

ANNALS OF THE ICRP

PUBLICATION 148

Radiation Weighting for Reference Animals and Plants

VOLUME 50 NO. 2, 2021

ISSN 0146-6453 • ISBN 9781529777468



Annals of the ICRP

Published on behalf of the International Commission
on Radiological Protection

Aims and Scope

The International Commission on Radiological Protection (ICRP) is the primary body in protection against ionising radiation. ICRP is a registered charity and is thus an independent non-governmental organisation created at the 1928 International Congress of Radiology to advance for the public benefit the science of radiological protection. ICRP provides recommendations and guidance on protection against the risks associated with ionising radiation from artificial sources such as those widely used in medicine, general industry, and nuclear enterprises, and from naturally occurring sources. These are published approximately four times each year on behalf of ICRP as the journal *Annals of the ICRP*. Each issue provides in-depth coverage of a specific subject area.

Subscribers to the journal receive each new publication as soon as it appears so that they are kept up to date on the latest developments in this important field. While many subscribers prefer to acquire a complete set of ICRP publications, single issues of the journal are also available separately for those individuals and organisations needing a single publication covering their own field of interest. Please order through your bookseller, subscription agent, or direct from the publisher.

ICRP is an independent international network of specialists in various fields of radiological protection, typically numbering more than two hundred eminent scientists, policy makers, and practitioners from around the world. ICRP is composed of a Main Commission, a Scientific Secretariat, four standing Committees (on radiation effects, doses from radiation exposure, protection in medicine, and the application of ICRP recommendations), and generally about twenty Task Groups.

The Main Commission consists of a Chair and twelve other members. Committees typically comprise just over 15 members each. Task Groups are usually chaired by an ICRP Committee member and usually contain a number of specialists from beyond the Main Commission and Committees. They are assigned the responsibility for drafting reports on various subjects, which are reviewed and finally approved by the Main Commission. These reports are then published as *Annals of the ICRP*.

For further information please visit www.icrp.org, or contact *Annals of the ICRP* Editor-in-Chief and ICRP Scientific Secretary C.H. Clement at sci.sec@icrp.org.

Annals of the ICRP

ICRP PUBLICATION 148

Radiation Weighting for Reference Animals and Plants

Editor-in-Chief
C.H. CLEMENT

Associate Editor
H. FUJITA

Authors on behalf of ICRP
K. Higley, A. Real, D. Chambers

PUBLISHED FOR

The International Commission on Radiological Protection

by



Please cite this issue as 'ICRP, 2021. Radiation weighting
for Reference Animals and Plants. ICRP Publication 148.
Ann. ICRP 50(2).'



CONTENTS

GUEST EDITORIAL	05
ABSTRACT	09
MAIN POINTS	11
1. INTRODUCTION	12
1.1. The Commission's position on environmental protection	13
1.2. Relevance of relative biological effectiveness to Reference Animals and Plants	15
2. RELATIVE BIOLOGICAL EFFECTIVENESS OF TRITIUM BETA PARTICLES	19
2.1. Introduction	19
2.2. Relative biological effectiveness values for tritium beta particles for different biological endpoints	20
2.3. Conclusions	22
3. RELATIVE BIOLOGICAL EFFECTIVENESS OF ALPHA PARTICLES	25
3.1. Introduction	25
3.2. Relative biological effectiveness values for alpha particles for different biological endpoints	26
3.3. Conclusions	28
4. OVERALL CONCLUSIONS AND RECOMMENDATIONS	29
REFERENCES	31
ANNEX A. RELATIVE BIOLOGICAL EFFECTIVENESS IN THE CONTEXT OF PROTECTION OF THE ENVIRONMENT	33
A.1. Relative biological effectiveness	33
A.2. Modelling of dose response for cell survival	40
A.3. Prior reports on relative biological effectiveness	42
A.4. References	44
ANNEX B. RELATIVE BIOLOGICAL EFFECTIVENESS OF TRITIUM BETA PARTICLES	47

B.1. Review of experimental studies on relative biological effectiveness of tritium beta particles	48
B.2. Other literature reviews of relative biological effectiveness of tritium beta particles.	71
B.3. Overall evaluation of relative biological effectiveness of tritium beta particles.....	78
B.4. References.....	78
ANNEX C. RELATIVE BIOLOGICAL EFFECTIVENESS OF ALPHA-EMITTING RADIONUCLIDES	81
C.1. Review of experimental studies of relative biological effectiveness of alpha-emitting radionuclides	81
C.2. Concluding remarks on relative biological effectiveness of alpha particles.....	118
C.3. References.....	123
GLOSSARY.....	129
ACKNOWLEDGEMENTS.....	131

Guest Editorial

SENSIBLE ADVICE FOR MAKING MORE REALISTIC ASSESSMENTS OF DOSE FOR BIOTA UNDER DIFFERENT EXPOSURE SITUATIONS

One of the first issues to arise in the development of a set of Reference Animals and Plants by the International Commission on Radiological Protection (ICRP) was that of allowing for factors such as relative biological effectiveness (RBE) in considerations of estimates of dose (ICRP, 2003, 2008). The issue was not a new one. The need to consider such factors had been widely recognised for many years, and for several reasons. Firstly, RBE obviously applies to animals other than humans; indeed, much of the RBE information used in human radiological protection had been derived from both in-vivo and in-vitro animal studies. It thus seemed reasonable that allowance should be made for such information in assessments of the relationship between dose and effects for those same animals in the context of their exposures to radiation in an environmental context. Secondly, it was known that many animals and plants can accumulate concentrations of naturally occurring alpha-particle-emitting nuclides within their tissues to very high levels, and thus there had been arguments for the use of 'weighting factors' to normalise assessments of comparative radiation background dose rates amongst different types of fauna and flora. Finally, because of the presence of alpha-particle-emitting nuclides (and, in some cases, tritium) in many environmental areas, as a result of different exposure situations, there had been concerns that their potential effects on wildlife would be underestimated if allowances for RBE were not taken into account.

Due to these uncertainties, various attempts to address them, or at least to highlight them, were made for some considerable time. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1996) suggested that a weighting factor of 5 should be used for internal alpha emitters based on an evaluation of reproductive (tissue reaction) endpoints for all living things other than humans, but no recommendations were made for low-energy beta-particle-emitting nuclides. Subsequently, and in view of the apparent general lack of interest in pursuing the issue further, a number of approaches were proposed by various groups and individuals. One was simply to refer to high- and low-linear energy transfer (LET) components of the dose rate separately; however, this approach was considered to be too clumsy. Another approach was to use a dose equivalent for fauna and flora, being the product of Gy and a 'qualifying factor'; the starting place for the latter was the LET of radiation in water as it was thought that this

could be used until more reliable or relevant information became available (Pentreath, 1999). The term ‘dose equivalent for fauna and flora’ was chosen deliberately because it gave the acronym ‘DEFF’ – a term deemed appropriate at the time because all of the relevant bodies appeared to be turning a deaf ear to various requests to resolve the issue.

However, interest in the problem was growing. At about the same time, Trivedi and Gentner (2000) suggested a somewhat different approach – deriving a weighting factor, the ‘ecodosimetry weighting factor (e_R)’, except for stochastic effects at low doses, because it was believed that not all non-human species developed cancer. Yet another suggestion came from a working group of the International Atomic Energy Agency (IAEA, 2000). They suggested that the term ‘(radiation) weighted absorbed dose (rate)’ should be used generally for protection of the environment. This group defined w_R as the ‘radiation weighting factor appropriate to the organism, effects endpoint and dose rate’. Kocher and Trabalka (2000) made a case for incorporating relevant biological effectiveness of different radiation types when expressing dose or dose limits for biota. Their work was related to the ongoing effort by the US Department of Energy (2002) to develop and implement a comprehensive system of radiological protection of the environment. At about the same time, Environment Canada (2000) proposed an RBE weighting factor for the ecological assessment of ecologically significant alpha-particle-emitting radionuclides in the environment under Canada’s Priority Substances List 2. This was based on work subsequently published by Thompson et al. (2003). The Canadian Nuclear Safety Commission’s Advisory Committee on Radiological Protection (ACRP, 2002) recommended that such a radiation weighting factor would be appropriate for protecting all biota against ‘ecologically relevant deleterious effects’. They concluded that all studies implying higher RBEs for some endpoints in animals had serious problems, either with alpha dosimetry or with poor statistics, and a Canadian consulting firm also commented on the methodological flaws in the studies that purported to support high RBEs for alpha-particle emitters (SENES, 2005). On a more practical basis, Chambers et al. (2006) identified 66 relevant measurements of alpha RBE and assigned them to one of three broad categories: population-relevant tissue reaction endpoints such as cell mortality, oocyte mortality, and sperm mortality; other tissue reaction endpoints such as haemopoiesis, sperm head abnormality, and lens opacity; and stochastic endpoints such as chromosomal aberration, double-stranded breaks, and mutation.

There had therefore been no shortage of suggestions with regard to how best to allow for RBE in assessing dose rates to non-human biota, and no shortage of suggestions on what any necessary term should be called. The issue became more acute, however, when the framework developed by ICRP required dose rates for Reference Organisms to be compared with bands of derived consideration reference levels (DCRLs) that had been based on radiation effects data for different types of biota (Reference Animals and Plants) because the results of such comparisons were

intended to guide what action might be considered in different exposure situations (ICRP, 2008). Quite simply: how, when the principal nuclides of concern were alpha-particle emitters or those of low LET, could one calculate realistic dose rates to biota in order to compare them with the DCRLs?

Unfortunately, none of the studies that had been undertaken contained exhaustive reviews of all of the available data, although there had been various suggestions about what numerical values might be appropriate. There is, of course, a difference between RBE, which is a biological observation in a particular experimental setting, and a weighting factor, which is a practical aggregation of data to inform and assist protective measures. Bearing this in mind, ICRP established a task group to examine the issue with regard to the framework it had developed for non-human biota. This was back in 2007. Since then, there have been many iterations of draft texts; many consultations and views aired, including by way of the ICRP symposia (Higley et al., 2012); and further analyses of databases and suggestions of values made, such as that of 10 for alpha-particle emitters by UNSCEAR (2008). It is therefore to the great credit, and no doubt great relief, of those members of Task Group 72 that this undertaking has at last been brought to a conclusion. There will be many, no doubt, who will still debate the issue, and that is how it should be. However, at least it is now possible to bring some uniformity to the various studies that have related – and future studies that will relate – exposure to dose for biota in different environmental exposure situations, as now set out by ICRP (2014), and it provides a basis for further numerical examination of this issue.

RICHARD JOHN (JAN) PENTREATH
EMERITUS MEMBER, MAIN COMMISSION, ICRP

References

- ACRP, 2002. Protection of Non-human Biota from Ionizing Radiation. Advisory Committee on Radiological Protection. INFO-0703. Canadian Nuclear Safety Commission, Ottawa, ON.
- Chambers, D.B., Osborne, R.V., Garva, A.L., 2006. Choosing an alpha radiation weighting factor for doses to non-human biota. *J. Environ. Radioact.* 87, 1–14.
- Environment Canada, 2000. Priority Substances List Assessment Report (PSL2). Releases of Radionuclides from Nuclear Facilities (Impact on Non-human Biota). Environment Canada and Health Canada, Ottawa, ON.
- Higley, K.A., Kocher, D.C., Real, A.G., et al., 2012. Relative biological effectiveness and radiation weighting factors in the context of animals and plants. *Ann. ICRP* 41 (3/4), 233–245.
- IAEA, 2000. Department of Nuclear Safety, Division of Radiation and Waste Safety. Specialists' Meeting on Protection of the Environment from the Effects of Ionizing Radiation: International Perspectives. Working Group on Dosimetry, Quantities and Units and Compliance. International Atomic Energy Agency, Vienna.

- ICRP, 2003. A framework for assessing the impact of ionising radiation on non-human species. ICRP Publication 91. Ann. ICRP 33(3).
- ICRP, 2008. Environmental protection – the concept and use of Reference Animals and Plants. ICRP Publication 108. Ann. ICRP 38(4–6).
- ICRP, 2014. Protection of the environment under different exposure situations. ICRP Publication 124. Ann. ICRP 43(1).
- Kocher, D.C., Trabalka, J.R., 2000. On the application of a radiation weighting factor for alpha particles in protection of non-human biota. *Health Phys.* 79, 407–411.
- Pentreath, R.J., 1999. A system of radiological protection of the environment: some initial thoughts and ideas. *J. Radiol. Prot.* 19, 117–128.
- SENES, 2005. Review and Evaluation of Published Literature on Alpha Radiation Weighting Factors for Non-human Biota. COGEMA, Saskatoon, SK.
- Thompson, P.A., Macdonald, C.R., Harrison, F., 2003. Recommended RBE Weighting Factor for the Ecological Risk Assessment of Alpha-emitting Radionuclides. Third International Symposium on Protection of the Environment from Ionizing Radiation (SPEIR 3), 22–26 July 2002, Darwin, Australia, pp. 93–102.
- Trivedi, A., Gentner, N.E., 2000. Ecdosimetry Weighting Factor (e_R) for Non-human Biota. 10th International Conference of the International Radiation Protection Association, 14–19 May 2000, Hiroshima, Japan.
- UNSCEAR, 1996. Sources and Effects of Ionizing Radiation. Report to the General Assembly, with Scientific Annex. United Nations Sales Publication E.96.IX.3. United Nations Scientific Committee on the Effects of Atomic Radiation, New York.
- UNSCEAR, 2008. Effects of Ionizing Radiation. UNSCEAR 2006 Report to the General Assembly, with Scientific Annexes. Annex E. Effects of Ionising Radiation on Non-Human Biota. United Nations Scientific Committee on the Effects of Atomic Radiation, New York.
- US Department of Energy, 2002. A Graded Approach for Evaluating Radiation Doses to Aquatic and Terrestrial Biota. DOE-STD-1153-2002. US Department of Energy, Washington, DC.

RADIATION WEIGHTING FOR REFERENCE ANIMALS AND PLANTS

ICRP PUBLICATION 148

Approved by the Commission in May 2019

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 determined experimentally 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. RBE values have been measured for a variety of endpoints 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 the 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 by 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. This publication reviews RBE data relevant to biota for one low-energy beta emitter (tritium) and for alpha-emitting radionuclides. 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 substantially higher. It is proposed that an RBE weighted absorbed dose should be used for protection purposes, with an RBE weighting for biota of 1 for all low-LET radiations and 10 for alpha particles. 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, the use of higher RBE values may be warranted.

© 2021 ICRP. Published by SAGE.

Keywords: DCRL; RBE; tritium; radiation weighting

MAIN POINTS

- This publication reviews data from studies of the relative biological effectiveness (RBE) of: (i) low-energy beta particle emissions from tritium; and (ii) alpha-particle-emitting radionuclides. RBE values are determined experimentally 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.
- 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 weightings of absorbed dose for biota to apply to all population-relevant endpoints as single values for all Reference Animals and Plants (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 derived consideration reference level (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 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 (UNSCEAR, 2008). Due to 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 12 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 1.1).

Table 1.1. Identification and description of the Reference Animals and Plants 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 day^{-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. 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 of a population thus exposed. The DCRLs considered to be most appropriate, based on the current level of knowledge, are shown in Fig. 1.1. The DCRLs as presented in Fig 1.1 do not include radiation weighting.

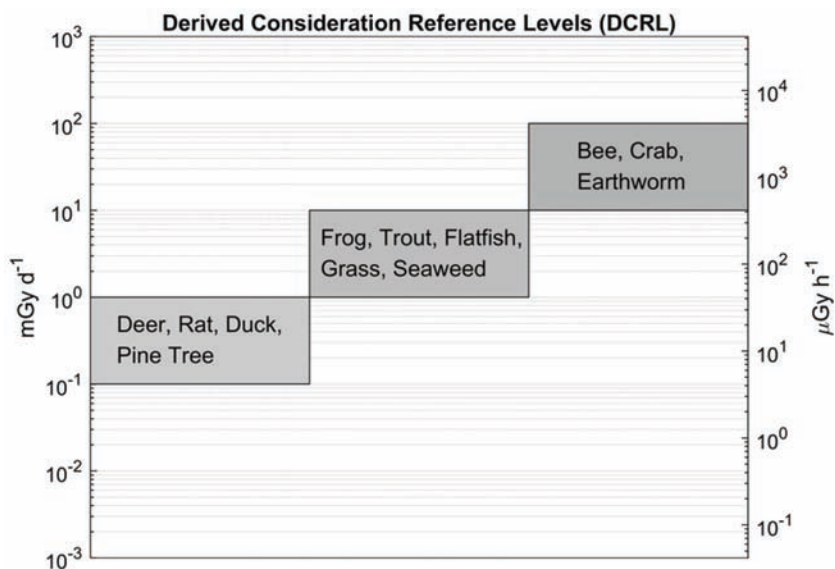


Fig. 1.1. Derived consideration reference levels for environmental protection for the Reference Animals and Plants.

(3) As 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 differences in such factors then need to be taken into account, and the impact on the final decision on the RBE value to use, 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 ($\mu\text{Gy h}^{-1} \text{Bq}^{-1} \text{kg}$) averaged over the mass of the organism. For internal exposures, values are given separately for alpha particles, low-energy beta particles and gamma radiation (effective dose <10 keV), and all other beta and gamma radiations (effective dose >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 sieverts (Sv). The w_R values are chosen largely on the basis of experimental data on the relative biological effectiveness (RBE) of different radiation types determined for biological endpoints 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 publication 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 radiation weighted absorbed dose rates for comparison with DCRLs and corresponding data for ROs. This publication has also identified the considerable need for collection of RBE data for additional species.

1.2. Relevance of relative biological effectiveness 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, and 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). Based on the current paucity of 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 not currently assessed for their impact on 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 publication, biological data are considered in four categories: mortality, reproductive dysfunction, 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 chromosomal damage are included together with directly relevant data on tissue reactions.

(9) ICRP has previously reviewed RBE data on stochastic effects as the basis for setting w_R values for the calculation of equivalent and effective dose (Sv) for humans (ICRP, 2003, 2007). Effective dose is used to set limits, constraints, and reference levels, and in the optimisation of protection against cancer and heritable effects. ICRP also sets limits on equivalent dose to tissues to prevent tissue reactions (hand, feet, skin, lens of the eye) (ICRP, 2007), 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 4, with higher values at lower energies. A w_R value of 20 is used for alpha particles for all cancer types and hereditary effects, although the available data suggest that RBE will differ for different endpoints (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 non-human species, 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 RBE 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 species or populations. To that end, it may be important to take RBE into account 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 effects are deterministic or stochastic. There is much research that remains to clarify the mechanisms that may be at work in causing 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 has also previously reviewed RBE data on tissue reactions, considering alpha particles, neutrons, and heavy ions; the data and analyses provided are referred to in Annexes A and C (ICRP, 1990). 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 RBE data reviewed in detail in Annexes B (tritium) and C (alpha-emitting radionuclides), and conclude by providing radiation weighting factors 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 RBE of 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 studied the most frequently (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 RBE values 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, 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 used more frequently (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 the 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 (mean 5.7 keV), the track average LET of tritium in water from secondary electrons is $4.70 \text{ keV } \mu\text{m}^{-1}$. This can be compared, for example, with the 0.22 and $0.52 \text{ keV } \mu\text{m}^{-1}$ track average LET in water generated from the 1173- and 1332-keV gamma rays of ^{60}Co (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 the gamma rays of ^{60}Co (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 administered internally and the absorbed dose estimated. Although the range of tritium beta particles in tissues is low, the uniform distribution of tritium as HTO 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 rays 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 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 dysfunction, morbidity, and chromosomal damage and mutations.

(22) In the summaries provided below for the different endpoints, 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 the reference radiation than when the comparison is with x rays.

2.2. Relative biological effectiveness 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 of 1.0–1.7 (three values available) for a rodent and a terrestrial vascular plant (Fig. 2.1). All relate to HTO.

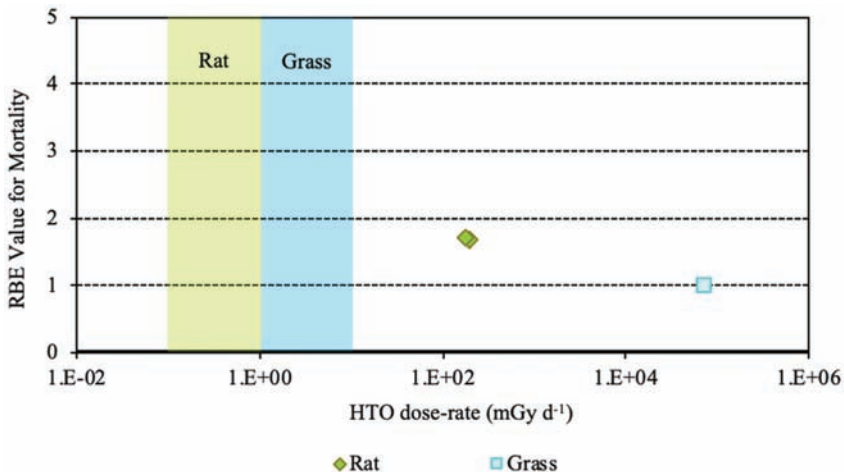


Fig. 2.1. Relative biological effectiveness (RBE) as a function of dose rate from tritium beta particles [tritiated water (HTO)] for early mortality. The derived consideration reference levels (mGy day⁻¹) for environmental protection for each Reference Animal and Plant are shown as coloured bands of green and blue.

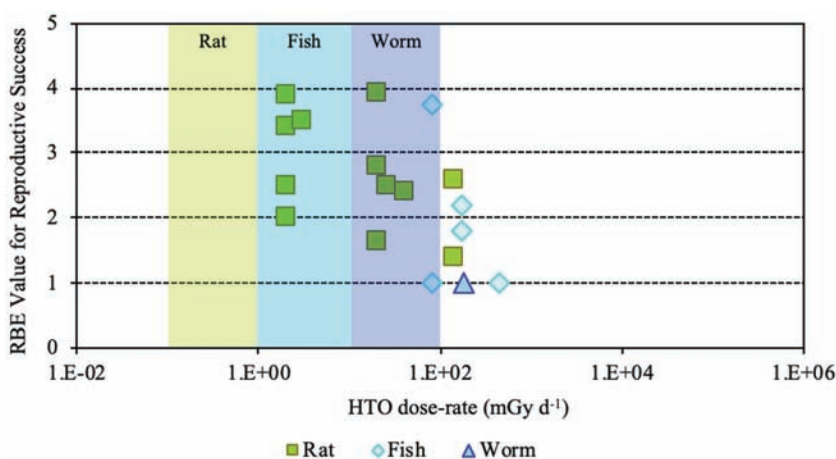


Fig. 2.2. Relative biological effectiveness (RBE) as a function of dose rate from tritium beta particles [tritiated water (HTO)] for reproductive dysfunction. The derived consideration reference levels (mGy day^{-1}) for environmental protection for each Reference Animal and Plant are shown as coloured bands of green, blue, and darker blue.

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

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

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

(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 endpoints 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.

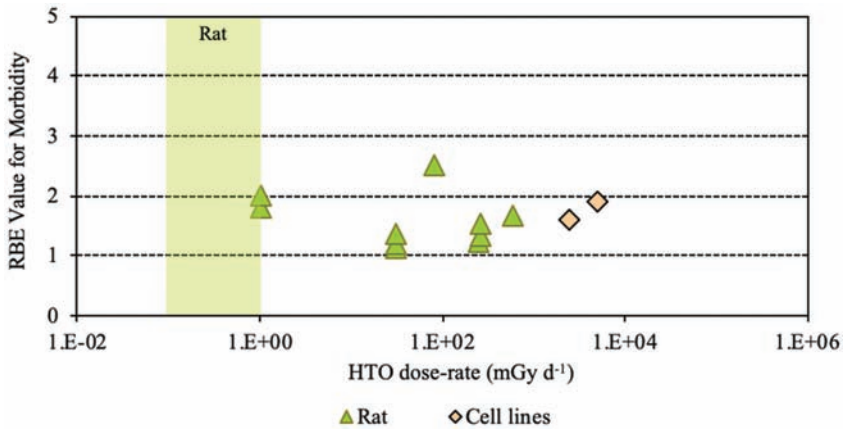


Fig. 2.3. Relative biological effectiveness (RBE) as a function of dose rate from tritium beta particles [tritiated water (HTO)] for morbidity. The derived consideration reference levels (mGy day⁻¹) for environmental protection for the Reference Animal is shown as a coloured band of green.

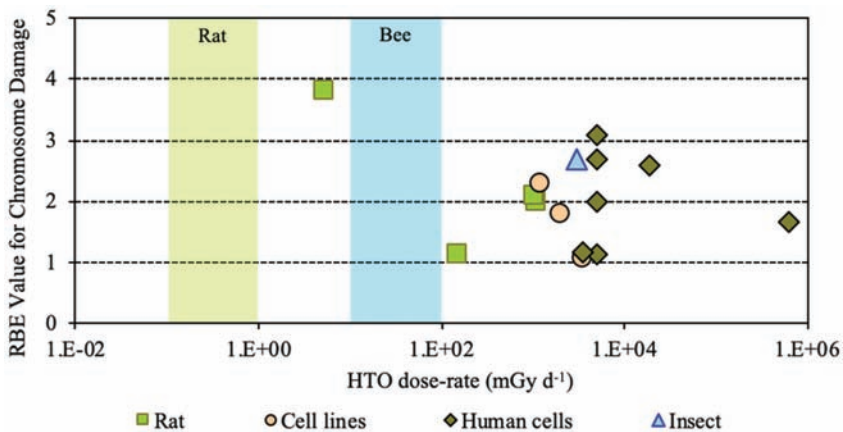


Fig. 2.4. Relative biological effectiveness (RBE) as a function of dose rate from tritium beta particles [tritiated water (HTO)] for chromosomal damage and mutation. The derived consideration reference levels (mGy day⁻¹) for environmental protection for each Reference Animal and Plant are shown as coloured bands of green and blue.

2.3. Conclusions

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

Table 2.1. Ranges of relative biological effectiveness (RBE) values described in the literature for tritium beta particles (tritium administered as tritiated water).

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; chromosomal aberrations; vertebral abnormality; tumour incidence	Embryo survival; chromosomal aberrations; cell survival; mutations	42	Fish; plant; marine invertebrate; mammals (mouse, rat, hamster, human primary cells, cell lines)
2–3	Reproductive capacity (germ cell 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; dicentric aberrations; mutations	25	Fish; insect; mammals (mouse, rat, human primary cells, cell lines)
3–4	Reproductive capacity; chromosomal aberrations and mutations	Chromosomal aberrations; mutations	7	Fish; mammals (mouse, human primary cells, cell lines)

(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 with other radionuclides, the majority (approximately 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 higher-energy electrons.

(31) The spread of data for fish are from 1 to nearly 4, with a value for an aquatic invertebrate of approximately 1. The same range was seen for rats, showing consistency across species. For reduced reproductive success, 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).

3. RELATIVE BIOLOGICAL EFFECTIVENESS OF ALPHA PARTICLES

3.1. Introduction

(33) A review of the data available on RBE of alpha particles and corresponding citations are given in Annex C; a summary of the main data is included here. Approximately 90 articles were found that discussed studies relevant to the RBE of alpha particles 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.

Table 3.1. Summary of reported relative biological effectiveness (RBE) values* 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, mouse, hamster, rat, cell lines, tumour cells)

*RBE values are as reported from the original reference. Thirty-six studies provided sufficient information to calculate RBE_m (maximum RBE for tissue reactions), with 72% of values <10. Fourteen studies had sufficient information to calculate RBE_M (maximum RBE for stochastic endpoints), with 64% of values <10. See Annex C for more information.

(34) Most of the reviewed papers either reported RBE values directly, or provided sufficient data from exposure–effect models or survival curves from which the RBE for alpha particles 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 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 publication.

3.2. Relative biological effectiveness values for alpha particles for different biological endpoints

(36) In mammals, mortality is a result of extensive irradiation that causes severe cell depletion, leading to dysfunction of major organs. Death of the organism 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 dysfunction. 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 RBE values obtained using x rays as the reference radiation 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 1–5, with very few papers reporting RBE values for alpha particles >5 . Most RBE values were obtained from studies using rodents or rodent cells exposed to high doses at high dose rates. Reported RBE values vs dose rate are shown in Fig. 3.1 for studies related to reproductive dysfunction.

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

(39) Twenty-six 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 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

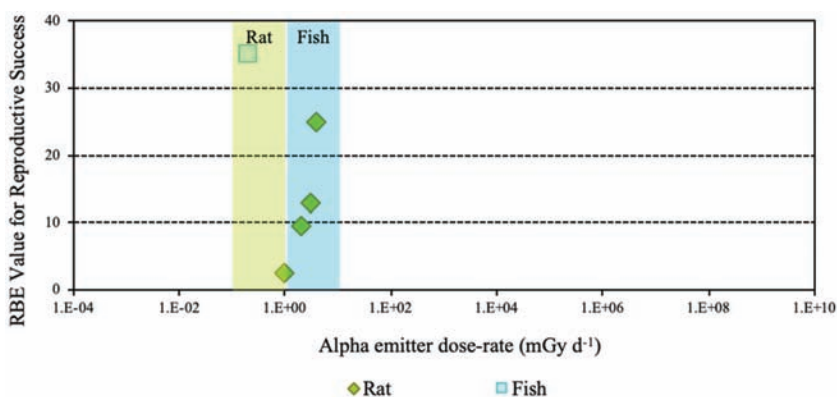
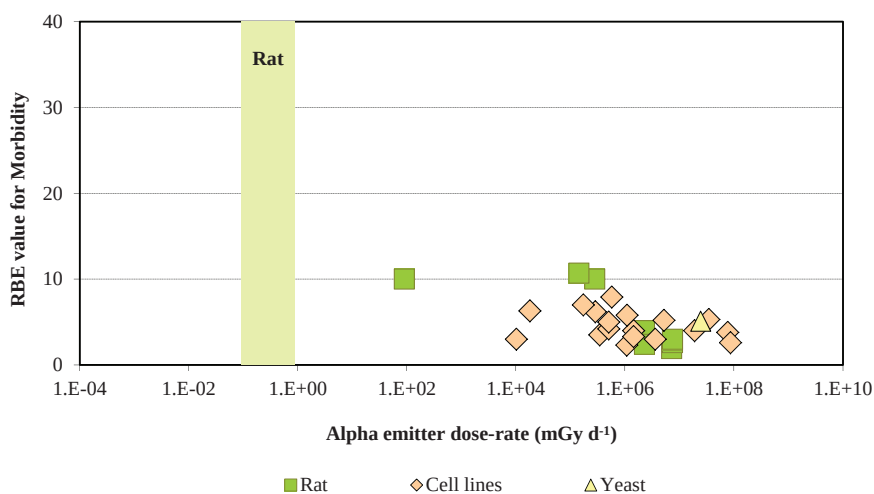


Fig. 3.1. Relative biological effectiveness (RBE) as a function of dose rate from alpha emitters for reproductive dysfunction. The derived consideration reference levels (mGy day^{-1}) for environmental protection for each Reference Animal and Plant are shown as coloured bands of green and blue.



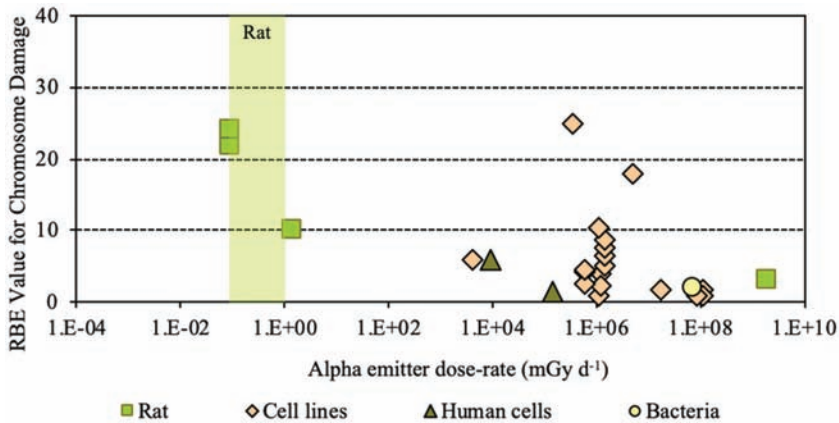


Fig. 3.3. Relative biological effectiveness (RBE) as a function of dose rate from alpha emitters for chromosomal damage and mutations. The derived consideration reference level (mGy day^{-1}) for environmental protection for the Reference Animal and Plant is shown as a coloured band of green. Cell lines include rodent fibroblasts and human lymphocytes.

(40) In the graphical and tabulated summaries provided below for the different endpoints, 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 the reference radiation than when the comparison is with x rays.

3.3. Conclusions

(41) As for tritium, it is evident that the data available for alpha emitters are primarily relevant to vertebrates – essentially to small mammals – and with respect to reproductive dysfunction and morbidity. Overall, the non-human biota data on RBE of alpha particles 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 <35 represented an upper limit, and that the actual value was more likely to be in the range of $7\text{--}<20$. Additionally, alpha dosimetry is complex due to its heterogeneous distribution and the short range of energy deposition. Such factors should be considered in detail when assessing impacts from alpha emitters.

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

4. OVERALL CONCLUSIONS AND RECOMMENDATIONS

(43) This publication 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 endpoint 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 Section 1). This publication has also identified the considerable need for collection of RBE data for additional species.

(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 survival, these considerations are complicated by the existence of thresholds below which no effects are observed. However, it appears that extrapolated RBE values 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 publication, 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 endpoints were considered in four categories: mortality, reproductive dysfunction, morbidity, and chromosomal damage/mutations. While the first two categories can clearly be considered as tissue reactions and relevant to survival, some of the morbidity studies and all chromosomal damage/mutation studies relate to stochastic effects, and their relevance in the context of this publication 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 no clear difference in the ranges of RBE values observed for the various endpoints. In proposing radiation weighting for general application, therefore, it is reasonable to consider the entirety of the available data.

(46) Consistent with the approach taken in specifying weighting factors used in the protection of humans, it is recommended that an RBE weighting factor of 1 should be used for all low-LET radiations, and a value of 10 should be used for alpha particles in assessments of exposures and comparison of estimated doses with the relevant DCRL. If internal 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 of the absorbed doses 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 of beta and gamma radiation. The 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.

REFERENCES

- Environment Canada, Health Canada, 2003. Priority Substances List Assessment Report. Releases of Radionuclides from Nuclear Facilities (Impact on Non-Human Biota). PSL2. Environment Canada and Health Canada, Ottawa.
- ICRP, 1990. RBE for deterministic effects. ICRP Publication 58. Ann. ICRP 20(4).
- ICRP, 2003. Relative biological effectiveness, radiation weighting and quality factor. ICRP Publication 92. Ann. ICRP 33(4).
- ICRP, 2007. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Ann. ICRP 37(2–4).
- ICRP, 2008. Environmental protection – the concept and use of Reference Animals and Plants. ICRP Publication 108. Ann. ICRP 38(4–6).
- ICRP, 2014. Protection of the environment under different exposure situations. ICRP Publication 124. Ann. ICRP 43(1).
- ICRP, 2017. Dose coefficients for non-human biota environmentally exposed to radiation. ICRP Publication 136. Ann. ICRP 46(2).
- ICRU, 1970. Linear energy transfer. ICRU Report 16. International Commission on Radiation Units and Measurements, Bethesda, MA.
- Knowles, J.F., 2001. An Investigation into the Effects of Chronic Radiation on Fish. R&D Technical Report P3-053/TR. Centre for Environment, Fisheries & Aquaculture Science, Lowestoft, pp. 1–42.
- Kocher, D.C., Apostolaei, A.I., Hoffman, F.O., 2005. Radiation effectiveness factors for use in calculating probability of causation of radiogenic cancers. Health Phys. 89, 3–32.
- Little, M.P., Lambert, B.E., 2008. Systematic review of experimental studies of relative biological effectiveness of tritium. Radiat. Environ. Biophys. 47, 71–73.
- Nikjoo, H., Goodhead, D.T., 1991. Track structure analysis illustrating the prominent role of low energy electrons in radiobiological effects of low-LET radiations. Phys. Med. Biol. 36, 229–238.
- Straume, T., Carsten, A.L., 1993. Tritium radiobiology and relative biological effectiveness. Health Phys. 65, 657–672.
- UNSCEAR, 2008. Sources and Effects of Ionizing Radiation. UNSCEAR 2008 Report to the General Assembly, with Scientific Annexes. Annex E. Effects of Ionising Radiation on Non-Human Biota. United Nations Scientific Committee on the Effects of Atomic Radiation, New York.
- UNSCEAR, 2016. Sources, Effects and Risks of Ionizing Radiation. UNSCEAR 2016 Report to the General Assembly with Scientific Annexes. Annex C. Biological Effects of Selected Internal Emitters – Tritium. United Nations Scientific Committee on the Effects of Atomic Radiation, New York.

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

(A1) 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 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 RBE. The term ‘RBE’ applies to observations from experimental studies, and is specific to the endpoint and system studied, and 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 RBE values obtained in studies at high doses to low doses of concern to radiological protection, especially extrapolation of RBE values for tissue reactions; and extrapolation of RBE values for cells to higher levels of biological organisation including whole organisms.

A.1. Relative biological effectiveness

(A2) 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), or that each dose response be a proportional (linear) relationship.

(A3) In most studies to estimate RBE, 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 tritium decay), and the reference radiation is higher-energy gamma rays (photons), such as those emitted in ^{60}Co decay. Any radiation of interest and reference radiation can be chosen, provided that they differ in quality (LET).

(A4) When an RBE value 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 type

(stochastic or deterministic), or to other radiations of similar LET, the resulting inference about biological effectiveness is not strictly RBE as this term is defined above. Nonetheless, the term ‘RBE’ is widely used to describe inferred RBE that is based on specific radiobiological studies.

A.1.1. Factors that influence relative biological effectiveness

(A5) 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 type). Certain other factors can also be important.

A.1.1.1. Choice of reference radiation

(A6) Reference radiations used in radiobiological studies to estimate RBE are usually 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 radiation.

(A7) 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 NCRP (1990) and ICRP (2003) suggest that, at low doses of interest in the radiological protection of humans, the biological effectiveness of orthovoltage x rays is approximately twice (1.5–2 times) the biological effectiveness of higher-energy photons (e.g. ^{60}Co gamma rays). This difference in biological effectiveness has also been recognised in the BEIR VII report (National Research Council, 2006). Recognition of a difference of this magnitude is important when comparing RBE values for stochastic effects that were obtained in studies using different low-LET reference radiations. This is especially the case in comparing RBE values for lower-energy, low-LET radiations, such as tritium beta particles.

(A8) 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 NCRP (1967) indicated that, at high dose rates where such effects occur, the biological effectiveness of orthovoltage x rays is only approximately 20% higher than the biological effectiveness of photons emitted in ^{60}Co decay. Such small differences are relatively unimportant compared with uncertainties in RBE values estimated using either reference radiation.

(A9) *Publication 92* (ICRP, 2003) recommends that the preferred low-LET reference radiation for use in radiobiological studies is high-energy photons emitted in ^{60}Co decay. This choice has a number of advantages including: (i) 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 (ii) 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.

A.1.1.2. Dose, dose rate, and dose fractionation

(A10) The magnitude of the absorbed dose and dose rate and the extent of dose fractionation 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 to 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, RBE for the high-LET radiation at higher doses is approximately 2 and increases to approximately 5 at lower doses.

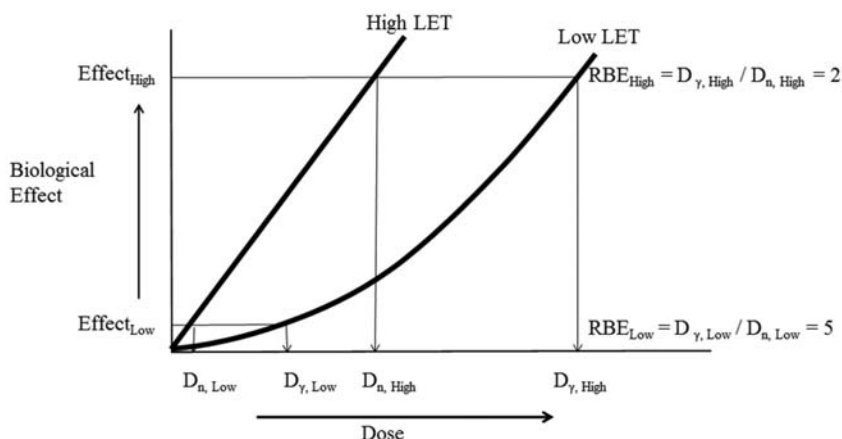


Fig. A.1. Biological effect as a function of dose for high- and low-linear energy transfer (LET) radiation. The graph illustrates how the calculated value of relative biological effectiveness (RBE) can differ based on the dose (high or low) used for the calculation (adapted from CNSC, 2002).

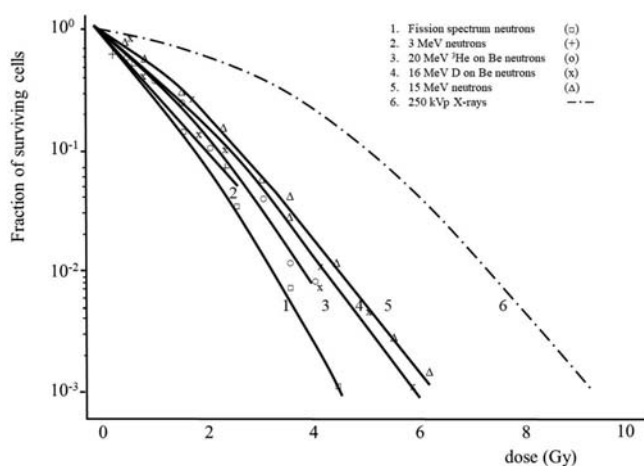


Fig. A.2. Dose-survival curves for cultured cells of human origin irradiated with different beams of fast neutrons and with 250-kVp x rays [Fig. 3B from ICRP (1990) and from Barendsen (1968)].

(A11) 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 2 as the dose of the reference radiation decreases from 10 to ≤ 0.1 Gy. The dependence of RBE on dose is less pronounced in the cases of exposure to the two higher-energy, high-LET radiations.

A.1.1.3. Type of biological endpoint

(A12) Estimates of RBE generally depend on the nature of the biological endpoint under study; that is, whether the effect is stochastic, in which case the probability of a response is a function of dose without a 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.

(A13) 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 that complete underlying repair is not possible. The severity of the effect therefore increases with higher doses.

(A14) 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 chromosomal and cellular levels do not usually translate into detriment at population level, and hence 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 individual level that could lead to impact on the maintenance of biological diversity or the conservation of species, such as reduced reproductive success, arising, for example, from effects on fertility, fecundity, growth, and early mortality.

(A15) Although most biological effects can be classified as either stochastic or tissue reactions, there can be substantial variations in RBE 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 value 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 the most sensitive species in radiological protection of the environment.

(A16) It should also be noted that a recent ICRP report on tissue effects (ICRP, 2012) suggests that, at least for some endpoints (e.g. circulatory disease and damage to the lens of the eye), the same threshold has been proposed for acute, and either fractionated or protracted (chronic) doses, somewhat blurring the distinction between stochastic effects and tissue reactions.

(A17) RBE values for high-LET radiations in inducing tissue reactions are generally lower than RBE values for those radiations in inducing stochastic effects. For example, at doses of interest in radiological protection, the reduction in RBE values for tissue reactions induced by alpha particles and fission neutrons compared with RBE values for stochastic effects appears to be approximately a factor of 2–3 (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.

A.1.1.4. Other potentially important influences

(A18) Other factors can influence estimates of RBE 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 can also confound an evaluation of the relevance of RBE to radiological protection of humans or the environment.

A.1.2. Extrapolation of relative biological effectiveness to low doses and dose rates

(A19) 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 and radiation weighting factors should be established on the basis of estimates of RBE values 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 ($R_L = \alpha_L D + \beta_L D^2$), RBE at low doses and dose rates, denoted by RBE_M , is the ratio of the 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.

(A20) 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); RBE for tissue reactions at low doses, which is equivalent to RBE_M for stochastic effects, is denoted by RBE_m to indicate that this is a maximum value. Although 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.

(A21) Although the definition and use of RBE_M for stochastic effects for purposes of radiological protection is relatively straightforward, there is a conceptual difficulty with use of RBE_m for tissue reactions that arises from the assumption that their dose–response relationships have thresholds. However, it appears that extrapolated RBE values for tissue reactions are largely independent of dose below a level that may be comparable to a threshold.

(A22) On the basis of the considerations discussed above, including that estimates of RBE_m are expected to be maximum values, the practice of estimating RBE_m by extrapolation of data on dose response for tissue reactions induced by a radiation of

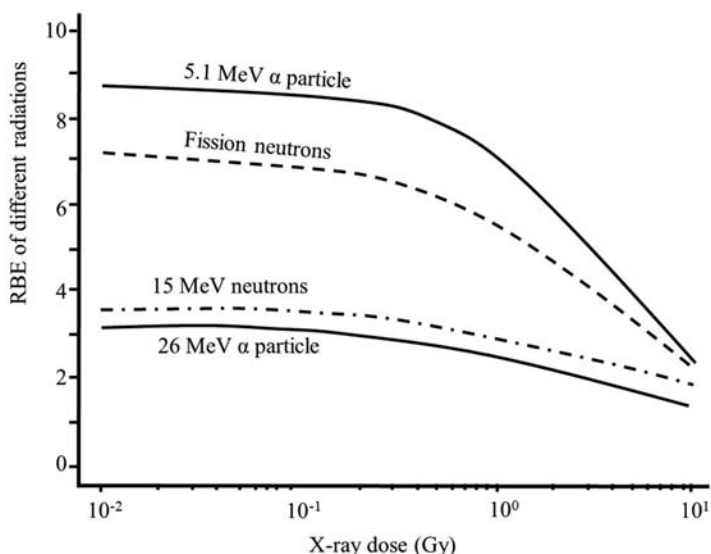


Fig. A.3. Relative biological effectiveness (RBE) vs dose curves illustrating that RBE values approach RBE_m (maximum RBE for tissue reactions) values at doses $<10^{-1}$ Gy of x rays [Fig. 5 from ICRP (1990)].

interest (e.g. alpha particles or tritium beta particles) and a reference low-LET radiation is continued in this publication. 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 relative biological effectiveness for tissue reactions through levels of biological organisation

(A23) As indicated previously, the most common studies of RBE for tissue reactions involve irradiation of mammalian cells in culture, and most studies measured cell reproductive death. This is especially the case in studies in which the radiation of interest is alpha particles. Less common are studies of RBE for tissue reactions in whole organs, tissues, or whole organisms of direct relevance to radiological protection of the environment.

(A24) 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, tissues, or 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, RBE for the mean lethal dose within 4 days ($LD_{50/4d}$) was similar to RBE 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).

(A25) On the basis of the arguments and supporting studies discussed in *Publication 58* (ICRP, 1990), it is assumed in this publication that estimates of RBE obtained from studies of cell reproductive death (cell survival) can be used to infer RBE for induction of tissue reactions in whole organs, tissues, or whole organisms.

A.2. Modelling of dose response for cell survival

(A26) As indicated previously, reproductive death of irradiated mammalian cells is the most common biological endpoint in studies to estimate RBE values for alpha particles in inducing tissue reactions. Cell killing is another frequent endpoint in studies to estimate RBE values for tritium beta particles.

(A27) 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 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’.

(A28) 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 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

(A29) The most commonly used mathematical description of the dose–response relationship for cell survival is the linear-quadratic 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 linear-quadratic model is a consequence of the theory of dual radiation action, which has some biological basis. This theory is used to derive the linear-quadratic 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:

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

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.