for laboratory animals

(697) Following intravenous administration of technetium isotopes to rats, 73% of the administered activity was recovered in urine and 15% in faeces after 24 h (Durbin et al., 1957, Durbin, 1960). At 24 h the gastrointestinal tract, bone, liver, and thyroid contained 9.0%, 0.4%, 0.7%, and <0.1%, respectively, of the administered amount. At 8 d after intravenous administration of technetium isotopes to rats the only tissues containing measureable amounts of activity were the skin, kidney and liver (Hamilton, 1948).

(698) Following intravenous administration of ^{99m}Tc as pertechenate to mice, the organ with the highest accumulation was the stomach, which contained 10% of the administered amount (corrected for radioactive decay) at 1-3 h and 14% at 6 h (McAfee et al., 1964). From 1 to 6 h the small intestine content increased from 2 to 6% and the large intestine content from 2 to 9% of administered technetium.

(699) Matthews and Mallard (1965) studied the distribution and tumor uptake of ^{99m}Tc pertechenate in the first few hours after its intravenous administration to rats and compared its behavior with that of other tracers. The distribution was found to be broadly similar to that of ^{131}I administered as iodide. Pertechnetate equilibrated rapidly with the extracellular spaces of several organs. Some observed differences from ^{131}I as iodide were that the liver accumulated 3 times as much ^{99m}Tc as ^{131}I, the kidneys accumulated 2-5 times as much ^{99m}Tc as ^{131}I, and the ^{99m}Tc content of the intestines continued to rise for 4.25 h while that of ^{131}I reached a peak relatively quickly and then began to decline. The content of ^{99m}Tc in the liver decreased from 8.7% of the administered amount at 0.57 h to 4.2% at 4.25 h. At 3-4 h after injection the concentration of ^{99m}Tc in the liver was about 2.5 times that in bone and 7 times that in muscle.

(700) Yeh and Kriss (1967) compared the biokinetics of ^{99m}Tc pertechnetate and a ^{99m}Tc citrate complex in mice over the first 24 h after intravenous administration. The pertechnetate showed high concentration in the salivary glands, stomach, thyroid, and colon. The liver content decreased from 8.5% of the administered amount at 0.5 h to 2.8% at 24 h. The kidney content was 1.8% at 0.5 h and below the detection limit at 24 h. Total-body retention was 70% at 0.5 h and 16.5% at 24 h. The citrate complex showed a much higher urinary excretion rate than pertechenate and in contrast to pertechnetate was not localized in the salivary glands, stomach, or thyroid. The liver content was roughly 2.5% of the administered amount from 0.5 to 2 h and declined to 1.5% at 24 h. The kidney content decreased from 2.3% at 0.5 h to 0.8% at 24 h. Total-body retention was 20% at 0.5 h and 7% at 24 h.

(701) McRae et al. (1974) studied the effects of stannous tin on the distribution of pertechnetate in rats. The following distribution was determined at 1 h after intravenous administration of $^{99m}TcO_4$ to control animals: liver, 4.3% of administered activity; kidneys, 1.0%; stomach, 17.1%; intestines, 7.2%; skeleton, 7.3%; muscle, 11.3%, and skin, 27.2%.

(702) Coffee et al. (1984) studied the biokinetics of intravenously injected $^{95m}TcO_4$ or $^{99m}TcO_4$ administered to rats with and without a $^{99}TcO_4$ carrier. Retention in all organs was reduced substantially by administration of the carrier. Total-body retention of $^{95m}TcO_4$ was about 9% at 7 d and >1% at 6 mo when administered with no carrier, 5% at 7 d and 0.6% at 6 mo when administered with 2.4 mg $^{99}TcO_4$/kg, and ~2.1% at 7 d and <0.2% at 6 mo when administered with 24 mg $^{99}TcO_4$/kg. The relative concentrations in tissues at 24 h after injection of $^{99m}TcO_4$ with no carrier were liver, 0.15; kidneys, 0.82; stomach, 0.40; large intestine, 0.05; and skin, 0.11.

(703) Maize containing bound ^{99}Tc was introduced acutely into the rumen of sheep (Kirchmann et al., 1986). The ^{99}Tc concentration in the kidneys over the period 1-28 d after administration was an order of magnitude greater than that in the liver and three orders of magnitude greater than that in muscle. The biological half-times for ^{99}Tc in kidneys, liver, and muscle based on measurements at 7 and 28 d after administration were about 6 d, 9 d, and 9 d, respectively.

(704) The biokinetics of ^{99}Tc was studied in sheep following its introduction into the rumen as pertechnetate or biologically bound to algae (Bruwaene et al., 1986). Tissue concentrations and urinary and faecal excretion rates were determined up to 3 mo after administration. The biokinetics of ^{99}Tc administered in algae appeared to be broadly similar to that for ^{99}Tc administered as pertechnate except for possible differences in uptake and retention by the thyroid, but variability in the data for ^{99}Tc administered in algae hampered precise characterization of its biokinetics. Gastrointestinal absorption of ^{99}Tc was low. Urinary excretion amounted to about 1% of the dosage. Highest concentrations of ^{99}Tc were found in thyroid tissue, followed by liver and kidney. Relatively high concentrations were also found in the skin and wool. Two components of total-body retention were observed following administration of ^{99}Tc either as pertechnetate or algae. Two components of retention were also evident for the liver, kidneys, and thyroid following administration of ^{99}Tc as pertechnetate. Following administration as pertechnetate, the size (coefficient) of the first component of retention was about 35 times that of the second component for the total-body, 6 times that of the second component for the kidneys, and 2 times that of the second component for the thyroid; the size of the second component was not determined for the liver. The estimated biological half-time of the long-term components for the total-body and individual tissues were in the range 20-50 d.

(705) Holm and Rioseco (1987) investigated the transfer of ^{99}Tc from lichens to reindeer in a region of central Sweden. Activity was measured in reindeer tissues during the period 1963-1981. Activity concentrations in the liver and kidneys typically were much higher than those in muscle. The mean activity concentration in bone expressed on a wet weight basis was about 2.5 times that in liver and 10 times that in muscle. Compact and trabecular bone showed similar concentrations of ^{99}Tc.

(706) Gerber et al. (1989) compared the biokinetics of ^{95m}Tc in rats (a monogastric animal) and sheep (a polygastric animal) following its intravenous injection or ingestion as TcO_4 or biologically incorporated in maize. The pattern of absorption and excretion and, to some extent, the organ distribution and retention depended on the animal species and the form of administered activity. Pertechnetate given orally was better absorbed by rats than by sheep. Absorption of activity bound to maize was roughly equal to that of TcO_4 in sheep but much less than that of TcO_4 in rats. Endogenous excretion of injected activity by rats was primarily in urine and by sheep was primarily in faeces. The highest tissue concentration at 3 and 7 d following intravenous administration to sheep and all modes of administration to rats was found in the thyroid, followed by the kidneys. Following ingestion of either form of ^{99m}Tc by sheep, the kidneys showed the highest tissue concentration. Bone, skin, muscle, and liver contributed significantly to the total-body burden. Biological half-times for tissues of sheep were estimated from tissue concentrations up to 90 d and characterized for each tissue as a sum of two exponential terms. The half-time of the first component of retention was about 5 d for all tissues. The half-time of the second component was about 20 d for kidneys, 40 d for liver, and 50 d or longer for bone, muscle, and skin.

(707) Jones (1989) studied the intestinal absorption and systemic biokinetics of ^{95m}Tc following its administration to female goats and swine. At 200 h after administration the highest tissue concentration in both species was found in the thyroid, followed by kidneys

and then liver. In swine the total content of the liver was roughly three times the content of the kidneys or thyroid.

(708) Ennis et al. (1989) studied the transfer of technetium isotopes to milk and tissues of lactating goats. At 35-40 d after oral administration of ^{99}Tc pertechnetate, the concentration of ^{99}Tc in tissues and fluids decreased in the order thyroid > hair > kidney > mammary gland > liver > lower large intestine > muscle > blood > milk. The concentration of ^{99}Tc in the thyroid was roughly 20 times that in the kidneys, 100 times that in the liver, and 1000 times that in muscle.

(709) Zuckier et al. (2004) compared the time-dependent distributions of ^{125}I, ^{99m}Tc, and ^{188}Re in mice after their intravenous injection as iodide, pertechnetate ($^{99m}TcO_4$), and perrhenate ($^{188}ReO_4$), respectively. The early distributions of these three radionuclides were remarkably similar. Activity concentrations of all three in salivary glands and stomach were several times higher than the blood concentration, remained elevated over the initial 2 h, and subsequently declined. A broadly similar pattern of accumulation and decline of pertechnetate and perrhenate was observed in the thyroid. By contrast, the concentration of ^{125}I in the thyroid continued to increase through the 19-h time point, presumably due to organification of the iodide. At 20 min, the concentration of ^{99m}Tc decreased in the order stomach > salivary glands > thyroid > liver > kidney > spleen > muscle. This order was maintained at 2 h except that the concentration in the thyroid had become slightly greater than that in the salivary glands by this time.

(710) Valenca et al. (2005) investigated the effects of cigarette smoke on the initial distribution of intravenously injected ^{99m}Tc pertechnetate in mice. The following concentrations (% injected ^{99m}Tc/g) were determined in control animals at 1 h: stomach, 5.7; red blood cells, 3.6; lung, 1.7; thyroid, 1.1; kidney, 0.89; spleen, 0.36; bone, 0.26; and testis, 0.25.

15.2.3.2. Biokinetic model for systemic technetium

(711) The structure of the systemic model for technetium used in this report is shown in Figure 15-1. Transfer coefficients are listed in Table 15-3.

(712) The model structure is a modification of the generic structure for bone-volume-seeking radionuclides. Although technetium is not regarded as a bone seeker, that structure provides a convenient starting place for modeling its systemic kinetics. Compartments representing the thyroid, salivary glands, stomach wall, and right colon wall are added to the model because they have been identified in human or animal studies as important repositories for pertechnetate. The bone, kidneys, liver, thyroid, and other soft tissues are each divided into multiple compartments representing different phases of retention and, in the case of bone, also different types of tissue.

(713) Blood is treated as a well-mixed pool. The total outflow rate from blood is assumed to be 25 d^{-1} (half-time of 40 min). This initially understates the clearance rate of intravenously administered pertechnetate in human subjects but reproduces observed blood clearance reasonably well after 1-2 h. Outflow from blood is divided as follows: 9% goes to a fast turnover thyroid compartment (Thyroid 1), 25% to the stomach wall; 15% to the salivary glands, 7.5% to the urinary bladder contents, 15% to a fast-turnover liver compartment (Liver 1), 2.5% to a fast-turnover kidney compartment (Urinary path), 0.25% to a slow-turnover kidney compartment (Other kidney), 13% to the colon wall, 2% to cortical bone surface, 0.5% to trabecular bone surface, 0.5% to a soft-tissue compartment with relatively slow turnover (ST2), and the remaining 9.75% to a soft-tissue compartment with relatively fast turnover.

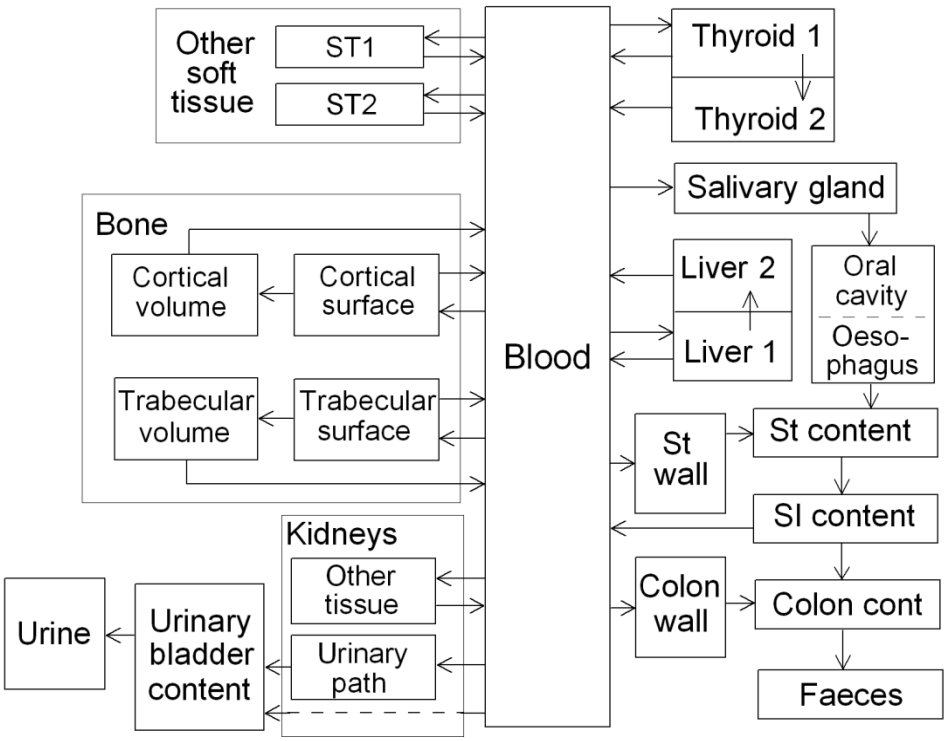

Figure 15-1. Structure of the biokinetic model for systemic technetium used in this report.

(714) It is assumed that 99% of activity entering Thyroid 1 returns to Blood and 1% enters Thyroid 2, representing relatively long-term retention in the thyroid. The transfer coefficient from Thyroid 1 to Blood is 36 d^{-1}, based on analogy with iodide (see the section on iodine). Activity transfers from Thyroid 2 to Blood at the rate 0.032 d^{-1}, corresponding to a half-time of 22 d. The 22-d half-time for this and other compartments in the model is based on the long-term component of retention of total-body technetium determined in the human study by Beasley et al. (1966).

(715) Activity transfers from the salivary glands to the oral cavity at the rate 36 d^{-1}, based on the estimate of Hays and Berman (1977) on healthy human subjects. The same value is applied here to transfer from the stomach wall to the stomach contents. The model of Hays and Berman does not include a separate compartment representing stomach wall, but the value 36 d^{-1} assumed here is reasonably consistent with the time course of movement of pertechnetate from plasma to a rapid turnover tissue compartment to stomach contents in their model. This transfer coefficient is also reasonably consistent with the value 50 d^{-1} applied to transfer from stomach wall and salivary glands to gastrointestinal contents in the model for iodide used in this report. The subsequent behavior of technetium entering the oral cavity or stomach content is described by default transfer coefficients of the Human Alimentary Tract Model and a reference gastrointestinal absorption fraction of 0.9 for technetium.

Table 15-3. Parameter values in the systemic model for technetium.

From	To	Transfer coefficient (d^{-1})
Blood	Thyroid 1	2.16
Blood	ST1	2.34
Blood	ST2	0.12
Blood	Urinary bladder content	1.8
Blood	Salivary glands	3.6
Blood	Stomach wall	6.0
Blood	Kidneys 1	0.6
Blood	Kidneys 2	0.06
Blood	Liver 1	3.6
Blood	Right colon wall	3.12
Blood	Trabecular bone surface	0.12
Blood	Cortical bone surface	0.48
Thyroid 1	Blood	36
Thyroid 1	Thyroid 2	0.364
Thyroid 2	Blood	0.032
ST1	Blood	0.433
ST2	Blood	0.032
Salivary gland	Oral cavity	36
Stomach wall	Stomach content	36
Kidneys 1	Urinary bladder content	8.32
Kidneys 2	Blood	0.032
Liver 1	Blood	8.234
Liver 1	Liver 2	0.0832
Liver 2	Blood	0.032
Right colon wall	Right colon content	0.693
Trabecular bone surface	Blood	0.429
Trabecular bone surface	Trabecular bone volume	0.00433
Cortical bone surface	Blood	0.429
Cortical bone surface	Cortical bone volume	0.00433
Trabecular bone volume	Blood	0.000493
Cortical bone volume	Blood	0.0000821

(716) Activity is removed from Liver 1 with a half-time of 2 h, with 99% returning to Blood and 1% moving to Liver 2, which represents relatively long-term retention in the liver. The removal half-time from Liver 2 to Blood is 22 d. Activity is removed from the kidney compartment called Urinary path to Urinary bladder contents with a half-time of 2 h. Activity is removed from the kidney compartment with relatively long-term retention (Other kidney tissue) to Blood with a half-time of 22 d. Activity is transferred from other soft tissue compartments ST1 and ST2 to blood with half-times of 1.6 d and 22 d, respectively; 1.6 d and 22 d are the fitted short-term and long-term half-times of removal from the body determined in the human study by Beasley et al. (1966) described earlier. Activity is lost from the right colon wall to the right colon contents with a half-time of 1 d. This is shorter than the half-time of 2.4 d estimated by Hays and Berman (1977), but this shorter half-time provides a better fit to the mean faecal excretion curve for technetium based on the human subjects of Beasley et al. (1966).

(717) The model for bone depicts a low rate of uptake of technetium by bone but a sizable portion of the total-body content in bone during chronic intake. Activity is removed from

bone surface with a half-time of 1.6 d, with 99% returning to blood and 1% entering the associated bone volume compartment. Activity is removed from bone volume at the reference rate of bone turnover for the given bone type.

(718) Model predictions of total-body retention of technetium as a function of time after its acute input to blood are compared in Figure 15-2 with a curve fit to observed values for human subjects (Beasley et al., 1966). Predictions of cumulative urinary and faecal excretion of technetium after its acute input to blood are compared in Figure 15-3 with mean values derived from results from the same study. The data for urine (circles) are based on measurements tabulated by Beasley et al. for a 25-day observation period. The data for faeces (plus signs) for days 1-8 are based on a graphical representation of cumulative faecal excretion over the first 8 d following intake. Data for faeces for later days were calculated as 100% minus estimated mean total-body retention (%) minus estimated mean cumulative urinary excretion (%).

15.2.3.3. Treatment of radioactive progeny

(719) All of the chain members addressed in this report in the derivation of dose coefficients for internally deposited isotopes of technetium are also isotopes of technetium. These chain members are assigned the biokinetic model for technetium as a parent radionuclide, starting at the time of production of the progeny in the body.

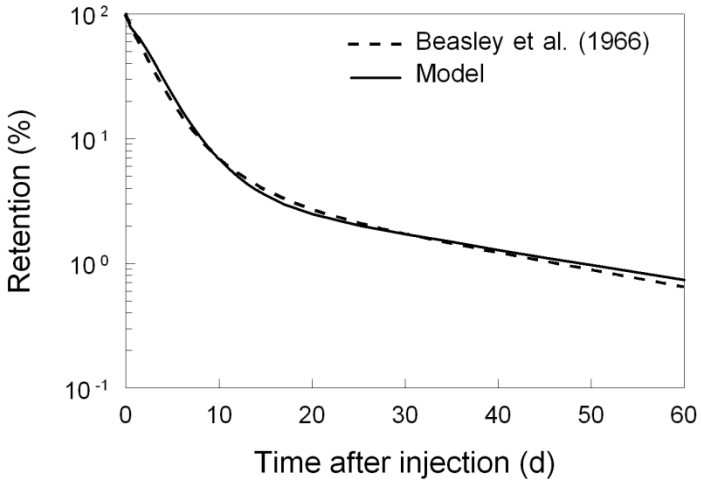

Figure 15-2. Model predictions of total-body retention of technetium following its acute input into blood, compared with a curve fit to observations for human subjects (Beasley et al., 1966).

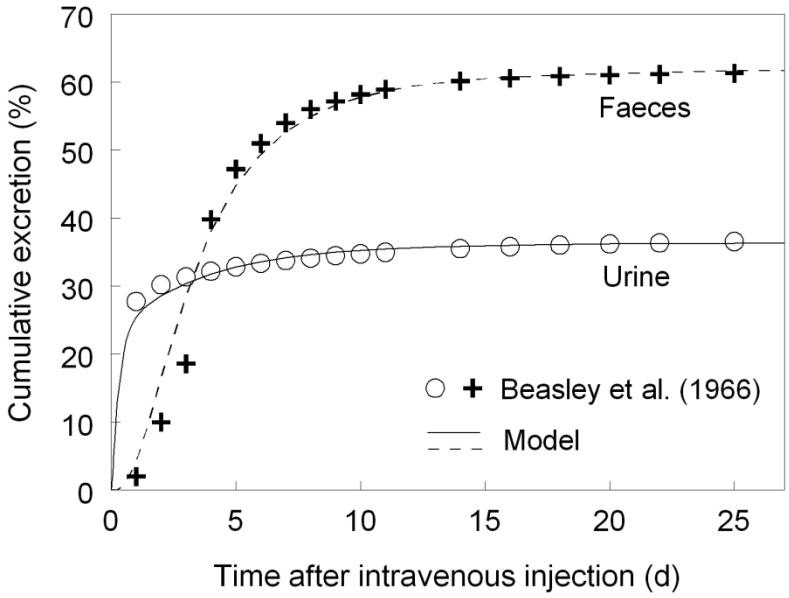

Figure 15-3. Model predictions of cumulative urinary and faecal excretion of technetium following its acute input into blood, compared with central estimates based on observations for human subjects (Beasley et al., 1966).

15.3. Individual monitoring

^{99}Tc

(720) ^{99}Tc is beta emitter. Monitoring of is done through urine bioassay techniques.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{99}Tc	Urine Bioassay	Liquid Scintillation Counting	1-5 Bq/L	1 Bq/L
^{99}Tc	Urine Bioassay	Beta proportional counting	4 Bq	0.04 Bq/L

^{99m}Tc

(721) Monitoring of ^{99m}Tc is in general accomplished through Whole Body Counting. In addition ^{99m}Tc may be detected through urine bioassay. If needed lung monitoring may be performed.

Isotope	Monitoring Technique	Method of Measurement	Typical Detection Limit	Achievable detection limit
^{99m}Tc	Urine Bioassay	γ-ray spectrometry	5-10 Bq/L	0.01 Bq/L
^{99m}Tc	Whole Body Counting	γ-ray spectrometry	90 Bq	25-30 Bq

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