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Radiation Weighting for Reference Animals and Plants

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Abstract- It has long been recognised that the degree of biological impact on an organism resulting from a given absorbed dose (in gray, Gy) of ionising radiation can vary depending upon the type of radiation involved. This difference has been experimentally quantified and reported as Relative Biological Effectiveness (RBE) of specific radiation types. RBE values are experimentally determined and are the ratio of doses of a test radiation and a low-LET reference radiation that produce the same level of observed effect. RBE values have been measured for a variety of end points in *in vitro* experiments that include human and animal cell lines, as well as in *in vivo* experiments with animals. Such studies have shown that the magnitude of a biological effect depends not only on dose and the type and energy of the radiation delivering the dose, but also on the rate at which the dose is delivered and, most importantly, the endpoint under study. The need to apply this knowledge to radiological protection of humans has led to an aggregation and analysis of RBE data to provide 'radiation weighting factors', and to the radiation protection quantity 'equivalent dose' (in sievert, Sv) where the absorbed dose is multiplied with the radiation weighting factor appropriate for the type of radiation considered. Whereas protection of humans has focused on avoiding tissue reactions (deterministic) and limiting stochastic (cancer/heritable) effects, protection of biota has largely focused on endpoints relevant to population viability. The present report reviews RBE data relevant to biota for one low energy beta emitter (tritium) and for alpha-emitting radionuclides. For tritium, values obtained centre around 1.5 – 2 compared with x-rays and 2 – 2.5 compared with gamma rays; values for alpha particles are generally substantially higher. It is proposed that for protection purposes, that an RBE weighted absorbed dose be used, with a RBE weighting for biota of 1 for all low-LET radiations and 10 for alpha particles, should be used for relevant RAPs, Use of a single value of 1 for all low-LET radiations is consistent with the approach taken to protection of humans. However, if exposures to tritium beta particles or other low-energy, low-LET radiations are estimated to be within or close to the Derived Consideration Reference Level (DCRL), assessment of the use of higher RBE values may be warranted.

CONTENTS

[GUEST] EDITORIAL

TITLE OF EDITORIAL (SAME STYLE AS LEVEL AS HEADINGS)

To be drafted.

CHRISTOPHER CLEMENT
SCIENTIFIC SECRETARY
EDITOR-IN-CHIEF

MAIN POINTS

- **This report reviews data from studies of the Relative Biological Effectiveness (RBE) of: (a) low energy beta particle emissions from tritium and (b) alpha particle emitting radionuclides. RBE values are experimentally determined and are the ratio of doses of a test radiation and a low-LET reference radiation that produce the same level of observed effect.**
- **RBE values showed no clear pattern of differences between species. For tritium, reported values centred around 1.5 – 2 compared with x-rays and 2 – 2.5 compared with gamma rays. Values for alpha particles were generally higher, of the order of 10.**
- **For protection purposes, it was considered reasonable on the basis of current knowledge to specify RBE weighted absorbed dose for biota to apply to all population relevant end-points as single values for all RAPs.**
- **RBE weighted absorbed dose rates to RAPs should be calculated using values of 1 for all low-LET radiations and 10 for alpha particles for comparison with the relevant DCRL.**
- **A caveat is made that if exposures to tritium beta particles, or to other low-energy, low-LET radiations, are within or close to the derived consideration reference level (DCRL) band, additional review, and possible modification of RBE weighting might be warranted.**

1. INTRODUCTION

1.1. The Commission's position on environmental protection

(1) The Commission's environmental protection aims are to prevent or reduce the frequency of deleterious radiation effects on biota to a level where they would have a negligible impact on the maintenance of biological diversity, the conservation of species, or the health and status of natural habitats, communities, and ecosystems (ICRP, 2007). The biological endpoints of most relevance are therefore those that could lead to changes in population size or structure. Because of the immense variety of biota, and their presumed response to radiation, any credible system needs to have some key points of reference which provide some form of auditable trail that links the basic elements of the framework together – or at least could do so if further data were forthcoming, and it is feasible to obtain such data. The Commission therefore developed a small set of twelve Reference Animals and Plants (RAPs), plus their relevant databases, for a few types of organisms that are typical of the major environments (ICRP, 2008) (Table 1).

Table 1. Identification and description of RAPS as first introduced in *Publication 108* (ICRP, 2008).

Reference organism	*Environment*	*Description*
Deer	Terrestrial	A large terrestrial mammal
Rat	Terrestrial	A small terrestrial mammal
Duck	Aquatic	An aquatic bird
Frog	Aquatic	An amphibian
Trout	Aquatic	A freshwater fish
Flatfish	Aquatic	A marine fish
Bee	Terrestrial	A terrestrial insect
Crab	Aquatic	A marine crustacean
Earthworm	Terrestrial	A terrestrial annelid
Pine tree	Terrestrial	A large terrestrial plant
Wild grass	Terrestrial	A small terrestrial plant
Brown seaweed	Aquatic	A seaweed

(2) After considering relevant radiation effects to these types of biota, a set of Derived Consideration Reference Levels (DCRLs) in units of absorbed dose per day, typically reported as mGy d^{-1}, was defined for the different types of RAPs (ICRP, 2008). The DCRL can be considered as a band of dose rate, spanning one order of magnitude, within which there is some chance of deleterious effect from ionising radiation occurring to individuals of that type of RAP, which may have a potentially deleterious effect on its population. Thus, when considered together with other relevant information, DCRLs can be used as points of reference to inform on the appropriate level of effort that should be expended on environmental protection,

dependent on the overall management objectives, the exposure situation, the actual fauna and flora present, and the numbers of individuals thus exposed. The DCRLs considered to be most appropriate, based on the current level of knowledge, are shown in Fig. 1.

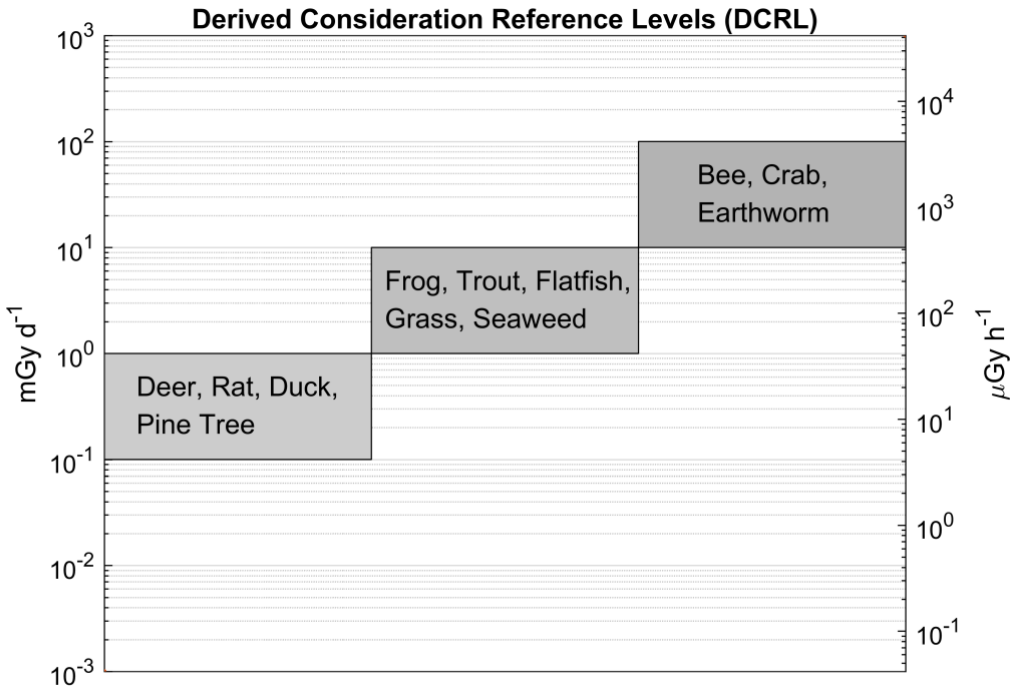

Fig. 1. Derived Consideration Reference Levels (DCRLs) for environmental protection for each RAP.

(3) Because the RAPs are, by definition, points of reference, it will also in some circumstances be necessary to identify Representative Organisms (ROs) relevant to the situations of exposure under consideration. The ROs may well be the same as, or similar to, the RAPs. Differences should be quantifiable, in relation to their basic biology, dosimetry, and radiation effects. The extent to which such factors then need to be taken into account, and their impact on the final decision, will depend on the circumstances of the assessment, as outlined in *Publication 124* (ICRP, 2014).

(4) *Publication 136* (ICRP, 2017) provides dose coefficients for RAPs, updating the data provided in *Publication 108* (ICRP, 2008). Data are provided for both internal and external exposures, as absorbed dose rates (μGy h^{-1} Bq^{-1} kg) averaged over the mass of the organism. For internal exposures, values are given separately for alpha particles, low-energy beta particles and gamma radiation (E <10 keV), and all other beta and gamma radiations (E >10 keV). This separation of dose contributions was done in recognition of differences between radiation types and energies in their effectiveness per absorbed dose in causing deleterious biological effects.

(5) In the system of protection as applied to humans (ICRP, 2007), absorbed doses to organs and tissues from different radiation types are multiplied by radiation weighting factors (w_R) before dose contributions are summed as equivalent dose in sievert (Sv). The w_R values are chosen on the basis largely of experimental data on the relative biological effectiveness (RBE) of different radiation types determined for biological end-points related to stochastic effects (cancer, hereditary effects). RBE values are experimentally determined and are the ratio of doses of a test radiation and a low-linear-energy-transfer (LET) reference radiation that produce the same level of observed effect.

(6) This report provides a review of RBE data relating to exposures to tritium beta particles, as an important example of low-energy, low-LET radiation. Data on RBE for biological effects caused by alpha particle emitting radionuclides are also reviewed. On the basis of the analyses of these data, RBE weightings for absorbed dose are proposed for use in relation to RAPs with the dose coefficients provided in *Publication 136* (ICRP, 2017). The intention is that these values will be used to calculate values of radiation weighted absorbed dose rates for comparison with DCRLs and corresponding data for ROs.

1.2. The relevance of RBE to Reference Animals and Plants

(7) The biological endpoints of most relevance to the protection of non-human biota are those that could lead to changes in population size or structure, including survival, fecundity, reproductive and developmental impairments. Such effects are generally classed as tissue reactions (formerly deterministic effects) and occur above thresholds with severity increasing with increasing dose (ICRP, 2007). Most likely, based on current knowledge and for the purpose of protection of non-human biota, biological endpoints such as DNA damage, chromosomal aberrations, mutation, and tumour induction, which are classed as stochastic effects, are less relevant for population viability. Such effects are taken to occur without thresholds and with probability (not severity) increasing with increasing dose (ICRP, 2003, 2007). Broadly speaking, effects termed stochastic, i.e. cancer and heritable effects, are caused by non-lethal mutational events in cells, while effects termed tissue reactions are typically caused by cell killing and other tissue abnormalities.

(8) In the reviews presented in this report, biological data are considered in four categories: mortality, reproductive failure, morbidity and chromosomal damage. Data on cancer induction are included in the morbidity category. Thus, for completeness and to allow comparisons to be made, less relevant stochastic data on cancer and chromosome damage are included together with directly relevant data on tissue reactions.

(9) ICRP (2003, 2007) has previously reviewed RBE data on stochastic effects as the basis for setting radiation weighting factors, w_R, for the calculation of equivalent and effective dose (Sv) for humans. Effective dose is used to set limits, constraints and reference levels and in the optimisation of protection against cancer and heritable effects. ICRP (2007) also sets limits on equivalent dose to tissues to prevent tissue reactions (hand, feet, skin, lens of the eye) although w_R values were intended to apply to stochastic effects.

(10) For photons and electrons of all energies, a w_R value of 1 is used (ICRP, 2007) despite recognised differences in RBE of up to a factor of four, with higher values at lower energies. A w_R value of 20 is used for alpha particles for all cancer types and hereditable effects, although the available data suggest that RBE will differ for different end-points (ICRP, 2007), with, for example, low values for alpha particle induced leukaemia (RBE = 1–2) and higher values for lung and liver cancer (RBE = 10–20). The intention of w_R was to balance scientific accuracy with a simple scheme of practical utility for protection purposes.

(11) Similarly, in using RBE data as the basis for the choice of RBE weighting values for the calculation of radiation weighted absorbed dose rates to RAPs, a simple scheme is required to apply across radiations, species and effects. However, there are important differences in application and specifically for environmental protection, the intention is that estimated dose rates will be compared with the most relevant DCRLs. Since DCRLs are set as order of magnitude dose rate bands of concern, the question is whether consideration of the relative biological effectiveness of radiations will result in the DCRL being reached or breached.

(12) Dose limits and dose constraints for protection of humans in planned exposure situations are set at levels where no tissue reactions occur and where inferred risks for stochastic effects are very small. Optimisation leads to actual exposures that are normally well below limits and constraints. A high level of protection is also afforded in existing exposure situations, where an appropriate reference level is selected that will inform optimisation efforts and which will be adjusted with time, as appropriate. DCRLs, however, are set at absorbed dose rates where deleterious effects may occur; the selection of an appropriate weighting factor thus has direct relevance for our understanding of likelihood of effects and need for protective measures. The relationship between optimisation (for environmental protection) and DCRLs in planned and existing exposure situations is outlined in *Publication 124* (ICRP, 2014).

(13) The Commission's approach for protection of the environment is intended to be a reasonable, yet prudent approach to understanding when there is a possibility of effects in the population. To that end it may be important to take into account the RBE, when the radiations of concern warrant. The Commission is not, at this time, suggesting a separate protection quantity, or a weighting factor terminology, as this could be seen as adding unnecessary complexity to the scheme. Likewise, the Commission is not treating protection of the environment in the same way as protection of humans, and is therefore not specifying whether population effects are deterministic or stochastic. There is much research that remains to clarify the mechanisms that may be at work in causing population effects of interest. When RBE weighting is used, there should be clear documentation of the original measurements, and the value of the weighting applied, in order to ensure transparency and reproducibility of the results.

(14) ICRP (1990) has also previously reviewed RBE data on tissue reactions, considering alpha particle, neutrons and heavy ions; the data and analyses provided are referred to in Annexes A and C. Alpha particle emitting radionuclides can be important contributors of dose to non-human biota, both in terms of anthropogenic sources and naturally occurring alpha-emitting nuclides. Tritium exposures can also be of concern in particular circumstances and a range of RBE studies have been undertaken using this radionuclide.

(15) The following sections provide summaries of the RBE data reviewed in detail in Annexes B (tritium) and C (alpha-emitting radionuclides) and conclude by providing w_B values based on these data. Annex A provides a detailed discussion of RBE and factors that influence RBE.

2. RELATIVE BIOLOGICAL EFFECTIVENESS OF TRITIUM BETA PARTICLES

2.1. Introduction

(16) A review of the data available on RBEs for tritium beta particles is given in Annex B. This section provides a summary of the main data and conclusions. Most studies have used tritiated water (HTO) as the radiation source. Information is scarce for organically bound tritium (OBT). Mammalian species have been the most frequently studied (80% of the data), either *in vivo* with laboratory bred animals (mainly mice) or *in vitro* (human cells or established cell lines). There is very limited information on RBEs for tritium beta particles that could be relevant to other RAPs: six RBE values for a fish (medaka) and single RBE values for an insect (*Drosophila*), a terrestrial plant, the broad bean, a vascular terrestrial plant (*Vicia faba*), and a polychaete worm (*Ophryotrocha diadema*). Both tissue reactions and stochastic endpoints have been analysed.

(17) Regarding the reference radiation used, gamma radiation (from ^{60}Co or ^{137}Cs) has been more frequently used (75% of the data) than orthovoltage x-rays. After critically reviewing the values of RBE when tritium was administered as HTO, in general, RBE values for tritium beta particles are almost two times higher when gamma rays are used as reference radiation rather than x-rays (Straume and Carsten, 1993; Environment Canada and Health Canada, 2003; Kocher et al., 2005; Little and Lambert, 2008; UNSCEAR, 2016).

(18) Due to its low beta particle energy (5.7 keV mean), tritium's track average LET in water from secondary electrons is 4.70 keV μm^{-1}. This can be compared (for example) to the 0.22 and 0.52 keV μm^{-1} track average LET in water generated from ^{60}Co's 1173 and 1332 keV gammas (ICRU, 1970). The net result is that the fraction of dose to tissue from tritium's low energy (0.1-5 keV) beta particles and/or secondary electrons is approximately 78%. This can be contrasted with the much smaller 33% contribution to dose from low energy secondary electrons resulting from ^{60}Co's gamma rays (Nikjoo and Goodhead, 1991).

(19) It also has to be noted that in all the studies reviewed here the reference radiation (either x-rays or gamma rays) is an external source whereas the tritium was internally administered and the absorbed dose estimated. Although the range of tritium beta particles in tissues is low, the uniform distribution of the radionuclide makes the comparison of averaged absorbed doses valid.

(20) Despite the fact that the intakes of tritium by biota in the natural environment will be by inhalation, skin absorption, or ingestion, almost all experimental *in vivo* studies have involved intraperitoneal or intravenous injection. However, in general the different routes of exposure/administration result in similar distribution of tritium in the various organs and tissues. Regarding the irradiation schedule, this has been performed either at exponentially decreasing dose rates (single tritium injection) or at constant dose rates (multiple injections or single injection followed by ingestion of tritium in drinking water). The reference radiation (gamma or x-rays) was administered at either a constant dose rate or an exponentially decreasing dose rate to mimic the time-course of tritium beta particle irradiation.

(21) Although the range of tritium beta particle doses and reference radiation doses and dose rates assayed has been wide, most of the studies have used doses and dose rates well above those found in the environment in planned or existing situations (but many are within the DCRL bands). Nevertheless, RBE values have been determined on the assumption that these data can be used for different biological endpoints: early mortality, reproductive failure, morbidity and chromosomal damage and mutations.

(22) In the summaries provided below for the different end-points, uncertainties on RBE values obtained from individual studies are not presented – this information is available in Annex B. Similarly, the reference radiation is not identified here but, as noted above, RBE values tend to be greater when gamma rays are used as reference than when the comparison is with x-rays.

2.2. RBE values for tritium beta particles for different biological endpoints

(23) RBE values for tritium beta particles for early mortality were determined to be in the range 1.0 to 1.7 (three values available) for a rodent and a terrestrial vascular plant (Fig. 2.1). All relate to HTO.

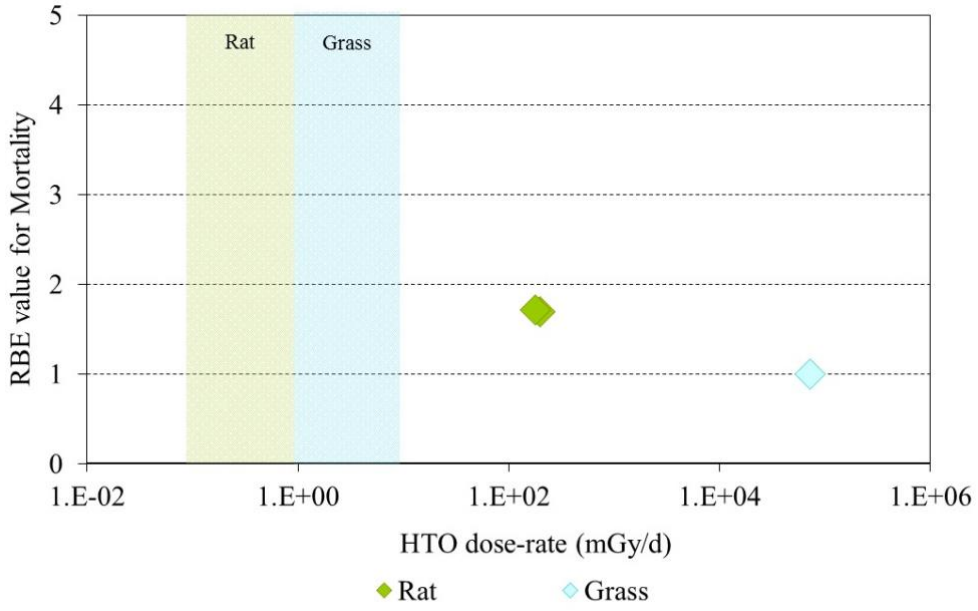

Fig. 2.1. RBE as a function of dose rate from tritium beta particles (HTO) for early mortality. The Derived Consideration Reference Levels (DCRLs, mGy d^{-1}) for environmental protection for each category of RAP are shown as coloured bands of green and blue.

(24) For reproductive failure, the RBE values for tritium beta particles were in the range 1.0 to 3.9 and relate to a rodent, a fish, and a polychaete worm (Fig 2.2). All were based on HTO.

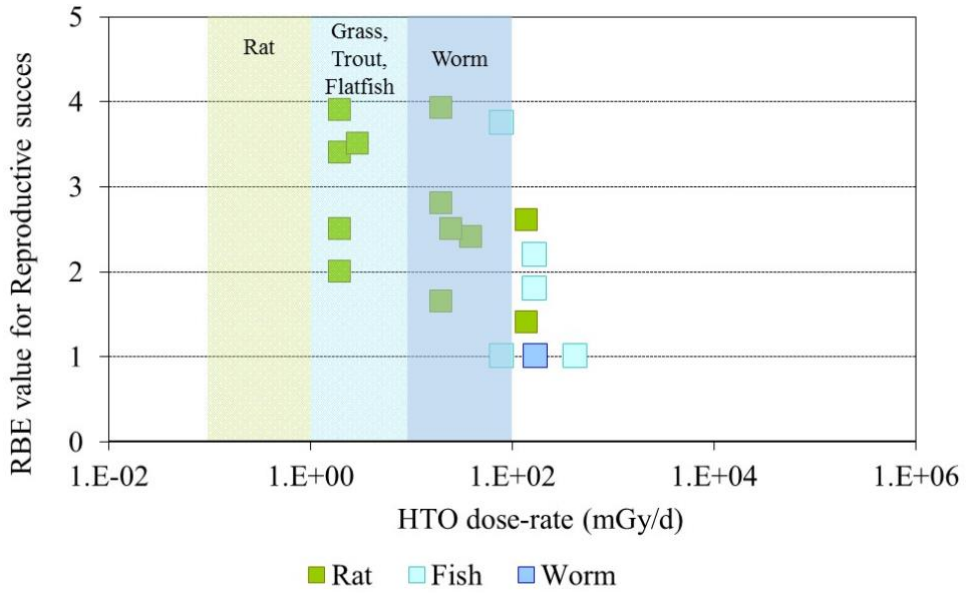

Fig. 2.2. RBE as a function of dose rate from tritium beta particles (HTO) for reproductive failure. The Derived Consideration Reference Levels (DCRLs, mGy d^{-1}) for environmental protection for each category of RAP are shown as coloured bands of green, blue and darker blue.

(25) The RBE values available for tritium beta particles relating to morbidity showed values in the range 1.0 to 2.5 (Fig. 2.3) and relate only to rodents (rats, mice, murine leukaemia cells, hamster cells) and using HTO.

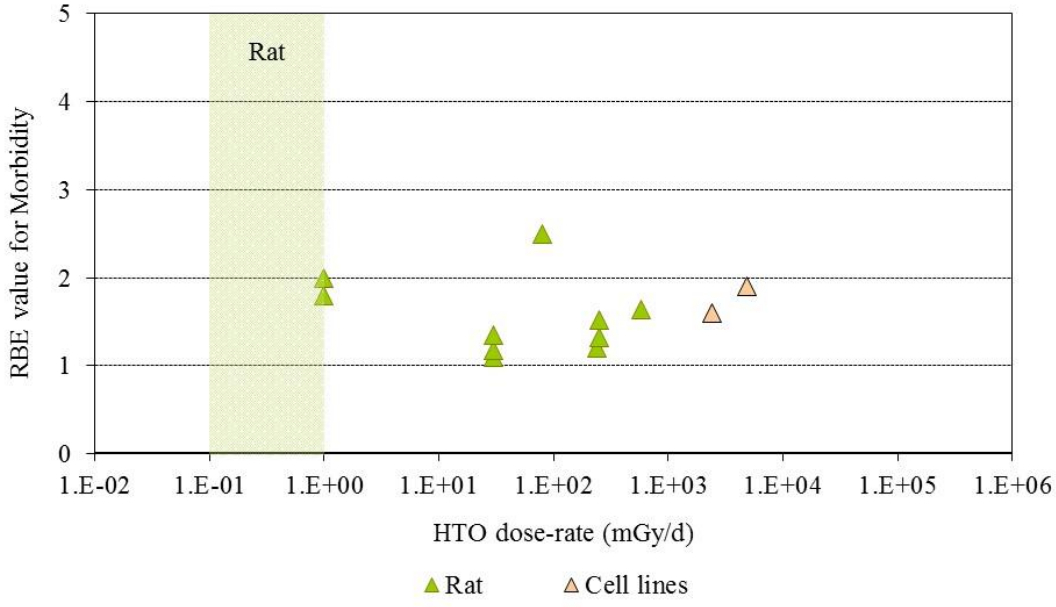

Fig. 2.3. RBE as a function of dose rate from tritium beta particles (HTO) for morbidity. The Derived Consideration Reference Levels (DCRLs, mGy d^{-1}) for environmental protection for the RAP is shown as a coloured band of green.

(26) For induction of chromosomal damage and mutations, RBE values for tritium beta particles were in the range of 1.0 to 3.8 (Fig. 2.4) and relate only to an insect and mammals.

All relate to HTO. It should be noted that there are substantial uncertainties in extrapolating from subcellular data such as chromosomal damage and mutation rates to observed effects in whole organisms. However, the data are presented for completeness.

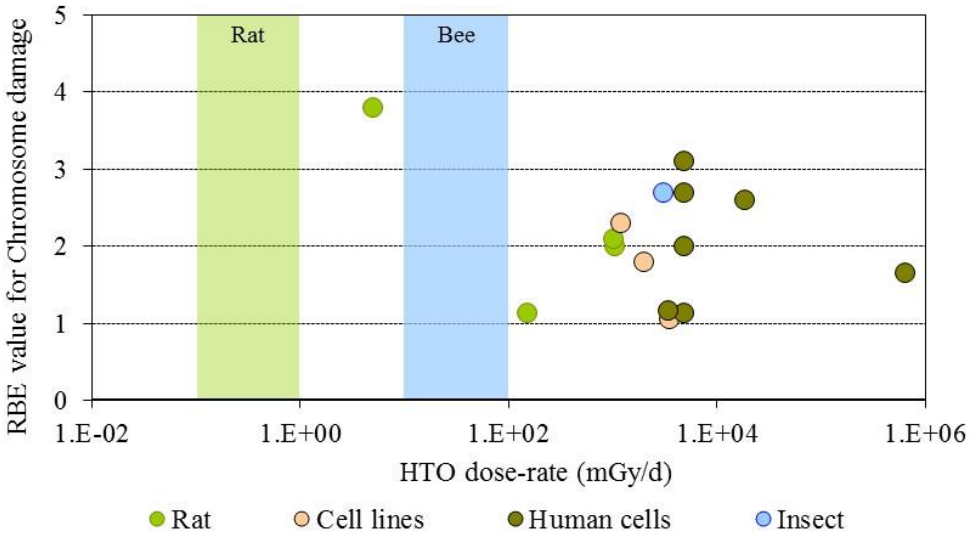

Fig. 2.4. RBE as a function of dose rate from tritium beta particles (HTO) for chromosome damage and mutation. The Derived Consideration Reference Levels (DCRLs, mGy d^{-1}) for environmental protection for each category of RAP are shown as coloured bands of green and blue.

(27) Regarding RBE values for tritium beta particles following tritium administration as DNA precursors (e.g. tritiated thymidine), in relation to any of the biological end points of interest, it was not possible to conclude anything from the four studies available because of the experimental conditions used, the biological endpoints chosen, and the dosimetric uncertainties.

2.3. Conclusions

(28) Overall, the non-human biota data on RBE for tritium beta particles, summarised in Table 2.1, cover a range of end-points and experimental conditions but relate primarily to small mammals.

(29) All values were obtained at dose rates that were in or above the relevant DCRL bands. RBE has been shown to increase with decreasing dose rate.

(30) In comparison to other radionuclides, the majority (~78%) of dose from tritium is due to the low energy beta and/or secondary electrons (0.1- 5 keV) which generate greater density of ionisations than do higher energy electrons.

(31) The spread of data for fish are from 1 to nearly 4 with values for aquatic invertebrates around 1. The same range was seen for rats, showing consistency across species. For reduced reproductive success, the RBE values were in the range of 1-3.9.

(32) Overall, as concluded by UNSCEAR (2016), values centred around 1.5 – 2 compared with x-rays and 2 – 2.5 compared with gamma rays (see Annex B).

Table 2.1. Ranges of RBE values described in the literature for tritium beta particles (tritium administered as HTO).

RBE range	*Endpoint analysed*		*Number of RBE values reported*	*Test models*
	In vivo/Ex vivo	In vitro		
1-2	Mortality; Reproductive capacity (fertility and fecundity); Cell survival; Chromosome aberrations; Vertebral abnormality; Tumour incidence	Embryo survival; Chromosome aberrations; Cell survival; Mutations	42	Fish; Plant; Marine invertebrate; Mammals (Mouse; Rat; Hamster; Human primary cells; Cell lines)
2-3	Reproductive capacity (germ cells survival and anomalies in total implants; Dominant lethal and sex-linked recessive lethal mutations in germ cells); Cell survival; Tumour development	Survival of haematopoietic progenitors; Chromosomal aberrations; Dicentrics; Mutations	25	Fish; Insect; Mammals (Mouse; Rat; Human primary cells; Cell lines)
3-4	Reproductive capacity; Chromosome aberrations and mutations	Chromosome aberrations; Mutations	7	Fish; Mammals (Mouse; Human primary cells; Cell lines)

3. RELATIVE BIOLOGICAL EFFECTIVENESS OF ALPHA PARTICLES

3.1. Introduction

(33) A review of the data available on the relative biological effectiveness of alpha particles and corresponding citations are given in Annex C; a summary of the main data is included here. About ninety articles were found that discussed studies relevant to alpha RBE for non-human biota. Of these, 58 were reviewed in detail; the remainder were considered to have inadequate precision with regard to dosimetry, or had other limitations. Table 3.1 provides an overall summary of RBE values for internally deposited alpha particles.

(34) Most of the reviewed papers either reported RBE values directly, or provided sufficient data from exposure–effect models, or survival curves, from which alpha particle RBE values could be calculated. Maximum values for RBE_m or RBE_M where m and M denote values for tissue reactions and stochastic endpoints, respectively, were calculated wherever possible from the slopes of survival curves (see Annex A for discussion, and glossary for definition). These data are included in Annex C.

(35) In addition to RBE values obtained from studies of internally deposited alpha emitters *per se*, some data on RBE were also derived from experimental studies involving external exposure to fission neutrons (which have similar LET to that for alpha particles for common internal emitters) have also been considered in this review.

3.2. Alpha particle RBE values for different biological end points

(36) In mammals, mortality is a result of extensive irradiation that causes severe cell depletion, in turn leading to dysfunction of major organs. Death of the organisms occurs due to injury of specific organs. Few RBE studies have been conducted for this endpoint.

(37) Of the 58 papers reviewed, 14 examined the effects of alpha emitters on reproductive failure. The reference radiations used in these studies were x-rays, ranging from 60 to 120 kVp, and high-energy gamma rays from sources such as ^{60}Co. It is important to note that the RBE values obtained using x-rays as the reference may be up to a factor of 2 lower than those using ^{60}Co. The alpha emitters commonly used were ^{238}Pu, ^{239}Pu and ^{210}Po. A wide range of RBE values were reported or calculated; however, most were in the range of 1 to 5, with very few papers reporting alpha RBE values >5. Most RBE values were obtained from studies using rodents or rodent cells exposed to high doses and at high dose rates. Reported RBE values vs. dose rate are shown in Fig. 3.1 for studies related to reproductive failure.

(38) Only 6 publications reported alpha particle RBE in relation to morbidity. The reference radiations used were ^{60}Co gamma rays and 220kVp x-rays. The alpha emitters commonly used were isotopes of Pu and Ra. A range of RBE and RBE maximum values were reported, all below 11, with the majority below 5 (Fig. 3.2).

(39) Some 26 articles analysed chromosomal damage and mutations caused by alpha emitters. It should be noted however, that these effects are stochastic in nature and at present, it is uncertain how to extrapolate such effects to relevant population endpoints. The reference radiation used in these studies was ^{60}Co gamma rays or x-rays ranging from 80 to 300 kVp. Alpha emitters commonly used to irradiate cell lines, tissues or cell cultures were ^{238}Pu, ^{239}Pu, ^{241}Am and ^{226}Ra. Most RBE values were obtained using rodents or rodent cells exposed to high doses at high dose rates giving values in the ranges of 1 to 10, with very few papers describing

alpha RBE values greater than 20 (Fig. 3.3). As discussed in Annex A, RBE is a function of dose, with values decreasing as dose increases, and this factor must be considered in any interpretation of the data.

(40) In the graphical and tabulated summaries provided below for the different end-points, uncertainties on RBE values obtained from individual studies are not presented – this information is available in Annex C. Similarly, the reference radiation is not identified here but, as noted above, RBE values tend to be greater when gamma rays are used as reference than when the comparison is with x-rays.

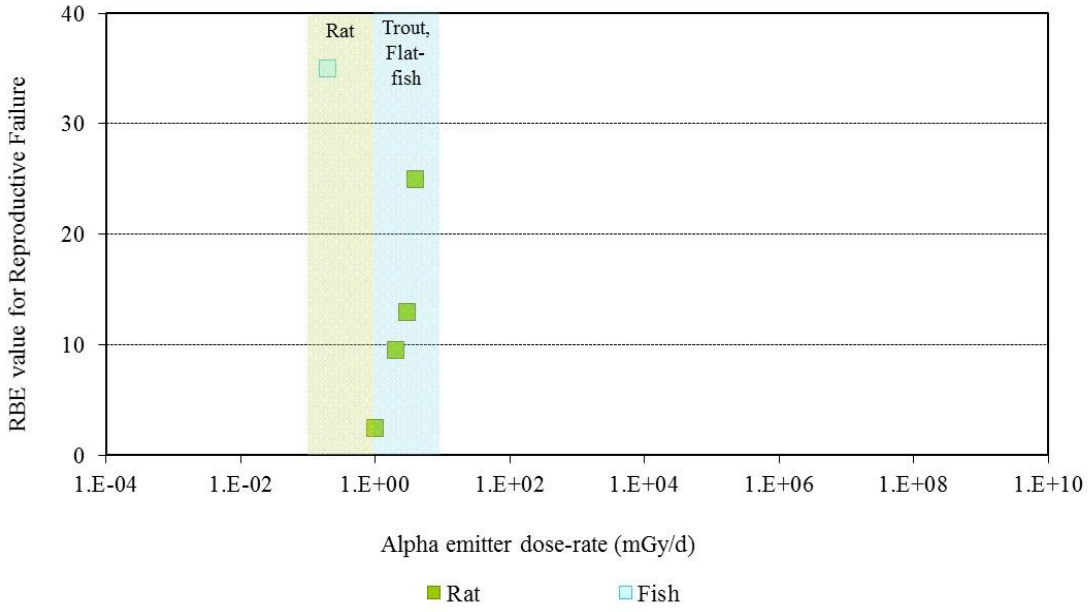

Fig. 3.1. RBE as a function of dose rate from alpha emitters for reproductive failure. The Derived Consideration Reference Levels (DCRLs) for environmental protection for each category of RAP are shown as coloured bands of green and blue.

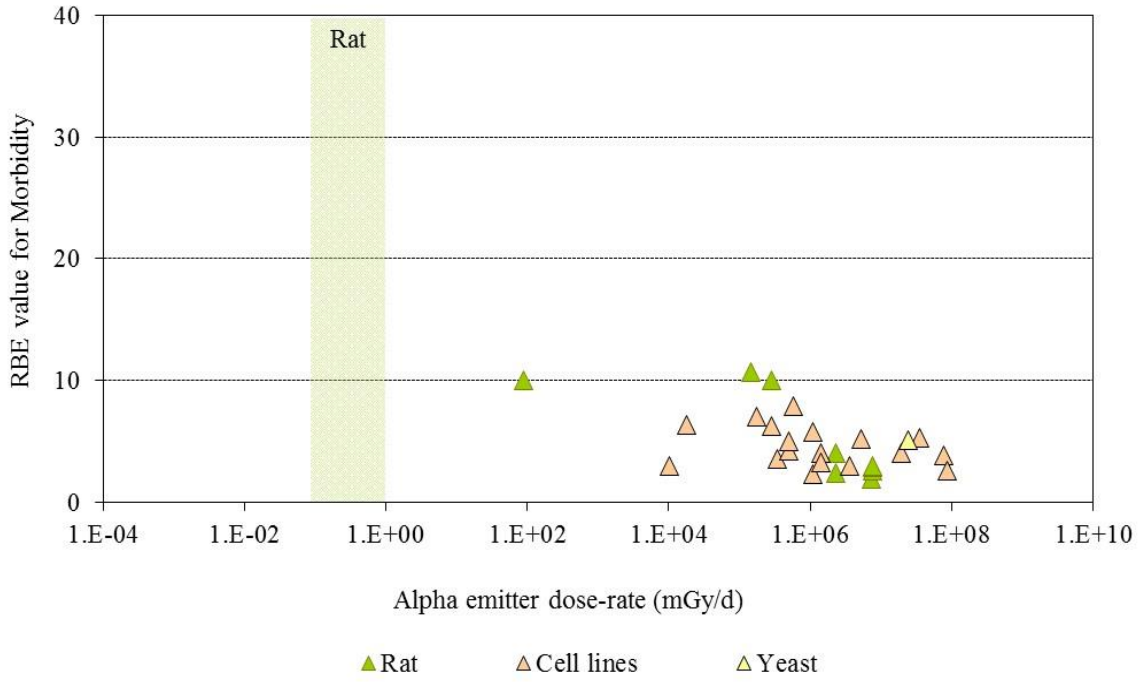

Fig. 3.2. RBE as a function of dose rate from alpha emitters for morbidity. The Derived Consideration Reference Levels (DCRLs, mGy d^{-1}) for environmental protection for the RAP is shown as a coloured band of green. Cell lines include rodent fibroblasts and tracheal epithelium, and human skin fibroblasts.

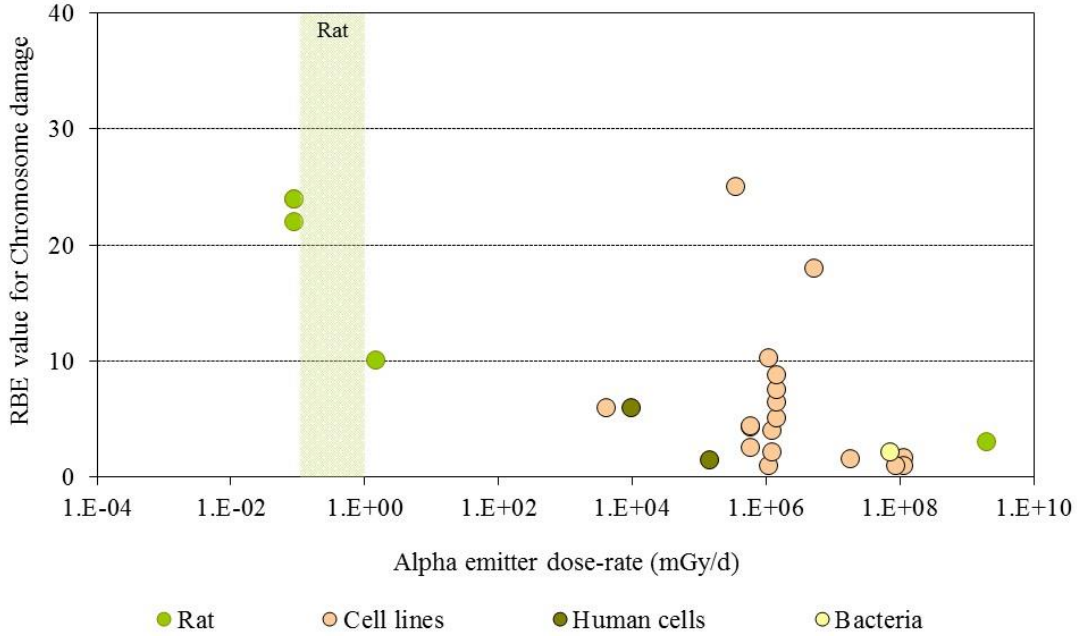

Fig. 3.3. RBE as a function of dose rate from alpha emitters for chromosomal damage and mutations. The Derived Consideration Reference Levels (DCRLs, mGy d^{-1}) for environmental protection for the RAP category is shown as a coloured band of green. Cell lines include rodent fibroblasts, and human lymphocytes.

Table 3.1. Summary of reported RBE values[a] for alpha particles.

RBE Range	*Endpoint analysed*		*Nº of RBE values reported*	*Test Models*
	In vivo/Ex vivo	In vitro		
0-4	Tumour Induction; Organ/Tissue effects	Cell survival, DNA damage and Double strand breaks; Chromosomal aberrations and Cell transformations	33	Mammals (Dog; Mouse; Rat; Cell lines); Fish
5-10	Tumour induction; Organ/Tissue effects	Cell survival, DNA damage and Double strand breaks, Chromosomal aberrations and Cell transformations	24	Mammals (Dog; Mouse; Rat; Cell lines; Tumour cells)
11-20	Tumour induction	DNA Double strand breaks and Chromosomal aberrations	4	Mammals (Dog; Mouse; Rat; Cell lines)
>20	Tumour induction; Effect on haematopoietic tissue	Chromosomal aberrations	7	Mammals (Dog; Mice; Hamster; Rat; Cell lines; Tumour cells)

[a] RBE values are as reported from the original reference. Thirty-six studies provided sufficient information to calculate RBE_m with 72% of these values less than 10. Fourteen studies had sufficient information to calculate RBE_M, with 64 % of the RBE less than 10. See Annex C for more information.

3.3. Conclusions

(41) As for tritium, it is evident that the data available are primarily relevant to vertebrates – essentially to small mammals, and with respect to reproductive failure and morbidity. Overall the non-human biota data on RBE for alpha particle irradiation are limited. The single value for a fish (Fig. 3.1) is of interest, although the authors (Knowles, 2001) had reservations about the results and commented that a value of < 35 represented an upper limit, and that the actual value was more likely to be in the range of 7 to <20.

(42) The RBE values summarised here were all obtained at dose rates that were in or above the relevant DCRL bands. The values obtained are in a wide range but centre around values of the order of 10.

4. OVERALL CONCLUSIONS AND RECOMMENDATIONS

(43) This review examined RBE data for tritium beta particles and alpha particles for biological effects in non-human biota to consider whether radiation weighting factors for biota should be used to modify estimates of absorbed dose rate for comparison with DCRLs. RBE values vary according to factors including the end-point being studied, the dose and dose rates employed, and the reference radiation. However, in general, there appears to be some consistency in numerical values obtained across species and for various cell lines, as might be expected in relation to the common physical basis for differences in the effectiveness per Gy of the different radiation types. This similarity across organisms suggests that, in the absence of better information, RBE weighting can reasonably be applied to all RAPs and to ROs identified under particular circumstances of exposure (see 1. Introduction).

(44) The available RBE data for tritium beta particles and alpha particles were obtained at dose rates at or above the corresponding DCRLs. As discussed in detail in Annex A, RBE values tend to increase to a maximum as doses and dose rates decrease. For the tissue reactions of most concern in terms of population survival, these considerations are complicated by the existence of thresholds below which no effects are observed. However, it appears that extrapolated RBEs for tissue reactions are largely independent of dose below a level that may be comparable to a threshold (see Annex A). For the purposes of this report, therefore, it is considered reasonable to base proposals for radiation weighting factors for biota on the observed RBE data without further adjustment to obtain RBE_m values for tissue reactions and RBE_M values for stochastic effects, although RBE_m and RBE_M values were calculated for some studies with alpha particle emitting radionuclides (Annex C).

(45) Biological end-points were considered in four categories: mortality, reproductive failure, morbidity and chromosomal damage/mutations. While the first two categories clearly can be considered as tissue reactions and relevant to population survival, some of the morbidity studies and all chromosome damage/mutation studies relate to stochastic effects and their relevance in the context of this report is more questionable. In general, RBE values for tissue reactions tend to be lower than values for stochastic effects. However, particularly in the case of tritium, but also for alpha particles, there was not a clear difference in the ranges of RBE values observed for the various end-points. In proposing radiation weighting for general application, therefore, it is considered reasonable to consider the entirety of the available data.

(46) Consistent with the approach taken in specifying weighting factors used in protection of humans, it is recommended that an RBE weighting factor of 1 be used for all low LET radiations and a value of 10 for alpha particles in assessments of exposures and comparison of estimated doses with the relevant DCRL. If exposures to tritium beta particles or other low energy, low LET radiations, are within or close to the DCRL, additional review, and possible modification of weighting might be warranted.

(47) These recommendations are consistent with those of UNSCEAR (2008) for non-human biota. In Annex E of its report, the Committee recommended a nominal factor of 10 for internally deposited alpha radiation, and a nominal factor of 1 for RBE for beta and gamma radiation. There recommendations were meant to be applicable on a generic basis across all organisms and endpoints.

(48) These RBE weighting factors can be used with the dose coefficients provided in *Publication 136* (ICRP, 2017) which provides separate values of absorbed dose rate for internally deposited radionuclides for high LET and low and high energy low LET radiations.

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ANNEX A. RELATIVE BIOLOGICAL EFFECTIVENESS IN THE CONTEXT OF PROTECTION OF THE ENVIRONMENT

(A 1) Studies of dose-response relationships for different types of radiation in inducing a wide variety of effects in many biological systems, ranging from cells in culture to whole organisms, have shown that knowledge of the absorbed dose is not sufficient to characterise the biological response from a given dose. It is generally observed that radiation quality, as commonly represented by the linear energy transfer (LET), is important in determining the biological response from a given absorbed dose. In particular, high-LET radiations (e.g. alpha particles and neutrons) are more effective per unit absorbed dose than low-LET radiations (e.g. orthovoltage x-rays and higher-energy photons) in inducing biological effects. To account for this, the absorbed dose (in Gy) is often multiplied by a modifying factor in order to account for the Relative Biological Effectiveness (RBE). The term RBE applies to observations from experimental studies and is specific to the endpoint and system studied, environmental and exposure conditions (e.g. reference radiation, dose rate, and dose) amongst other factors. This section presents a definition of RBE and brief discussions of factors that influence RBE, extrapolation of RBEs obtained in studies at high doses to low doses of concern to radiological protection, especially extrapolation of RBEs for tissue reactions, and extrapolation of RBEs for cells to higher levels of biological organisation including whole organisms.

A.1. Relative Biological Effectiveness (RBE)

(A 2) For a specific radiation (A) of interest, RBE is a unitless quantity defined as the ratio of the dose of a reference radiation required to produce a specific level of biological response to the dose of radiation A required to produce an equal biological response, with all physical and biological variables, except radiation quality, being held as constant as possible (ICRP, 2007). RBE as so defined is a radiobiological quantity that does not depend on the dose-response relationships for the two radiations having the same functional form (e.g. a linear-quadratic relationship) and, or, that each dose response be a proportional (linear) relationship.

(A 3) In most studies to estimate RBEs, radiation A is a high-LET radiation and the reference radiation is a specified low-LET radiation. However, this need not be the case. For example, the radiation of interest in many studies is a lower-energy low-LET radiation (e.g. orthovoltage x-rays, lower-energy x-rays such as those used in mammography, or beta particles emitted in decay of tritium) and the reference radiation is higher-energy gamma rays (photons), such as those emitted in decay of ^{60}Co. Any radiation of interest and reference radiation can be chosen as long as they differ in quality (LET).

(A 4) When an RBE obtained in a study is extrapolated to other doses not included in that study using assumed dose-response relationships for the two radiations, to other biological systems, to other biological endpoints of the same kind (stochastic or deterministic), or to other radiations of similar LET, the resulting inference about biological effectiveness is not strictly an RBE as this term is defined above. Nonetheless, the term RBE is widely used to describe an inferred relative biological effectiveness that is based on specific radiobiological studies.

A.1.1. Factors that Influence RBE

(A 5) There are several factors that influence estimates of RBE obtained from radiobiological studies. Amongst others, these include the chosen reference radiation, the magnitude of the dose or dose rate and extent of dose fractionation, and the biological endpoint

under study (i.e. whether the endpoint is a stochastic effect or a tissue reaction and the particular effect of either kind). Certain other factors also can be important.

Choice of Reference Radiation

(A 6) Reference radiations used in radiobiological studies to estimate RBEs usually are orthovoltage (e.g. 150–300 kVp) x-rays or higher-energy photons (gamma rays). Many radiobiological studies have shown a significant difference in biological effectiveness of these two common types of reference radiations.

(A 7) Differences in biological effectiveness of orthovoltage x-rays and higher-energy photons are especially evident in some studies of stochastic effects. For example, reviews of data for stochastic effects by the NCRP (1990) and ICRP (2003) suggest that, at low doses of interest in radiological protection of humans, the biological effectiveness of orthovoltage x-rays is around twice (1.5–2 times) that of the biological effectiveness of higher-energy photons (e.g. ^{60}Co gamma rays). This difference in biological effectiveness also has been recognised in the BEIR VII report (National Research Council, 2006). Recognition of a difference of this magnitude is important when comparing RBEs for stochastic effects that were obtained in studies using different low-LET reference radiations. This is especially the case in comparing RBEs for lower-energy low-LET radiations, such as tritium beta particles.

(A 8) Differences in biological effectiveness of orthovoltage x-rays and higher-energy photons appear to be less important in studies of tissue reactions. For example, early studies of tissue reactions reviewed by the NCRP (1967) indicated that, at high dose rates where such effects occur, the biological effectiveness of orthovoltage x-rays is only about 20% higher than the biological effectiveness of photons emitted in decay of ^{60}Co. Such small differences are relatively unimportant in comparison to uncertainties in RBEs estimated using either reference radiation.

(A 9) *Publication 92* (ICRP, 2003) recommends that the preferred low-LET reference radiation for use in radiobiological studies is high-energy photons emitted in decay of ^{60}Co. This choice has a number of advantages including that (a) the photon energy is discrete and well defined, in contrast to the continuous and variable spectra of photons in studies using orthovoltage x-rays that depend on the tube potential (kVp) and filtration (filter material and thickness), and (b) the photon energy is closer to the average energy of photons in exposures of Japanese atomic-bomb survivors, studies of which provide the primary source of data on cancer risks from exposure to ionising radiation.

Dose, Dose Rate, and Dose Fractionation

(A 10) The magnitude of the absorbed dose and dose rate and the extent of dose fractionation all can influence estimates of RBE obtained in radiobiological studies. RBE depends on the dose, dose rate, and dose per fraction in fractionated exposures whenever the dose-response relationship for the radiation of interest, the reference radiation, or both is non-linear. This effect is illustrated in Fig. A.1 [adapted from CNSC (2002)] which shows the response as a function of dose, both on a linear scale, for induction of a stochastic effect by a high-LET radiation and a reference low-LET radiation. As observed in many studies, the dose-response for the high-LET radiation is assumed to be linear ($R = \alpha D$), whereas the dose-response for the reference radiation is assumed be linear-quadratic in form ($R = \alpha D + \beta D^2$). As a consequence of this difference in the dose-response relationships, in this example the RBE for the high-LET radiation at higher doses is about two and increases to about five at lower doses.

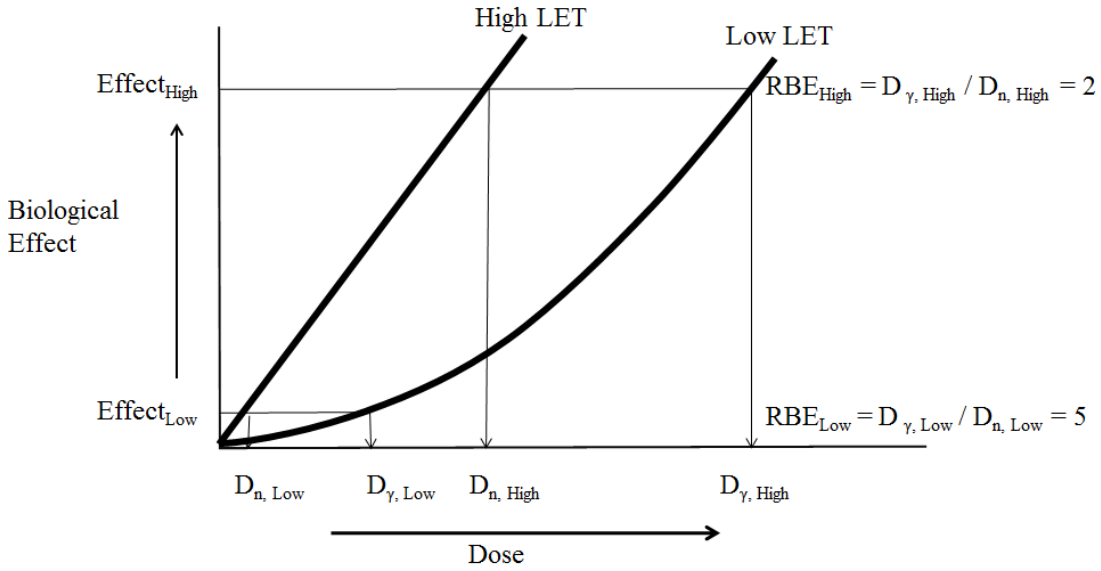

Fig. A.1. Biological effect as a function of dose for high- and low-LET radiation. The graph illustrates how the calculated value of RBE can differ based on the dose (high or low) used for the calculation (Adapted from figure INFO 0730, 2002).

(A 11) A similar dependence of RBE on dose is seen in many studies of tissue reactions. Examples of the dependence of RBE for various high-LET radiations on the dose of reference orthovoltage x-rays in studies of cell survival are shown in Fig. A.2 (ICRP, 1990). The curves in Fig. A.2 are based on assumptions of a survival function for high-LET radiations of the form $S = \exp(-\alpha D)$ and a survival function for the reference low-LET radiation of the form $S = \exp[-(\alpha D + \beta D^2)]$. These survival functions are discussed further below. In these examples, the dependence of RBE on energy is most pronounced in the case of exposure to 5.1 MeV alpha particles, where RBE increases by more than a factor of two as the dose of the reference radiation decreases from 10 to 0.1 Gy or less. The dependence of RBE on dose is less pronounced in the cases of exposure to the two higher-energy high-LET radiations.

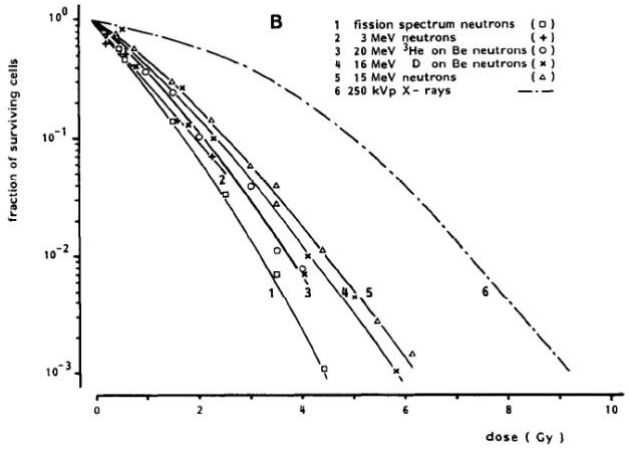

Fig. A.2. Dose-survival curves for cultured cells of human origin irradiated with different beams of fast neutrons and with 250 kVp X rays [Fig. 3B from ICRP (1990) and from Barendsen (1968)].

Type of Biological Endpoint

(A 12) Estimates of RBE generally depend on the nature of the biological endpoint under study—i.e. whether the effect is stochastic, in which case the probability of a response is a function of dose without threshold, or a tissue reaction, in which case the severity of an effect but not its probability is a function of dose and a threshold usually exists.

(A 13) Tissue reactions include impairment of tissue integrity and function, but also include cellular responses. Cellular reproductive death is presumed to be a significant source of tissue reactions (ICRP, 1984, 2012). Tissue reactions are presumed to have a threshold, and occur because sufficient damage has occurred such that complete underlying repair is not possible. The severity of the effect therefore increases with higher doses.

(A 14) Stochastic radiation effects are characterised by the lack of a threshold. Conceptually, this means that a single event (i.e. radiation damage to one cell) is sufficient to cause the effect. In humans, the main stochastic effect is cancer, with the assumption of hereditary effects based on mouse data (ICRP, 2007). The frequency of the effect is related to the dose, but not its severity. However, radiation effects at the chromosome and cellular levels usually do not translate into detriment at the population level and hence, the RBE for stochastic effects in an individual member of the species is of limited concern for population level effects in non-human biota. Radiological protection of non-human biota has largely focused on endpoints at the individual level that could lead to changes at the population level, such as reduced reproductive success, arising for example from effects on fertility, fecundity, growth and early mortality.

(A 15) Although most biological effects can be classified as either stochastic or tissue reactions, there can be substantial variations in RBEs for either type of effect, depending on the particular effect and the biological system under study. As a consequence, judgement is often required in evaluating whether an RBE for a particular endpoint in a particular biological system is relevant to the principal concern in a system of radiological protection of non-human biota, for example maintaining the viability (reproductive capability) of populations of the most sensitive species in radiological protection of the environment.

(A 16) It should also be noted that a recent ICRP report on tissue effects (ICRP, 2012) suggests that at least for some endpoints, such as circulatory disease, and damage to the lens of the eye for example, the same threshold has been proposed for acute, and either fractionated or protracted (chronic) doses, thus, somewhat blurring the distinction between stochastic effects and tissue reactions.

(A 17) RBEs for high-LET radiations in inducing tissue reactions generally are lower than RBEs for those radiations in inducing stochastic effects. For example, at doses of interest in radiological protection, the reduction in RBEs for tissue reactions induced by alpha particles and fission neutrons compared with RBEs for stochastic effects appears to be about a factor of 2 to 3 (ICRP, 1990; Kocher and Trabalka, 2000). A reasonable explanation for this effect is that even at the lowest doses where significant tissue reactions are observed, occurring only in the event of severe damage to or death of a substantial fraction of cells in organs and tissues, the density of ionisation of the nominally low-LET reference radiation is relatively high and closer to the organ-averaged density of ionisation of a high-LET radiation of interest than is the case at lower doses where only stochastic effects are induced.

Other Potentially Important Influences

(A 18) Other factors can influence estimates of RBEs in some studies (ICRP, 1990). Potentially important factors can include the time interval between an irradiation and observation of an effect, the conditions of the biological system under study, such as the proliferative state and cell cycle distribution, and the presence or absence of sensitising or

protecting compounds, such as reactive oxidative species. Such factors also can confound an evaluation of the relevance of an RBE to radiological protection of humans or the environment.

A.1.2. Extrapolation of RBEs to Low Doses and Dose Rates

(A 19) In radiological protection of humans, where limitation of the risk of cancer is the primary concern and the risk is assumed to be non-zero at any dose, it is generally accepted that quality factors (Q) and radiation weighting factors (w_R) should be established on the basis of estimates of RBEs for stochastic effects at low doses and low dose rates that are obtained by extrapolation to zero dose of assumed dose-response relationships for a radiation type of interest and a reference radiation. For example, when the dose-response for a stochastic effect induced by a high-LET radiation (H) is assumed to be linear ($R_H = \alpha_H D$) and the dose-response for the reference low-LET radiation (L) is assumed to be linear-quadratic ($R_L = \alpha_L D + \beta_L D^2$), the RBE at low doses and dose rates, denoted by RBE_M, is the ratio of slope of the dose-response for the high-LET radiation to the slope of the dose-response for the reference radiation as $D \rightarrow 0$: $RBE_M = \alpha_H/\alpha_L$. Given the dependence of RBE on dose discussed in Section A.1.1, RBE_M is a maximum value for the stochastic effect under study.

(A 20) A similar approach of extrapolating observed dose-response relationships for tissue reactions induced by a high-LET radiation of interest and a reference low-LET radiation to obtain an estimate of RBE at low doses (i.e. as $D \rightarrow 0$) for purposes of radiological protection of humans is used in *Publication 58* (ICRP, 1990); the RBE for tissue reactions at low doses, which is equivalent to RBE_M for stochastic effects, is denoted by RBE_m to again indicate that this is a maximum value. Even though dose-response relationships for tissue reactions are presumed to have a threshold, estimation of RBE_m was judged to be 'necessary for assessing the risk of exposure conditions where a small dose of high-LET radiation is delivered together with low-LET radiation' (ICRP, 1990). That is, for purposes of radiological protection, use of RBE_m was considered necessary to address induction of tissue reactions from exposure to mixed radiation fields in which, for example, the dose from a low-LET radiation is above a threshold dose but the dose from a high-LET radiation may be orders of magnitude below the threshold.

(A 21) Although the definition and use of an RBE_M for stochastic effects for purposes of radiological protection is relatively straightforward, there is a conceptual difficulty with use of an RBE_m for tissue reactions that arises from the assumption that their dose-response relationships have thresholds. However, it appears that extrapolated RBEs for tissue reactions are largely independent of dose below a level that may be comparable to a threshold.

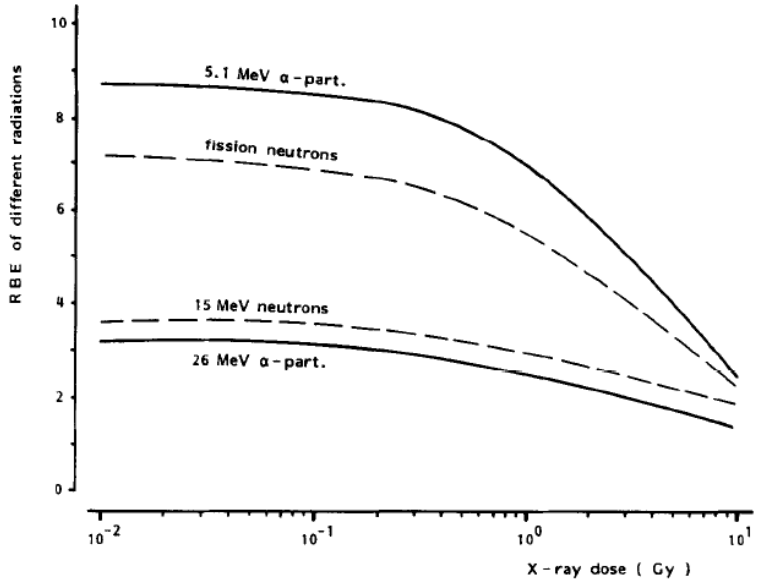

Fig. A.3. RBE versus dose curves illustrating that the RBE values approach RBE_m, values at doses below 10^{-1} Gy of x-rays. [Fig. 5 from ICRP (1990)].

(A 22) On the basis of the considerations discussed above, including that estimates of RBE_m are expected to be maximum values, the practice of estimating an RBE_m by extrapolation of data on dose-response for tissue reactions induced by a radiation of interest (e.g. alpha particles or tritium beta particles) and a reference low-LET radiation is continued in this report. This approach is considered appropriate for the purposes of deriving weighting factors relevant to non-human biota and radiological protection of the environment.

A.1.3. Extrapolation of Data on RBE for Tissue Reactions through Levels of Biological Organisation

(A 23) As previously indicated, the most common studies of RBEs for tissue reactions involve irradiation of mammalian cells in culture, specifically cell reproductive death. This is especially the case in studies in which the radiation of interest is alpha particles. Less common are studies of RBEs for tissue reactions in whole organs or tissues or in whole organisms of direct relevance to radiological protection of the environment.

(A 24) The problem of extrapolating estimates of RBE obtained from studies of reproductive death in cultured cells to obtain estimates of RBE for tissue reactions in whole organs or tissues or in whole organisms is addressed in *Publication 58* (ICRP, 1990) by comparing data for responses in whole tissues with data for survival of the critical cells in the same tissues. For example, in studies of early damage to the intestinal tract from irradiation by orthovoltage x-rays or 15 MeV neutrons, an RBE for the mean lethal dose within four days ($LD_{50/4d}$) was similar to RBEs for survival of intestinal crypt stem cells. This and other studies of exposure of various tissues and their critical cells were used to support an assumption that cell reproductive death is mainly responsible for tissue injury (ICRP, 1990).

(A 25) On the basis of the arguments and supporting studies discussed in *Publication 58* (ICRP, 1990), it is assumed in this report that estimates of RBE obtained from studies of cell reproductive death (cell survival) can be used to infer an RBE for induction of tissue reactions in whole organs or tissues or in whole organisms.

A.2. Modelling of Dose-Response for Cell Survival

(A 26) As indicated by the review in Annex C Section 7, reproductive death of irradiated mammalian cells is the most common biological endpoint in studies to estimate RBEs for alpha particles in inducing tissue reactions. Cell killing also is a frequent endpoint in studies to estimate RBEs for tritium beta particles.

(A 27) In *Publication 58* (ICRP, 1990), analyses of data on cell survival from exposure to high- and low-LET radiations were based on an assumption that the dose-response relationship can be described by a linear-quadratic (LQ) model. However, some studies have used a different description of the dose-response relationship for cell survival, which is referred to as a single-hit, multi-target model.

(A 28) This section discusses two models to describe the dose-response relationship for cell survival. These discussions emphasise the properties of the two models at high and low doses and use of the models to estimate an RBE at low doses, RBE_m, which is the quantity of interest in radiological protection. A concluding discussion compares the two models and considers the extent to which they are compatible.

A.2.1. Linear-Quadratic Model and Its Characteristic Parameters

(A 29) The most commonly used mathematical description of the dose-response relationship for cell survival is the LQ model. This model is based on an assumption that cell reproductive death can be caused by damage caused by a single track or by an accumulation of damage caused by two or more tracks of ionising particles (ICRP, 1990). The LQ model is a consequence of the theory of dual radiation action, which has some biological basis. This theory also is used to derive the LQ model for induction of stochastic effects, in which the frequency of an effect, F, at dose D is assumed to be described by the equation:

$$F(D) = a_1 D + a_2 D^2 \qquad \text{(A.1)}$$

The model in eq. (A.1) is widely used to describe dose-response relationships for stochastic effects in biological systems ranging in complexity from single cells to whole organisms.

(A 30) In the LQ model to describe the dose-response relationship for cell survival, the surviving fraction, S, of cells that receive a dose D, assuming that all unirradiated cells survive [$S(0) = 1$], is described by the equation:

$$S(D) = \exp[-(\alpha D + \beta D^2)] \qquad \text{(A.2)}$$

The parameters of this model are α (unit of Gy^{-1}) and β (Gy^{-2}); α is a measure of the contribution to the frequency of cell killing by a single track, and β is a measure of the contribution from an accumulation of damage by two or more tracks.

(A 31) Cell survival curves typically are displayed as plots of the natural logarithm of S as a function of dose D:

$$\ln S(D) = -(\alpha D + \beta D^2) \qquad \text{(A.3)}$$

The value of α determines the initial slope of the survival curve at low doses, where the quadratic term βD^2 is negligible and the survival curve is essentially linear. The ratio α/β (Gy) is equal to the dose at which the linear and quadratic terms contribute equally to cell killing.

(A 32) Many curves of cell survival in cases of exposure to low-LET radiation are described by eq. (A.3). In cases of exposure to high-LET radiation, it is commonly observed that $\beta \approx 0$ and ln S is essentially a linear function of dose at any dose, in a manner similar to the usual linearity in dose-response relationships for stochastic effects. Examples of survival curves for various radiations are shown in Fig. A.4 (ICRP, 1990). The survival curve for 250 kVp x-rays (Curve 8) shows the influence of the quadratic term ($\beta \neq 0$) for low-LET radiation, whereas the survival curves for alpha particles of energy typical of energies of alpha particles emitted in radioactive decay (Curves 2, 3, and 4) are essentially linear.

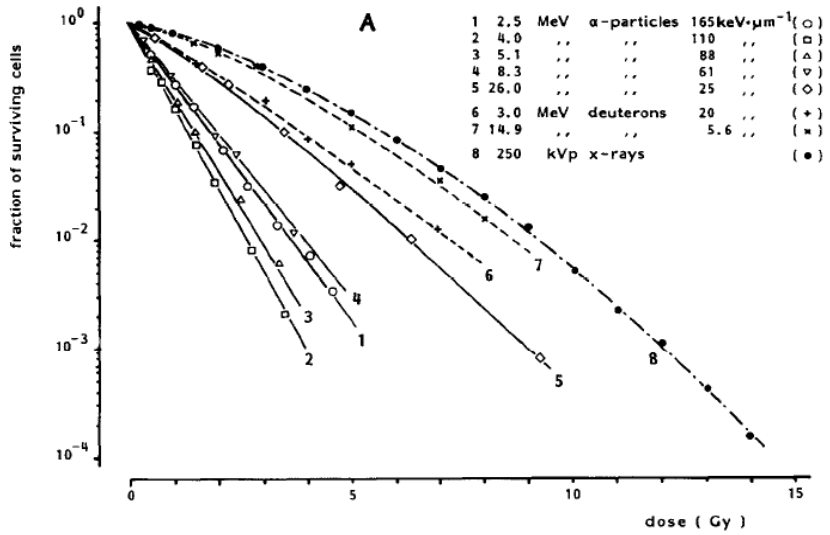

Fig. A.4. Dose-survival curves for cultured cells of human origin obtained with radiations of different LET (Barendsen, 1968).

(A 33) The description of a cell survival curve in eq. (A.3) has two important properties. As noted previously, at low doses, where the quadratic term is negligible, the survival curve is essentially linear with a slope given by:

$$\mathrm{d}[\ln S(D)]/\mathrm{d}D \approx -\alpha \qquad \text{(A.4)}$$

(A 34) At higher doses where the quadratic term is not negligible, the survival curve is non-linear, with a slope that is a function of dose given by:

$$\mathrm{d}[\ln S(D)]/\mathrm{d}D = -(\alpha + 2\beta D) \qquad \text{(A.5)}$$

(A 35) When the LQ model is used to describe cell survival, the RBE of a high-LET radiation (H) of interest at low doses (i.e. as $D \rightarrow 0$) is estimated as the ratio of the value of α in the survival curve for that radiation to the value of α in the survival curve for the reference low-LET radiation (L):

$$\mathrm{RBE_m} = \alpha_H/\alpha_L \qquad \text{(A.6)}$$

The LQ model thus lends itself to estimation of an RBE of interest in radiological protection.

A.3. Prior Reports on RBE

(A 36) This evaluation of the biological effectiveness of alpha particles and tritium beta particles in inducing tissue reactions of potential relevance to population viability of RAPS examined previous reports by ICRP and other organisations or investigators. Most of those reports were prepared to support the development of recommendations on biological effectiveness for purposes of radiological protection of humans. Nonetheless, given that much of the available data was obtained from studies of radiation effects in biological systems other than those of human origin, portions of the previous work were directly relevant to protection of the environment.

(A 37) Several reports by ICRP and other advisory groups that develop recommendations on radiological protection, provided information of use to this report. These reports include ICRU *Report 40* (ICRU, 1986), *Publication 58* (ICRP, 1990), *Publication 92* (ICRP, 2003), NCRP Report No. 89 (NCRP, 1987), and NCRP Report No. 104 (NCRP, 1990). An earlier report by ICRP, *Publication 31* (ICRP, 1980), was used to a lesser extent.

A.3.1. ICRU *Report 40*

(A 38) ICRU *Report 40* (ICRU, 1986), which was prepared by a joint task group of ICRP and ICRU, was concerned with theoretical considerations, calculations, and experimental data that could be used to develop recommendations on effective quality factors for use in radiological protection of humans. That report is concerned mainly with RBEs at low doses for a variety of stochastic effects in biological systems ranging from cells to whole organisms. However, some information on RBEs for tissue reactions induced by fission neutrons is also presented.

(A 39) Several presentations in the ICRU report were relevant to the development of this report. These include discussions on (a) the potential importance of differences in biological effectiveness between high-energy gamma rays (photons of energy greater than about 250 keV) and lower-energy photons (e.g. orthovoltage x-rays) or tritium beta particles, as indicated by calculations and available data, (b) the weak energy-dependence of the effective quality factor for alpha particles at energies of 4 to 9 MeV, which encompass the energies of alpha particles emitted by most potentially important radionuclides in the environment, and (c) available data on RBEs for stochastic effects induced by high-LET radiations, mainly data for fission or other neutrons but also including more limited data for alpha particles and heavy ions.

A.3.2. ICRP *Publication 58*

(A 40) For the purposes of this report, *Publication 58* (ICRP, 1990) is the most important source of information on RBEs for tissue reactions induced by high-LET radiations, including alpha particles, neutrons, and heavy ions. RBEs for stochastic effects are not discussed in that report. In addition to an extensive review of studies of RBEs for high-LET radiations in inducing tissue reactions in cultured mammalian cells and whole organs or tissues of animals and humans, *Publication 58* discusses basic aspects of deterministic radiation effects and the use of data on RBE for purposes of radiological protection, especially extrapolation of estimates of RBE at high doses to lower doses of potential importance in radiological protection.

(A 41) Discussions in this report make considerable use of information in *Publication 58* (ICRP, 1990). Important examples include descriptions of dose-response relationships for cell survival using a LQ model, the dependence of RBEs for tissue reactions on dose and

extrapolation of RBEs to low doses of concern to radiological protection, and the reviews and evaluations of data on RBEs for neutrons and heavy ions, which can be used in evaluating data on RBEs for alpha particles.

A.3.3. ICRP *Publication 92*

(A 42) *Publication* 92 (ICRP, 2003) presents a review of data on RBEs for induction of stochastic effects by low- and high-LET radiations and recommendations on quality factors (Q) and radiation weighting factors (w_R) for different radiation types for use in radiological protection of humans that were developed on the basis of the available data and other considerations. That report is not concerned with RBEs for tissue reactions.

(A 43) Information in *Publication 92* that was used in this report mainly concerns RBEs for alpha particles. Given the emphasis of *Publication 92* on protection of humans, much of the discussion on RBEs for alpha particles focuses on estimates obtained from studies of lung cancer, bone sarcomas, leukaemia, and liver cancer in humans. However, *Publication 92* also discusses RBEs for those effects in animals and RBEs obtained from studies of neoplastic transformation in animal cells and dicentric chromosome aberrations in human lymphocytes.

A.3.4. NCRP Report No. 89

(A 44) NCRP Report No. 89 (NCRP, 1987) is concerned with induction of stochastic genetic effects from exposure to radionuclides that are incorporated in mammalian cells or whole organisms. The report focuses primarily on data on genetic effects from incorporated alpha emitters and comparisons with genetic effects from incorporated higher-energy beta emitters for the purpose of estimating the risk from alpha particles relative to the risk from beta particles. However, data on genetic effects from exposure to incorporated tritium also are presented.

A.3.5. NCRP Report No. 104

(A 45) NCRP Report No. 104 (NCRP, 1990) presents an extensive review of data on RBEs for induction of stochastic effects by low- and high-LET radiations, principally x-rays (low-LET) and neutrons and alpha particles (high-LET). RBEs for tissue reactions were not considered. A wide variety of data is discussed including data on cytogenetic effects in plant, animal and human cells, transformation and mutation in mammalian cells *in vitro*, several hereditable effects, carcinogenesis in animals from external high-LET radiation (principally neutrons but also including limited data for heavy ions), data on several endpoints in cells and whole organisms from incorporated radionuclides, and data on life shortening in mice.

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ANNEX B. RELATIVE BIOLOGICAL EFFECTIVENESS OF TRITIUM BETA PARTICLES

(B 1) Tritium is the only radioactive isotope of the element hydrogen. Its nucleus contains one proton and two neutrons. It decays by beta particle emission, with a half-life of 12.3 years, to form stable helium (two protons and one neutron). Its atoms can replace hydrogen atoms in any molecule. Beta particles from decay of tritium travel only about 6.0 mm in air, and they do not penetrate the dead layer of the skin. Tritium beta particles are completely absorbed by a sheet of glass, plastic or metal. Therefore, the main hazard associated with tritium is when it is incorporated into the organism (ingestion, inhalation, absorption through the skin) and beta particles are emitted inside the body.

(B 2) In living tissues, tritium beta particles travel only about 6 μm (the average diameter of a typical cell is 10–20 μm, and a nucleus is 6–15 μm). Due to its low initial energy and short range, the average ionisation density (the linear energy transfer, LET) produced by the emitted beta particle is higher than that produced by higher-energy beta particles or photons. Tritium beta particles (mean 5.7 keV) have a track average LET in water of 4.70 keV μm^{-1}, compared with LET values of 0.22, 0.52 and 1.7 keV μm^{-1} for ^{60}Co gamma rays (1,173 and 1,332 keV), ^{90}Sr beta rays and 200 kVp x-rays, respectively (ICRU, 1970). It has been calculated that the fraction of dose to tissue from tritium delivered by low-energy beta particle and/or secondary electrons (energies between 0.1-5 keV), is approximately 78%. This is in contrast to 33% for ^{60}Co gamma rays (Nikjoo and Goodhead, 1991).

(B 3) Since tritium is an isotope of hydrogen, it reacts chemically to form compounds in the same manner as hydrogen does and, thus, can be a constituent atom of a wide variety of molecules, such as water or several organic compounds. Tritium can be found in oxide form (tritiated water), bound to organic compounds, or as tritiated gas. Tritium in gaseous form (HT) is readily oxidised to HTO in the atmosphere, or through microbial agents near the soil surface. Therefore, HT in the environment generally does not imply an important exposure of humans or other organisms.

(B 4) Tritium is most commonly found in the environment as tritiated water (HTO). Tritiated water has the same chemical properties as water. Once the tritiated water is incorporated into the organism, it quickly reaches equilibrium with water in the body and is distributed uniformly among all soft tissues. For plants, tritium may label organic matter as organically bound tritium through metabolic processes, such as photosynthesis (Boyer et al, 2009). Tritiated water is eliminated from the organism at the same rate as water.

(B 5) Organically bound tritium (OBT) refers to those forms in which tritium has been incorporated into organic molecules such as carbohydrates, fats, or proteins. Two types of OBT can be distinguished: exchangeable and non-exchangeable. When tritium atoms are bonded to oxygen, sulphur, nitrogen or phosphorus atoms, the tritium can readily exchange with hydrogen in body water and, therefore, is considered exchangeable. Exchangeable tritium in OBT compounds exhibits kinetics indistinguishable from HTO. When a tritium atom is bonded to a carbon atom in an organic molecule, it is non-exchangeable and can only be released by enzymatic reactions. Non-exchangeable tritium in OBT compounds exhibits kinetics characteristic of the OBT molecules concerned and their turnover in body tissues.

(B 6) When HTO is incorporated into animals, it will be almost homogeneously distributed throughout the body's fluids within a short time after intake, since tritium exchanges easily and rapidly with other hydrogen atoms. A small proportion is incorporated non-exchangeably into organic molecules during their synthesis (becomes non-exchangeable OBT). Tritium can also be ingested by animals as OBT in foods. The biological half-time (time required for half of the activity to be physically removed from the body) in adult humans is 10

days for HTO and 40 days for non-exchangeable OBT (ICRP, 1993). Biokinetic and dosimetric models have been developed for humans of different ages and have been used to calculate dose coefficients for intakes of tritium as HTO, OBT or HT (tritiated gas) (ICRP, 1989, 1993, 1994, 1995, 1996).

(B 7) Studies of tritium exposure to plants shows fast equilibrium between above and below ground parts and environmental concentrations in air and soil, with halftimes on the order of hours to a few days (Boyer et al, 2009).

(B 8) When tritium is incorporated into DNA (for example, after administration of tritiated thymidine), the beta doses received by cells will depend on the length of their division cycles. Cells rapidly dividing will have more chance of incorporating tritiated thymidine, but they will also eliminate it more rapidly. In cells with small proliferating rates, the probability of incorporating tritiated thymidine will be much lower, but retention times will be longer. Estimation of beta doses received from OBT has much more uncertainties than the estimation of the dose received from HTO (NCRP, 1979; Straume and Carsten, 1993).

B.1. Review of experimental studies on RBE for tritium beta particles

(B 9) In this report, published data on RBE for tritium beta particles has been considered, provided that enough details on the experimental procedures used and the results obtained were reported.

(B 10) The experimental data on RBE for tritium beta particles have been grouped in this report within one of the four biological endpoints: early mortality, reproductive success, morbidity or chromosomal damage and mutations; only the first three are considered relevant to population viability (ICRP, 2008).

B.1.1. Data on RBE for early mortality

(B 11) The RBE for tritium beta particles for lethal effects on plants (broad bean root, *Vicia faba*) was estimated by Spalding et al. (1956). Bean roots were exposed to HTO at cumulative doses of 1.8–4.6 Gy (dose rates of 72 Gy d^{-1}) or were acutely irradiated with 175 kVp x-rays at total doses of 2.0–4.7 Gy (dose rates of 72 Gy d^{-1}). The mortality of the beans was quantified in both groups, and an RBE of 1.0±0.06 was calculated.

(B 12) The effects of tritium beta particles on survival of mice were studied by Furchner (1957). Adult mice (CF1 strain) received a single intraperitoneal injection of HTO and their mortality was recorded 30 days after the injection (cumulative doses over 30 days in the range of 5.3–16.5 Gy). The mortality at 30 days was also analysed in a group of mice chronically exposed to ^{60}Co gamma rays (reference radiation) at total doses of 12.3–16.5Gy. Gamma irradiation was performed at decreasing dose rates (0.41-0.55 Gy d^{-1}) to mimic the exponential decay of tritium. An RBE of 1.7±0.1 was calculated from the slopes of the regression lines of the dose-response curves.

(B 13) Yamada et al. (1982) studied the effects of *in vitro* irradiation with tritium beta particles and gamma rays on mouse embryo survival. Mouse embryos [BC3F1 (C3H/C57BL)] in pronuclear or 2 cell stage were cultured *in vitro*, and HTO was added to the culture medium at concentrations leading to dose rates of 0.2–4.1 Gy d^{-1} (after 3 days the accumulated dose was in the range of 0.6 to 16.3 Gy). ^{60}Co gamma rays were used as reference radiation (chronic irradiation during 3 days at dose rates of 0.48 Gy d^{-1} and total doses of up to 19.2 Gy). RBEs as calculated from LD_{50} values were 1.0, 1.7 and 1.3 for pronuclear, early 2 cells, and late 2 cells embryos, respectively.

(B 14) In summary, all the studies to estimate an RBE for tritium beta particles for reduced survival of individuals have used tritiated water as the radiation source. The species used have plants (*Vicia faba*), and mice (BC3F1 embryos and CF1 adult mouse). Each of the studies involved chronic irradiation at high cumulative doses administered at high dose rates. The values of RBE for increased mortality were in the range 1.0–1.7 (Table B.1).

Table B.1. Data on RBE for tritium beta particles for early mortality.

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose)[a]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose)[b]	**Reported RBE (±SE)**	**Comments**	**Reference**
Plant (*Vicia faba*)	Beans mortality	175 kVp x-rays (A) 72 Gy d^{-1} (Constant dose-rate) Total dose: 2.0 - 4.7 Gy	HTO (A) 72Gy d^{-1} (Constant dose-rate) Total dose: 1.8 - 4.6 Gy	1.00 ± 0.06	-	Spalding et al. (1956)
Mouse (Embryos, BC3F1)	Embryo survival (blastocist formation LD50)	^{60}Co gamma (C) 4.8 Gy d^{-1} (Constant dose-rate) Total dose up to 19.2 Gy	HTO (C) 0.2 - 4.1Gy d^{-1} (Constant dose-rate) Total dose 0.6 - 16.4 Gy	1.00 - 1.70	RBEs of 1.0; 1.7 and 1.3 for pronuclear, early 2 cells and late 2 cells embryos, respectively. RBE calculated from LD50 values	Yamada et al. (1982)
Mouse (Adult, CF1)	Mortality at 30 days	^{60}Co gamma (C) 0.41 - 0.55 Gy d^{-1} (Exponentially decreasing dose-rates) Total dose: 12.3 - 16.5 Gy	HTO (C) 0.18 - 0.55 Gy d^{-1} (Exponentially decreasing dose-rates) Total dose: 5.3 - 16.5 Gy	1.72 ± 0.13	RBE calculated from the slopes of the regression lines	Furchner (1957)

[a] Unless specified, external irradiation.
[b] Unless specified, internal irradiation.

B.1.2. Data on RBE for reduction of reproductive success

(B 15) Etoh and Hyodo-Taguchi have published three studies on the RBE for tritium beta particles for alteration of the reproductive capacity of medaka fish (*Oryzias latipes*) using gamma rays as reference radiation (Etoh and Hyodo-Taguchi, 1983; Hyodo-Taguchi and Etoh, 1986, 1993). In the first study (Etoh and Hyodo-Taguchi, 1983), medaka fertilised eggs were exposed to HTO within two hours after fertilisation at concentrations giving dose rates of 0.17–1.70 Gy d^{-1} (cumulative doses absorbed by the eggs in 10 days of 1.8–17.0 Gy). Another group of fertilised eggs was chronically irradiated with ^{137}Cs gamma rays at dose rates of 0.11–2.12 Gy d^{-1} (total doses received by eggs of 4.3–21.2 Gy). The doses needed to reduce survival of germ cells (female and male) to 50% were 1.95 Gy for tritium beta particles and 3.5 for ^{137}Cs gamma rays, giving an RBE value of 1.8. The doses needed to reduce female germ cells survival to 50% were 1.4 Gy for tritium beta particles and 3.05 for ^{137}Cs gamma-rays, giving an RBE of 2.2.

(B 16) Hyodo-Taguchi and Etoh (1986) studied the effects of tritium beta particles and ^{137}Cs gamma rays on fertility and fecundity of medaka fish. Medaka fertilised eggs were treated during 10 days with HTO at cumulative doses of 0.85–34.0 Gy (dose-rates in the range 0.085–1.70 Gy d^{-1}) or were chronically irradiated with ^{137}Cs gamma rays at total doses of 0.61–25.4 Gy (dose-rates of 0.06–2.54 Gy d^{-1}). The authors did not estimate an RBE. However, the doses needed to reduce the female reproductive capacity to 50% were 4.0 Gy for tritium beta particles and 15.0 Gy for gamma rays, giving an estimated RBE of 3.75. No differences were seen in the capacity of tritium beta particles and gamma rays to reduce male reproductive capacity.

(B 17) Hyodo-Taguchi and Etoh (1993) analysed the capacity of tritium beta particles and gamma rays to induce vertebral malformations in medaka fish (*Oryzias latipes*). The fertilised fish eggs were exposed during approximately 9 days to HTO (dose rates of 0.43–1.70 Gy d^{-1} and cumulative doses of 3.7–16.7 Gy) or to ^{137}Cs gamma rays (dose rates of 0.44–1.89 Gy d^{-1} and total doses of 4.2–18.8 Gy). The RBE for tritium beta particles to induce vertebral malformations, estimated from the regression analysis of the dose-response curves, was 1.

(B 18) Knowles and Greenwood (1997) studied the RBE of tritium beta particles to alter the reproductive capacity of aquatic invertebrates. Mature adult polychaete worms (*Ophryotrocha diadema*) were continuously irradiated from immediately prior to egg laying until development into mature adult. After the treatment, the reproductive output of these adults was analysed. HTO was administered at concentrations delivering dose rates of 0.175 Gy d^{-1}. A group of worms was chronically irradiated with ^{137}Cs gamma rays at the same dose rates. In both experimental groups, the reproductive performance of worms (sacs/worm; eggs/worm; larvae/worm; % survival eggs to larvae; days to first egg) was studied. The authors stated that the study examined only a single dose rate for tritium beta particles and gamma radiation and that no attempt to estimate an RBE was made. However, they conclude that the two radiation types produced very similar effects on the reproductive capacity of the aquatic invertebrate *Ophryotrocha diadema*.

(B 19) Chopra and Heddle (1988) studied reduction in testes weight in mice, using 250 kVp x-rays as the reference radiation. Adult mice (CBA/H strain) received a single intraperitoneal injection of HTO (dose rates in the range 0.14–0.43 Gy d^{-1} and cumulative doses of 1.43–4.34 Gy) with the testes weight determined after 10 days.

X-ray exposures were continued for a period of 10 days (dose-rates 0.13–0.33 Gy d^{-1}, and total doses of 1.33–3.36 Gy), with the testes weight determined after the irradiation ended. The estimated RBE for reduction in mouse testes weight was in the range of 1.07–1.40.

(B 20) Carr and Nolan (1979) studied the effects of HTO and tritiated thymidine (^{3}HTdR) on testis mass in adult CBA mice, comparing these effects with those produced by ^{60}Co gamma rays. Gamma radiation exposures were in 15 fractions to mimic tritium exposure (total dose 0.578 Gy). Tritium (HTO or ^{3}HTdR) was administered by single intraperitoneal injection, with average cumulative doses to testes of 0.145–0.58 Gy for HTO and 0.03–0.50 Gy for ^{3}HTdR. Testes mass was determined in each experimental group up to 24 weeks after irradiation started. RBEs for tritium beta particles were calculated from the slopes of the corresponding dose-response curves (integrated fractional mass loss as a function of the calculated average absorbed dose in the testis up to 10 weeks after irradiation), and values of 1.43±0.19 for HTO and 2.07±0.25 for ^{3}HTdR were obtained. It should be noted that only one dose of ^{60}Co was used in this study, so the reported RBEs apply to that dose only.

(B 21) The relative effectiveness of tritium beta particles to kill resting primary spermatocytes, compared with x-rays, was studied in adult DBA2 mice (Lambert, 1969). Both tritiated water (HTO) and tritiated thymidine (^{3}HTdR) were used in this study. A group of mice received a single intraperitoneal injection of HTO at concentrations that produced dose rates in the range of 0.04–0.06 Gy d^{-1} (cumulative doses of 0.05–0.12 Gy). ^{3}HTdR was also injected intraperitoneally at concentrations giving dose rates in the range 0.06–0.11 Gy d^{-1} (cumulative doses of 0.084–0.19 Gy). Simultaneously, a group of mice was chronically irradiated during 72 hours with x-rays at decreasing dose rates in the range of 0.02–0.16 Gy d^{-1} (total doses of 0.05–0.50 Gy). The resting primary spermatocytes were quantified at 19 and 72 hours after tritium injection (HTO or ^{3}HTdR) or x-rays exposure. For HTO, RBEs for tritium beta particles of 2.3 and 2.4 at 19 and 72 h after exposure, respectively, were estimated, whereas estimated RBEs for ^{3}HTdR were 1.3 and 1.6 at 19 and 72 h after exposure, respectively. In the discussion of the paper, the authors highlight that the RBE values calculated in the study must be viewed with circumspection, due to the assumptions made in calculating the doses. Furthermore, the authors do not provide much detail about the experimental design (e.g. the number of animals used in each group and the statistical methods used).

(B 22) Zhou et al. (1989) studied the effects of tritium beta particles and gamma rays on the survival of primary oocytes and spermatogonia in juvenile mice. Two different treatments with HTO were used: a) a single intraperitoneal injection (exponentially decreasing dose rate), or b) a single intraperitoneal injection followed by tritium administration in drinking water (constant dose rate). The cumulative doses received over 10 days from HTO beta particles were in the range of 0.2–1.0 Gy. Another group of mice was chronically irradiated with ^{60}Co gamma-rays over 10 days (total doses of 0.7–2.8 Gy), either at an exponentially decreasing dose rate or at a constant dose rate. For an exponentially decreasing dose rate, the RBE for tritium beta particles, as calculated from the slopes of the dose-response curves, was 1.4-2.0 for primary oocyte survival and 2.1–2.8 for spermatogonia survival. When the irradiation took place at a constant dose rate, the RBE was 1.65 for primary oocyte survival and 2.3–2.5 for spermatogonia survival.

(B 23) Swiss-Webster mice were used to study the RBE for tritium beta particles to reduce primary oocyte survival, compared with ^{60}Co gamma-rays (Dobson and Kwan, 1976). Mice were exposed to HTO during 33 days, from conception to 14 days

after birth, at doses rates in the range 2.20–19.80 mGy d^{-1} (cumulative doses of 0.07–0.65 Gy). Another group of mice was chronically irradiated with ^{60}Co gamma rays (during 33 days, from conception to 14 days after birth) at doses rates in the range 10.08–31.92 mGy d^{-1} (total doses of 0.33–1.05 Gy). At 14 days after birth, the number of primary oocytes was quantified in the female offspring of each experimental group. The RBE for tritium beta particles increased as the dose administered decreased, with values of 1.8 at 0.4 Gy of the reference gamma radiation and 2.5 at 0.2 Gy.

(B 24) In 1977 Dobson and Kwan published a more complete follow-on study. They used the same experimental system (non-inbred Swiss-Webster mice) and approach (exposure to HTO or ^{60}Co during 33 days from conception to 14 days after birth), but different dose ranges. The HTO was administered at concentrations giving dose rates in the range of 24.96–51.52 mGy d^{-1} (cumulative doses of 0.57–0.83 Gy). Cobalt-60 gamma radiation was administered at dose rates of 8.0–38.0 mGy d^{-1} (total doses of 0.26–1.25 Gy). An RBE for tritium beta particles of 2.5 for oocyte survival at low doses was estimated. As in the previous study (Dobson and Kwan, 1976) the RBE values decreased at higher doses and dose rates.

(B 25) Satow and co-workers studied the RBE for tritium beta particles for murine oocyte survival. Juvenile mice (ICR strain, 14 days-old), received a single intraperitoneal injection of HTO (cumulative doses during 14 days of 0.04–0.25 Gy) or a chronic irradiation with ^{137}Cs gamma rays at decreasing dose-rates to mimic exposure to HTO (dose rates in the range of 0.03–0.09 Gy d^{-1}, and cumulative doses during 14 days of 0.06–0.21 Gy). The RBE for tritium beta particles, as calculated from survival curves using the single-target model, was in the range 1.1–3.5. The authors also observed that the RBE increased with decreasing doses, as previously described by Dobson and Kwan (1976, 1977). The highest RBE of 3.5 was seen at the lower dose used (0.04 Gy) (Satow et al., 1989a).

(B 26) The same group studied the teratogenic effects of tritium beta particles and ^{137}Cs gamma rays in rats. In these experiments, mature rats (Donryu strain) received a single intraperitoneal injection of HTO on day 8 or 9 of pregnancy (dose-rates of 0.14–1.06 Gy d^{-1} and cumulative doses of 1.75–6.80 Gy). Another group of rats was chronically irradiated with ^{137}Cs gamma rays from day 9 to 18 of pregnancy (the dose rates used were similar to those from HTO and the total doses received were of 1.75–6.80 Gy). The percentage of foetuses surviving and the frequency of foetuses with anomalies were estimated in both groups of rats. The RBEs for tritium beta particles to produce 50% and 20% anomalies in total implants were 1.8 and 2.4, respectively. RBEs to produce anomalies in surviving foetuses of 50% and 20% were also estimated; the values were 2.0 and 2.6, respectively (Satow et al., 1989b).

(B 27) The effects of tritium beta particles and gamma rays on the frequency of dominant lethal mutations in mice oocytes were studied by Zhou et al. (1986). Adult female mice (LACA strain) received a single intraperitoneal injection of HTO (total absorbed ovarian doses of 39–912 mGy). Another group of mice was chronically irradiated during 10 days with ^{60}Co gamma rays at decreasing dose rates (total doses of 0.53–2.70 Gy). Twenty-one days after irradiation, females were mated with non-irradiated males. Eighteen days after breeding, females were sacrificed to examine their ovaries for the number of corpora luteae, viable embryos, and early and late embryonic deaths, in order to estimate the frequency of induced dominant lethal mutations. The estimated RBE for tritium beta particles, as calculated from the slopes of the linear curves, was 2.5.

(B 28) Zhou et al. (1989) published a more complete study, in which they analysed the genetic effects (dominant lethal mutations on oocytes and spermatocytes;

dominant skeletal mutations in spermatogonia) of tritium beta particles and gamma rays in juvenile mice. HTO was administered in a single intraperitoneal injection (exponential decreasing dose rate). The cumulative doses of beta particles over 10 days were in the range of 0.2–1.0 Gy. Another group of mice received chronic irradiation with ^{60}Co gamma rays over 10 days at an exponentially decreasing or a constant dose rate (total doses of 0.7–2.8 Gy). The RBE for tritium beta particles, as calculated from the slopes of the dose-response curves, was in the range of 2.8–3.4 for dominant lethal mutations in oocytes, 3.5–3.9 for dominant lethalmutations in spermatogonia, and 1.6–3.9 for dominant lethal mutations in spermatocytes (Zhou et al., 1989).

(B 29) In summary, most of the studies to estimate an RBE for tritium beta particles to reduce reproductive success have used small mammals (rodents) (Lambert, 1969; Dobson and Kwan, 1976, 1977; Carr and Nolan, 1979; Zhou et al., 1986, 1989; Chopra and Heddle, 1988; Satow et al., 1989a,b). Three studies have been done in fish (Medaka) (Etoh and Hyodo-Taguchi, 1983; Hyodo-Taguchi and Etoh, 1986, 1993) and one in an aquatic invertebrate (*Ophryotrocha diadema*) (Knowles and Greenwood, 1997). Most studies used tritium administered as HTO, with two studies using ^{3}HTdR.

(B 30) Several endpoints related to reproductive success have been analysed: reproductive capacity and performance, testis weight loss, germ cell (female and male) survival, and dominant lethal mutations. There is not a clear correlation between the biological endpoint studied and estimates of RBE for tritium beta particles.

(B 31) The vast majority of the studies of RBE for tritium beta particles to reduce reproductive success have used gamma rays as the reference radiation. Only two studies have compared the effects of tritium beta particles with those of x-rays (Lambert, 1969; Chopra and Heddle, 1988). In all the studies, both tritium and reference radiation were chronically administered at dose rates ranging from 2 to 1,700 mGy d^{-1}. There is not a clear correlation between the dose rate used in the study and the estimated RBE value. Equal numbers of studies administered the reference radiation at constant or exponentially decreasing dose rates, with no clear influence of this parameter on estimates of RBE.

(B 32) For reduced reproductive success, the RBE values for tritium beta particles (tritium administered as HTO or ^{3}HTdR) were in the range 1.0–3.9. Only 5 out of 23 RBE values for tritium beta particles, were above 3.0 (Table B.2).

1243 Table B.2. Data on RBEs for tritium beta particles for reduced reproductive success.

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE (±SE)**	**Comments**	**Reference**
Fish (Medaka fertilised eggs)	Vertebral malformations	^{137}Cs gamma (C) 0.44 - 1.89 Gy d^{-1} (Constant dose rate) Total dose: 4.2 - 18.8 Gy	HTO (C) 0.43 -1.70 Gy d^{-1} (Constant dose rate) Total dose: 3.7 - 16.7 Gy	1.00	-	Hyodo-Taguchi and Etoh (1993)
Aquatic invertebrate (Ophryotrocha diadema)	Reproductive performance	^{137}Cs gamma (C) 0.175 Gy d^{-1} (Constant dose rate) Total dose: ≈13.5 Gy[c]	HTO (C) 0.175Gy d^{-1} (Constant dose rate) Total dose: ≈13.5 Gy[c]	1.00	Single dose rate used. The study was not designed to calculate RBE values	Knowles and Greenwood (1997)
Fish (Medaka fertilised eggs)	Male reproductive capacity	^{137}Cs gamma (C) 0.06 - 2.54 Gy d^{-1} (Constant dose rate) Total dose: 0.61 - 25.40 Gy	HTO (C) 0.08 - 1.7 Gy d^{-1} (Constant dose rate) Total dose: 0.85 - 34.00 Gy	1.00	RBE calculated for 50% loss of male reproductive capacity	Hyodo-Taguchi and Etoh (1986)
Mouse (Adult CBA/H)	Testes weight	250 kVp x-rays (C) 0.13 - 0.33 Gy d^{-1} (Exponentially decreasing dose rates) Total dose: 1.33 - 3.36 Gy	HTO (C) 0.14 - 0.43 Gy d^{-1} (Exponentially decreasing dose rates) Total dose: 1.43 - 4.34 Gy	1.07 - 1.40	-	Chopra and Heddle (1988)
Mouse (Adult male, DBA2)	Survival of resting primary spermatocytes	200 kVp x-rays (C); 0.02 - 0.16 Gy d^{-1} (Exponentially decreasing dose rate) Total dose: 0.05 - 0.5 (Gy)	^{3}HTdR (C) 0.06 - 0.11 Gy d^{-1} ≈ 3.0- 12.5 Gy d^{-1} Total dose: 0.08 - 0.19 Gy	1.30 - 1.60	RBE calculated from doses reducing the surviving fraction by 27%	Lambert (1969)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (±SE)	Comments	Reference
Mouse (Adult, male, CBA)	Testis mass	^{60}Co gamma (Protracted) 15 fractions Total dose: 0.58 Gy	HTO (C) Unknown dose rate Total dose: 0.14 - 0.58Gy[d]	1.43 ± 0.19	Only one gamma dose used. HTO doses not specified within the text (only in a figure)	Carr and Nolan (1979)
Mouse (Juvenile)	Primary Oocyte Survival	^{60}Co gamma (C) Total dose: 0.74 - 2.07 Gy[e]	HTO (C) Unknown dose rate Total dose: 0.2 - 0.6 Gy[e]	1.65	RBE for lower beta dose used (0.2 Gy) (RBE = 1.5 for 0.6 Gy)	Zhou et al. (1989)
Fish (Medaka fertilised eggs)	Germ cell (female and male) survival	^{137}Cs gamma (C) 0.11 - 2.12 Gy d^{-1} (Constant dose rate) Total dose: 4.3 - 21.2 Gy	HTO (C) 0.17 - 1.7 Gy d^{-1} (Constant dose rate) Total dose: 1.7 - 17 Gy	1.80	RBE calculated from LD50	Etoh and Hyodo-Taguchi (1983)
Mouse (Juvenile)	Primary Oocyte Survival	^{60}Co gamma (C) (Exponential decreasing dose rate) Total dose: 0.74 - 2.07 Gy[e]	HTO (C) 0.002 - 0.006 Gy d^{-1}(Exponential decreasing dose rate) Total dose: 0.2 - 0.6 Gy[e]	2.00	RBE for beta dose of 0.2 Gy (RBE = 1.4 for 0.6 Gy)	Zhou et al. (1989)
Mouse (Adult male)	Testis mass	^{60}Co gamma (Protracted) 15 fractions Total dose: 0.58 Gy	^{3}HTdR (C) Unknown dose rate Total dose: 0.03 - 0.50 Gy	2.07 ± 0.25	Only one gamma dose used. ^{3}HTdR doses not specified within the text (only in a figure)	Carr and Nolan (1979)
Fish (Medaka fertilised eggs)	Female germ cell survival	^{137}Cs gamma (C) 0.11 - 2.12 Gy d^{-1} (Constant dose rate) Total dose: 4.3 - 21.2 Gy	HTO (C) 0.17 - 1.7 Gy d^{-1} (Constant dose rate) Total dose: 1.7 - 17 Gy	2.20	RBE calculated from LD50	Etoh and Hyodo-Taguchi (1983)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (±SE)	Comments	Reference
Mouse (Adult male, DBA2)	Survival of resting primary spermatocytes	200 kVp x-rays (C) 0.02 - 0.16 Gy d^{-1} (Exponentially decreasing dose rates) Total dose: 0.05 - 0.50 Gy	HTO (C) 0.04 - 0.06 Gy d^{-1} (Exponentially decreasing dose rates) Total dose: 0.05 - 0.12 Gy[f]	2.30 - 2.40	RBE calculated from doses reducing the surviving fraction by 27%. Due to dosimetry assumptions RBE values should be considered with caution.	Lambert (1969)
Mouse (Juvenile)	Spermatogonia Survival	^{60}Co gamma (C) Unknown dose rate Total dose: 0.74 - 2.87 Gy[e]	HTO (C) Unknown dose rate Total dose: 0.2 - 0.6 Gy[e]	2.30 - 2.50	-	Zhou et al. (1989)
Mouse (in utero, Swiss-Webster)	Primary oocyte survival	^{60}Co gamma (C) 0.01 - 0.03 Gy d^{-1} (Constant dose rate) Total dose: 0.33 - 1.05 Gy	HTO (C) 0.002 - 0.02 Gy d^{-1} (Constant dose rate) Total dose: 0.07 - 0.65 Gy	2.50	RBE at gamma doses of 0.2 Gy (RBE = 1.8 at gamma doses of 0.4Gy)	Dobson and Kwan (1976)
Mouse (In utero, Swiss-Webster)	Primary oocyte survival	^{60}Co gamma (C) 0.008 - 0.038 Gy d^{-1} (Constant dose rate) Total dose: 0.26 - 1.25 Gy	HTO (C) 0.025 - 0.051 Gy d^{-1} (Constant dose rate) Total dose: 0.57 - 0.83 Gy	2.5	RBE for the lower dose used. RBE varied inversely with dose (dose-rate)	Dobson and Kwan (1977)
Mouse (Adult females, LACA)	Dominant lethal mutation in oocytes	^{60}Co gamma (C) Unknown dose rate Total dose: 0.53 - 2.70 Gy	HTO (C) Unknown dose rate Total dose: 0.04 - 0.91 Gy	2.50	RBE calculated from the slopes of the curves	Zhou et al. (1986)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (±SE)	Comments	Reference
Rat (Donryu)	Anomalies in survived foetuses	^{137}Cs gamma (C) Similar dose rates than HTO (Exponentially decreasing dose rate) Total dose: 1.75 - 6.80 Gy	HTO (C) 0.14 - 1.06 Gy d^{-1} (Exponentially decreasing dose rate) Total dose: 1.75 - 6.80 Gy	2.60	RBE for 20 % appearance of anomalies (RBE = 2.0 for 50% appearance of anomalies)	Satow et al. (1989b)
Mouse (Juvenile)	Spermatogonia survival	^{60}Co gamma (C) Unknown dose rate Total dose: 0.74 - 2.87 Gy[e]	HTO (C) Unknown dose rate Total dose: 0.2 - 1.01 Gy[e]	2.8	RBE for beta doses of 0.6 Gy (RBE = 2.1 for 0.2 Gy)	Zhou et al. (1989)
Mouse (Juvenile)	Dominant Lethal Mutations in Oocytes	^{60}Co gamma (C) Unknown dose rate Total dose: 0.74 - 2.07 Gy[e]	HTO (C) 0.002 - 0.006 Gy d^{-1} (Exponential decreasing dose rate) Total dose: 0.2 - 0.6 Gy[e]	3.40	RBE for beta doses of 0.2 Gy (RBE = 2.8 for 0.6 Gy). RBE calculated from the slopes of the dose-response curves	Zhou et al. (1989)
Mouse (Juvenile, ICR)	Oocyte survival	^{137}Cs gamma (C) 0.03 - 0.09 Gy d^{-1} (Exponential decreasing dose rate) Total dose: 0.06 - 0.21 Gy[g]	HTO (C) ≈ 0.003 - 0.018 Gy d^{-1} (Exponential decreasing dose rate) Total dose: 0.04 - 0.25 Gy[g]	3.50	RBE value at 0.04 Gy (RBE=1.1 at 0.24 Gy). RBE calculated from survival curves using single-target model	Satow et al. (1989a)
Fish (Medaka fertilised eggs)	Female reproductive capacity	^{137}Cs gamma (C) 0.06 - 2.54 Gy d^{-1} (Constant dose rate) Total dose: 0.61 - 25.40 Gy	HTO (C) 0.08 - 1.7 Gy d^{-1} (Constant dose rate) Total dose: 0.85 - 34.00 Gy	3.75	RBE calculated for 50% loss of female reproductive capacity	Hyodo-Taguchi and Etoh (1986)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (±SE)	Comments	Reference
Mouse (Juvenile)	Dominant Lethal Mutations in Spermatocytes	^{60}Co gamma (C) Unknown dose rate Total dose: 0.74 - 2.07 Gy[e]	HTO (C) 0.002 - 0.006 Gy d^{-1} (Exponential decreasing dose rate) Total dose: 0.2 - 0.6 Gy[e]	3.90	RBE for beta doses of 0.2 Gy (RBE = 1.6 for 0.6 Gy). RBE calculated from the slopes of the dose-response curves	Zhou et al. (1989)
Mouse (Juvenile)	Dominant Skeletal Mutations in Spermatogonia	^{60}Co gamma (C) Unknown dose rate Total dose: 0.74 - 2.87 Gy[e]	HTO (C) Unknown dose rate Total dose: 0.2 - 1.01 Gy[e]	3.92	RBE for beta doses of 0.6 Gy (RBE = 3.48 for 0.2 Gy). RBE calculated from the slopes of the dose-response curves	Zhou et al. (1989)

[a] Unless specified, external irradiation.
[b] Unless specified, internal irradiation.
[c] Total doses received have been calculated taking into account that he irradiation period extended from the egg (prior to its being laid) to when the worms were approaching the end of their lives, at about 11 weeks, as is described in the paper;
[d] Average absorbed dose in the testis over 16 weeks.
[e] Total doses received during 10 days.
[f] Estimated dose to testis.
[g] Total doses accumulated during 14 days.

B.1.3. Data on RBE for morbidity effects

(B 33) The RBE for tritium beta particles to induce cancer *in vivo* has been estimated in three studies with rodents (rat and mouse). Gragtmans et al. (1984) studied the effects of tritium beta particles and x-rays on induction of mammary tumours in rats. Sprague-Dawley female rats received a first intraperitoneal injection of HTO, which was repeated 4 more times at 2-day intervals, to maintain a constant dose rate (cumulative doses in the range of 0.49–4.10 Gy). Another group of rats was chronically irradiated with 200 kVp x-rays during 10 days with total doses of 0.3–2.0 Gy. An RBE for tritium beta particles was calculated from the initial slopes of the dose-response curves (best-fit linear relationship). For cumulative tumour incidence per 100 animals at risk, the RBE was of 1.02±0.13 when all doses from exposure to HTO were included and 1.17±0.18 when the highest dose of 3.85 Gy was excluded. When the endpoint considered was the cumulative percentage of animals with tumours, the RBE was 0.85±0.15 when all doses were included and 1.35±0.13 when the dose of 3.85 Gy was excluded. When the endpoint analysed was the time required to develop mammary tumours in 50% of the animals at risk, the RBE was 0.67±0.13 (all doses) and 1.12±0.18 (dose of 3.85 Gy excluded). None of the RBE values was statistically different from 1.0.

(B 34) Johnson et al. (1995) studied the effectiveness of tritium beta particles and x-rays to induce myeloid leukaemia in the mouse. CBA/H mice received a single intraperitoneal injection of HTO (cumulative beta doses of 0.85–3.04 Gy). Another group was chronically irradiated with 150–200 kVp x-rays during 10 days at dose rates of 0.24–0.72 Gy d^{-1} (total doses of 1.06–2.64 Gy). An RBE for tritium beta particles was calculated considering different fits to the dose-response for the incidence of myeloid leukaemia per 10^4 mouse-days at risk, with values ranging from 1.1 to 1.24. The best estimate gave an RBE of 1.2±0.3.

(B 35) The effects of tritium beta particles and ^{137}Cs gamma rays on tumour development in different organs have been studied in mice (Seyama et al., 1991). Adult female mice (C57BL/6N and BCF1) received a single intraperitoneal injection of HTO (cumulative beta doses of 0.27 or 2.7 Gy). Another group of mice was chronically irradiated with ^{137}Cs gamma rays (total dose of 0.27 or 2.7 Gy administered at 0.08 and 0.76 Gy d^{-1}, respectively). The RBE for tritium beta particles, as calculated from the data on tumour incidence at 500 days after exposure to 2.7 Gy, was 2.5.

(B 36) The RBE for tritium beta particles in causing splenic and thymic atrophy was studied in adult female mice (CF1) using radium gamma rays as the reference radiation (Storer et al., 1957). Mice received a single intraperitoneal injection of HTO followed by administration of HTO in the drinking water in order to maintain a constant tritium concentrations over 5 days (cumulative doses of 1.25–3.50 Gy). The exposure to gamma rays took place during 5 days at dose rates similar to those from exposure to HTO (total doses of 1.25–3.5 Gy). For splenic atrophy, the RBE for tritium beta particles was 1.32±0.12, and for thymic atrophy the RBE was 1.52±0.15. The authors also studied the capacity of tritium beta particles, compared with ^{60}Co gamma rays, to reduce ^{59}Fe uptake by red cells in adult rats (Sprague-Dawley) at the same dose rates and doses as used in the experiments described above. The RBE for tritium beta particles for ^{59}Fe uptake by red cells was 1.64±0.05.

(B 37) Ijiri (1989) studied the RBE of tritium beta particles for cell death (apoptosis) in the crypts of adult male mice (C57Bl/6). HTO was injected

intraperitoneally at concentrations giving dose rates in the range 0.001–1.164 Gy d^{-1} (cumulative doses up to 2.0 Gy). Another group of mice was chronically irradiated with ^{137}Cs gamma rays at dose rates of 0.014–11.52 Gy d^{-1} (total doses up to 2.9 Gy). Using estimates of the maximum number of apoptotic cells per crypt section, calculated as the mean of the data obtained at the three highest doses, RBEs for tritium beta particles were calculated for the small intestine (1.6±0.2) and descendant colon (1.4±0.1). The RBE was also calculated from D_0 values (doses that reduce the survival fraction to 37%) obtained from the corresponding beta particle and gamma ray dose-response curves, with values of 2.0±0.2 for the small intestine and 1.8±0.2 for the descendent colon.

(B 38) The RBE for tritium beta particles for cell survival *in vitro* has been estimated in experiments using transformed cell lines. Ueno et al. (1982) studied the effects of tritium beta particles, with tritium administered as HTO, and ^{60}Co gamma rays on L5178Y cell survival. HTO was added to the culture medium at a concentration of 22.2-166.5 MBq ml^{-1} (total doses up to about 11 Gy). Another cell line sample was exposed to ^{60}Co gamma radiation over a period of 4.5-100 hours at dose rates of 2.9-11.5 Gy d^{-1} (total doses up to 11.0 Gy). The RBE for tritium beta particles at 50% survival was 1.4 when linear models were used to fit the survival curves and 1.6 using linear-quadratic models.

(B 39) Bedford et al. (1975) used a murine leukaemic cell line (L5178Y) and a Chinese hamster cell line (V79B) in their cell survival studies. The cell lines were exposed to tritiated water (HTO) or tritiated thymidine (^{3}HTdR) at cumulative beta doses of 1.0–16.0 Gy (dose rate of 4.8 Gy d^{-1}). The reference radiation was ^{60}Co gamma rays at the same dose rate and total doses. The irradiations were carried out with cells held in the frozen state (to prevent cell division) or at 5ºC. For ^{3}HTdR, the RBE for tritium beta particles for L5178Y and V79B cell survival (irradiated in the frozen state) was 3.0 and 4.4, respectively. However, the authors noted uncertainty in the dose calculations; ^{3}HTdR is incorporated into DNA and average cell dose will underestimate effects. For V79B cells irradiated at 5ºC, the RBE was 1.7-1.9 for the two forms of administered tritium.

(B 40) In summary, the RBE for tritium beta particles to produce morbidity effects when tritium was administered as HTO has been studied in small mammal systems only, either *in vivo* (mouse and rat) or *in vitro* (transformed cell lines like murine lymphocytic leukaemia, L5178Y, or Chinese hamster V79B). Only 2 studies have used x-rays as the reference radiation (Gragtmans et al., 1984; Johnson et al., 1995). Cesium-137, ^{60}Co or Ra gamma rays were used as the reference radiation in the remaining studies.

(B 41) Several endpoints related to morbidity have been analysed in studies of RBE for tritium beta particles, including tumour induction (mammary tumours, myeloid leukaemia) (Gragtmans et al., 1984; Seyama et al., 1991; Johnson et al., 1995), tissue damage in experimental animals (splenic and thymic atrophy, descendent colon and intestine cell survival, depression of ^{59}Fe uptake) (Storer et al., 1957; Ijiri, 1989), and cell survival in transformed cell lines (Bedford et al., 1975; Ueno et al., 1982).

(B 42) The values of RBE for tritium beta particles to produce morbidity effects, when tritium was administered as HTO, were in the range of 1.0–2.5. Most RBE values were below 2.0 (10 values out of 12) (Table B.3). One study using ^{3}HTdR administered to cell lines suggested RBE values in the range of 1.7–4.4, depending on the temperature at which the cell line was irradiated, and on the cell type used in the study (Table B.3).

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System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE (±SE)**	**Comments**	**Reference**
Rat (Adult female, Sprague-Dawley)	Mammary tumours (Time to develop tumours in 50% of animals at risk)	200 kVp x-rays (C) 0.03 - 0.20 Gy d^{-1} Total dose: 0.3 - 2.0 Gy	HTO (C) Unknown dose rate Total dose 0.49 -4 .10 Gy[(c)]	1.12 ± 0.18[(d)]	RBE when the higher dose of HTO was excluded (RBE= 0.67±0.13 when all HTO doses were included). RBE calculated from the initial slopes of the dose-response curves	Gragtmans et al. (1984)
Rat (Adult female, Sprague-Dawley)	Mammary tumours (Cumulative tumour incidence per 100 animals at risk)	200 kVp x-rays (C) 0.03 - 0.2 Gy d^{-1} Total dose: 0.3 - 2.0 Gy	HTO (C) Unknown dose rate Total dose: 0.49 - 4.10 Gy[(c)]	1.17 ± 0.18[(d)]	RBE when the higher dose of HTO was excluded (RBE = 1.02±0.13 when all HTO doses were included). RBE calculated from the initial slopes of the dose-response curves	Gragtmans et al. (1984)
Mouse (Adult, CBA/H)	Myeloid leukaemia	150 - 200 kVp x-rays (C) 0.24 - 0.72 Gy d^{-1} Total dose: 1.06 - 2.64 Gy	HTO (C) Unknown dose rate Total dose: 0.85 - 3.04 Gy	1.20 ± 0.30	RBE for best fit of dose-response curves	Johnson et al. (1995)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE (±SE)**	**Comments**	**Reference**
Mouse (Adult female CF1)	Splenic atrophy (weight loss)	Radium gamma (5 days) Dose rates similar for HTO and gamma (Constant dose rate) Total dose: 1.25 - 3.5 Gy	HTO (5 days) Dose rates similar for HTO and gamma (Constant dose-rate) Total dose: 1.25 - 3.5 Gy	1.32 ± 0.12	-	Storer et al. (1957)
Rat (Adult female, Sprague-Dawley)	Mammary tumours (Cumulative % of animals with tumours)	200 kVp x-rays (C) 0.03 - 0.2 Gy d^{-1} Total dose: 0.3 - 2.0 Gy	HTO (C) Unknown dose rate Total dose: 0.49 - 4.10 Gy[c]	1.35 ± 0.13[d]	RBE when the higher dose of HTO was excluded (RBE= 0.85±0.15 when all HTO doses were included). RBE calculated from the initial slopes of the dose-response curves	Gragtmans et al. (1984)
L5178Y (Murine lymphocytic leukaemia cell line)	Survival	^{60}Co gamma (C) 2.88 - 11.52 Gy d^{-1} (Constant dose rate) Total dose: 0.5-11.0 Gy	HTO (C) ≈ 2.4- 9.6 Gy d^{-1}[e] (Constant dose rate) Total dose: 1.0 - 11.0 Gy	1.40 - 1.60	RBE calculated for LD50.	Ueno et al. (1982)
Mouse (Adult female CF1)	Thymic atrophy (weight loss)	Radium gamma (5 days) Dose-rates similar for HTO and gamma (Constant dose rate) Total dose: 1.25 - 3.5 Gy	HTO (5 days) Dose-rates similar for HTO and gamma (Constant dose rate) Total dose: 1.25 - 3.5 Gy	1.52 ± 0.15	-	Storer et al. (1957)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (±SE)	Comments	Reference
Rat (Adult, male Sprague-Dawley)	Depression of ^{59}Fe uptake by red cells	^{60}Co gamma (5 days) Dose rates similar for HTO and gamma (Constant dose rate) Total dose: 1.25 - 3.5 Gy	HTO (5 days) Dose-rates similar for HTO and gamma (Constant dose rate) Total dose: 2.92 - 5.91 Gy	1.64 ± 0.05	-	Storer et al. (1957)
V79B (Chinese hamster cell line)	Survival	^{60}Co gamma (C) ≈ 4.8Gy d^{-1} (Constant dose rate) Total dose: ≈ 1.0 - 16.0 Gy[e]	HTO (C) ≈ 4.8 Gy d^{-1} (Constant dose rate) Total dose: ≈ 1.0 - 16.0 Gy[e]	1.70 - 1.90	Cells irradiated at 5 ºC	Bedford et al. (1975)
V79B (Chinese hamster cell line)	Cell survival	^{60}Co gamma (C); ≈ 4.8Gy d^{-1} Total dose: ≈ 1.0 - 16.0 Gy[e]	^{3}HTdR (C) ≈ 4.8Gy d^{-1} Total dose: ≈ 1.0 - 16.0 Gy[e]	1.70 -1.90	Cells irradiated at 5 ºC	Bedford et al. (1975)
Mouse (Adult male, C57Bl/6)	Apoptosis in descendent colon	^{137}Cs gamma (C) 0.014-11.52 Gy d^{-1} (Constant dose rate) Total dose: Up to 2.9 Gy	HTO (C) 0.001-1.164 Gy d^{-1} (Constant dose rate) Total dose: Up to 2.0 Gy	1.80 ± 0.20	RBE calculated for D_0	Ijiri (1989)
Mouse (Adult male, C57Bl/6)	Apoptosis in small intestine	^{137}Cs gamma (C) 0.014-11.52 Gy d^{-1} (Constant dose rate) Total dose: Up to 2.9 Gy	HTO (C) 0.001-1.164 Gy d^{-1} (Constant dose rate) Total dose: Up to 2.0 Gy	2.00 ± 0.20	RBE calculated for D_0	Ijiri (1989)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE (±SE)**	**Comments**	**Reference**
Mouse (Adult female, C57BL/6N and BCF1)	Tumour development (in different organs)	^{137}Cs gamma (C) 0.08 or 0.76 Gy d^{-1} Total dose: 0.27 or 2.7 Gy	HTO (C) Unknown dose rate Total dose: 0.27 or 2.7 Gy	2.50	RBE calculated for carcinogenicity at 500 days after 2.7 Gy exposure	Seyama et al. (1991)
V79B (Chinese hamster cell line)	Cell survival	^{60}Co gamma (C); ≈ 4.8Gy d^{-1} Total dose: ≈ 1.0 - 16.0 Gy[e]	^{3}HTdR (C) ≈ 4.8Gy d^{-1} Total dose: ≈ 1.0 - 16.0 Gy[e]	3.0	Cells irradiated in frozen state.	Bedford et al. (1975)
L5178Y (Murine lymphocytic leukaemia cell line)	Cell survival	^{60}Co gamma (C); ≈ 4.8Gy d^{-1} Total dose: ≈ 1.0 - 16.0 Gy[e]	^{3}HTdR (C) ≈ 4.8Gy d^{-1} Total dose: ≈ 1.0 - 16.0 Gy[e]	4.4	Cells irradiated in frozen state.	Bedford et al. (1975)

[a] Unless specified, external irradiation.
[b] Unless specified, internal irradiation.
[c] Including 50% of dose from mammary lipid-bound tritium. When no dose from lipid bound tritium was considered, the estimated doses were 0.46–3.85 Gy.
[d] RBE value not statistically different from 1.0.
[e] Range of doses used not described in the text (Estimated from a Figure).

B.1.4. Data on RBE for chromosomal damage and mutations

(B 43) Using drosophila germ cells, Byrne and Lee (1989) estimated the RBE for tritium beta particles to induce mutations. Adult drosophila males were exposed over 48 hours to HTO or ^{60}Co gamma rays at total doses of 6.4–25.5 Gy. In the different experimental groups, sex-linked recessive lethal mutations in germ cells were analysed. The RBE for tritium beta particles, as calculated from the slopes of the dose-response curves for gene mutations transmitted to successive generations, was 2.7±0.3.

(B 44) Matsuda et al. (1986) studied the efficacy of tritium beta particles to induce chromosomal aberrations in mice fertilised eggs, compared with gamma radiation. The fertilised eggs in early pronuclear stage were treated *in vitro* with HTO over 2 hours at dose rates of 1.02–4.08 Gy d^{-1} and total doses of 0.085–0.34 Gy or exposed for 2 hours to ^{60}Co gamma radiation at dose rates of 0.62–3.54 Gy d^{-1} and total doses of 0.05–0.30 Gy. The results showed that the dose-response curves for tritium beta particles and ^{60}Co at doses above 0.05 Gy were approximately linear. Thus, linear regression coefficients from fits at those doses were used to calculate an RBE for tritium beta particles of 2.0. Using the results on chromosomal aberration frequency in murine fertilised eggs exposed to acute doses of x-rays as the reference radiation (results obtained by this group in previous studies), an RBE of 1.6 was calculated (Matsuda et al., 1983, 1985a,b).

(B 45) Two groups have studied the RBE for tritium beta particles for induction of chromosomal aberrations in murine spermatocytes. Zhou et al. (1989) studied the induction of chromosomal aberrations in juvenile mice spermatocytes. Mice received a single intraperitoneal injection of HTO, followed by tritium administration in drinking water to keep the dose rate constant. Cumulative doses of beta radiation were in the range of 0.2–1.0 Gy (dose rates of 0.005–0.05 Gy d^{-1}). Another group of mice received chronic irradiation with ^{60}Co gamma rays over 10 days at a constant dose rate (total doses of 0.43–2.04 Gy administered at dose-rates of 0.04–0.20 mGy d^{-1}). RBE values of 2.9–3.8 were calculated.

(B 46) Chopra and Heddle (1988) analysed the RBE of tritium beta particles to produce chromosomal aberrations in murine primary spermatocytes and peripheral blood lymphocytes. Mice (CBA/H) received a single intraperitoneal injection of HTO or were irradiated with 250 kVp x-rays during 10 days at total doses of beta and x-rays of 1.5–6.0 Gy. Dose response curves for different types of chromosomal aberrations were generated and an RBE calculated from their slopes. The RBE for tritium beta particles to induce chromosome translocations in primary spermatocytes was 1.21 [95% confidence interval (CI) of 0.8–1.9]. The RBE for induction of dicentrics and centric rings in primary spermatocytes was 1.26. The RBE for induction of chromosomal aberrations in peripheral blood lymphocytes was 1.14 (95% CI of 0.8–1.5). The authors concluded that the different RBE values were not statistically different from 1.0.

(B 47) The RBE for tritium beta particles to induce chromosomal aberrations in human spermatozoa has been studied by Kamiguchi et al. (1990a,b). The sperm samples were treated *in vitro* with HTO (57 to 900 MBq mL^{-1}) for 80 minutes. The authors argued that since it was difficult to accurately determine the absorbed dose received by the spermatozoa, doses were expressed as a range between the estimated minimum dose (MIN dose) and the estimated maximum dose (MAX dose). MIN and MAX doses were estimated to be in the range of 0.14–2.06 Gy and 0.25–3.74 Gy,

respectively. Dose rates were not calculated. Other sperm samples were irradiated *in vitro* with 220 kVp x-rays at a dose rate of 628 Gy d^{-1} and total doses of 0.23–1.82 Gy. After irradiation, both samples were analysed for chromosomally abnormal spermatozoa and for different types of aberrations (breakages, exchanges, chromosome and chromatid-type). The RBEs for tritium beta particles for the different endpoints were in the ranges 1.89–3.00 (MIN) and 1.04–1.65 (MAX). The authors considered that the MAX doses estimates were more reliable (Kamiguchi et al., 1990a,b).

(B 48) Kozlowski et al. (2001) assessed the capacity of tritium beta particles and x-rays to induce chromosomal aberrations in bone marrow cells of mice exposed *in utero*. Pregnant mice were treated with tritium either in the drinking water or in cress, from day 1 post-conception until parturition on day 20. After ingestion of HTO or tritiated cress, the accumulated doses during pregnancy were estimated to be 0.6 and 0.3 Gy, respectively. The estimated cumulative doses during the 4 weeks after birth were of 0.1Gy for both HTO and tritiated cress. Another group of female pregnant mice were irradiated acutely with 250 kVp x-rays on day 7 or 14 of pregnancy at a total dose 0.5 Gy. Chromosomal aberrations were quantified in bone marrow cells of the mothers and offspring of each experimental group. Similar levels of stable chromosomal aberrations were quantified in bone marrow of the mothers and their offspring in the 3 irradiated groups (HTO, tritiated cress and x-rays). The authors did not calculate an RBE for tritium beta particles, but they stated that the results were consistent with an RBE value in the range of 1.0–2.0.

(B 49) Several groups have studied the RBE of tritium beta particles for induction of chromosomal aberrations in human peripheral blood lymphocytes *in vitro*. Bocian et al. (1978) treated blood samples with HTO for a period of 2 hours at dose rates of 3.36–30.48 Gy d^{-1} and cumulative doses of 0.28–2.55 Gy or irradiated them acutely with 180 kVp x-rays at a dose rate of 2,736 Gy d^{-1} and total doses of 0.5–3.0 Gy. From the dose-response curves for chromosomal aberration frequency (dicentrics + centric rings) in peripheral lymphocytes after acute exposure, an RBE for tritium beta particles of 1.17 ± 0.02 was calculated. In another study by Vulpis (1984), the peripheral blood samples were exposed to HTO for 20 to 150 min at estimated dose rates of 18.14–66.53 Gy d^{-1} and accumulated doses of 0.25–7.0 Gy, and the number of dicentrics in lymphocytes was quantified. To calculate an RBE for tritium beta particles, those investigators used the data obtained in the same laboratory, under the same conditions, for blood samples exposed acutely to 250 kVp x-rays at total doses of 0.4–9 Gy. RBE was calculated from the ratio of alpha coefficients obtained by fitting the aberration yield curves with a linear-quadratic dose response. An RBE of 2.6 was calculated at a dose of 0.25 Gy. RBE decreased with increasing dose, with an RBE of 1.1 calculated at 7.0 Gy.

(B 50) Tanaka et al. (1994) studied the production of chromosomal aberrations in human peripheral blood lymphocytes and human bone marrow cells by tritium beta particles. The peripheral blood and bone marrow samples were treated with HTO at a beta dose rate of 4.8 Gy d^{-1} and total dose of 0.13–1.11 Gy or irradiated with ^{60}Co or ^{137}Cs gamma rays at a dose rate of 28.8 Gy d^{-1} and total doses of 0.25–2.0 Gy for ^{60}Co and a dose rate of 0.29 Gy d^{-1} and total dose of 2.0 Gy for ^{137}Cs. In human peripheral blood lymphocytes, the RBE for tritium beta particles for induction of chromosomal aberrations and dicentrics was 2.2–2.7 and 2.1–2.3, respectively, when ^{60}Co rays were the reference radiation. The RBE for induction of chromosomal aberrations was 2.0 when ^{137}Cs gamma rays were the reference radiation. In human bone marrow cells,

the RBE for induction of chromosomal aberrations and chromatid aberrations was 1.13 and 3.10, respectively, when ^{60}Co gamma rays were the reference radiation.

(B 51) Dewey et al. (1965) exposed a Chinese hamster cell line to HTO or ^{3}HTdR (tritiated thymidine) for a period of 10 hours; dose rates and doses were not reported. Other cell samples were irradiated with ^{60}Co gamma rays over the same period at dose rates of 3.5–20.7 Gy d^{-1} and total doses of 1.47–8.65 Gy. In each group, the incidence of chromosomal aberrations was quantified. RBEs for tritium beta particles were calculated from the doses needed to produce 2 visible aberrations per cell (8.2 Gy for ^{3}HTdR; 4.9 Gy for HTO, and 5.2 Gy for ^{60}Co gamma-rays), giving estimated RBEs of 1.06 for exposure to HTO and 1.0 for exposure to ^{3}HTdR.

(B 52) Ueno et al. (1982) studied the RBE of tritium beta particles, with tritium administered as HTO, to induce mutations and micronuclei in the murine lymphocytic leukaemia cell line L5178Y using ^{60}Co gamma rays as the reference radiation. In the mutation studies, the cell lines were exposed to cumulative doses of tritium beta particles of 1.5–5.0 Gy at dose rates of 2.0–6.0 Gy d^{-1} or irradiated with ^{60}Co at total doses of 2.0–6.0 Gy and dose rates of 2.40–7.20 Gy d^{-1}. In the studies of micronuclei, the cell line was exposed to total doses of 1.0–8.0 Gy for tritium beta radiation or 2.0–9.0 Gy for ^{60}Co gamma rays at doses rates of 1.2–9.6 Gy d^{-1} and 2.40–10.80 Gy d^{-1} for the beta and gamma radiation, respectively. An RBE for tritium beta particles of 1.8 for mutation induction was estimated. From the doses needed to produce 25 and 50 micronuclei per 1,000 cells, RBE values of 2.3 and 1.8, respectively, were calculated (Ueno et al., 1982).

(B 53) In summary, the majority of the studies of RBE for tritium beta particles for chromosomal damage and mutations have been done *in vitro* with mammalian cells and tritium administered as HTO. One study done with a Chinese hamster cell line used ^{3}HTdR. The experimental systems used included mouse fertilised eggs (Matsuda et al., 1986), human cell samples (bone marrow, peripheral blood lymphocytes, sperm) (Bocian et al., 1978; Vulpis, 1984; Kamiguchi et al., 1990b; Tanaka et al., 1994), and cell lines (Chinese hamster and murine lymphocytic leukaemia) (Dewey et al., 1965; Ueno et al., 1982). One *in vitro* study was done in Drosophila (Byrne and Lee, 1989). Three *in vivo* studies on chromosomal damage were performed using mice (Chopra and Heddle, 1988; Zhou et al., 1989; Kozlowski et al., 2001).

(B 54) The other end-points studies were mutations and micronuclei in the murine lymphocytic leukaemia cell line L5178Y (Ueno et al., 1982) and sex-linked recessive lethal mutations in Drosophila (Byrne and Lee, 1989).

(B 55) All the studies but two (Matsuda et al., 1986; Kozlowski et al., 2001) used tritium beta doses >1 Gy administered at constant dose-rates over a range of 0.005-66.50 Gy d^{-1}. More studies have used gamma rays (10 out of 16) than x-rays (6 out of 16) as the reference radiation.

(B 56) The estimates of RBE for tritium beta particles to produce chromosomal damage and mutations varied from 1.0 to 3.8. Only two RBE estimates were above 3.0 (8 values in the range 1.0–1.9, 6 values in the range 2.0–2.9) (Table B.4).

Table B.4. Data on RBE for tritium beta particles for chromosomal damage and mutations.

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE (±SE)**	**Comments**	**Reference**
Chinese hamster cell line	Chromosomal aberrations	^{60}Co gamma (C) 3.5 - 20.7 Gy d^{-1} Total dose: 1.47 - 8.65 Gy	^{3}HTdR (C) Unknown dose rate Unknown total dose	1.00	RBE calculated from the doses needed to produce 2 visible aberrations per cell	Dewey et al. (1965)
Human sperm	Chromosomal aberrations	220 kVp x-rays (A) 628 Gy d^{-1} Total dose: 0.23 - 1.82 Gy	HTO (A) Unknown dose rate Total dose: MIN= 0.14 - 2.06 Gy MAX= 0.25 - 3.74 Gy	1.04 - 1.65	RBE value for MAX dose (Authors state that the true RBE is very close to this value). RBE also calculated for MIN dose (RBE = 1.89 - 3.00)	Kamiguchi et al. (1990b)
Mouse (In utero, CBA/H)	Stable chromosomal aberrations in bone marrow cells	250 kVp x-rays (A) 1,05 Gy d^{-1} Total dose: 0.5 Gy	HTO and tritiated food (C) Unknown dose rate Total dose: 0.7 Gy HTO and 0.4 Gy tritiated cress	1.00 - 2.00	RBE values estimated by the authors for both HTO and tritiated cress	Kozlowski et al. (2001)
Chinese hamster cell line	Chromosomal aberrations	^{60}Co gamma (C) 3.5 - 20.7 Gy d^{-1} Total dose: 1.47 - 8.65 Gy	HTO (C) Unknown dose rate Unknown total dose	1.06	RBE calculated from the doses needed to produce 2 visible aberrations per cell	Dewey et al. (1965)
Human bone marrow	Chromosome-type aberrations	^{60}Co gamma (A) 28.8 Gy d^{-1} (Constant dose rate) Total dose: 0.25 - 2.0 Gy	HTO (A) 4.8 Gy d^{-1} (Constant dose rate) Total dose: 0.13 - 1.11 Gy	1.13	-	Tanaka et al. (1994)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Tritium Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE (±SE)**	**Comments**	**Reference**
Mouse (CBA/H)	Chromosome aberrations in peripheral blood lymphocytes	250 kVp x-rays (C) ≈ 0.15 - 0.6 Gy d^{-1} (Exponentially decreasing dose rates) Total dose: 1.5 - 6.0 Gy	HTO (C) ≈ 0.15 - 0.6 Gy d^{-1} (Exponentially decreasing dose rates) Total dose: 1.5 - 6.0 Gy	1.14	RBE not statistically different from 1.0 (95% CI = 0.8 - 1.5)	Chopra and Heddle (1988)
Human peripheral blood lymphocytes	Chromosomal aberrations	180 kVp x-rays (A) 2,736 Gy d^{-1} (Constant dose rate) Total dose: 0.5 - 3.0 Gy	HTO (A) 3.36 - 30.48 Gy d^{-1} (Constant dose rate) Total dose: 0.28 - 2.55 Gy	1.17 ± 0.02	-	Bocian et al. (1978)
Mouse (CBA/H)	Chromosomal aberrations in primary spermatocytes	250 kVp x-rays (C) Unknown dose rate Total dose: 1.5 - 6.0 Gy	HTO (C) Unknown dose rate Total dose: 1.5 - 6.0 Gy	1.21	RBE not statistically different from 1.0 (95% CI= 0.8 - 1.9)	Chopra and Heddle (1988)
L5178Y (Murine lymphocytic leukaemia cell line)	Mutation frequency	^{60}Co gamma (C) ≈ 2.40- 7.20 Gy d^{-1}[(c)] (Constant dose rate) Total dose: ≈ 2.0 - 6.0 Gy[(c)]	HTO (C) ≈ 2.0- 6.0 Gy d^{-1}[(c)] (Constant dose rate) Total dose: ≈ 1.5 - 5.0 Gy[(c)]	1.8	-	Ueno et al. (1982)
Human peripheral blood lymphocytes	Chromosomal aberrations	^{137}Cs gamma (A) 0.29 Gy d^{-1} Total dose: 2 Gy	HTO (A) 4.8 Gy d^{-1} Total dose: 0.13 - 1.11 Gy	2.00	-	Tanaka et al. (1994)
Mouse eggs (early pronuclear stage)	Chromosomal aberrations	^{60}Co gamma (A) 0.62 - 3.54 Gy d^{-1} Total dose: 0.05 - 0.30 Gy	HTO (A) 1.02 - 4.08 Gy d^{-1} Total dose: 0.085 - 0.34 Gy	2.00	RBE calculated from linear regression coefficients over 0.05 Gy	Matsuda et al. (1986)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (±SE)	Comments	Reference
Human peripheral blood lymphocytes	Chromosomal aberrations	^{60}Co gamma (A) 28.8 Gy d^{-1} Total dose: 0.2 - 2.0 Gy	HTO (A) 4.8 Gy d^{-1} Total dose: 0.13 - 1.11 Gy	2.30 - 2.70	RBE values for different chromosomal aberrations (centric and dicentric rings)	Tanaka et al. (1994)
L5178Y (Murine lymphocytic leukaemia cell line)	Micronuclei frequency	^{60}Co gamma (C) ≈ 2.40 - 10.80 Gy d^{-1}[c] (Constant dose rate) Total dose: ≈ 2.0 - 9.0 Gy[c]	HTO (C) ≈ 1.2 - 9.6 Gy d^{-1}[c] (Constant dose rate) Total dose: ≈ 1.0 - 8.0 Gy[c]	2.3	RBEs, calculate from doses needed to produce 25 MN/1000 cells (RBE = 1.8 from doses needed to produce 50 MN/1000 cells)	Ueno et al. (1982)
Human peripheral blood lymphocytes	Chromosomal aberrations	250 kVp x-rays (A) 509 Gy d^{-1} (Constant dose rate) Total dose: 0.05 - 9 Gy	HTO (A) 18.14-66.53 Gy d^{-1} (Constant dose rate) Total dose: 0.25 - 7.0 Gy	2.60	RBE at 0.25 Gy. RBE decreased with increasing doses (RBE=1.1 at 7 Gy)	Vulpis (1984)
Insect (Drosophila, adult male)	Sex-linked recessive lethal	^{60}Co gamma (C) ≈ 3.0 - 12.5 Gy d^{-1} (Constant dose rate) Total dose: 6.4 - 25.5 Gy	HTO (C) ≈ 3.0 - 12.5 Gy d^{-1} (Constant dose rate) Total dose: 6.4 - 25.5 Gy	2.70 ± 0.30	-	Byrne and Lee (1989)
Human bone marrow	Chromatid-type aberrations	^{60}Co gamma (A) 28.8 Gy d^{-1} (Constant dose rate) Total dose: 0.25 - 2.0 Gy	HTO (A) 4.8 Gy d^{-1} (Constant dose rate) Total dose: 0.13 - 1.11 Gy	3.10	-	Tanaka et al. (1994)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [(a)]	Tritium Exposure (Acute/Chronic, Dose Rate, Total Dose) [(b)]	Reported RBE (±SE)	Comments	Reference
Mouse (Juvenile)	Chromosome aberrations in spermatocytes	^{60}Co gamma (C) 0.04 - 0.20 Gy d^{-1} (Constant dose-rate) Total dose: 0.43 - 2.04 Gy	HTO (C) 0.005 - 0.05 Gy d^{-1} (Constant dose-rate) Total dose: 0.2 - 1.0 Gy	3.80	RBE for lower beta dose used (0.2 Gy) (RBE = 2.9 for beta doses of 0.6 Gy)	Zhou et al. (1989)

[(a)] Unless specified, external irradiation.
[(b)] Unless specified, internal irradiation.
[(c)] Range of doses (dose-rates) used not described in the text (Estimated from a figure).

B.2. Other literature reviews of RBEs for tritium beta particles

(B 57) Several reviews of RBE data for tritium beta particles have been published in the last two decades. Most of these reviews were concerned with assessing health risks in humans. Thus, the more relevant endpoints were considered to be those directly related to induction of cancer and heritable effects at low doses and low dose rates (stochastic effects). The information analysed in each of these reviews has been almost the same: estimates of tritium in studies performed *in vivo* or *in vitro*, using either orthovoltage x-rays or gamma radiation as the reference radiation. Thus, as would be expected, the conclusions of the different reviews are quite similar (Table B.5). There were some minor differences in the criteria used to select the information for review. Some authors only reviewed papers published in peer reviewed journals (Little and Lambert, 2008), while others have also considered data published in conference proceedings (Fairlie, 2007).

(B 58) The only published review in which non-human biota were the primary focus was from Environment Canada and Health Canada (2003). The data on RBE for tritium beta particles were analysed with emphasis on those effects related to loss of reproductive capacity due to their relevance for maintenance of populations. The aim of that review was to estimate what the investigators called an 'ecodosimetry weighting factor' to be applied to tritium beta particles to calculate 'equivalent doses' to biota. Environment Canada assumed that orthovoltage x-rays were two times more effective in inducing biological effects than gamma radiation. Thus, the estimated RBE values when x-rays were used as the reference radiation were multiplied by 2 to compare them with the estimated RBE values using gamma rays as the reference radiation. For impairment of reproductive capacity, estimated RBE values for tritium beta particles ranged from 1.7 to 3.8, while estimates for genetic endpoints were in the range from 1.5 to 2.9. The authors concluded that the majority of the RBE values are in the range of 2.0-3.0, with a few values for ecologically relevant endpoints as high as 3.8. Accordingly, Environment Canada proposed an ecodosimetry weighting factor of 3.0 for calculating an equivalent dose from exposure to tritium when high-energy gamma radiation is used as the reference radiation.

(B 59) A more recent review was published by the Canadian Nuclear Safety Commission (CNSC, 2010). In that report, a detailed description of each of the previously published reviews was presented, together with an analysis by CNSC of the experimental studies to estimate an RBE for tritium beta particles that were available in the literature. The report focused on analysing the possibility of choosing an appropriate single value of RBE that could be applied for human radiological protection purposes.

(B 60) UNSCEAR (2016) Annex C provides a review of scientific information on the characteristics of tritium including various physical and chemical forms, biokinetic models, dosimetry and radiobiological effects associated with human exposure to tritium. UNSCEAR notes that over several decades, tens of experiments have been conducted using mammals (mostly mice) and their cells to determine RBE for tritium under various experimental conditions and considering a range of biological end points. UNSCEAR's evaluation concludes from some 50 different experiments, RBE values for tritium beta in animals or animal cells have been reported as ranging from 1.0 to 5.0 (centred around 2–2.5) and 0.4–8.0 (centred around 1.5–2) with gamma rays and orthovoltage x-rays as reference radiation, respectively. UNSCEAR also notes that there is tendency for RBE values to increase with decreasing doses and that RBE values for stochastic effects are generally higher (centred around 2.5–3 compared

with prolonged gamma radiation) than those obtained from studies of tissue reactions (cell killing in vivo and in vitro).

B.3. Overall Evaluation of RBEs for tritium beta particles

(B 61) The RBE values for tritium beta particles in the available studies were all obtained at dose rates that were in or above the relevant DCRL bands. The calculated values were all <4 with the majority of values <3. The data for fish are from 1 to nearly 4 with aquatic invertebrates around 1; these data are consistent with the data observed for mammals.

Table B.5. Summary of conclusions in several published reviews on RBE values for tritium beta particles.

Authors, year	**RBE value**	
	X-rays Reference radiation	**Gamma rays reference radiation**
Straume and Carsten, 1993	1.8 (mostly in 1.0 - 2.0 range)	2.3 (mostly in 2.0 - 3.0 range)
Environment Canada, 2003	Multiplied by 2 to be 'gamma comparable'	Reproduction: majority in the 2.0 - 3.0 range
HPA, 2007	1.0 to 2.0	2.0 to 3.0
Fairlie, 2007	1.0 - 3.0 (although the data are scarce)	1.3 to 3.4. Mean value of 2.0.
Little and Lambert 2008	Stochastic endpoints 1.17 (95% CI 0.96, 1.39)	2.19 (95% CI 2.04, 2.33)
CNSC, 2010	1.4	2.2
UNSCEAR, 2016	0.4 to 8.0 (centred around 1.5 - 2)	1.0 to 5.0 (centred around 2 - 2.5)

B.4. References

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ANNEX C. RELATIVE BIOLOGICAL EFFECTIVENESS OF ALPHA-EMITTING RADIONUCLIDES

(C 1) An alpha particle has two protons and two neutrons and is identical to the nucleus of a ^{4}He atom. Alpha particles are positively charged (+2) particles of energy about 4–9 MeV that are emitted by certain radionuclides in response to a low neutron–to-proton ratio in the nucleus. Radioactive isotopes that emit alpha particles include, for example, ^{241}Am, ^{239}Pu, and several radionuclides in the natural uranium and thorium decay chains, such as ^{238}U, ^{226}Ra, ^{222}Rn, ^{210}Po and ^{232}Th.

(C 2) Alpha particles have very low penetration power in matter compared with gamma rays and are primarily injurious when alpha-emitting radionuclides are deposited internally, although higher energy alpha particles can penetrate the outer layer of dead skin and irradiate the underlying basal layer. The dosimetry of alpha emitters is complicated by a number of factors, among them, their non-uniform distribution in organs and tissues and the short range of alpha particles, which can result in non-uniform localised doses to cells.

(C 3) In general terms, radiation quality can be specified by the fluence spectrum of the ionising particles of different charge and velocity that deposit energy in the system considered, which in turn determine the numbers of ionisations within the affected volume. To illustrate, Goodhead (1992) notes that a secondary electron track produced by an incident gamma ray that traverses the nucleus of a mammalian cell with a diameter of about 8 µm gives rise to 60–80 ionisations, resulting in an absorbed dose of the order of 1 mGy, whereas an alpha particle traversing the same nucleus results in some 23,000 ionisations within the same volume and an absorbed dose of the order of 400 mGy.

(C 4) Such differences in ionisation density or LET are the basis of observed differences in effectiveness per Gy in causing deleterious effect in cells and tissues. In general, alpha particles and neutrons can produce observable damage at much lower average absorbed doses than beta or gamma radiation.

C.1. Review of experimental studies of RBE for alpha-emitting radionuclides

(C 5) Several criteria were used to evaluate the literature describing experiments related to RBE for alpha particles, among them life stage, endpoints, LET, dose rates, total dose, and reference radiation. The papers reviewed varied greatly in the level of detail provided.

(C 6) Most of the reviewed papers either reported RBE values or provided sufficient data, such as the coefficients α and β linear-quadratic exposure-effect models or survival curves (see Annex A), that could be used to calculate RBE values. The reported or calculated RBE values for alpha particles were obtained in studies in which x-rays, high-energy gamma rays, or in some cases, higher energy beta particles were used as the reference radiation Maximum RBE (RBE_m or RBE_M) values were calculated where data were available, as for example from the slopes of survival curves provided in the reviewed papers.

(C 7) The RBE values differ between experiments due to a number of factors, including differences in species and strains, cell lines, genetic modifications, and dose rate. It should be noted that the route of administration in many of the experimental studies was injection, whereas intakes in the natural environment will arise via ingestion or inhalation. The following sections provide a brief overview of available data from experimental studies of RBE for alpha-emitting radionuclides and fission neutrons of relevant LET (Tables C.1 to C.4).

C.1.1. Data on RBE to produce early mortality

(C 8) In mammals, early mortality is a result of extensive irradiation that causes severe cell depletion in turn leading to dysfunction of major organs. Death of the organisms occurs due to injury of specific organs caused by exposure to radiation. Few studies have been conducted to test this endpoint using alpha–emitting radionuclides. One study of interest but not direct relevance (Mays et al., 1969) reported RBE values of 6 (^{239}Pu), 8 (^{228}Th), and 2 (^{228}Ra) relative to ^{226}Ra as a reference radiation in a study of early mortality from radiation-induced bone cancer in Beagle dogs (Table C.1). This variation in toxicity of alpha particle emitting radionuclides per Gy average bone dose is attributable to their different patterns of deposition in relation to the location of target cells for induction of bone cancer near to inner bone surfaces.

(C 9) Animals in the wild also develop cancer, but the effects of cancer morbidity on the ability to reproduce and the effect on overall mortality is not clear at environmentally relevant doses. Overall, the possibility of cancer as an endpoint is generally considered of relatively little interest for populations of non-human biota compared to reproductive endpoints.

C.1.2. Data on RBE to reduce reproductive success

(C 10) Fourteen publications were identified that considered the effects of alpha particles on reproductive success (Table C.2). The alpha-emitting radionuclides most commonly used in these studies were ^{238}Pu, ^{239}Pu and ^{210}Po and the most common reference radiation was 60-120 kVp x-rays.

(C 11) Depending on the species considered, a wide range of RBE and RBE-maximum values were reported for endpoints related to reduced reproductive success, among them, numbers of surviving offspring, sperm head survival and testis weight. Although a few papers reported alpha RBE values >10 (see Section C.2), most were in the range of from 1 to 10. Most RBE values were obtained using rodents or rodent cells exposed to high doses and dose rates.

C.1.3. Data on RBE to produce morbidity effects

(C 12) As per *Publication 108*, all forms of morbidity in animals and plants leads to reduced fitness. This can influence an organism's life span and reproductive capacity. There are few data on larger mammals, with most experiments conducted in mesocosms.

(C 13) Alpha-emitting radionuclides commonly used to irradiate cell lines, tissues or cell cultures were ^{238}Pu, ^{239}Pu and ^{210}Po. The common reference radiation used in studies of this endpoint was 250-kVp x-rays.

(C 14) Thirty-five publications reported alpha RBE values for a variety of morbidity effects, notably, cell survival (Table C.3). The RBE and RBE maximum values were calculated whenever possible from the slopes of the survival curves provided at low dose. Depending on the species considered, a wide range of RBE and RBE maximum values were reported. The majority of RBE values calculated were below 5 and almost all the RBE values provided for cell survival were below ten.

C.1.4. Data on RBE to produce chromosomal damage and mutations

(C 15) Thirty-three publications discussed chromosomal damage and mutations caused by exposure to alpha-emitting radionuclides (Table C.4). Alpha-emitting radionuclides commonly used to irradiate cell lines, tissues or cell cultures were ^{238}Pu, ^{239}Pu, ^{241}Am and ^{226}Ra. The common reference radiations in these studies were ^{60}Co gamma rays and 80-300 kVp x-rays.

(C 16) The majority of the reviewed publications that analysed chromosomal damage and mutations reported RBE values or provided enough data on fitted dose-response functions to allow calculation of RBE values. Most RBE values were obtained using rodents or rodent cells based on exposures to high doses and dose rates. Few papers reported alpha RBE values greater than 20, and most reported values are in the range of 1 to 10.

(C 17) Most of the studies were concerned with chromosomal damage and mutation effects caused by alpha emitters were conducted on hamster cells *in vitro* and mice *in vivo*. It should be noted that while these data indicate an increase in the biological effectiveness of alpha radiation compared to the reference radiations, there are limitations to the quantitative use of these data. Moreover, the relation, if any, between chromosomal damage and mutational events at the cellular level observed in laboratories and observable population level effects on environmental populations of non-human biota remains to be determined.

Table C.1. Summary of publications studying RBE for alpha particles to produce early mortality.

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
Beagle dogs (Young adult)	Average time to death with osteosarcomas	^{226}Ra (Int) (A), Unknown dose-rate, Unknown total dose	^{228}Ra alphas, (A), Unknown dose-rate, 5.6 - 6.5 Gy (1 year after injection)	2.5	N.E.	RBE calculated using data of death from osteosarcoma 8 years after injection	Mays et al. (1969)
Beagle dogs (Young adult)	Average time to death with osteosarcomas	^{226}Ra (Int) (A), Unknown dose-rate, Unknown total dose	^{239}Pu, alphas, (A), Unknown dose-rate, 1.4 - 15.0 Gy (1 year after injection)	6.0	N.E.	RBE calculated using data of death from osteosarcoma 8 years after injection	Mays et al. (1969)
Beagle dogs (Young adult)	Average time to death with osteosarcomas	^{226}Ra (Int) (A), Unknown dose-rate, Unknown total dose	^{228}Th alphas, (A), Unknown dose-rate, 4.8 - 19.0 Gy (1 year after injection)	8.0	N.E.	RBE calculated using data of death from osteosarcoma 8 years after injection	Mays et al. (1969)

[a] Unless specified, external irradiation.

[b] Unless specified, internal irradiation.

N.E. Not estimated. Difficult to estimate RBE_m due to lack of information.

1784 Table C.2. Summary of publications studying RBE for alpha particles to reduce reproductive success.

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/RBE_M**	**Comments**	**Reference**
C3H10T1/2 (Mouse fibroblast cell line) , Chinese hamsters; rats	A variety of endpoints including cell reproductive death.	^{137}Cs gamma and 300 kVp x-rays, Unknown dose-rate, Unknown total dose	^{239}Pu alpha, Unknown dose-rate, Unknown total dose (Experimental details given in Ullrich, 1984, and Lundgren et al., 1987).	5 (For DNA-sized targets), 4 (For nucleosome-sized targets), >100 (for chromatin-sized targets, for slow protons and alpha particles)	N.E.	Alpha RBE was calculated through computer modelling using Monte Carlo track structure computations. Cells from a Chinese hamster were irradiated in vitro with 1.0 MeV neutrons at dose rates of 3.0 and 1.0.	Barendsen (1989) (Review Paper)
Mouse (Adult females F1(C3H/HeH x101/H))	Total number of offspring produced by female surviving to sterility	^{60}Co gamma, (C), 0.10 - 0.20 Gy d^{-1}, Unknown total dose	^{239}Pu alpha (130 keV μm^{-1}), (A), 7.5-13.5 mGy d^{-1} (after 3rd litter) to 8.9 - 24.4 mGy d^{-1} (5-10 $\mu Ci\ kg^{-1}$)	2.5	N.E.	Questionable assumption about homogeneous distribution of alpha dose	Searle et al. (1980)
Mouse (Young male Swiss Webster)	Sperm head survival rate	120 kVp x-rays, (A), Unknown dose-rate, Unknown total dose	^{212}Pb alpha and decay products (100 keV μm^{-1}) (Ext), (A), Unknown dose rate, 0.14 or 0.48 Gy	4.7 ± 0.5	N.E.	RBE at 0.14 Gy (at 0.48 Gy RBE= 4.1±0.5). ^{212}Pb and ^{212}Bi yield a mixed radiation field of photons, beta particles and alpha particles	Howell et al. (1994)
Mouse (Young male Swiss Webster)	Sperm head survival	120 kVp x-rays, (A), Unknown dose-rate, Unknown total dose D37 = 0.67 +/- 0.03 Gy (from Rao et al., 1988)	^{223}Ra alpha (50 keV μm^{-1}), (A), Unknown dose rate, Unknown total dose D37= 0.124 +/- 0.020 Gy	5.4 ± 0.9	N.E.	RBE for 10% survival	Howell et al. (1997)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/RBE_M**	**Comments**	**Reference**
Mouse (Young Swiss Webster)	Survival of spermatogonial cells	60 -120 kVp x-rays, Unknown type of exposure, Unknown dose rate, Unknown total dose	^{210}Po-citrate alpha (5.3 MeV), (A), Unknown dose rate, Unknown total dose	6.7	N.E.	RBE calculated for 37% survival	Rao et al. (1989)
Mouse (Young male Swiss Webster)	Sperm head survival	120 kVp x-rays, (A), Unknown dose-rate, Unknown total dose D37 = 0.67 +/- 0.03 Gy (from Rao et al., 1988)	^{148}Gd alpha (50 keV μm^{-1}), (A), Unknown dose rate, Unknown total dose D37= 0.0090 +/- 0.029 Gy	7.4 ± 2.4	N.E.	RBE for 37% survival	Howell et al. (1997)
Mouse (Young Harvard Swiss Wistar)	Oocyte survival.	^{60}Co gamma, Unknown type of exposure, Unknown dose rate, 40 - 143 mGy	^{210}Po alpha (5.3 MeV; 135 keV/μm), (A), Unknown dose rate, 0.1 - 106.4 mGy	7.8	N.E.	Reported RBE for 5.3% survival. The highest RBE reported (377) is too high by a factor of at least 4 due to statistical errors in ^{210}Po dosimetry al low doses (homogeneous distribution assumed). RBE of 50 - 100 is reasonably substantiated by data at low doses (0.1 - 2.7 mGy). For doses between 10.6 and 106.4 mGy there is not a relationship between RBE and dose (RBEs of 1.6, 7.5, 1.4 and 4.8 for 48.5%, 45.0%, 18.0% and2.7% survival)	Samuels (1966)
Mouse (Young Swiss Webster)	Survival of spermatogonial cells	60 -120 kVp x-rays Unknown type of exposure, Unknown dose rate, Unknown total dose	^{125}I Auger electrons (100 keV μm^{-1}), (A), Unknown dose rate, Unknown total dose	7.9	N.E.	RBE calculated for 37% survival	Rao et al. (1989)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/RBE_M**	**Comments**	**Reference**
Mouse (Young male (C57BL/6J x BALB/cJ) F1 B.16CF)	Testis weight	^{60}Co gamma, (A, C), 0.03 - 0.06 Gy d^{-1}, 0.6 - 10.5 Gy	^{239}Pu alpha (5.15 MeV; 130 keV μm^{-1}), (C), 0.75-1.50 mGy d^{-1} (5-10 $\mu Ci\ kg^{-1}$), Unknown total dose	9.5 ± 4.0	N.E.	RBE calculated using 'effect per rad' coefficients, which were calculated from weighted least squares linear regressions. The RBE values may have been high by a factor of 3 or more since dose was calculated based on testis weight at the beginning of the study where results indicated that it decreased. Distribution of ^{239}Pu assumed to be uniform within the gonad.	Grahn, et al. (1979)
Mouse (Young male (C57BL/6J x BALB/cJ) F1 B.16CF)	Dominant lethal mutations	^{60}Co gamma, (A, C), 0.03 - 0.06 Gy d^{-1}, 0.6 - 10.5 Gy^{-1}	^{239}Pu alpha (5.15 MeV; 130 keV μm^{-1}), (C), 0.75 - 1.50 mGy d^{-1} (5 - 10 $\mu Ci\ kg^{-1}$), Unknown total dose	13.0 ± 3.0	N.E.	RBE calculated using 'effect per rad' coefficients, which were calculated from weighted least squares linear regressions. The RBE values may have been high by a factor of 3 or more since dose was calculated based on testis weight at the beginning of the study where results indicated that it decreased. Distribution of Pu-239 assumed to be uniform within the gonad.	Grahn, et al. (1979)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/RBE_M**	**Comments**	**Reference**
Mouse (Young male (C57BL/6J x BALB/cJ) F1 B.16CF)	Abnormal sperm	^{60}Co gamma, (A, C), 0.03 - 0.06 Gy d^{-1}, 0.6 - 10.5 Gy	^{239}Pu alpha (5.15 MeV; 130 keV μm^{-1}), (C), 0.75 - 1.50 mGy d^{-1} (5 - 10 µCi kg^{-1}), Unknown total dose	25.0 ± 8.0	N.E.	RBE calculated using 'effect per rad' coefficients, which were calculated from weighted least squares linear regressions. The RBE values may have been high by a factor of 3 or more since dose was calculated based on testis weight at the beginning of the study where results indicated that it decreased. Distribution of ^{239}Pu assumed to be uniform within the gonad.	Grahn, et al. (1979)
Mouse (Young male (C57BL/6J x BALB/cJ) F1 B.16CF)	Chromatid fragments in early meiosis.	^{60}Co gamma, (A, C), 0.03 - 0.06 Gy d^{-1}, 0.6 - 10.5 Gy	^{239}Pu alpha (5.15 MeV; 130 keV μm^{-1}), (C) 0.75-1.50 mGy d^{-1} (5-10 µCi kg^{-1}), Unknown total dose	33.0 ± 5.0	N.E.	RBE calculated using 'effect per rad' coefficients, which were calculated from weighted least squares linear regressions. The RBE values may have been high by a factor of 3 or more since dose was calculated based on testis weight at the beginning of the study where results indicated that it decreased. Distribution of ^{239}Pu assumed to be uniform within the gonad.	Grahn, et al. (1979)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/RBE_M**	**Comments**	**Reference**
Fish (Zebrafish *Danio rerio*)	Egg production	^{137}Cs gamma, (C), Approx: 7.2; 24.0 and 177.6 mGy d^{-1}, Unknown total dose	^{210}Po Alpha (5.4MeV), (C) (Estimated ^{210}Po activity per meal (2 times a week) were 7, 20, 155 and 620 Bq g^{-1}), 0.2 - 17.7 mGy d^{-1}, Unknown total dose	<35.0	N.E.	RBE alpha = Dose rate of gamma -radiation causing an effect (ceased egg production) / Dose rate of alpha -radiation causing the same effect. This RBE value (< 35) represents the upper limit. Using data from the gamma irradiated group (3 dose rates) the alpha RBE ranged from <20 to <7, which authors notes may represent closer estimates.	Knowles (2001)
Mouse (Adult male Swiss Webster)	Abnormalities in sperm heads	120-kVp x-rays, (A) Unknown dose rate, Unknown total dose (Experimental details in Rao et al., 1988)	^{210}Po-citrate alpha, (A), 2980 Gy MBq^{-1} injected in right testes, Unknown dose rate, Unknown total dose	245 ± 23	N.E.	RBE calculated from initial slopes of dose-response curves for induction of abnormalities. Authors assumed uniform polonium distribution.	Rao et al. (1991)

[(a)] Unless specified, external irradiation.
[(b)] Unless specified, internal irradiation.
N.E. RBE_m not estimated due to lack of information.

1788 Table C.3. Summary of publications studying RBE for alpha particles to produce morbidity effects.

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
Mouse (Adult female LAF1)	Survival of lymphoma cells	230 kV x-rays, (A), 2,880 - 3,168 Gy d^{-1}, Unknown total dose	He ions alpha; (C); 910 MeV, 17 keV μm^{-1}; 85 meV, 180 keV μm^{-1}; 118MeV, 80 keV μm^{-1}; 32 MeV, 220 keV μm^{-1}; 7,200 - 43,200 Gy d^{-1}; Unknown total dose	0.95 - 1.90	N.E.[(d)]	Reported RBE value for hypoxic conditions. For hyperoxic conditions the RBE was1.04 - 1.20. The RBEs were calculated by dividing the mean lethal dose from x-rays by the mean lethal dose from He ions.	Feola et al. (1969)
V79 (Chinese hamster cell line)	Cell survival	250 kVp x-ray, (A), 1,152 Gy d^{-1}, Unknown total dose	^{238}Pu alpha (3.5 MeV; 110 keV μm^{-1}), (A), 76,896 Gy d^{-1}, Unknown total dose	1.38 - 3.80	RBE_m 1.7 - 6.5 (based on survival curves)	Reported RBE for 10% survival. RBE = 1.3 - 3.2 for 1% survival	Zyuzikov et al. (2001)
Rat Tracheal Epithelial Cells.	Cell survival	250 kVp x-ray, Unknown type of exposure, 432 Gy d^{-1}, 0.5 - 9.0 Gy	^{238}Pu alpha (5.5 MeV; 137 keV μm^{-1}), Unknown type of exposure, 2,290 Gy d^{-1}, 0.5 - 5.0 Gy	1.5 - 4.0	RBE_m= 2.8 from survival curves		Thomassen et al. (1990)
C-18 (Chinese Hamster Ovary cell line)	Cell survival	250 kVp x-ray, (A), 8.6; 18.8 and 19.2 Gy d^{-1}, 1.15 - 8.83 Gy	^{212}Bi (3.2 MeV;113 keV μm^{-1}), ^{222}Rn (3.8 MeV; 103 keV μm^{-1}) and ^{238}Pu (3.5 MeV; 110 keV μm^{-1}); Unknown type of exposure; 3 - 3,000 Gy d^{-1} (^{212}Bi), 0.7 - 12.2 Gy d^{-1} (^{222}Rn), 2,851 Gy d^{-1} (^{238}Pu); Unknown total dose	1.7-3.2 (37% survival), 2.2-3.8 (1% Survival)	Radon RBE_m = 5 (From survival curves)	The dose at 1% survival for the ^{222}Rn and ^{212}Bi exposures was similar (2.95 to 3.01 Gy). The dose for the ^{238}Pu source was 2.45 Gy. Higher RBEs at 1% survival may be due to non-linear survival curves for alphas.	Schwartz et al. (1992)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
Yeast (Saccharomyces cerevisiae strains)	Colony forming ability and cell repair ability	^{60}Co gamma, Unknown type of exposure, 14,400 Gy d^{-1}, 35 - 60 Gy (Further details on exposure in Petin, 1979)	^{239}Pu alpha (134 keV μm^{-1}), Unknown type of exposure, 24,480 Gy d^{-1}, 17 - 32 Gy (Further details on exposure in Petin, 1979)	1.9 - 5.1	N.E.	Reported RBE is for diploid strains (37% survival). For haploid strains RBE =1.6 - 3.2 (7% survival) Experimental points in each survival curve have a standard error of approximately 2%.	Petin and Kabakova (1981)
V79-379A (Chinese Hamster cell line)	Cell survival	X-ray, 250 kVp, (A), 2,592 Gy d^{-1}, 50 Gy	Neutrons (2.3 MeV), (A), 1,080 Gy d^{-1}, 1.7 and 5.6 Gy (From Graph)	2.3	RBE_m = 5.8	Reported RBE was calculated for 1% survival.	Prise et al. (1987)
Rat Tracheal Epithelial Cells.	Cell transformation	250 kVp x-ray, Unknown type of exposure, 432 Gy d^{-1}, 0.5 - 9.0 Gy	^{238}Pu alpha (5.5 MeV; 137 keV μm^{-1}), Unknown type of exposure, 2,290 Gy d^{-1}, 0.5 - 5.0 Gy	2.4			Thomassen et al. (1990)
V79-379A (Chinese Hamster cell line)	Cell survival	X-ray, 250 kVp, (A), 2,592 Gy d^{-1}, 50 Gy	^{238}Pu Alpha (3MeV; 125 keV μm^{-1}), (A), 1,080 Gy d^{-1}, 1.7 and 5.6 Gy (From Graph)	2.6	RBE_m = 7.5 (from linear quadratic fits to survival curves)	Reported RBE was calculated for 1% survival.	Prise et al. (1987)
Rat (Adult male, Albino CD strain)	Hair Follicle Survival and damage	Electrons (0.32 Mev), (A), Unknown dose rate, 8.1 - 123 Gy	Cyclotron-accelerated alpha particles (37 MeV, 34 keV μm^{-1}), (A), 7,488 Gy d^{-1}, 2.1 - 68.5 Gy	2.6 ± 0.4	N.E .	RBE for hair follicle damage (RBE =2.1± 0.7 for hair follicle survival)	Burns et al. (1968)
Rat (Adult male, Albino CD strain)	Tumour Induction	Electrons (0.32 Mev), (A), Unknown dose rate, 8.1 - 123 Gy	Cyclotron-accelerated alpha particles (37 MeV, 34 keV μm^{-1}), (A), 7,488 Gy d^{-1}, 2.1 - 68.5 Gy	2.9 ± 0.5	N.E		Burns et al. (1968)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
Rat (Adult male, Albino CD strain)	Acute Skin Injury	Electrons (0.32 Mev), (A), Unknown dose rate, 8.1 - 123 Gy	Cyclotron-accelerated alpha particles (37 MeV, 34 keV μm^{-1}), (A), 7,488 Gy d^{-1}, 2.1 - 68.5 Gy	3.0 ± 1.0	N.E		Burns et al. (1968)
C3H 10T1/2 (Mouse fibroblast cell line)	Neoplastic transformation	^{60}Co gamma, (C), 720 Gy d^{-1}, Unknown total dose	^{241}Am alpha (2.7 MeV; 147 keV μm^{-1}), (C), 288 Gy d^{-1} and 1,195 - 3,600 Gy d^{-1}, Unknown total dose	3.0	RBE_m = 12	Gamma data was not a main objective in study and is subject to considerable uncertainties; therefore, this data was not fitted to a numerical relation.	Hieber et al. (1987)
GHE (Primary golden hamster embryo cell line)	Cell survival and cell transformation	^{60}Co gamma, (A), 1,584 Gy d^{-1}, Approx. 0 - 8 Gy (from survival curves)	^{14}N (530 keV μm^{-1}), ^{4}He (36 keV μm^{-1}), ^{4}He (77 keV μm^{-1}); 1,000 - 1,440 Gy d^{-1} (^{14}N), 1,440 - 3,744 Gy d^{-1} (^{4}He); Approx. 0 - 4 Gy (from survival curves)	3.3	RBE_m = 4.6 (From survival curves)	Reported RBE for 37% survival. The RBEs for morphological transformations were about 3.3 for ^{14}N; 2.4 for ^{4}He (36 keV μm^{-1}) and 3.3 for ^{4}He (77keV μm^{-1}).	Suzuki et al. (1989)
3T3 (Mouse embryo fibroblast cell line)	Cell Survival	250 kVp x-ray, (A), 1,152 Gy/d, 0 - 6.0 Gy (from graph)	^{238}Pu alpha (5.3 MeV; 148 keV μm^{-1}), (A), 345.6 Gy d^{-1}, 0 - 2.5 Gy (from Graph)	3.5	RBE_m = 6.2 (from survival curves) RBE_m = 3.0 (transformation)	Reported RBE for 50% survival. The effective RBE for alpha particles would thus be increased to 5, when recovery was allowed to take place.	Roberston et al. (1983)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
V79-379A (Chinese Hamster lung fibroblasts cell line)	Cell survival	300kVp x-rays, (A), 720 Gy d^{-1}, 4 Gy	^{239}Pu Alpha (Average of 118 keV μm^{-1}, 179 keV μm^{-1} and 201 keV μm^{-1}); (A); 12,960, 19,008 and 73,440 Gy d^{-1}; 0.21, 0.28 and 0.38 Gy	4.0	RBE_m =13, (based on figures provided)	Reported RBE value for 10% survival (RBE=3.7 for 1% survival). As LET increased, the effectiveness of alpha-particles to inactivate V79 cells increased initially until, at the highest LET tested, effectiveness decreased again.	Manti et al. (1997)
Co631 (Chinese Hamster embryo cell lines)	Cell survival	^{60}Co gamma, (A), 1,584 Gy d^{-1}, 7.9 Gy	^{241}Am Alpha (120 keV μm^{-1}); (A); 504 Gy d^{-1}; D37=0.85Gy, D10= 0.85 Gy	4.2	RBE_m = 9.3 (37 % survival)	Reported RBE value for 10% survival.	Lücke-Huhle et al. (1986)
Human skin fibroblasts (Primary fibroblasts and AT2BE cell line)	Survival	^{60}Co gamma, (A), 2,160 Gy d^{-1}, 0.27-3.0 Gy	^{241}Am alpha (4 MeV, 120 keV μm^{-1}), (A), 504 Gy d^{-1}, 0.27 - 3.0 Gy	5.0	RBE_m = 5.6 (primary fibroblast)	Reported RBE value was calculated for 10% survival of primary fibroblast. An RBE of 1.9 was calculated for 10% survival of AT2BE cell line.	Coquerelle et al. (1987)
GM 10 (Human - diploid embryonic skin fibroblast cell line)	Cell survival	250 kVp x-rays, (A), 2,880 Gy d^{-1}, 1.3 Gy	^{238}Pu alpha (2.9 MeV; 100 keV μm^{-1}), (A), 5,184 Gy d^{-1}, 2.5 Gy	5.2	N.E.	RBE for 37% survival. The RBE was calculated using data from the survival curves after alpha irradiation and the Do values for x-rays. Only the cells in the central part of the dish were uniformly irradiated due to the geometry of the alpha source.	Chen et al. (1984)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
V79-4 (Chinese Hamster Cell line)	Cell survival	^{60}Co gamma rays, (A), 5,472 Gy d^{-1}, Unknown total dose	^{238}Pu Alpha (120 keV μm^{-1}, (A), 34,560 Gy d^{-1}, Unknown total dose	5.3	RBE_m = 12	Reported RBE value for 10% survival (RBE= 4.0 for 1% survival). Slopes of survival curves are provided in this paper but difficult to deduce.	Jenner et al. (1993)
V79-4 (Chinese Hamster cell line)	Cell survival	250 kVp x-ray, (A), 1,094 Gy d^{-1}, 6.0 Gy	^{238}Pu alpha (100 keV μm^{-1}); Using the 2 independent methods, the dose rate was approximately 10.8 rad per 18.6 sec; range of total dose range 0 - 2.8 Gy (Approximately)	5.8	RBE_m = 12.8 (from survival curves)	Reported RBE for 70% survival. RBE = 4.8 and 3.5 for 37% and 10% survival, respectively. Surviving fraction not calculated relative to unirradiated controls, but relative to number of cells respread per dish.	Thacker et al. (1982)
C3H 10T1/2 (Mouse fibroblast cell line)	Cell survival	^{60}Co gamma, (C), 720 Gy d^{-1}, Unknown total dose	^{241}Am alpha (2.7 MeV; 147 keV μm^{-1}), (C), 288 Gy d^{-1} and 1,195 - 3,600 Gy d^{-1}, Unknown total dose	6.2	RBE_m = 12	Reported RBE value for 10% survival (RBE = 4.0 for 50% survival); Gamma data was not a main objective in study and is subject to considerable uncertainties; therefore, this data was not fitted to a numerical relation.	Hieber et al. (1987)
C3H 10T1/2 (Mouse fibroblast cell line)	Cell survival	250 kVp x-ray, (A), 18 Gy d^{-1}, 0 - 8.5 Gy (From Graph)	Protons, deuterons and ^{3}He ions (10-120 keV μm^{-1}), Unknown dose rate, 0.2 - 6.0 Gy	Specific RBE values not stated.	RBE_m = 6.3 and 7.2 at the two highest LETs.	RBE was determined from the slopes of the survival curves provided for different LETs.	Hei et al. (1988)
Tracheal cells (Adult male Fischer F344 rats)	Cell survival	300 kVp x-rays, (A), Unknown dose-rate (2.58 - 5.16 x 10^{-4} C kg^{-1} of air per second), 0.45 - 6.55 Gy	^{210}Po alpha (135 keV μm^{-1}), (A), Unknown dose rate, 0.25 - 1.25 Gy	6.35	RBE_m is approx. 16 from survival curve	Reported RBE value for 37% survival.	Ford and Terzaghi-Howe (1993)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
SHE (Golden Syrian Hamster Embryo cell line)	Cell survival	250kVp x-rays, (A), 1,440 Gy d^{-1}, 15 Gy	^{4}He Alpha (90 - 200 keV μm^{-1}), (A), 173 - 1,440 Gy d^{-1}, Unknown total dose (Experimental details in Miller et al. 1980)	RBE (LET in keV μm^{-1})= 4.8 (90), 5.0 (100), 7.0 (120), 5.4 (150), 3.8 (180), 3.6 (200)	RBE_m (LET in keV μm^{-1}) = 9 (90), 10 (100), 12 (120), 10 (150), 8 (180), 7 (200)	RBE_m values for morphological transformation induction ranged from 3 to 60, with the LETs of 90 and 100 keV μm^{-1} being the most effective with RBE_m values of 60 and 37, respectively. However, the RBE_m for the 90 keV μm^{-1} LET had a standard deviation of +45, -30 (poor statistics)	Martin et al. (1995)
C3H 10T1/2 (Mouse fibroblast cell line)	Cell survival	^{60}Co gamma, (A, C), 43,200 Gy d^{-1}, 0.9 - 8.0 Gy	^{238}Pu alpha (124 keV μm^{-1}; (A, C), 576 - 2,448 Gy d^{-1} (high dose rate), Mean lethal dose 0.6 Gy	7.9	RBE_m = 8.9 (From survival curves)	Reported RBE value for 80% survival at high dose rates (RBE= 6.2 and 4.6 for 37% and 5% survival, respectively)	Roberts and Goodhead (1987)
Tracheal epithelial cells (Male Sprague-Dawley rats)	Cell survival.	^{60}Co gamma, (A), 864 Gy d^{-1}, 1.0 - 5.0 Gy	^{241}Am alpha, (A), 280.8 Gy d^{-1}, 0.5 - 6.0 Gy	~10	RBE_M = 10 (From initial linear slopes of the curves)	Reported RBE for doses up to 0.5 Gy. Above 0.5 Gy RBE gradually decreased; it was 5.1 at 1 Gy and 1.1 at 5 Gy. No LET given.	Kugel et al. (2002)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
Mouse (Young female NMRI)	Induction of osteosarcoma	^{177}Lu (short-lived beta) and ^{90}Sr (long-lived beta) (Int), (C), 0.36-12.8 Gy d^{-1} (^{177}Lu) and 0.19 to 0.93 Gy d^{-1} (^{90}Sr), 0.9 and 20 Gy (total skeletal dose for beta emitter)	^{224}Ra; ^{226}Ra alpha; (C); 0.9 - 432 cGy d^{-1} (^{224}Ra), 3 - 15 cGy d^{-1} (^{226}Ra); Unknown total dose	10 (beta doses as reference radiation)	N.E.	Reference experiments with long-lived alpha and beta emitters (^{226}Ra and ^{90}Sr) showed that the incidence of osteosarcomas per Gy could be lower than that observed when the same skeletal dose was applied by protraction of short-lived radionuclides.	Muller et al. (1983)
Rat (Adult female Wistar)	Incidence of lung carcinomas	220kVp x-rays, (A), 144 - 864 Gy d^{-1}, 0.5 - 10 Gy	$^{239}PuO_2$ aerosols (42.5 keV µm^{-1}), (A), Unknown dose rate, 0.5 to 10.0 Gy	10.7	RBE_M = 11.3 (from the slopes of the curves)	The incidence of lung tumour lesions distributed in the rat's lung were about 2-fold more in Alpha emitting $^{239}PuO_2$ compared to those of thoracic x-ray irradiation.	Oghiso and Yamada (2003)
C3H 10T1/2 (Mouse fibroblast cell line)	Cell survival and oncogenic transformation	250kVp x-rays, Unknown type of exposure, Unknown dose-rate, Unknown total dose (Experimental details in Miller et al., 1989, 1990)	^{3}He (75 keV µm^{-1}), ^{4}He (90 - 200 keV µm^{-1}); (A); Unknown dose rates; 6 Gy (deuteron), 3 Gy (proton).	No RBE values stated	RBE_m for oncogenic transformation peaked at around 20 for reference radiation of 20 (120keV µm^{-1})	Authors state that the difference in RBE_m values between C3H 10T1/2 cells and the Syrian Hamster embryo cell line (Martin et al., 1995) were likely caused by the differences in the two systems.	Miller et al. (1995)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [(a)]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [(b)]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
Beagle dog and Mouse (female CF1)	Induction of bone sarcomas	^{90}Sr beta (Int); (A); Unknown dose rate; 0 - 101 Gy (beagles), 0 - 120 Gy(mice) [c]	^{226}Ra Alpha, (A), Unknown dose-rate, 0 - 134 Gy (beagles) and 0 - 289 Gy (mice)[c]	In Beagles RBE = 26 (8.7% incidence); 5 (66.7% incidence). In Mice RBE= 25 (7.7% incidence); 1 (86.4% incidence)	RBE_M = 800 (8.7% incidence in beagles), RBE_M = 230 (7.7% incidence in mouse)	RBE was calculated as the ratio of ^{90}Sr dose/ ^{226}Ra dose at a given level of incidence of bone sarcoma, with one of these values coming directly from the data and the other being interpolated from a graph. RBE progressively increased as the dose decreased.	Mays and Finkel (1980)
Mouse (In utero: from conception to birth; Offspring until 8 weeks of age)	Long-term effect to haematopoietic tissue	^{60}Co gamma, (A), Unknown dose-rate, Unknown total dose	^{238}Pu alpha, (A), Unknown dose rate, Doses to foetal liver were 8.7, 12.9 and 41.3 mGy	150	N.E.	The relatively high RBE value could be due to heterogeneity in alpha particle dosimetry or the ineffectiveness of the gamma radiation to cause the biological effect at low doses.	Lord and Mason (1996)
Mouse (Young, BDF1(C57B1 x DBA2))	Spleen colony forming units (CFU-S) in liver	^{60}Co gamma, (A, C), 864 Gy d^{-1}, Unknown total dose	^{239}Pu alpha, (A), 30 Bq g^{-1} i.v. injected, Unknown dose rate, Unknown total dose	250 - 360	N.E.	RBE for chronic irradiation (both alpha and gamma). A repeat experiment gave an RBE of 150. For acute gamma irradiation RBE = 130-180. Uniform distribution assumed. The RBE would be lower if the ^{239}Pu was assumed to be heterogeneously distributed in the liver.	Jiang et al. (1994)

System(s) Studied	**Endpoint**	**Reference Radiation Exposure** (Acute/Chronic, Dose Rate, Total Dose) [a]	**Test Radiation Exposure** (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	**Reported RBE** (95 % CI, where indicated)	**RBE_m/ RBE_M**	**Comments**	**Reference**
Varied, including pig, mouse, rat and several unstated species; rat for determination of alpha RBE	Impairment of tissue integrity and function; specifically spinal cord damage for alpha RBE	X-rays or gamma rays. The reference is just listed as low-LET radiation (Ext, 0.5 - 20 Gy x-rays)	Neutrons of energy ranging from 1 to 50 MeV, heavy ions including carbon, neon and argon ions, and high energy alpha particles. Specific information not provided	For high energy alpha particles, values in the range of 1.0 - 1.5 were obtained for damage to the rat spinal cord.	RBE_m: 4 - 12 (1 - 5MeV Neutrons), 3 - 8 (5 - 50MeV Neutrons), 2 - 5 (Heavy Ions: C, Ne, Ar)	This review paper makes generalisations about RBE and quality factor based on results from previous papers involving different animals, exposure methods and endpoints. Only a single range is given for alpha RBE.	Barendsen (1992)
Mouse (B6D2F1 or BDF1)	Haematopoietic tissue	^{60}Co gamma; (C); 50, 100 and 150 mGy d^{-1}; 0.3 Gy	^{239}Pu Alpha, (A), Unknown dose rate, 0.2 - 0.28 (dose equivalent)	RBE was not calculated in this paper.	Difficult to estimate RBE_m (Survival curves not provided).	The alpha dose from plutonium was calculated assuming a dose equivalent quality factor of 20 (for adults); however, this factor may not be representative for effects in the foetus.	Mason et al. (1992)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute/Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
V79 (Chinese Hamster cell line), HeLa (human cell line), and C3H 10T1/2 (mouse fibroblastcell line)	Cell survival	Alpha particles (30 and 35 MeV; 20 and 23 keV μm^{-1}), (C), 115,200 - 158,400 Gy d^{-1}, 5.04 - 6.24 cGy	Protons (1.2 and 1.4 MeV; 20 and 23 keV μm^{-1}) (Ext), (C), 158,400 - 230,400 Gy d^{-1}, 7.26 - 8.06 cGy	Ratio B at low doses for LET of 20.3keV μm^{-1}: 1.69±0.42 (V79); 1.26±0.36 (HeLa); 0.94±0.27 (HeLa S3) and 0.91±0.18 (C3H 10T1/2). For LET of 23.0 keV μm^{-1}: 1.43±0.37 (V79); 1.31±0.27 (HeLa); 1.28±0.15 (HeLa S3) and 0.91±0.18 (C3H 10T1/2).	N.E.	At low doses, protons were more effective than alpha particles of the same LET in V79 and HeLa cells. C3H 10T½ cells did not show a higher effectiveness for protons compared to alpha particles of the same LET.	Goodhead et al. (1992)

[a] Unless specified, external irradiation.
[b] Unless specified, internal irradiation.
[c] Average skeletal dose, 1 year before death.
[d] N.E. Not estimated. Difficult to estimate RBE_m due to lack of information.

1794 Table C.4. Summary of publications studying RBE for alpha particles to produce chromosomal damage and mutations.

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
V79-4 (Chinese Hamster cell line)	DNA damage (double strand breaks)	250 kV x-rays, (A), 5,472 Gy d^{-1}, 40 - 150 Gy	Alpha (20 - 23 keV μm^{-1}), (A), 115,200 - 230,400 Gy d^{-1}, 40 - 150 Gy	0.68 - 1.68	Curves for all radiations appear linear	The RBE value varied depending on the assay used to analyse the DNA damage (sedimentation or precipitation assay). The RBE could be calculated by using the slope (units of 1/(Dalton*Gy)) of the corresponding curves of initial yield of dsb vs dose.	Jenner et al. (1992)
V79-4 (Chinese Hamster cell line)	DNA damage (double strand breaks)	250 kV x-rays, (A), 5,472 Gy d^{-1}, 40 - 150 Gy	Proton (20 - 23 keV μm^{-1}), (A), 115,200 - 230,400 Gy d^{-1}, 40 - 150 Gy	0.74 - 1.0	Curves for all radiations appear linear	The RBE value varied depending on the assay used to analyse the DNA damage (sedimentation or precipitation assay). The RBE could be calculated by using the slope (units of 1/(Dalton*Gy)) of the corresponding curves of initial yield of dsb vs dose	Jenner et al. (1992)
CHO-K1 (Chinese Hamster ovary cell line)	Mutation rate and primary DNA damage	^{60}Co gamma, Unknown type of exposure, Unknown dos rate, Unknown total dose	^{239}Pu alpha (4.3 MeV, 417 keV μm^{-1}), 4.08 Gy d^{-1}, 0.7 Gy	1.0 - 6.0	N.E. [c]	The RBE value depends upon the sources and endpoint considered. The values reported as RBEs are actually the relative frequencies. There is no explanation of how these values are calculated.	Fisher et al. (1985)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
V79-379A (Chinese Hamster cell line)	Double-Strand Breaks (dsb)	X-ray, 250 kVp, (A), 2,592 Gy d^{-1}, 50 Gy	^{238}Pu Alpha (3MeV; 125 keV μm^{-1}), Neutrons (2.3 MeV); (A); 1,080 Gy d^{-1}; 1.7 and 5.6 Gy (From Graph)	1.0	N.E.	The alpha and neutron irradiations showed a linear relationship (approximately) between dsb induction and lethal lesions, although different than for x-rays. For doses =< 10 Gy, the RBE for dsb induction for alpha particles is higher than the RBE for neutrons (>1), while at higher doses (>20 Gy) the RBE is less than 1.	Prise et al. (1987)
V79-379A (Chinese Hamster lung fibroblast cell line)	DNA double strand breaks (dsb)	250 kVp x-rays, (A), 2,520 Gy d^{-1}, 25 Gy	^{238}Pu alpha (4.3 MeV;105 keV μm^{-1}), (A), 86,400 Gy d^{-1}, Unknown total dose	1.0	RBE_M = 2.4 (calculated from the survival curve provided in figures of this paper)	RBE of 1 (dsb induction) not likely due to experimental conditions, since the survival curve is similar to that of Prise et al. (1987) which used a different method of cell exposure. This RBE (1 for dsb induction) is in agreement with Prise et al. (1987).	Fox and McNally (1990)
Bacteria (Escherichia coli)	Mutation	^{60}Co gamma, Unknown type of exposure, 72,000 - 432,000 Gy/d, 0 - 65 Gy	He ions (26 - 105 keV μm^{-1}), ^{210}Po, ^{238}Pu alpha (120 - 256 keV μm^{-1}); (A); Unknown dose-rate; 22 - 87 Gy (from graph)	1.3 - 2.1	RBE_m=1.06	The reported RBE is what authors call 'Relative lethal effectiveness'. Alpha particle sources or helium ions used in calculations were not consistent with chart and survival curve titles. An assumption was made that the more detailed description of ranges given in text and captions was correct while the use of strictly helium ions for all LETs as implied by chart titles was an oversight. Drosophila and T4 phage results for RBE at different LETs were from other studies.	Nikjoo et al. (1999)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
Human peripheral blood lymphocytes	Chromosome aberrations	^{137}Cs gamma, (A), 720 Gy d^{-1}, 0-4.0 Gy	^{241}Am alpha (2.7 MeV; 150 keV/µm), (A), 144 Gy d^{-1}, 0-1.0 Gy	1.5	RBE_M calculations questionable, due to dosimetry uncertainties	RBE calculated from the relationship of number of dicentrics per cell vs absorbed dose. There are some uncertainties with dosimetry and cell cycle kinetics.	Schmid et al. (1996)
EATC (Ehrlich ascites tumour cell line)	DNA double strand breaks	140 kV x-rays, Unknown type of exposure, 57,888 Gy d^{-1}, Unknown total dose	^{241}Am alpha (surface source Cyclotron exposure) (65 keV μm^{-1}) (Ext), Unknown type of exposure, 18,144 Gy d^{-1}, Unknown total dose	1.6 ± 0.4	N.E.	Details of irradiation procedure and dosimetry in Bertsche (1978), and Bertsche and Iliakis (1981, 1987).	Blöcher (1988)
HF-19 (Human fibroblast cell line)	DNA strand breaks	250 kVp x-rays, (A), 806.4 Gy d^{-1}, 0-9.0 Gy	^{238}Pu alpha (3.24 MeV; 128 keV μm^{-1}), (A), 1,238 Gy d^{-1}, 0 - 5.18 Gy	1.6 - 4.0			Bedford and Goodhead (1989)
V79 (Chinese Hamster Cell line)	Inactivation and mutation	^{60}Co gamma, Unknown type of exposure, Unknown dose rate, 0 - 7.0 Gy	He ions (20-100 keV μm^{-1}), Unknown type of exposure, 576 - 1728 Gy d^{-1}, Unknown total dose	1.7 - 4.3	RBE_m = 3.4-9.0	RBEα is stated as the ratio of the linear terms (alpha coefficients) of the respective dose-response curves. Hence the values were considered as RBE_m.	Cox et al. (1977)
C3H 10T1/2 (Mouse fibroblast cell line)	Dicentrics	80kVp x-rays, (A), 1,440 Gy d^{-1}, Unknown total dose	Alpha (Tandem Accelerator used) (177 keV μm^{-1}), (A), Unknown dose rate, 0 - 3.0 Gy	2.0		Reported RBE for 80% rate. For 37% rate the RBE = 1.8. What the authors call RBE is actually the ratio of effects at a given dose.	Durante et al. (1992)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
Bone marrow cells (Mouse CBA/H)	Chromosomal aberrations	250 kV x-rays; (A); 1,051 Gy d^{-1}, 0.73 Gy min^{-1}; 0.5 Gy	^{239}Pu, (A), 2 10E6Gy d^{-1}, 0.005 - 0.8 Gy	2.0 - 3.0	N.E.	No explanation as to how the RBEs were calculated. The authors noted that the RBE value of 50 - 100 (in utero) is only an estimate due to the uncertainty in the dose to target cells and the possibility of a transfer of clastogenic factors from maternal tissue to foetal haematopoietic tissue.	Kozlowski et al. (2001)
HF-19 (Human fibroblast cell line)	Chromosome breaks	250 kVp x-rays, (A), 806.4 Gy d^{-1}, 0 - 9.0 Gy	^{238}Pu alpha (3.24 MeV; 128 keV μm^{-1}), (A), 1,238 Gy d^{-1}, 0 - 5.18 Gy	2.16	RBE_M = 2.3 (based on figures provided)		Bedford and Goodhead (1989)
V79 (Chinese Hamster Cell line)	Inactivation	^{60}Co gamma, Unknown type of exposure, Unknown dose rate, 0 - 7.0 Gy	^{14}N ions (470 keV μm^{-1}), Unknown type of exposure, 576 - 1728 Gy d^{-1}, Unknown total dose	2.5	RBE_m = 6.2	RBEα is stated as the ratio of the linear terms (alpha coefficients) of the respective dose-response curves. Hence the values were considered as RBE_m.	Cox et al. (1977)
V79 (Chinese Hamster Cell line)	mutation	^{60}Co gamma, Unknown type of exposure, Unknown dose rate, 0 - 7.0 Gy	^{10}B ions (100 - 200 keV μm^{-1}), Unknown type of exposure, 576 - 1728 Gy d^{-1}, Unknown total dose	3.2 - 4.4	RBE_m = 5.2 and 7.9	RBEα is stated as the ratio of the linear terms (alpha coefficients) of the respective dose-response curves. Hence the values were considered as RBE_m.	Cox et al. (1977)
C3H 10T1/2 (Mouse fibroblast cell line)	Chromosome aberrations	80kVp x-rays, (A), 1,440 Gy d^{-1}, Unknown total dose	Alpha (Tandem Accelerator used) (177 keV/μm), (A), Unknown dose rate, 0 - 3.0 Gy	5.1	RBE_M = 2 -10 (Estimated from α/β for x-ray curve, mean lethal dose of alphas and RBEs)	Reported RBE for 80% rate. For 37% rate the RBE = 4.5. What the authors call RBE is actually the ratio of effects at a given dose.	Durante et al. (1992)
Human blood cells	Chromosome aberrations (dicentrics)	250 kVp x-rays and ^{60}Co gamma; Unknown type of exposure; Unknown dose rate; 1, 3 and 5 Gy	^{242}Cm alpha (4.4 MeV;140 keV μm^{-1}), Unknown type of exposure, 9.6 - 14.4 Gy d^{-1}, 0.10 - 4.18 Gy	6.0	RBE=17.9 (with respect to ^{60}Co gamma rays, at low doses)	Reported RBE with respect to x-rays (at the initial slope). ^{60}Co gamma and x-ray data from previous experiments were used.	Edwards et al. (1980)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
EATC (Ehrlich Ascites Tumour Cell line)	Total lethal damage, Unrepaired lethal damage, Potentially lethal damage	0.14 MeV x-rays, Unknown type of exposure, Unknown dose rate, Unknown total dose	Alpha particles (4.3 MeV; 100 keV μm^{-1}), Unknown type of exposure, Unknown dose rate, Unknown total dose	No RBE provided	RBE_m= 6.0 (total lethal damage), 11.6 (unrepaired lethal damage) and 0.8 (potentially lethal damage)	Approximate values of α had to be deduced from the published data (Bertsche and Iliakis, 1981), and this involves some uncertainties. Experimental details in Bertsche and Iliakis (1981).	Bertsche and Ilakis (1987)
C3H 10T1/2 (Mouse fibroblast cell line)	Chromatid aberrations	80kVp x-rays, (A), 1,440 Gy d^{-1} Unknown total dose	Alpha (Tandem Accelerator used) (177 keV μm^{-1}), (A), Unknown dose rate, 0 - 3.0 Gy	6.5		Reported RBE for 80% rate. For 37% rate the RBE = 6.0. What the authors call RBE is actually the ratio of effects at a given dose.	Durante et al. (1992)
C3H 10T1/2 (Mouse fibroblast cell line)	Chromosome breaks	80kVp x-rays, (A), 1,440 Gy d^{-1}, Unknown total dose	Alpha (Tandem Accelerator used) (177 keV μm^{-1}), (A), Unknown dose rate, 0 - 3.0 Gy	7.5		Reported RBE for 80% rate. For 37% rate the RBE = 6.3. What the authors call RBE is actually the ratio of effects at a given dose.	Durante et al. (1992)
C3H 10T1/2 (Mouse fibroblast cell line)	Interstitial deletions	80kVp x-rays, (A), 1,440 Gy d^{-1}, Unknown total dose	Alpha (Tandem Accelerator used) (177 keV μm^{-1}), (A), Unknown dose rate, 0 - 3.0 Gy	8.8		Reported RBE for 80% rate. For 37% rate the RBE = 6.9. What the authors call RBE is actually the ratio of effects at a given dose.	Durante et al. (1992)
Lung fibroblasts (Young male Wistar rats)	Induction of micronuclei	^{60}Co Gamma, (A), Unknown dose rate, Unknown total dose	Radon and its progeny (low energy); 0.98, 1.85 and 2.83 Gy h^{-1} (for 4 hour exposure), 0.06, 0.12 and 0.17 Gy h^{-1} (for 67 hour exposure); Average doses 3.9, 7.4 and 11.3 Gy (exposure details in Brooks et al., 1994),	10.1	RBE_M = 65.2 +/- 8.4 (radon; low dose-rates)	The reported RBE_M value could have been much lower if all the uncertainties were taken into account, as higher calibration values result in proportionally smaller RBE values.	Brooks et al. (1995)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
V79-4 Chinese Hamster Cells 2.3 Lifestage	Mutation frequency (HGPRT)	250 kVp x-ray, (A), 1,094 Gy d^{-1}, 6.0 Gy	^{238}Pu alpha (100 keV μm^{-1}), (Using the 2 independent methods, the dose rate was approximately) 10.8 rad rev^{-1}, 0 - 2.8 Gy (Approximately)	10.3		RBE calculated for HGPRT mutation induction at doses of x-rays reducing survival to 70% (quadratic fit of the x-ray dose response curve). RBE = 9.0 and 7.4 for doses producing 37% and 10% survival, respectively.	Thacker et al. (1982)
C3H/10T1/2 and BALB/3T3 (Mouse fibroblastic cell lines)	Sister chromatid exchanges	220 kVp x-rays, (A), 1,152 Gy d^{-1}, 0 - 6.0 Gy	^{238}Pu alpha (5.4 MeV; 130 keV μm^{-1}), (A), 351.4 Gy d^{-1}, 0 - 2.5 Gy	15.0 – 25.0	RBE_m =11	Reported RBE at low doses (2.5 - 5.0 cGy). It is not clear where the data are coming from as some data are from this paper and some are taken from other experiments.	Nagasawa et al. (1990)
GM 10 (Human - diploid embryonic skin fibroblast cell line)	Induction of mutations	250 kVp x-rays, (A), 2,880 Gy d^{-1}, 1.3 Gy	^{238}Pu alpha (2.9 MeV; 100 keV μm^{-1}), (A), 5,184 Gy d^{-1}, 2.5 Gy	18.0	N.E.	Reported RBE for mutation frequencies of 4 x 10^{-5}. RBE = 13.3 for mutation frequencies of 11 x 10^{-5}. Only the cells in the central part of the dish were uniformly irradiated due to the geometry of the alpha source.	Chen et al. (1984)
Mouse (C3Hx101/2 hybrid male mice mated with outbred 'R' female mice)	Dominant lethal mutations	^{60}Co gamma, (C), 0.057 Gy d^{-1}, 1.6 Gy	^{239}Pu alpha (very low intensities of protracted low LET plutonium irradiation), (A), 8.64 x 10^{-4} Gy d^{-1}, 0.025 Gy	22	N.E.	The alpha RBE was calculated by taking the ratio of the rate of induction of aberrations per rad for the alpha and gamma radiation for each endpoint.	Searle et al. (1976)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
Mouse (C3Hx101/2 hybrid male mice mated with outbred "R" female mice)	Reciprocal translocation	^{60}Co gamma, (C), 0.057 Gy d^{-1}, 1.6 Gy	^{239}Pu alpha (very low intensities of protracted low LET plutonium irradiation), (A), 8.64 x 10^{-4} Gy d^{-1}, 0.025 Gy	24	N.E.	The alpha RBE was calculated by taking the ratio of the rate of induction of aberrations per rad for the alpha and gamma radiation for each endpoint.	Searle et al. (1976)
Mouse (C3Hx101/2 hybrid male mice mated with outbred "R" female mice)	Chromosome fragments	^{60}Co gamma, (C), 0.057 Gy d^{-1}, 1.6 Gy	^{239}Pu alpha (very low intensities of protracted low LET plutonium irradiation), (A), 8.64 x 10^{-4} Gy d^{-1}, 0.025 Gy	24	N.E.	The alpha RBE was calculated by taking the ratio of the rate of induction of aberrations per rad for the alpha and gamma radiation for each endpoint.	Searle et al. (1976)
Chinese Hamster ovary cells	Sister Chromatid Exchange	220 kVp x-rays, (A), 1,152 Gy d^{-1}, 4.0 Gy	^{238}Pu alpha (3.7 MeV;130 keV μm^{-1}), (A), 211.7 Gy d^{-1}, 0.31 to 49 mGy	> 100	N.E.	For calculating the RBE, the authors used x-ray data from a previous study for various hamster cell lines and didn't identify the Chinese Hamster cell lines in this paper.	Nagasawa and Little (1992)
Bone marrow cells (Male mouse CBA/H)	Cytogenetic aberrations in individual colonies of haematopoietic cells	250 kV x-rays, (A), 1,080 Gy d^{-1}, 3.0 Gy	^{238}Pu alpha (3.3 MeV; 121 keV μm^{-1}) , (A), 288 - 1,152 Gy d^{-1}, 0.25, 0.50 and 1.00 Gy	Infinite	N.E.	Study suggests an effective alpha RBE approaching infinity.	Kadhim et al. (1992)

System(s) Studied	Endpoint	Reference Radiation Exposure (Acute or Chronic, Dose Rate, Total Dose) [a]	Test Radiation Exposure (LET, Acute/Chronic, Dose Rate, Total Dose) [b]	Reported RBE (95 % CI, where indicated)	RBE_m/ RBE_M	Comments	Reference
C3H10T1/2 (Mouse fibroblast cell line	Cell transformation in vitro (with comparisons made to cell reproductive death mutation and chromosome aberrations	^{137}Cs gamma rays and 300 kVp x-rays, Unknown type of exposure, Unknown dose rate, Unknown total dose	^{239}Pu was used in the studies by Ullrich (1984) and Lundgren et al. (1987). Unknown type of exposure, Unknown dose-rate, Unknown total dose	5 (For DNA-sized targets), 4 (For nucleosome-sized targets), >100 (for chromatin-sized targets), for slow protons and alpha particles	N.E.	Alpha RBE value wasn't calculated for specific biota, but rather calculated through computer modeling using Monte Carlo track structure computations. Cells from a Chinese hamster were irradiated in vitro with 1.0 MeV neutrons at dose rates of 3.0 and 1.0.	Barendsen (1989) (a review paper)
C3H 10T1/2 (Mouse fibroblast cell line)	Total, unrepaired and potentially lethal damage	225 kVp x-ray, (A), 1,728 Gy d^{-1}, 0 - 7.0 Gy	^{28}Si (50 keV μm^{-1}), ^{12}C (128 keV μm^{-1}); 1,440 - 4,320 Gy d^{-1}; Approximately 0-6.5 Gy (From Graphs)	RBE = 1.0-4.0	RBE_M for total damage = 2.3 (^{28}Si), 7.7 (^{12}C) RBE_M for unrepaired damage 4.23 (^{28}Si) 18.4 (^{12}C) RBE_M for potentially lethal damage = 1.0 (^{28}Si) 0 (^{12}C)		Yang et al. (1985)
V79-4 (Chinese hamster cell line)	Mutation induction (hprt)	Alpha particle beams of incident energy (measured at the entrance cell surface) (35.7 and 30.5 MeV) (Ext), (C), 1,728 - 3,168 Gy d^{-1}, 0.5 - 4.0 Gy	Alpha particles (35.7 and 30.5 MeV; 20.3 - 23 keV μm^{-1}) (Ext), (C), Unknown dose rate, Unknown total dose	The ratio of the coefficient for the protons to that for the alpha particles is 1.85 and 2.07.	N.E.	Effectiveness did not change significantly with the small change in LET of each kind of particle, but for the different particles at the same LET, protons were more effective in mutation induction than alpha particles of the same LET by a factor of about 2 (1.85 at 20 keV μm^{-1} and 2.07 at 23 keV μm^{-1}).	Belli et al. (1992)

[a] Unless specified, external irradiation.
[b] Unless specified, internal irradiation.
[c] N.E. Not estimated. Difficult to estimate RBE_m due to lack of information.

C.1.5. Alpha RBE and experimental system

(C 18) A wide range of experimental test systems, *in vitro* and *in vivo*, have been considered in studies of RBE. A 1967 report of the NCRP presents experimental curves of RBE versus LET for a wide variety of test organisms and endpoints including among others, T1 bacteriophage in broth, haploid yeast survival in air, artemia eggs hatching or emerging, various mammalian tissues, broad leaf bean root effects on growth and survival and others.

(C 19) Studies reported by Chen at al. (1984), Coquerelle et al. (1987), Edwards et al. (1980), Bedford et al. (1989) and Schmid et al. (1996) all focused on alpha RBE with respect to human cells; however, these studies are considered relevant to all mammalian cells and relevant to the current evaluation.

(C 20) Studies of bone carcinoma induction in beagle dogs were reviewed and interpreted in terms of RBE comparing alpha-emitting ^{226}Ra and beta-emitting ^{90}Sr (Mays and Finkel 1980). Amongst other observations, the data indicated that RBE approached or was greater than 20 in the lowest dose ranges but was less at high doses. It was concluded that the RBE for the alpha emitter increased as an inverse function of dose, which was attributed to be mainly due to the relatively low effectiveness per Gy of ^{90}Sr beta particles at low doses and dose rates.

(C 21) The data summarised for mice show a considerable range in RBE for endpoints involving reproductive and haematopoietic systems. Rao et al. (1991) reported an RBE of 245 for sperm head abnormalities from ^{210}Po exposure and a RBE of 6.7 at 37% cell survival (Rao et al., 1989).

(C 22) Knowles (2001) reported studies of fish and found that there was no dose-effect relationship for zebrafish (*Danio rerio*) exposed to alpha particles, since none of the alpha doses were sufficiently high to result in the desired effect of cessation of egg production. Only an upper limit to the RBE could be estimated, which could be a conservative upper limit to the RBE value.

(C 23) Mouse embryo-derived fibroblastic cell lines (C3H 10T1/2 and BALB/3T3) in culture were the model systems used in several of the morbidity studies referenced in this report here.

(C 24) Cell lines from the Chinese hamster, V79 and CHO-K1, were the main model systems used in the in-vitro studies. Reported RBEs ranged from 1 to 7, with an average of approximately 3. The calculated RBE_m ranged from 1.7 to 12.8, with an average of approximately 8.

(C 25) Suzuki et al. (1989) reported on survival of Golden hamster embryo cells and cell transformation due to exposure to heavy ions.

(C 26) Rats (*In Vivo/Ex Vivo):* Reported experimental RBEs for rats in vivo and ex vixo range from 1.1 to 10.7, with an average of approximately 4.

C.2. Concluding remarks on RBEs for alpha particles

C.2.1. Other literature reviews

(C 27) This Section briefly reports on previous evaluations of RBE data other than those previously developed by the ICRP for humans.

(C 28) As previously noted, NCRP (1967) provided a discussion of the concept of RBE of radiation from internal emitters, including discussions of RBE values for somatic effects in mammals and RBE data derived from dose-effect curves for a number of end-points. It was

concluded that the effects of high LET radiations were insensitive to dose rate while effects of low LET radiations were dose-rate dependent. The NCRP report presents experimental curves of RBE versus LET for a variety of test organisms and endpoints and suggests a maximum RBE of about 10 for radiation with a LET of about 300 keV μm^{-1} for human cells in culture.

(C 29) Thompson et al. (2002) summarised RBE values for alpha particles that were estimated in several experiments using various endpoints (Table C.5).

(C 30) Chambers et al. (2005) reviewed published data and summarised their conclusions concerning the range of RBE for different endpoints (Table C.6). Overall, these authors recommended a nominal (biota) radiation weighting factor for alpha particles of 5 for population-relevant endpoints but, to reflect the limitations in the experimental data, also suggested uncertainty ranges of 1–10 and 1–20 for tissue reactions and stochastic endpoints, respectively.

Table C.5. Alpha RBE values (Thompson et al., 2002).

Test System	Endpoint	Alpha Emitter	RBE	Reference
Human Diploid Fibroblasts	chromosome breaks	^{238}Pu	2.16 ± 0.13	Bedford and Goodhead (1989)
Erlich ascites tumour cells	double strand breaks	^{241}Am	2.7 ± 0.4 3.8 ± 1.2 (10 Gy)	Blöcher (1988)
Rat lung fibroblasts	binucleated cells; micronuclei	Radon	65.2 ± 8.4*	Brooks et al. (1995)
Human fibroblasts	cell mortality mutation frequency	^{238}Pu	5.2 13.3, 18	Chen et al. (1984)
Human peripheral lymphocytes	chromosomal aberrations		15	Schmid et al. (1996)
C3H 10T1/2 cells	cell death		4.5 - 5.1 (at 80% cell survival)	Durante et al. (1992)
V79-4 Chinese Hamster cells	double strand breaks	^{238}Pu	1.19 ± 0.18, 1.16 ± 0.16 (23 keV·μm^{-1})	Jenner et al. (1992)
V79-4 Chinese Hamster cells	10% cell survival	^{238}Pu	5.3	Jenner et al. (1993)
V79-4 Chinese Hamster cells	double strand breaks	^{238}Pu	0.68 ± 0.12 (anaerobic = 3.0)	Jenner et al. (1993)
SV40 – transformed Chinese hamster embryo cells	gene sequences	^{238}Pu	6	Lücke-Huhle et al. (1986)
Syrian Hamster embryo cells	10% cell survival	Radon progeny	7 to 12	Martin et al. (1995)
Syrian Hamster embryo cells	Morphological transformation	Radon progeny	60 to 90	Martin et al. (1995)
C3H 10T1/2 cells	cell survival	^{238}Pu	4.6 to 7.9	Roberts and Goodhead (1987)
Chinese Hamster ovary cells	Chromosome damage		15 to 20	Brooks (1975)

(C 31) The reports discussed above and various other authors, among them, Copplestone et al. (2001), Environment Canada and Health Canada (2003), FASSET (2003), Trivedi and Gentner (2002), and UNSCEAR (2008), have provided nominal values (or ranges of values) for a radiation weighting factor, which are summarised in Table C.7. In considering these values, it is important to note that the estimates of RBE are specific to the endpoint studied, the biological, environmental, and exposure conditions (e.g. reference radiation, dose rate, and dose), and other factors. Thus, as noted in a FASSET report (FASSET, 2003), it is difficult to develop a generally valid radiation weighting factor for use in an environmental risk assessment.

Table C.6. Range of RBE Values for alpha particles Reported in Review by Chambers et al. (2005).

Description	Examples	RBE - Median	RBE Range
Population-Relevant Deterministic Endpoints	Cell, Oocyte or Sperm Mortality, Egg Production	3.8	1.3 – 7.9
Other Deterministic Endpoints	Haematopoiesis, Spermhead Abnormality, Lens Opacification	1.22	1.22
Stochastic Endpoints	Chromosomal Aberrations, Mutation, Sister Chromatid Exchange, DSB, Micronuclei	4.8	<1 - 19

Table C.7. Radiation Weighting Factors for Alpha Particles in Non-Human Biota (Relative to Low LET Radiation).

Source	Nominal Value	Comment
NCRP (1991)	1	Built-in conservatism in dose model
IAEA (1992)	20	Keep same as for humans
Barendsen (1992)	2 - 10	Non-stochastic effect of neutrons and heavy-ions
UNSCEAR (1996)	5	Average for tissue reactions
Trivedi and Gentner (2002)	10	Deterministic population-relevant endpoints
Copplestone et al. (UK Environment Agency) (2001)	20	Likely to be conservative for tissue reactions
Environment Canada and Health Canada (2003)	40	Includes studies with high RBEs
ACRP (2002)	5 - 20 (10)	5-10 tissue reactions (cell killing, reproductive) 10-20 cancer, chromosome abnormalities 10, nominal central value
FASSET Deliverable #3 (2003)	5 - 50 (10)	10 o illustrate effect of α RBE

C.2.2. Overall evaluation of alpha RBE

(C 32) Previous evaluations of RBE data for alpha particle emitting radionuclides and the specification of radiation weighting factors for non-human biota include those of FASSET (2003) and UNSCEAR (Annex E, 2008). In order to account for the effect of radiation quality in cases of exposure to internally deposited alpha emitters, FASSET recommended that the absorbed dose be modified by a radiation weighting factor of 10 (FASSET, 2003; Larsson, 2004). In its most recent evaluation of the effects of ionising radiation on non-human biota, UNSCEAR (Annex E, 2008) recommended a modifying factor of 10 to reflect its judgement of the available data on RBE for alpha particles.

(C 33) The current evaluation considered *in vivo* and *in vitro* experimental data. Two significant features were evident from the *in vivo* studies. Firstly, the studies were carried out at relatively low doses and dose rates, and therefore, they were much closer to environmental exposure conditions than *in vitro* tests, which used higher doses and dose rates. Secondly, the endpoints studied were critical from the standpoint of the maintenance of populations of organisms (reproductive performance, effects on oocytes, sperm and immune system health). The majority of studies, notably those showing data for population relevant endpoints, report RBE values <10.

C.3. References

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GLOSSARY

α/β value or ratio

A measure of the curvature of the cell survival curve. The α/β value is also the dose at which the linear and quadratic components of cell killing are equal. For tissues, the α/β value is a measure of their sensitivity to changes in dose fractionation. In vivo, the α component describes the dose–response slope at low doses, which is often considered independent of dose rate, but it is likely that it can be modified in chronic radiation scenarios by cell renewal and cell competition processes. The β component describes the increase in slope at higher doses due to cumulative damage, which is repairable during fractionated or low-dose-rate exposures.

Absorbed dose, *D*

The quotient of dε by d*m*, where dε is the mean energy imparted by ionising radiation to matter of mass d*m*. The unit of absorbed dose is J kg^{-1} and its special name is gray (Gy).

Activity, A

The expectation value of the number of nuclear transformations occurring in a given quantity of material per unit time. The SI unit of activity is per second (s^{-1}) and its special name is becquerel (Bq).

Apoptosis

A mode of cell death in which the cell nucleus displays characteristic densely staining globules, and at least some of the deoxyribonucleic acid (DNA) is subsequently broken down into internucleosomal units. Sometimes postulated to be a ‘programmed’ and therefore potentially controllable process.

Becquerel (Bq)

The special name for the SI unit of activity, 1 Bq = 1 s^{-1} (≈ 2.7 10^{-11} Ci).

Biological half-life

The time required, in the absence of further input, for a biological system or compartment to eliminate, by biological processes, half the amount of a substance (e.g. radioactive material) that has entered it.

Bystander effect

A response in unirradiated cells that is triggered by signals received from irradiated neighbouring cells.

Derived consideration reference level, DCRL

A band of dose rate within which there is likely to be some chance of deleterious effects of ionising radiation occurring to individuals of that type of Reference Animal or Plant (derived from a knowledge of defined expected biological effects for that type of organism) that, when considered together with other relevant information, can be used as a point of reference to optimise the level of effort expended on environmental protection, dependent upon the overall management objectives and the relevant exposure situation.

Deterministic effects

See tissue reactions.

Dose Modifying Factor (DMF)

The ratio of doses with and without modifying agents, causing the same level of biological effect.

Dose Conversion Factor (DCF)

A value that enables the dose to an organism to be calculated on the assumption of a uniform distribution of a radionuclide within or external to the organism, assuming simplified dosimetry, in terms of $(\text{Gy d}^{-1})/(\text{Bq kg}^{-1})$.

Emergency exposure situation

An unexpected situation that occurs during the operation of a practice, requiring urgent action. Emergency exposure situations may arise from practices.

Environmental exposures

All additional radiation exposures of biota in the natural environment as a result of human activities.

Environmental radiological protection

Measures taken to prevent or reduce the frequency of deleterious radiation effects in animals and plants (biota) in their natural environmental setting to a level where they would have a negligible impact on the maintenance of biological diversity, the conservation of species, or the health and status of natural habitats, communities, and ecosystems.

Existing exposure situation

A situation that already exists when a decision on control has to be taken, including natural background radiation and residues from past practices that were operated outside the Commission's recommendations.

Exposure

The co-occurrence or contact between the endpoint organism and the stressor (radiation or radionuclide).

Exposure pathway

A route by which radiation or radionuclides can reach a living organism and cause exposure.

Fluence, Φ

The quotient of dN by da, where dN is the number of particles incident on a sphere of cross-sectional area da. The unit of fluence is m^{-2}.

Gray (Gy)

The special name for the SI unit of absorbed dose: 1 Gy = 1 J kg^{-1}.

Intake, I

Activity that enters the body through the respiratory tract or the gastrointestinal tract or the skin.

Acute intake: A single intake by inhalation or ingestion, taken to occur instantaneously.

Chronic intake: An intake over a specified period of time.

Justification

The process of determining whether either (1) a planned activity involving radiation is, overall, beneficial, i.e. whether the benefits to individuals and to society from introducing or continuing the activity outweigh the harm (including radiation detriment) resulting from the activity; or (2) a proposed remedial action in an emergency or existing exposure situation is likely, overall, to be beneficial, i.e. whether the benefits to individuals and to society (including the reduction in radiation detriment) from introducing or continuing the remedial action outweigh the cost and any harm or damage it causes.

LD_{50}

Dose that is lethal for half of the exposed individuals.

Linear energy transfer (L or LET)

The average linear rate of energy loss of charged particle radiation in a medium, i.e., the radiation energy lost per unit length of path through a material. That is, the quotient of dE by dl where dE is the mean energy lost by a charged particle owing to collisions with electrons in traversing a distance dl in matter:

$$L = \frac{\mathrm{d}E}{\mathrm{d}l}$$

The unit of L is J m^{-1}, often given in keV μ^{-1}.

Linear-quadratic (LQ) dose-response model

A statistical model that expresses the risk of an effect E (e.g. disease, death, or abnormality) as the sum of two components: one proportional to dose (linear term) and the other proportional to the square of dose (quadratic term). $E = \alpha D + \beta D^2$, where D is dose. For cell survival: S =exp -(αD+ βD^2).

Natural environment

A collective term for all of the physical, chemical, and biological conditions within which wild animals and plants normally live.

Optimisation of protection (and safety)

The process of determining what level of protection and safety makes exposures, and the probability and magnitude of potential exposures, as low as reasonably achievable, economic and societal factors being taken into account.

Planned exposure situations

Everyday situations involving the planned operation of sources including decommissioning, disposal of radioactive waste and rehabilitation of the previously occupied land. Practices in operation are planned exposure situations.

Quality factor, Q(L)

The factor characterising the biological effectiveness of a radiation, based on the ionisation density along the tracks of charged particles in tissue. Q is defined as a function of the unrestricted linear energy transfer, L_∞ (often denoted as L or LET), of charged particles in water:

$$Q(L) = \begin{cases} 1 & L < 10 \text{ keV}/\mu\text{m} \\ 0.32L - 2.2 & 10 \leqslant L \leqslant 100 \text{ keV}/\mu\text{m} \\ 300/\sqrt{L} & L > 100 \text{ keV}/\mu\text{m} \end{cases}$$

Q has been superseded by the radiation weighting factor in the definition of equivalent dose, but it is still used in calculating the operational dose equivalent quantities used in monitoring.

Radiation weighting factor, w_R

A practical method (function or numerical value) used to represent relative biological effectiveness for a specific type of radiation, based on existing scientific knowledge and adopted by consensus or via recommendations. Within the system of human radiological protection, it is used to define and derive the equivalent dose from the mean absorbed dose in an organ or tissue.

Reference Animal or Plant, RAP

A hypothetical entity, with the assumed basic biological characteristics of a particular type of animal or plant, as described to the generality of the taxonomic level of family, with defined anatomical, physiological, and life history properties, that can be used for the purposes of relating exposure to dose, and dose to effects, for that type of living organism.

Relative Biological Effectiveness, RBE

The ratio of a dose of a low-LET reference radiation (usually of ^{60}Co γ-rays or kilovoltage x-ray quality) to a dose of the test radiation considered that gives an identical biological effect. RBE values vary with the dose, dose fractionation, dose rate, and biological endpoint considered.

RBE_m

Maximal value of RBE derived from tissue reactions data. There is a dose-dependence to RBE, which reaches a maximal value as the dose drops below approximately 0.1 Gy of x-rays. RBE_m is the calculated ratio of slopes of the dose effect curves at zero dose.

RBE_M

Maximal value of RBE derived for stochastic effects, e.g. carcinogenesis. There is a dose-dependence to RBE, which reaches a maximal value as the dose drops below approximately 0.1 Gy of x-rays. RBE_M is the calculated ratio of slopes of the dose effect curves at zero dose.

Representative organism (RO)

A particular species or group of organisms selected during a site-specific assessment. In many cases the representative organisms chosen for this purpose may be the same

as, or very similar to, the Reference Animals and Plants; but in some cases they may be very different.

Stochastic effects of radiation

Malignant disease or heritable effects; the probability of an effect occurring, but not its severity, is regarded as a function of dose without threshold.

Threshold dose for tissue reactions

Dose estimated to result in only 1% incidence of tissue reactions.

Tissue reactions

Injury in populations of cells, characterised by a threshold dose and an increase in the severity of the reaction as the dose is increased further. Tissue reactions were previously called ‘deterministic effects’. In some cases, tissue reactions are modifiable by postirradiation procedures including health care and biological response modifiers.

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This report provides a review and summary of studies that allow the derivation of radiation weighting factors for alpha emitting radionuclides and low energy beta emitters such as tritium for application in dose assessment for Reference Animals and Plants (RAPs) taking into account different endpoints that are relevant for protection of populations of biota (mortality, fertility, morbidity). The use of the proposed values is discussed.

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