German Commission on
Radiological Protection

Office of the
German Commission on Radiological Protection
Postfach 12 06 29
D-53048 Bonn

http://www.ssk.de

Basic principles of determining radiation exposure limits for the general public

Statement by the German Commission
on Radiological Protection (SSK)

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CONTENTS

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Stellungnahme der Strahlenschutzkommission

1 Introduction

1.1 Advisory mandate and approach

On 19 March 2014, the Federal Ministry for the Environment commissioned the German Commission on Radiological Protection (SSK) to investigate the basic principles for determining dose limits and dose constraints. In response, the SSK drew up the recommendation "Basic principles of determining dose limits for occupationally exposed persons" (SSK 2018) in a first step. In this document, the SSK recommends, among other things, retaining the concept of limiting the occupational lifetime dose, continuing the discussion on the value for the lifetime occupational dose limit and raising the issue of the tolerable cancer risk from exposures at various workplaces with other responsible ministries.

This statement is devoted to the basic principles of determining dose limits for the general population. Dose limits and their role in public radiation protection are first described along with their historical development. This is followed by a description of public exposure to radiation[1] from natural and anthropogenic sources. In the next step, an overview of biological mechanisms of cancer development due to radiation exposure is provided and the available information on the dose-response relationship at very low doses is outlined. The lifetime risk of additional cancers after radiation exposure is then estimated in the range of the dose limit in utero, in childhood and adolescence, and in adulthood. All solid tumours together, thyroid cancer and leukaemia are examined in the process. For comparison purposes, the regulation of exposure to chemical genotoxic carcinogens in food and in the environment is described.

With regard to health effects, this statement is limited to the discussion of cancer risks[2]. Hereditary defects play a minor role in the total extent of the impairment due to radiation-induced damage to health, as determined in the so-called detriment as defined by the ICRP, and are not considered further here. The SSK considers radiation-induced cardiovascular diseases to be of secondary importance when setting the effective dose limit (SSK 2018). The SSK published a separate statement on benign tumours (SSK 2017). Other harmful non-carcinogenic effects on health are regulated by organ dose limits, which are not the subject of this statement. The SSK published a separate recommendation on radiation effects in organs for which there are no organ dose limits (SSK 2020).

The justifications for dose constraints and reference levels are not the subject of this statement. It is the SSK's view that there should be a separate review of the basic principles for determining the dose constraints and reference levels and a discussion of whether an acceptable risk should be defined for public radiation protection – similar to occupational radiation protection (Rühm et al. 2020). Furthermore, the basic principles for distinguishing between emergency, existing and planned exposure situations should be discussed in this context.

1.2 The radiation protection system

Traditionally, radiation protection distinguishes between stochastic and deterministic effects. In the case of deterministic effects, a threshold organ dose is assumed to exist below which these effects do not occur, while their severity increases above the threshold as the dose

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[1] In the following, public exposure to radiation means exposure of members of the public to radiation as defined in Section 5(14) of the German Radiation Protection Act (Strahlenschutzgesetz, StrlSchG), with the exception of occupational or medical radiation exposure.

[2] This statement uses the term cancer as a collective term for malignant tumours and haematological neoplasms (including leukaemia, lymphoma and multiple myeloma).

increases. The level of the respective threshold depends on the type of effect and varies based on individual factors in the population. Deterministic effects include acute radiation syndrome and various organ injuries. In the case of stochastic effects, it is assumed that the probability of occurrence depends on the organ dose and that the occurrence of damage cannot be ruled out with certainty at any dose greater than zero. Cancer and hereditary disorders are traditionally considered radiation-induced stochastic effects. The SSK assumes that radiation-induced benign tumours also arise through stochastic modes of action (SSK 2017).

According to more recent findings, there are health effects that do not conform to this traditional classification. These may include cardiovascular diseases and cataracts. The International Commission on Radiological Protection (ICRP) groups such damage and deterministic effects under the term "tissue reactions". The ICRP formed a task group in 2022 to clarify whether the classification used to date still reflects current scientific knowledge (ICRP TG 123[3]).

The main goal of radiation protection is to keep radiation exposure low enough so that radiation-induced stochastic effects do not exceed an acceptable level and that deterministic effects are prevented. This is achieved by applying the three principles of radiation protection of justification, optimisation and dose limitation and, in Germany, also through a legal obligation (Section 8(2) StrlSchG) to keep any exposure or contamination of people and the environment, even below the dose limits, as low as possible (principle of dose reduction). Radiation exposure caused by human activities must be justified, i.e. it must be more beneficial than harmful. Unnecessary exposure must be prevented.

According to the classification of exposure situations in ICRP Publication 103 (ICRP 2007) into planned, existing and emergency exposure situations, limits apply only in planned exposure situations in which the source of the radiation can be controlled. In the other exposure situations, only reference levels are specified. Dose limits represent tolerance thresholds beyond which any additional radiation exposure is unacceptable. The effective dose limit for the population in planned exposure situations is 1 mSv in a calendar year[4]. This limit is intended to keep the risk of stochastic effects below a tolerable level. In addition to the effective dose limit, organ dose limits serve to restrict tissue reactions. The SSK has ascertained that there is no evidence for radiation-induced tissue reactions that would require dose limits beyond those specified in the Radiation Protection Act (Strahlenschutzgesetz) (SSK 2020).

Occupational radiation exposure is divided into the three categories: unacceptable, tolerable and acceptable (Rühm et al. 2020). The effective dose limit for the population can be regarded as the boundary between unacceptable and tolerable risks. The radiation protection principle of optimisation for radiation exposure at doses below the limits is intended to achieve radiation exposure that is as low as reasonably achievable, taking into account economic and societal factors (ALARA – As Low As Reasonably Achievable). In occupational radiation protection, the aim of optimisation is to achieve an acceptable radiation risk for the given situation (Rühm et al. 2020). Numerical values of acceptable risks are not defined in radiation protection.

The dose limits that are set depend on the risks a society considers tolerable. The role of scientific advisers in this societal process is to present facts and boundary conditions as a basis for decision-making and recommendations. While existing dose limits both internationally and in German radiation protection law distinguish between the range of additional radiation exposures that are tolerable and the range of radiation exposures that are unacceptable, a value

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[3] ICRP Task Group 123 "Classification of Harmful Radiation-induced Effects on Human Health for Radiological Protection Purposes" (https://www.icrp.org/icrp_group.asp?id=194)

[4] The unit of measurement "mSv in a calendar year" is abbreviated in this document as "mSv a^{-1}".

that represents the acceptable risk below which no further optimisation is required has not been defined.

1.3 Historical development of dose limits

Until World War II, radiation protection mainly aimed to protect workers. Extensive damage to the health of scientists and doctors working with X-rays led to the first proposals for limiting radiation exposure at the end of the 1920s. Following initial uncertainty about the level of risk and the definition of dose levels, an annual dose limit corresponding to an effective dose of 500 mSv was recommended. From today's point of view, this dose limit is sufficient for preventing deterministic health effects. The annual dose limit for occupational radiation exposure was lowered to 150 mSv in 1950 and then to 50 mSv in 1956.

Only after increased cancer rates were reported among the survivors of the atomic bombings of Hiroshima and Nagasaki did public radiation protection become a relevant issue. Fear of impending nuclear conflicts, but also the expansion of nuclear power, prompted the development of comprehensive radiation protection.

As nuclear power began to expand, the ICRP formulated a dose limit for radiation exposure of the population of 5 mSv per year in 1956 (ICRP 1958). According to ICRP Publication 26 (ICRP 1977), it was deemed reasonable to consider the magnitude of radiation risks to the general public in the light of the public acceptance of other risks of everyday life. This acceptance could be motivated by the benefits that would not otherwise be received, by an assessment of the social cost of achieving a possible reduction of risk, or by an implicit judgment that the risk is negligible. The socially accepted mortality risk in everyday life was considered to be in the range of 10^{-6} to 10^{-5} per year. Assuming a mortality risk of 10^{-2} from an effective dose of 1 Sv, consistent with the state of knowledge at the time, the upper limit of the above risk range is reached by a radiation exposure of 1 mSv. In line with the previous recommendation, the ICRP recommended an effective dose limit of 5 mSv in a calendar year for critical groups[5] in the population (ICRP 1977).

Since the annual dose limit for occupational radiation exposure was lowered to 20 mSv in 1990, the ICRP has also recommended a lower dose limit of 1 mSv per year for public radiation exposure from planned exposure situations (ICRP 1991), at the time referred to as activities. The ICRP also justifies the dose limit of 1 mSv per year on the grounds that the mean value of the annual dose from natural sources without radon is 1 mSv, and 2 mSv is a typical value for higher altitude areas and for areas with geologically higher natural radiation. ICRP Publication 26 (ICRP 1977) stated that there was no reason to assume that regional differences in exposure to naturally occurring radiation would affect acceptable health risks more than regional differences in other natural risk factors such as meteorological conditions or volcanic activity.

In Germany, the dose limit for public radiation exposure was 5 mSv per year from 1960 (StrlSchV 1960) to 1989 (StrlSchV 1989) and was then reduced to 1 mSv per year in line with the above-mentioned ICRP recommendations. This limit still applies today.

[5] Definition of the critical group concept in ICRP Publication 26 (ICRP 1977, paragraph 26). This concept was subsequently replaced by the term "representative person" (ICRP 2006, ICRP Publication 101a).

2 Exposure to ionising radiation

2.1 Natural sources

Exposure to natural radiation has two causes: the first is cosmic radiation that is mainly comprised of protons and helium nuclei as well as gamma rays. It interacts with the components of the Earth's atmosphere, where it produces secondary radiation, primarily photons and muons, and also neutrons at higher altitudes in particular, as well as cosmogenic radionuclides, e.g. ^{14}C, ^{3}H, ^{7}Be and ^{10}Be. The latter enter the human body through the food chain and result in a mean annual effective dose of 12 µSv. These and the following dose specifications reflect the global mean limits according to (UNSCEAR 2008, Annex B). The external exposure caused by secondary cosmic rays increases on the Earth's surface with increasing altitude and proximity to the poles. It yields a population-weighted mean annual effective dose of 0.38 mSv. In particular, the neutron component increases with altitude. Depending on the altitude, the average effective doses range from 0.3 mSv to 2 mSv [6].

The second cause of natural radiation exposure is terrestrial radiation, i.e. radiation from primordial radionuclides, mainly ^{40}K, ^{238}U, ^{235}U, ^{232}Th and their decay products. Ingestion of these radionuclides results in an annual effective dose of 0.29 mSv (0.2 mSv to 0.8 mSv)[7]. The external radiation exposure they cause leads to an annual effective dose of 0.48 mSv (0.2 mSv to 1 mSv)[8]. The gaseous radionuclides ^{222}Rn and ^{220}Rn, and particularly their decay products, contribute by far the largest share to the inhalation dose, namely an effective dose of 1.25 mSv per year (0.2 mSv to 10 mSv). In ICRP Publication 65 (ICRP 1993), the global mean value for radon activity concentration in dwellings is given as 40 Bq m^{-3} (geometric mean 20; geometric standard deviation 2.5). When assessing these values, the considerable variability indicated must be taken into account: contributions can vary by more than one order of magnitude between different regions of the world; UNSCEAR gives a range of annual effective doses of between 1 mSv and 13 mSv from radon and its decay products (UNSCEAR 2008). The 95th percentile is given as 4 mSv a^{-1}. Extreme values, e.g. in parts of India, Brazil and Iran, are not covered by this.

In Germany, the annual effective dose based on natural sources typically falls in the range of 2 mSv to 3 mSv (BMU 2021). The contribution of radon can vary considerably. Indoor concentrations from 27 Bq m^{-3} to 68 Bq m^{-3} (25th percentile to 75th percentile) result in effective doses of 0.64 mSv a^{-1} to 1.72 mSv a^{-1} when using the dose factor in (StrlSchV 2018). However, there are as many as 345,000 residential buildings in Germany in which the indoor concentration of ^{222}Rn exceeds 300 Bq m^{-3} (Petermann and Bossew 2021), which corresponds to 7.6 mSv a^{-1}. In individual cases, maximum values of up to 10,000 Bq m^{-3} have been recorded indoors (BMU 2021). In (BMU 2021), a range of 1 mSv a^{-1} to 6 mSv a^{-1} is specified for the dose caused by radon in Germany. The variation of natural radiation without radon is approx. 0.9 mSv a^{-1} to 1.9 mSv a^{-1} in Germany.

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[6] The lower value applies to sea level, the upper value to people living above an altitude of 3,000 m who receive a disproportionate share of the collective dose due to cosmic radiation (according to UNSCEAR 2008)

[7] (UNSCEAR 2000) specifies this as a "typical range" and refers to the composition of foods and drinking water. In addition, extremely varied country-specific and individual eating habits make it difficult to specify more precise values.

[8] Ranges represent the difference between the 5th percentile and 95th percentile of the values (UNSCEAR 2000). It must be kept in mind that only around 25% of countries and 40% of the world's population are represented by this data.

2.2 Anthropogenic sources in planned exposure situations

In planned exposure situations, members of the general public may be exposed to radiation of both anthropogenic origin (e.g. from the use of nuclear fission) and natural origin released by, emanating from, or used in technical processes (e. g. from the NORM[9] range). This includes exposure to radon if it arises from an authorised activity. The exposure of patients to radiation in medical applications is not considered here, as no dose limit is set for such a situation and it must be justified by a valid indication.

To regulate anthropogenic radiation exposure, secondary dose limits for mass-, volume- or surface-related activity are derived by modelling from the effective dose limit of 1 mSv per year, enabling measurement-based proof of compliance with the primary limit. This is where the concept of the "representative person" developed by the ICRP comes into play.

Causes of anthropogenic radiation exposure of the population in Germany range from discharges of radionuclides with exhaust air or wastewater from nuclear installations or facilities and direct radiation from these installations and facilities (limited by 1 mSv per year) to the clearance of residues, buildings or ground surfaces (regulated by the dose criterion of 10 µSv per calendar year), the handling of excepted materials such as consumer goods and exposure to radiation from patients who have been administered radioactive substances for diagnostic or therapeutic purposes, to the use of mobile gamma radiography and the transport of radioactive substances. Handling NORM in industrial processes and the recovery or disposal of the resulting residues also lead to anthropogenic radiation exposure, but these are regulated by the concept of a reference level. The total resulting radiation exposure of members of the general population can be classified as follows:

- Operation and decommissioning of nuclear installations and other facilities: Calculated and real doses fall below the limit values (0.3 mSv a^{-1} per discharge type, 1 mSv a^{-1} in total) by at least one order of magnitude, usually by several orders.
- Clearance of NORM residues from monitoring or continued monitoring: Here, too, it must be ensured that the annual effective dose for an individual member of the population does not exceed 1 mSv a^{-1}. Modelling of this dose is possible in far less detail in the case of NORM residues than in the case of discharges from nuclear installations.

In addition, exposure to radiation in the order of 1 mSv a^{-1} can certainly occur when natural radionuclides are handled, for example in the context of existing exposure situations or during remediation of abandoned mines. However, these cases are not regulated by a dose limit, but by a reference level for public radiation exposure.

3 Carcinogenic effects of exposure to ionising radiation

Cancer is a very common disease, the cause of which can in most cases not be clearly identified. Nevertheless, many biological, chemical and physical toxins are known to increase the incidence of cancer in individuals having been exposed accordingly. At the beginning of this chapter, basic information on how cancer develops is outlined and modes of action are discussed, such as how exposure to ionising radiation can increase the incidence of cancer. Following a brief summary of the state of knowledge on cancer risks caused by radiation

[9] NORM = Naturally occurring radioactive material is material that only contains radionuclides of natural origin (radionuclides of the decay series of ^{238}U, ^{235}U and ^{232}Th and ^{40}K).

exposures at different ages, lifetime risks of ionising radiation with low effective dose are estimated for the general population. Based on the current state of knowledge, individual risks cannot be estimated and the risks of vulnerable population groups can only be estimated to a limited extent.

The lifetime risks are calculated for the following two exposure scenarios:

- homogeneous whole-body exposure to X-ray or gamma radiation, in which the risks of malignant tumours are related to the dose absorbed by the colon and those of leukaemia to the dose absorbed by the bone marrow
- incorporation of radioactive iodine, in which the risk of thyroid cancer relates to the dose absorbed by the thyroid gland

Cancer incidence risks were calculated because mortality risks depend on the state of the health system and to achieve comparability with the regulation of carcinogenic substances. The calculated incidence risks form the basic foundation for further discussion.

3.1 Modes of action

Cancer cells differ from their normal progenitor cells in a number of functional changes that occur mainly as a result of mutations. Such mutations can occur spontaneously as a result of errors in normal cellular processes or as a result of exposure to noxious agents that cause DNA damage. Like other noxious agents that damage DNA, radiation may play a role in multistep and multifactorial carcinogenesis. Experiments have shown changes in various cancer-related processes even at very low energy doses in the range of around 1 mGy to 10 mGy. Primary damage to DNA largely exhibits a linear dependence on dose. For cellular response reactions, on the other hand, nonlinear dependencies (sublinear, supralinear, or multiphasic) in the range of small doses and qualitative differences between small and larger doses are often described. In addition, radiation can influence the increased growth of mutant cells through various effects on the microenvironment of mutant cells, their neighbouring cells and the immune system. How these effects and the observed nonlinear dose dependencies of the different biological effects at low doses interact and potentially determine the resulting cancer risk is currently unknown. Experiments on cancer development in animal models after exposure to radiation also do not permit any conclusive statements to be made at present concerning the dose-effect relationship.

3.2 Cancers risk due to in utero exposure

Radiation exposure during prenatal development can lead to an increased incidence of malignant tumours and leukaemias. These can occur during both childhood and adulthood.

There are a number of studies on cancer risks during childhood after radiation exposure in utero. The largest case-control study on mortality from cancers after diagnostic X-ray imaging, the Oxford Survey of Childhood Cancer (OSCC), found evidence of increased cancer risks at in utero doses of the order of 10 mGy. As described in the SSK statement on childhood leukaemia in the vicinity of nuclear power plants (SSK 2008), this statement assumes an excess relative risk per uterine dose of 40 Gy^{-1} for both malignant tumours and leukaemias.

For cancer risks in adulthood after radiation exposure in utero, the Japanese atomic bomb survivors (Life Span Study, LSS) represent by far the most important source of information. The most recent and largest study of malignant tumour mortality in the LSS cohort found an

excess relative rate (ERR)[10] per uterine dose of 1.84 Gy^{-1} for females exposed in utero (Sugiyama et al. 2021[11]). No increase in risk was found for males exposed in utero. The relative risks in adulthood are thus significantly lower than in childhood. However, the higher spontaneous rates in adulthood have to be taken into account for the calculation of the radiation-induced absolute lifetime risks. For leukaemia, the number of cases in the LSS was not sufficient to ascertain a risk. For an estimate of the order of magnitude of lifetime risks for adult leukaemia after exposure in utero, this statement therefore also assumes an excess relative risk per uterine dose of 1.84 Gy^{-1} for women.

3.3 Cancer incidence risks due to exposure during childhood or adolescence

Exposure to ionising radiation in childhood bears a higher risk of cancer incidence than exposure during adulthood, and this risk persists into old age. The LSS remains an important source of epidemiological evidence on this risk due to the size of the cohort, the particularly long follow-up period, the good dose reconstruction and the detailed risk models that have been published.

A systematic review of the recent literature showed that there are many informative studies on cancers in children and adolescents following radiation exposure during childhood and adolescence, including in particular computed tomography (CT) scans, which to date account for a large part of the current total diagnostic exposure in many countries. In addition, there are a number of studies on natural background radiation. Their findings are consistent with studies on cancer in children, adolescents and young adults following CT scans in childhood (see literature in UNSCEAR 2019). Risk estimates from meta-analyses and pooled studies (Lubin et al. 2017, Little et al. 2018) are compatible with those of the LSS, but mostly pertain only to childhood cancer. There is not sufficient data in these studies to quantify an age dependency into old age.

The risk estimates undertaken for this statement are therefore based on the models derived for the LSS for the incidence of malignant tumours of (Grant et al. 2017), of leukaemias of (Hsu et al. 2013) and of thyroid carcinoma of (Furukawa et al. 2013).

3.4 Cancer risk due to exposure during adulthood

The International Nuclear Workers Study (INWORKS) is a prominent study among studies investigating cancer mortality risk after longer-term exposure of workers to ionising radiation (Richardson et al. 2015, Leuraud et al. 2015). Even when the cohort was restricted to members with colon doses less than 100 mGy, there was evidence of an increased risk of malignant

[10] Many radiation epidemiological studies determine the quotient of the rate of an event (e.g. disease or death) in an exposed population and that in a non-exposed population reduced by 1. This value, or ERR for short, is sometimes referred to in the literature as “excess relative risk” or “excess relative rate”. According to (UNSCEAR 2012) and (SSK 2018), a distinction should be made between the concept of “excess relative rate”, which relates to the analysis of a specific study with a specific population with a specific exposure, and “excess relative risk”, which provides a risk estimate for populations that have not yet been exposed or for which the events to be investigated are not yet (conclusively) known. These prospective risk estimates indicate a detriment-weighted probability that is inferred by assessing the available knowledge, e.g. by considering the results of different studies. This conceptual distinction is taken into account in this statement and in the scientific background. However, since original literature is sometimes cited that does not reflect this distinction, the relevant passages are marked here and in the following text if the authors have used the term “excess relative risk” for the result of a specific study.

[11] The authors use the term “excess relative risk”.

tumours and an increased risk of leukaemia when restricted to bone marrow doses less than 300 mGy. UNSCEAR calculated cancer risks for age at exposure, exposure duration, age at end of follow-up and colon or bone marrow dose that approximate the mean values in the INWORKS study. Given the uncertainties, risks calculated with models based on the LSS and INWORKS are consistent (UNSCEAR 2019). This confirms the SSK's assessment that the cancer risks per dose from acute and longer-term radiation exposure to low and moderate doses are comparable (SSK 2014).

Due to the relatively short follow-up in INWORKS, the study is not suitable for calculating risks over longer periods of time into older age (UNSCEAR 2019). This is why the SSK has calculated lifetime risks on the basis of the LSS results. As is the case for radiation exposure during childhood and adolescence, this statement uses the current models of increased incidence rates for malignant tumours of (Grant et al. 2017), for leukaemia of (Hsu et al. 2013) and for thyroid carcinomas of (Furukawa et al. 2013) also for calculations of the cancer risk after radiation exposure during adulthood.

3.5 Lifetime risks

To determine the lifetime risks, cumulative probabilities for the induction of malignant tumours or leukaemia are estimated at different ages. First the probabilities are calculated for an external whole body exposure. As there is no epidemiological evidence for the level of risks at doses close to the effective dose limit of 1 mSv a^{-1}, risks are specified here for a higher annual dose of 3 mSv a^{-1}. In the range of the cumulative doses, there is evidence for increased cancer risks from protracted/repeated radiation exposure. Possible implications for radiation exposure with 1 mSv a^{-1} will be discussed.

Three different exposure periods will be considered: i) radiation exposure in utero (cumulative dose 3 mSv), ii) radiation exposure during childhood and adolescence until the end of the 17th year of life (cumulative dose 54 mSv) and iii) radiation exposure during adulthood until the end of the 89th year of life (cumulative dose 216 mSv). For the minimum latency period between exposure to ionising radiation and cancer diagnosis, five years were assumed for malignant tumours and two years for leukaemia.

Table 3-1 shows the probabilities calculated for additional malignant tumours in the respective sex and age group and in different lifetime periods on the basis of the preferred risk models described in the scientific background, as well as the spontaneous incidence in the German population for comparison purposes. Table 3-2 shows the incidence probabilities for additional leukaemias. For malignant tumours and leukaemia together, the cumulative lifetime cancer probabilities are 5.6:100 for women and 3.6:100 for men. The alternative models investigated produce a similar result for women. For men, the probabilities tend to be lower; in particular, the model with a linear-quadratic dose-response relationship yields a probability that is lower by a factor of 3.

The uncertainty of the specified lifetime risks cannot be reliably estimated according to the current state of knowledge. However, UNSCEAR has specified an uncertainty range of approximately one fifth to twice the best estimate for the specific case of risk of malignant tumours up to the age of 60 years after occupational external radiation exposures in the age range of 30 years to 45 years with a colon dose of 100 mGy (UNSCEAR 2019). Higher uncertainties are to be assumed for risks in other age ranges. This applies in particular after radiation exposure in utero or during childhood.

The probabilities shown in Table 3-1 do not include skin cancers of ICD-10 category C44 "other malignant neoplasms of skin". These neoplasms have a very high spontaneous incidence. However, epidemiological studies show no clear evidence of a radiation risk at skin doses below

1 Gy. The SSK is currently working on a separate recommendation that focuses on the risk of radiation for skin cancer.

The SSK assumes that the probabilities of malignant diseases such as lymphomas, multiple myelomas and myelodysplastic syndromes, which are not explicitly calculated, make only an insignificant contribution to the overall probability.

If the cancer risk from annual radiation exposure up to the age of 89 with annual effective doses of 1 mSv to 3 mSv shows a linear dependence on the cumulative dose, the lifetime incidence probability at 1 $mSv\,a^{-1}$ would be one third of the values provided in Tables 3-1 and 3-2, averaged over women and men in all models studied, in the order of 1:100 to 2:100. Such radiation exposure would thus increase the sex-averaged probability of developing malignant tumours [12] and leukaemia in Germany by the age of 89 for a person exposed in this way from approx. 41:100 (RKI and GEKID 2021) to 42:100 to 43:100.

In addition to the external radiation exposure scenario, the cancer risk from incorporation of ^{131}I was also estimated. Iodine accumulates in the thyroid gland. Other organs play a secondary role in the excess cancer risk. For the incorporation of iodine, only thyroid cancer is considered here. The tissue weighting factor of the thyroid gland is 0.04 (ICRP 2007). This means that an annual effective dose of 3 mSv per year is reached with an annual thyroid dose of 75 mGy when only the thyroid gland is exposed to radiation.

Table 3-3 shows the probabilities of additional thyroid cancers in different lifetime periods based on the preferred risk model described in the scientific background and, for comparison, the spontaneous incidence. For an annual thyroid dose of 75 mGy, the excess probability of developing thyroid cancer, cumulative over all exposure periods, would be 4.4:100 for women and 0.88:100 for men.

If the thyroid cancer probability from lifetime radiation exposure to annual thyroid doses from 75 mGy down to 25 mGy exhibits a linear dependence on the cumulative dose, the lifetime thyroid cancer probability at 25 $mGy\,a^{-1}$ is of the order of 0.9:100, averaged over women and men. This means that for the same effective dose, the probability of excess cancer is generally higher for homogeneous external radiation exposure than for an incorporation of radioiodine.

[12] without “other malignant neoplasms of skin” (category C44 in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10))

Table 3-1: Estimated incidence probability of malignant tumours in different lifetime periods due to external radiation exposure with an effective dose of 3 mSv per year and, for comparison, the background incidence probability in Germany in 2017 (cumulative values from RKI und GEKID 2021)

Cumulative colon or uterine dose / period of exposure	**Excess or spontaneous incidence[a] of developing a malignant tumour[b]**			
	Girls (0-17 years)	Boys (0-17 years)	Women (18-89 years)	Men (18-89 years)
216 mSv (18-89 years)	-	-	$260 \cdot 10^{-4}$	$165 \cdot 10^{-4}$
54 mSv (0-17 years)	$4.2 \cdot 10^{-4}$	$2.2 \cdot 10^{-4}$	$244 \cdot 10^{-4}$	$140 \cdot 10^{-4}$
3 mSv in utero	$1.2 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$	$20 \cdot 10^{-4}$	0
Total	$5.4 \cdot 10^{-4}$	$3.3 \cdot 10^{-4}$	$524 \cdot 10^{-4}$	$305 \cdot 10^{-4}$
Background incidence probability (incidence in Germany)				
	$15 \cdot 10^{-4}$	$16 \cdot 10^{-4}$	$3\,675 \cdot 10^{-4}$	$4\,269 \cdot 10^{-4}$

[a] in the respective sex and age group
[b] without other malignant neoplasms of skin (acc. to ICD10: C44)

Table 3-2: Estimated incidence probability of leukaemia in different lifetime periods due to external radiation exposure with an effective dose per year of 3 mSv and, for comparison, the background incidence probability in Germany in 2017 (cumulative values from RKI und GEKID 2021*)*

Cumulative bone marrow dose / period of exposure	**Excess or spontaneous incidence[a] of developing leukaemia**			
	Girls (0-17 years)	Boys (0-17 years)	Women (18-89 years)	Men (18-89 years)
216 mSv (18-89 years)	-	-	$24 \cdot 10^{-4}$	$36 \cdot 10^{-4}$
54 mSv (0-17 years)	$3.4 \cdot 10^{-4}$	$4.6 \cdot 10^{-4}$	$4.0 \cdot 10^{-4}$	$5.9 \cdot 10^{-4}$
3 mSv in utero	$0.7 \cdot 10^{-4}$	$0.9 \cdot 10^{-4}$	$0.5 \cdot 10^{-4}$	0
Total	$4.1 \cdot 10^{-4}$	$5.5 \cdot 10^{-4}$	$28.5 \cdot 10^{-4}$	$41.9 \cdot 10^{-4}$
Background incidence probability (incidence in Germany)				
	$7.3 \cdot 10^{-4}$	$9.4 \cdot 10^{-4}$	$98 \cdot 10^{-4}$	$140 \cdot 10^{-4}$

[a] in the respective sex and age group

Table 3-3: Estimated incidence probability of thyroid cancer in different lifetime periods due to incorporation of ^{131}I with a thyroid dose of 75 mGy per year and, for comparison, the background incidence probability in Germany in 2017 (cumulative values from RKI und GEKID 2021*)*

Cumulative thyroid dose / period of exposure	**Excess or spontaneous incidence[a] of developing thyroid cancer**			
	Girls (0-17 years)	Boys (0-17 years)	Women (18-89 years)	Men (18-89 years)
5 400 mGy (18-89 years)	-	-	$80 \cdot 10^{-4}$	$17 \cdot 10^{-4}$
1 350 mGy (0-17 years)	$10.4 \cdot 10^{-4}$	$2.3 \cdot 10^{-4}$	$353 \cdot 10^{-4}$	$69 \cdot 10^{-4}$
Total	$10.4 \cdot 10^{-4}$	$2.3 \cdot 10^{-4}$	$433 \cdot 10^{-4}$	$86 \cdot 10^{-4}$
Background incidence probability (incidence in Germany)				
	$0.9 \cdot 10^{-4}$	$0.4 \cdot 10^{-4}$	$89 \cdot 10^{-4}$	$38 \cdot 10^{-4}$

[a] in the respective sex and age group

3.6 Incidence probability, cancer mortality and detriment

The concept of effective dose is based on the detriment, i.e. the measure of harm defined by the ICRP for radiation damage to health (ICRP 2007). For the detriment, the risk of radiation-induced cancers and their lethality are essential parameters. Individual types of cancer differ, in some cases considerably, in their lethality risk. Other than the skin cancers not covered here, the most common cancers in the population are the same as those in the calculated lifetime risks for radiation-induced cancers. There is also no evidence that radiation-induced and non-radiation-induced cancers progress differently. According to this, on average, the lethality of a cancer induced by homogeneous whole-body exposure does not differ significantly from that for cancers in the general population. In Germany, the number of all cancer deaths[13] is roughly half the number of cancer cases (RKI und GEKID 2021). Accordingly, the overall lifetime risk for radiation-induced cancer mortality across all entities is about half that for the calculated incidence of radiation-induced cancer.

The ICRP has estimated a detriment per effective dose of 0.057 per Sv for a radiation exposure of a nominal global population[14] with low dose rates. For radiation exposure with an effective dose of 1 Sv, the ICRP assumes a lifetime excess probability of cancer (except skin cancer) of $831 \cdot 10^{-4}$ for women and of $560 \cdot 10^{-4}$ for men (Table 3-4).

Table 3-4: Incidence probability of cancer up to the age of 89 and detriment due to external radiation exposure up to the age of 84 with an effective dose of 1 Sv, according to Table A.4.18 in (ICRP 2007)[15]

Population	Incidence probability of cancer[a]	Detriment[a]
Females	$831 \cdot 10^{-4}$	$635 \cdot 10^{-4}$
Males	$560 \cdot 10^{-4}$	$455 \cdot 10^{-4}$
Total population	$696 \cdot 10^{-4}$	$545 \cdot 10^{-4}$

[a] without skin cancer (“skin”) and without hereditary damage (“gonads”)

External radiation exposure over 85 years with an annual effective dose of 3 mSv corresponds to a total dose of 0.255 Sv. Table 3-5 compares the incidence probabilities calculated by ICRP for this kind of radiation exposure with those calculated for this statement. The incidence probabilities calculated in this statement are higher than those of the ICRP values by a factor of approx. 2.5. The difference is explained by the fact that the ICRP, in contrast to this statement, used a dose and dose-rate effectiveness factor (DDREF) of 2. However, the numerical value of the DDREF is controversial in the literature (see e.g. Jacob et al. 2009, Shore et al. 2017, Hoel 2018, Little et al. 2020). The SSK does not see sufficient evidence for a risk reduction of this

[13] Cancer other than category C44 “other malignant neoplasms of the skin” defined in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

[14] The ICRP’s risk estimates are referred to as “nominal” because they refer to the exposure of a hypothetical population of females and males with a typical age distribution and are calculated by averaging across age groups and both sexes (ICRP 2007).

[15] Radiation exposure up to the age of 84 and risk up to the age of 89 corresponds to the common interpretation of ICRP Publication 103 (ICRP 2007). (Cléro et al. 2022, ICRP 2007) use these parameters for an update of ICRP Publication 103 and clarify, however, that the calculations in ICRP Publication 103 apply for radiation exposure up to age 89 and risk up to age 94. Accordingly, these cannot be directly compared with the calculations carried out for this statement. However, the resulting discrepancy is likely to have a negligible impact on the conclusions drawn in this section.

kind (SSK 2014). The SSK's assessment is shared by the WHO in its calculation of cancer risks after the Fukushima nuclear accident (WHO 2013) and by UNSCEAR in its most recent calculations of cancer risks in selected exposure scenarios (UNSCEAR 2019). In addition, only older modelling of leukaemia risks with very low values for longer periods after radiation exposure was available to the ICRP. Taking these two factors into account, the ICRP calculations and the calculations in this statement are in very close agreement despite the use of different models and data.

An 85-year incorporation of ^{131}I with an annual effective dose of 3 mSv corresponds to a total thyroid dose of 6.375 Sv. Averaged over both sexes, the ICRP and this statement calculate a similarly high thyroid cancer risk for this type of radiation exposure.

Table 3-5: Incidence probability of radiation-related cancer (excluding skin cancer) up to age 89 after 85 years of external radiation exposure from birth (excluding exposure in utero) with an effective dose per year of 3 mSv, ICRP: according to the cumulative dose of 0.255 Sv, the nominal risk coefficients according to Table A.4.18 in (ICRP 2007) were multiplied by 0.255 Sv. In the calculations, the ICRP reduced the risk factors found in the LSS for application to low doses by a factor of two. This explains most of the differences in the results.

Population	ICRP	This statement[a]
Females	$212 \cdot 10^{-4}$	$540 \cdot 10^{-4}$
Males	$143 \cdot 10^{-4}$	$354 \cdot 10^{-4}$
Total population	$177 \cdot 10^{-4}$	$447 \cdot 10^{-4}$

[a] because of the shorter minimal latency period, the contribution of leukemia in the present calculations refers to an exposure time of 88 years

4 Regulations of exposure to chemical carcinogens

Small amounts of carcinogenic substances in the environment, in food and at the workplace are often unavoidable despite improved occupational and environmental protection measures. Geogenic concentrations also contribute to the background levels of some carcinogens, such as arsenic.

The distinction between genotoxic and non-genotoxic carcinogens is considered particularly relevant for risk assessments in toxicology. For the latter substances, which are often classified as "tumour promoters", the existence of concentrations without adverse effects (thresholds) is postulated independently of various underlying mechanisms. In contrast, genotoxic carcinogens, their metabolic precursors and DNA-reactive metabolites are considered risk factors at all concentrations, since even one or a small number of DNA lesions can essentially lead to mutations and thus increase the risk of tumours.

4.1 The protection system

Various approaches exist for assessing and decreasing exposure to genotoxic carcinogens; these can be divided into pragmatic risk-reduction approaches, risk-based assessments and scientific approaches including a detailed consideration of the mode of action. Different concepts apply here for the population and for workplace exposure. A tolerable incidence lifetime risk of 4:1,000 and an acceptable lifetime risk of 4:10,000 or 4:100,000 (originally planned from 2018) are explicitly specified for individually assessed hazardous substances at the workplace, but not for the population.

The general (pragmatic) principle for the protection of the population from carcinogenic substances in food is the ALARA principle (as low as reasonably achievable), which aims to minimise the exposure of the population to carcinogenic substances, taking into account technical, economic and socio-economic aspects.

More precise in terms of accepted excess cancer risks to the population is the TTC (threshold of toxicological concern) approach, an exposure-based approach that relies on a risk-based assessment of known carcinogens. For substances without sufficient toxicity data, but for which a potential carcinogenic effect can be assumed based on the chemical structure, a daily intake is estimated. If this is lower than a value of 0.15 µg per person, which corresponds to an estimated excess lifetime cancer risk of less than 1:1,000,000 based on animal carcinogenicity data of known carcinogens, the substance is considered as not requiring priority treatment. Several substances with a presumably higher cancer risk are exempt from this procedure. The TTC approach is thus a screening and prioritisation tool to assess the safety of substances of unknown toxicity in food. For the protection of the population not additionally exposed occupationally, an estimated lifetime excess cancer risk of 1:1,000,000 per substance is therefore considered as a benchmark for different minimisation strategies.

If, on the other hand, carcinogenicity data from animal studies are available, prioritisation is based on the margin of exposure (MOE). This approach takes into account not only the substance-specific data but also the actual exposure; if this is a factor of 10,000 or more below the dose that produces tumours in 10% of animals in animal experiments (lower confidence bound), this substance is given a low priority for further risk management measures. This represents a lifetime cancer risk of 1:100,000. As with the TTC approach, this is a prioritisation approach and not a risk quantification; modes of action are also not taken into account.

4.2 Mode of action-based risk assessments

For many chemical carcinogens, the dose-response curves between the induction of DNA damage and the appearance of tumours are not linear across the entire dose range, but are often at least biphasic. While the first range has a flat slope determined by the induction of DNA damage and its conversion into mutations, it is often followed by a steeper gradient that can be explained mechanistically by the saturation of detoxification or repair mechanisms and/or by the induction of any kind of tumour promotion mechanism. In addition, some genotoxic metabolites, such as formaldehyde and acetaldehyde, but also reactive oxygen species, are also formed endogenously within the framework of amino acid metabolism or the respiratory chain; this is increasingly taken into account in quantitative risk assessments for toxicologically well-studied substances.

5 Summary and position

Radiation protection is based on the interplay between justification, optimisation and limitation. Anthropogenic exposure situations are categorised as planned, existing and emergency exposure situations. In categorising these situations, the processing and disposal of residues play a separate role in that occupational radiation exposures are considered planned, while resulting exposures of the general public are treated as existing exposure situations.

The basic principles of public radiation protection in planned exposure situations other than occupational and medical radiation exposure are summarised below and contrasted with those of protection of the public against cancer risks from chemical genotoxic carcinogens.

The Radiation Protection Act limits the effective dose to the public from ionising radiation from all planned exposure situations to 1 $mSv\,a^{-1}$. This limit remained unchanged for more than 30

years. In contrast to other planned exposure conditions, medical radiation exposures are not regulated by dose limits.

To understand the level of the dose limit, a comparison with radiation exposure from natural sources can be helpful. Radiation exposure from natural sources other than radon causes an effective dose of 1 mSv per year on average in Germany. Here, the range of variation of the effective dose from natural sources without radon is approximately the same as the level of the dose limit. The range of variation of the effective dose from all natural sources, i.e. including radon, is significantly larger than the dose limit for the population in planned exposure situations. For chemical genotoxic carcinogens, exposure from natural sources varies considerably. For arsenic, for example, concentrations can be reached for which linear extrapolations estimate cancer risks at levels similar to exposure from natural radiation sources without radon (see scientific background).

According to current calculation methods, planned radiation exposures from anthropogenic sources cause effective doses in the population in Germany that are at least one order of magnitude below the dose limit of 1 mSv per year. Moreover, these calculation methods significantly overestimate the real radiation exposures both for discharges from nuclear installations and generally also for the release of radioactive substances. Due to extensive restrictions imposed by the Radiation Protection Act regarding the addition of radioactive substances, consumer goods do not constitute a significant radiation exposure for the population. For a large number of types of consumer products, adding radioactive substances is also completely banned.

Incidence probabilities of additional cancers can be ascribed to an effective dose for given exposure scenarios. There is sufficient evidence to estimate cancer risks of longer-term radiation exposure to X-rays and gamma radiation with an annual dose of 3 mSv. Model calculations show an excess cancer risk of 6:100 for women and 4:100 for men, cumulative over the entire lifetime. This estimate is subject to considerable uncertainty, which cannot be reliably determined at this point in time. If the radiation risk from lifetime radiation exposure with annual doses in the range of 1 mSv to 3 mSv exhibits a linear dependence on the dose, a lifetime radiation exposure with an annual dose of 1 $mSv\,a^{-1}$ results in a sex-averaged excess cancer risk in the order of 1:100 to 2:100. The effective doses to the population calculated for planned exposure situations are at least one order of magnitude below the dose limit and thus correspond to a cancer risk of less than 1:1,000. Due to the conservative calculation methods, the real effective doses are even lower.

Due to genotoxicity as the main mode of action, there are similarities between ionising radiation and chemical genotoxic carcinogens. Still the protection of the population is based on different approaches. While dose limits are defined in radiation protection, the protection system for the population against cancer risks from chemical genotoxic carcinogens has no general dose limit. Prioritisation procedures regarding risk assessment are first applied to the large number of carcinogenic and possibly carcinogenic substances. Substances for which sufficient toxicity data is not available, but whose estimated intake by members of the public is below a level that corresponds on average to a lifetime cancer risk of 1:1,000,000 for a large number of carcinogens, are not prioritised. If sufficient toxicity data is available, a decision is made on the basis of the margin-of-exposure (MOE) approach as to which substances are to be prioritised with the aim of carrying out mode-of-action-based risk estimates and exposure reduction measures for them. If, taking into account animal experimental data and known exposure, the estimated risk of a carcinogen is below 1 in 100,000, it is not prioritised for further risk management measures to reduce population exposure.

When comparing the values of cancer risks involved in the regulations of public exposure to ionising radiation and to chemical genotoxic substances, two sets of opposing factors should be considered. On the one hand, in the case of chemical genotoxic substances, only individual carcinogens are considered. For substances for which explicit risk calculations can be made, only the dominant exposure pathway and the cancer type with the highest risk are considered. In contrast, radiation protection looks at the overall risk from all radionuclides, all exposure pathways and all cancer types for planned exposure situations. There is no such overall assessment in the area of chemical genotoxic substances. On the other hand, the decision criterion used for chemical genotoxic substances is based on the lower limit of a confidence interval of the dose (lifetime intake amount) that causes a given risk. An estimated exposure of the population is thus ascribed a higher risk than if the decision criterion were based on the best estimate of the risk coefficient, as is the case in radiation protection.

Overall, the approaches for protecting the population from ionising radiation and from chemical genotoxic carcinogens are very different. In addition to the above-mentioned differences in the calculation methods of risks, there is a significant conceptual difference. While there is a generally applicable dose limit in the radiation protection system for the population, protection against exposure to chemical genotoxic carcinogens is based on prioritisation procedures for individual carcinogens.

For all planned exposure situations, the actual radiation exposures of the population are at least one order of magnitude lower than the dose limit, among other things as a result of the optimisation principle and the dose reduction principle. Accordingly, a reduction in the dose limit would not have a direct additional protective effect on the population. However, any such decision would have to take into account the relationship between the negative effects and benefits of such an adjustment and what consequences an adjustment of the dose limit would have, among other things, for the system of radiation protection. Whether the dose limit should be adjusted is ultimately a political decision that must include a discussion not only of the scientific principles outlined here, but also, for example, of the social acceptance of risks and ethical issues.

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German Commission on
Radiological Protection

Office of the Commission on Radiological Protection
PO Box 12 06 29
53048 Bonn
Germany

http://www.ssk.de

Basic principles of determining radiation exposure limits for the general public

Scientific background to the statement of the German Commission on Radiological Protection

Adopted at the ___ meeting of the German Commission on Radiological Protection on __ / __. ____ 20__

CONTENTS

1 Dose limits in the radiation protection system

1.1 Basic principles for setting dose limits in the radiation protection system

1.1.1 Principles and approach

Dose limits, dose constraints and reference levels for exposure to noxious agents are designed to prevent or to reduce the likelihood of injury to health.

According to the classification of exposure situations for ionising radiation into planned, existing and emergency exposure situations according to ICRP Publication 103 (ICRP 2007a), limits apply only in planned exposure situations in which the source of the radiation can be controlled. In the other exposure situations, only reference levels are recommended in the form of ranges.

This chapter provides a brief outline of the principles for determining the limits and the current radiation protection system.

Traditionally, a distinction is made in radiation protection between stochastic and deterministic radiation effects.

It is assumed in the case of deterministic effects that a threshold exists below which such effects do not occur, whereas above the threshold the severity of the effects increases with the dose. The level of the respective threshold depends on the nature of the effects and also varies according to individual factors in the population. Deterministic radiation effects include acute radiation sickness and various organ injuries. The purpose of defining limits for organ equivalent doses ("organ doses") is to prevent deterministic effects.

It is assumed in the case of stochastic effects that the probability of occurrence depends on the dose and that the occurrence of damage cannot be ruled out with certainty at any dose level. Cancer and hereditary disorders are traditionally considered radiation-induced stochastic effects. The purpose of the effective dose limit is to restrict stochastic effects to a tolerable level. The SSK assumes that radiation-induced benign tumours are also caused by stochastic effects (SSK 2017b).

According to more recent findings, there are health effects that do not correspond to the traditional classification previously mentioned. These probably include cardiovascular diseases and cataracts. The ICRP summarises these and the deterministic effects under the term "tissue reactions" (ICRP 2007a). In its statement on limits for organ equivalent doses (SSK 2020), the SSK considers diseases that are neither cancer, benign tumours nor hereditary genetic disorders. The SSK notes that there is no evidence to suggest that limits other than those given in the Radiation Protection Act are required for radiation-induced tissue reactions (SSK 2020). Having issued a recommendation on the "Basic principles of determining dose limits for occupationally exposed persons" in 2018, (SSK 2018), this statement from the SSK now presents the basic principles of determining radiation exposure limits for the general public[8] in planned exposure situations. The justification of reference levels for the protection of the public in existing and emergency exposure situations is not covered by this statement. The question of the circumstantial, acceptable or tolerable risks in existing and emergency exposure situations will be addressed in a future statement/recommendation.

[8] Radiation exposure of the public, when mentioned below, refers to the exposure of individuals to radiation with the exception of occupational and medical exposure.

1.1.2 Relationship between risk and dose

The level of risk depends on the dose – sometimes also the dose rate – received by an individual through exposure. While the *determination of the level* of tolerable or acceptable risks is a societal process, the relationship between (tolerable or acceptable) risks and the respective dose levels is based on assumptions and scientific facts.

Various approaches are taken to risk quantification. In radiation protection, risk refers to the probability of a specific endpoint occurring during a defined period and in a specified population group. Concerning cancer, radiation protection focused for a long time mainly on cancer mortality, i. e. *death* from cancer. However, since medical advances have brought about changes in cancer mortality, the focus has shifted onto the risk of cancer occurrence. The availability of good cancer registries has enabled the reliable documentation of new cancer cases.

Historically, the recommendations of the ICRP likewise focused on the mortality endpoint, although with the introduction of the detriment as a concept for measuring the harmful effects, non-fatal cancers were also considered; see also (SSK 2018). The detriment is determined from the lifetime risk of cancer and accounts for the variable lethality, loss of quality of life and years of life lost. Hereditary disorders were also considered.

Other measures of risk, such as the YLL (years of life lost per 100,000 population) as part of the DALY (age-standardised disability-adjusted life years attributable to the environment), QALY (quality-adjusted life years) or HALE (health-adjusted life expectancy) concepts, have not gained a footing in radiation protection.

1.1.3 Effective dose and dose limits

The effective dose, which weights the organ doses according to the efficacy of diverse types of radiation and the sensitivity of the individual organs to stochastic effects and their consequences, serves as a measure of radiation exposure in relation to stochastic effects. The effective dose thereby reflects age-, sex- and population-weighted risks. The current limit for the general public relating to planned cases of exposure in Germany of 1 mSv (Radiation Protection Act, StrlSchG) relates to the annual effective dose.

To assess the radiation exposure limits for the general public, population risks for cancer will be considered in the present scientific background. Based on the knowledge currently available it is not possible to estimate individual risks, while the risks in vulnerable population groups can only be estimated to a limited extent. The population risks are calculated for men and women, three periods of exposure (in utero, childhood and adolescence, adulthood up to and including 89 years) and cumulatively for childhood and adolescence on the one hand and for adulthood on the other. This permits an estimation of the radiation exposure that contributes most significantly to the lifetime risk and the phases of life during which these major risks occur.

1.1.4 Tolerance and acceptance thresholds

What is acceptable and what is tolerable depends on the respective situation and the circumstances as well as social factors. What may be tolerated or accepted in an emergency is neither tolerable nor acceptable in existing or planned exposure situations. However, the principle of proportionality applies to all specifications from the regulator, i. e. the specifications must be necessary, suitable and appropriate (reasonable).

The risk-related concept of measures of the Technical Rules for Hazardous Substances (TRGS910)) for protection against carcinogenic substances in the workplace entails a construct

that comprises various risk areas. A distinction is made between three risk areas which are separated from one another by the acceptance and the tolerance thresholds (Figure 1-1):

- An area of “low” or “acceptable” risk below the acceptance threshold
- An area of “medium” or “tolerable” risk between the acceptance threshold and the tolerance threshold
- An area of “high” or “not tolerable” risk above the tolerance threshold.

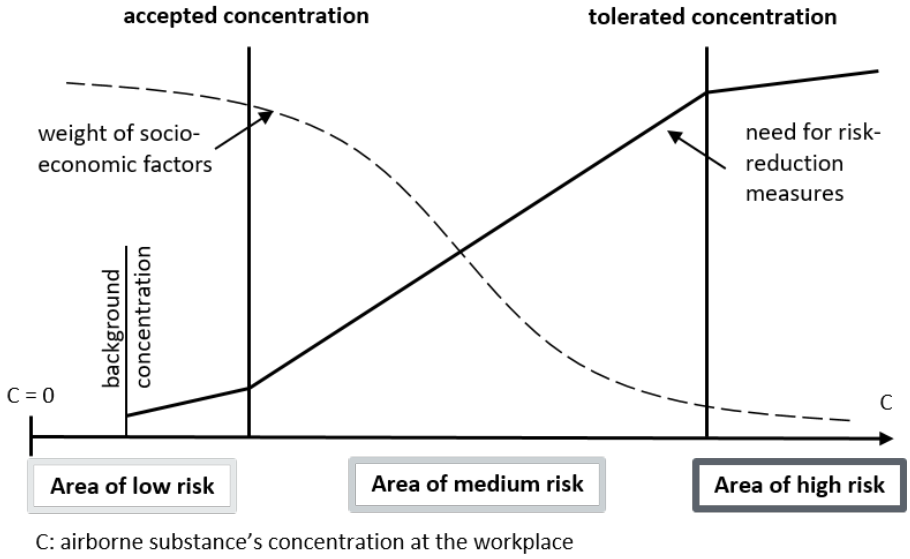

Figure 1-1: Relationship between risk areas and measures (figure modified from TRGS 910). By way of example, the figure shows (non-quantitatively) that the closer the concentration (C) of an airborne substance at the workplace comes to the tolerable concentration, the greater the need for risk-reduction measures. The dashed line illustrates the variable importance of socioeconomic factors in the different risk areas.

A diagram with tolerance and acceptance thresholds could also be a solution for communication in radiation protection. The tolerance and acceptance thresholds should be developed only in the context of numerous parameters and are subject to social discourse. This scientific background to the statement addresses the principles for potentially justifying a tolerable risk to the general public in planned exposure situations.

A fundamental difference between the concepts of TRGS 910 (Figure 1-1) and other assessment systems is the estimation of the background concentration and natural radiation exposure, respectively. The background concentration is considered acceptable according to TRGS 910, whereas other authors (e. g. Jung et al. 2000) set the tolerance threshold below the level of natural radiation exposure.

Without pre-empting future discussions of acceptance thresholds, Table 1-1 provides a summary of the acceptance and tolerance thresholds described or proposed in the literature which relate partly to cancer (incidence), partly to cancer mortality and partly to mortality due to other causes. They demonstrate that there are no consistent answers at present to the questions of what is acceptable or tolerable. On the other hand, it should be stressed that, to protect the public, the tolerance and acceptance thresholds are set at levels 10 to 100 times lower than those for protecting people in the workplace. However, there is no standardised approach here either.

Regulations applicable in Germany for protection against occupational exposure to chemical genotoxic carcinogens are described in chapter 10.

Table 1-1: Ranges of acceptance and tolerance thresholds given by various authors which relate partly to cancer (incidence), partly to cancer mortality and partly to mortality due to other causes (data according to Kalberlah et al. 2005).

	Acceptance thresholds		**Tolerance thresholds**	
	Lifetime risk per year of exposure	Lifetime risk from exposure over entire (occupational) life	Lifetime risk per year of exposure	Lifetime risk from exposure over entire (occupational) life
Workers Occupational life of 40 years	$1 \cdot 10^{-6} – 1 \cdot 10^{-4}$	$4 \cdot 10^{-5} – 4 \cdot 10^{-3}$	$1 \cdot 10^{-5} – 1 \cdot 10^{-3}$	$4 \cdot 10^{-4} – 4 \cdot 10^{-2}$
General public Lifespan of 70 years	$1 \cdot 10^{-8} – 1 \cdot 10^{-5}$	$7 \cdot 10^{-7} – 7 \cdot 10^{-4}$	$7 \cdot 10^{-7} – 1 \cdot 10^{-4}$	$5 \cdot 10^{-5} – 7 \cdot 10^{-3}$

In the legal framework in Germany, the specification of tolerable or acceptable risks and the resulting dose limits, dose constraints or reference levels forms part of the parliamentary legislative procedure, which takes European and international regulations and recommendations into consideration. In radiation protection, the Atomic Energy Act (AtG 1985), the Radiation Protection Act (StrlSchG 2017) and the Radiation Protection Ordinance (StrlSchV 2018) have resulted from this procedure. The regulation concerning the risk assessment and the handling of genotoxic carcinogens at the workplace are laid down in the Technical Rule for Hazardous Substances (TRGS 910), which is adopted by the Committee on Hazardous Substances (AGS).

1.1.5 Evaluation in the social and scientific context

Dose limits, dose constraints and reference levels must be justified. Though they are ultimately based on social consensus, scientific evaluation is also necessary.

Dose limits and constraints are set as the result of social discourse which ends in a majority decision or a decision by mandate holders or governments. This discourse involves assessing the risks, evaluating their significance and weighing up the protective measures that are suitable, necessary and reasonable. The principle of proportionality must also be observed when setting dose limits.

The assessment of risks by individuals is always subjective. It results from people’s basic attitudes while accounting for scientific facts, insofar as the respective level of knowledge is sufficient. Perception of risk plays a crucial role in the assessment of risks, as does the question whether the limits set and their basis can be communicated.

In radiation protection, this discourse is driven mainly by the ICRP, which endeavours to broaden the scope of the recommendations through public discussion of draft recommendations. International organisations such as the IAEA (International Atomic Energy Agency), UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation), WHO (World Health Organization) and ILO (International Labour Organisation) are also involved in the discussion, along with the national and international professional societies.

Recommendations of the ICRP are then incorporated into the International Basic Safety Standards of the IAEA and, in Europe, into the EURATOM Basic Safety Standards, which in turn form the basis for the national regulations.

1.2 The radiation protection system

The aim of radiation protection is to reduce radiation-induced cancers and hereditary disorders to an acceptable level and to prevent deterministic health effects.

To achieve this, the radiation protection system is founded upon three principles of radiation protection which are formulated in ICRP Publication 103 (ICRP 2007a) as follows:

- "*Principle of Justification: Any decision that alters the radiation exposure situation should do more good than harm.*"
- *"The Principle of Optimisation of Protection: The likelihood of incurring exposure, the number of people exposed, and the magnitude of their individual doses should all be kept as low as reasonably achievable, taking into account economic and societal factors."*
- *The Principle of Application of Dose Limits: The total dose to any individual from regulated sources in planned exposure situations other than medical exposure of patients should not exceed the appropriate limits specified by the Commission* [ICRP]."

The limit represents the boundary between tolerable and not tolerable risks. The objective of optimisation is to achieve an acceptable risk under the given circumstances.

The three principles of radiation protection have been incorporated into international and national regulations and laws. They apply in all planned exposure situations: occupational radiation exposure, medical radiation exposure and public radiation exposure, as well as exposure to radiation for the purpose of non-medical imaging, e. g. for forensic purposes. In existing and emergency exposure situations where a generally applicable limit is not appropriate, ranges of reference levels are defined which, combined with the optimisation principle, are designed to guarantee the best possible protection for workers and members of the general public.

To understand the basic principles and rationale behind the limits, their historical development needs to be considered; this is presented in chapter 2.

Since dose limits, dose constraints and reference levels are seldom differentiated and their meaning is frequently misunderstood, the terms are explained below based on the glossary provided in ICRP Publication 103 and the definitions of the Radiation Protection Act (StrlSchG 2017).

- A **dose limit** is the value of the effective dose or the equivalent dose to individuals from planned exposure situations that shall not be exceeded.
- A **dose constraint** according to ICRP Publication 103 serves as a prospective and source-related restriction on the individual dose from a source in planned exposure situations which provides a basic level of protection for the most highly exposed individuals from a source and serves as an upper bound on the dose in optimisation of protection against that source. For occupational exposure, the dose constraint is a value of individual dose used to limit the range of options considered in the process of optimisation. For public exposure, the dose constraint is an upper bound on the annual doses that members of the public should receive from the planned operation of any controlled source.
- A **reference level** represents the level of dose or risk in emergency or existing controllable exposure situations above which it is judged to be inappropriate to plan to allow exposures to occur, and below which optimisation of protection should be implemented. The chosen value for a reference level will depend upon the prevailing

circumstances of the exposure under consideration. According to ICRP Publication 103, a value of 1 mSv per year is considered the goal of optimisation in existing exposure situations.

– One anomaly is the value of 10 µSv a^{-1} with respect to **clearance**. It does not represent a dose limit (but rather a criterion according to the Radiation Protection Ordinance (StrlSchV)) and involves a dose "in the range of 10 µSv a^{-1}". For dose levels below this range, a statutory rule is not deemed necessary (de minimis principle). Relevant sources can be formally dismissed from the scope of the radiation protection legislation.

– In Publication 103, the ICRP lays down the following system of ranges for dose constraints and reference levels (Table 1-2).

Table 1-2: *Framework for source-related dose constraints and reference levels with examples of constraints for workers and the public from single dominant sources for all exposure situations that can be controlled (after (ICRP 2007a)).*

Bands of constraints and reference levels[a] (mSv)	**Characteristic of the exposure situation**	**Radiological protection requirements**	**Examples**
Greater than 20 to 100 [b,c]	Individuals exposed by sources that are not controllable, or where actions to reduce dose would be disproportionately disruptive. Exposures are usually controlled by action on the exposure pathways the exposure pathways.	Consideration should be given to reduce doses. Increasing efforts should be made to reduce doses as they approach 100 mSv. Individuals should receive information on radiation risk and on the actions to reduce doses. Assessment of individual doses should be undertaken.	Reference level set for the highest planned residual dose from an radiological emergency.
Greater than 1 to 20	Individuals will usually receive benefit from the exposure situation but not necessarily from the exposure itself. Exposures may be controlled at source or, alternatively, by action in the exposure pathways.	Where possible, general information should be made available to enable individuals to reduce their doses. For planned situations, individual assessment of exposure and training should take place.	Constraints set for occupational exposure in planned situations. Constraints set for comforters and carers of patients treated with radiopharmaceuticals. Reference level for the highest planned residual dose from radon in dwellings.
1 or less	Individuals are exposed to a source that gives them little or no individual benefit but benefits to society in general. Exposures are usually controlled by action taken directly on the source for which radiological protection requirements can be planned in advance.	General information on the level of exposure should be made available. Periodic checks should be made on the exposure pathways as to the level of exposure.	Constraints set for public exposure in planned situations.

a Acute or annual dose.
b In exceptional situations, informed volunteer workers may receive doses above this band to save lives, prevent severe radiation-induced health-effects, or prevent the development of catastrophic conditions.
c Situations in which the dose threshold for deterministic effects in relevant organs or tissues could be exceeded should always require action.

This table includes aspects of radiation exposure for the general public, occupational radiation exposure and unusual or extreme situations. The dose limits that constitute the boundary between the dose ranges are accepted worldwide and have been adopted in the EURATOM Basic Safety Standards (EURATOM 2014).

The system of dose limits, dose constraints and reference levels has been interpreted by (Michel et al. 2018) and (Völkle 2021) as a traffic light system, as follows:

- The **upper reference level** for existing and emergency exposure situations[9] constitutes the boundary between tolerable (yellow) and not tolerable (red). Optimisation is necessary in the tolerable range; in the not tolerable range, action must be taken and is almost always justified in emergency exposure situations.
- The **lower reference level** for existing and emergency exposure situations constitutes the boundary between acceptable (green) and tolerable (yellow). Optimisation is necessary in the tolerable range. If the exposure does not reach the lower reference level in an emergency exposure situation, the situation should be treated as an existing exposure situation.
- In planned exposure situations, a **dose limit** separates tolerable from not tolerable. The limit may not be exceeded. Optimisation is necessary below the respective limit.
- A **dose constraint** (as defined by German law) implies that anything below this limit is acceptable in any exposure situation. Further optimisation of the protection is no longer necessary in this case.
- A ***de minimis* level**, in planned exposure situations, constitutes a dose limit below which additional doses from a source would be excluded or exempted from legal regulations. Such doses are acceptable. Whether such a limit marks the boundary between acceptable and tolerable is disputed and shall be reserved for a future recommendation.
- A **dose constraint** according to ICRP Publication 103 lies in the tolerable range in planned exposure situations and represents an optimisation tool.

It must be noted here that in planned exposure situations the principle of optimisation helps to ensure that the limits are not exhausted. The actual radiation exposure is at least one order, and in many cases several (in the case of nuclear power plants more than three) orders of magnitude below the exposure limits. This should always be remembered when assessing the risks (refer also to the reports of the Federal Government on environmental radioactivity and radiation exposure (parliamentary reports)[10]).

Only the basic principles and rationale behind the dose limits are covered in this statement and scientific background. Whereas the rules for existing exposure and emergency exposure situations are not addressed in this statement and scientific background, they cannot always be ignored.

2 Historical development of radiation protection limits for the general public

Historically, limits for exposure of the public to radiation have been set in line with concepts for regulating occupational radiation protection. Hence, developments for setting occupational radiation exposure limits are also presented in this chapter along with those for public radiation exposure, as far as necessary. The historical development of radiation protection limits has been influenced by the development of risk assessments by the ICRP. After a brief historical overview (section 2.1.1), the three main ICRP recommendations are discussed in detail: ICRP

[9] Note that the ICRP assumes that emergency exposure situations are only of limited duration, whereas existing exposure situations can also last longer.

[10] https://www.bfs.de/SharedDocs/Downloads/BfS/EN/expert-info/parlamentsberichte-dip.html

Publication 26 in section 2.1.2, ICRP Publication 60 in section 2.1.3 and ICRP Publication 103 in section 2.1.4. Lastly, consideration is given to the historical development in Germany (section 2.2).

2.1 ICRP recommendations

2.1.1 Historical overview

The development of the limits for occupational radiation exposure (top) and radiation exposure of the general public (bottom) over time, based on the ICRP recommendations, is presented in Figure 2-1.

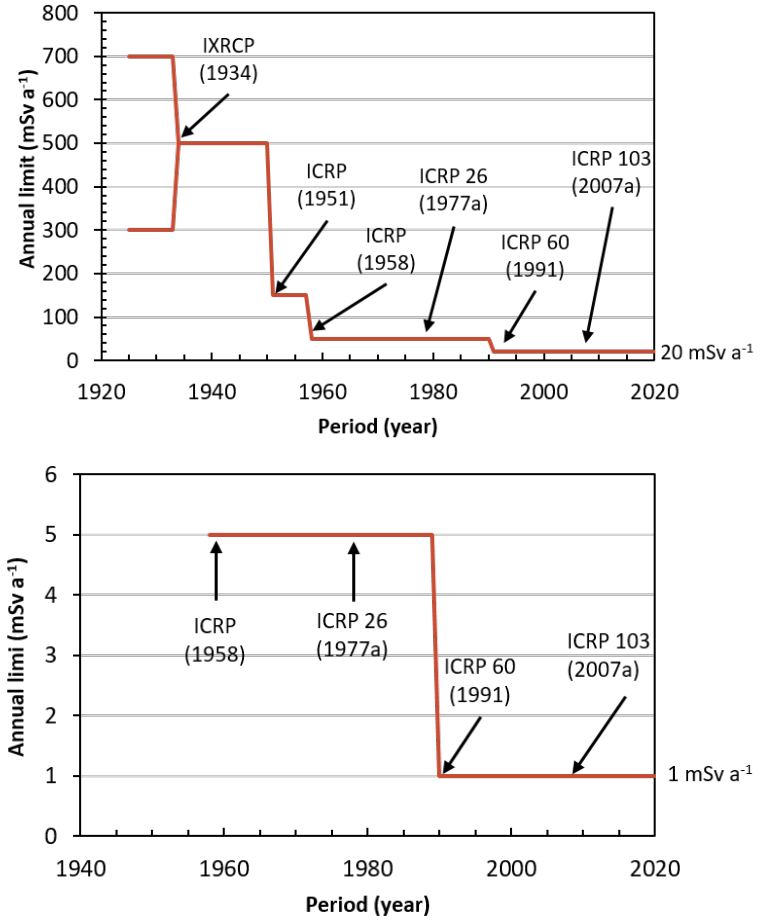

Figure 2-1: Development over time of the annual limits for various dose levels, applied here to the effective dose, for occupational radiation exposure (top) and radiation exposure of the general public (bottom). The range of the occupational radiation exposure limit as proposed by (Mutscheller 1925) and (Sievert 1925) was initially broad, illustrating the uncertainty at the time due to the lack of definitions for an appropriate dose quantity. The ICRP recommendations of 1950 and 1956 were not published until 1951 and 1958, respectively.

The regulatory framework for radiation protection has been established over time from advances in knowledge about the health effects of ionising radiation and has led to greater safety due to lowering the limits in response to new findings. The assessment of radiation risks and the resultant limits have essentially remained unchanged for about three decades.

When the development of radiation protection first began, attention was focused on the avoidance of deterministic effects. In 1925, (Mutscheller 1925) and (Sievert 1925) suggested that the annual dose be limited to 10 % of the erythema dose. This dose, defined by a health

effect, is a very vague limit in units of a physically defined dose, since 10 % of the erythema dose corresponds to approx. 30 R (Röntgen) per year for 100 kV X-rays and approx. 70 R per year for 200 kV X-rays (100 R in tissue amount to slightly less than 1 Gy or 1 Sv with low LET radiation, i. e. for beta, gamma and X-ray radiation). At that time, there was no reasonable unit for measuring radiation. This uncertainty is illustrated in Figure 2-1 by a corresponding range.

As radiation protection has developed, different terms have been used to describe the dose. Examples are the genetically significant dose, the whole-body dose and the effective dose. No such distinctions are made here. As far as possible, the discussion is conducted in effective dose units.

In 1925, the need to establish a radiation protection committee was discussed at the first International Congress of Radiology (ICR) in London. The *International X-Ray and Radium Protection Commission (*later the *International Commission on Radiological Protection* (ICRP)) was founded at the second congress in Stockholm in 1928 (Clarke und Valentin 2009). The objective of the ICRP was to establish the necessary standards of protection based on scientific knowledge. At the same time, it was clear that the harmful effects of radiation were a matter of the dose and that the curative effect of the ionising radiation for treating malignant diseases also depends on the dose applied. Hence, the *International X-Ray Unit Committee* (later the *International Committee for Radiological Units;* today the *International Commission on Radiation Units and Measurements* (ICRU)), which had likewise been envisaged at the first congress in 1925, was also established at the second congress. The first task of the ICRU was to define a unit for the measurement of radiation in medicine.

Dose limits for individuals exposed occupationally to radiation were first recommended by the International X-Ray and Radium Protection Commission (IXRPC), as the predecessor to the ICRP, in 1934. The aim of these limits was to avoid deterministic effects, which the ICRP formulated as follows: "*The known effects to be guarded against are: (a) Injuries to the superficial tissues. (b) Derangements of internal organs and changes in the blood. The evidence at present available appears to suggest that under satisfactory working conditions a person in normal health can tolerate exposure to X rays to an extent of about 0.2 international röntgens (r) per day.*" (IXRPC 1934).

It took another 16 years for the ICRP to consider a more complete list of the biological effects of radiation. It then identified five possible consequences of radiation exposure: "*It appears that the effects to be considered are: (1) Superficial injuries, (2) general effects on the body, particularly the blood and blood-forming organs, e. g., production of anaemia and leukaemia, (3) the induction of malignant tumours, (4) other deleterious effects including cataract, obesity*[11]*, impaired fertility, and reduction of life span, (5) genetic effects.*" (ICRP 1951).

Around 1950, there were fears of genetic damage in the descendants of survivors of the atomic bombings of Hiroshima and Nagasaki. These fears could not be confirmed, however. More recent studies also found no genetic damage in the descendants (Yeager et al. 2021). So far, such effects have only been observed in animal experiments. The incidence of leukaemia and malignant tumours was found to be increased in the survivors of the atomic bombings, however. This led to a change in radiation protection. It was no longer a matter of merely avoiding deterministic effects, but also of limiting the risk of stochastic effects to an acceptable or tolerable level.

[11] It is not clear whether the ICRP in fact regarded obesity as a radiation-induced effect. It appears as such in the recommendation, however (ICRP 1951).

Until 1956, radiation protection was aimed solely at workers handling radioactivity and radiation. In 1956, the ICRP introduced recommendations for limiting radiation exposure in the general population by a factor of 10 below the limit for occupational radiation exposure (ICRP 1958). It based its decision on the fear of genetic effects associated with the growing peaceful use of nuclear energy and the increasing use of radioactivity and radiation.

Since the scientific evidence – particularly with respect to genetic effects in humans – was unsatisfactory, the ICRP considered such a recommendation "*prudent*", i. e. reasonable based on the principle of prevention: "*Until general agreement is reached, it is prudent to limit the dose of radiation received by gametes from all sources additional to the natural background to an amount of the order of the natural background in presently inhabited regions of the earth.*" (ICRP 1958).

The ICRP thus recommended a limit for the genetically significant dose in the general population of 5 rems ≅ 50 mSv per year: "*(64) It is suggested that the genetic dose (see paragraph 63) to the whole population from all sources additional to the natural background should not exceed 5 rems plus the lowest practicable contribution from medical exposure. The background is excluded from the suggested value because it varies considerably from country to country.*" (ICRP 1958).

Furthermore, in paragraph (61) the ICRP established the linear no-threshold (LNT) model (ICRP 1958), which has since been used as the general approach for extrapolating the risks of stochastic effects from the disease rates observed at high doses to low (ICRP 1977a) doses for which no reliable estimates of radiation-induced disease rates are available. The ICRP has stressed repeatedly that the LNT model is designed for the purposes of radiation protection – e. g. for deciding on the action to be taken – and not for quantifying individual radiation risks.

The dose and dose-rate effectiveness factor (DDREF) was first mentioned in 1959: "*Dose Rate Effects … (b) Genetic effects – A linear dose-effect relationship unaffected by dose rate has been generally accepted in the past for gene mutations. Recent experimental work has shown, however, that at intermediate and higher levels of dose rate the number of mutations produced in test subjects may not be independent of dose rate.*" (ICRP 1960). The DDREF is still disputed today; see (SSK 2014).

2.1.2 ICRP Publication 26

The ICRP first formulated a complete radiation protection concept in Publication 26 (ICRP 1977a). It then distinguished between stochastic and non-stochastic effects and recommended extending radiation protection to the general population in addition to workers. It recommended not only dose limits but also radiation protection principles for justification and the ALARA principle (*as low as reasonably achievable*) while accounting for economic and social factors. ICRP Publication 26 also offered a general justification for the dose limits: "*The aim of radiation protection should be to prevent detrimental non-stochastic effects and to limit the probability of stochastic effects to levels deemed to be acceptable.*"

It should be noted here that the term "acceptable", as used in ICRP Publication 26 (ICRP 1977a), corresponds to the term "tolerable" in ICRP Publication 60 (paragraph (150); ICRP 1991) and deviates, moreover, from current usage. According to the SSK, cases of radiation exposure are tolerable if they fall below a tolerance threshold which, if exceeded, would be deemed inappropriate. The range of tolerable radiation exposures is limited downwards by an acceptance threshold, below which radiation exposure is acceptable without further optimisation of the protection.

Since a threshold must first be exceeded for deterministic effects to occur before the severity and – due to the differences in individual radiation sensitivity – the frequency of the disease

then increases with increasing doses, it is relatively easy to formulate dose limits for such radiation effects. To rule out deterministic effects, the limits must basically be significantly lower than the threshold doses. In Publication 26, therefore, the ICRP proposed an annual limit of 500 mSv for all organs except for the lens of the eye, where an annual dose limit of 300 mSv was recommended.

The situation surrounding stochastic effects is far more complex. In radiation protection, it is assumed that there are no threshold doses for stochastic risks (as for malignant tumours, leukaemia and genetic diseases) and the severity of the disease does not depend on the dose of radiation, whereas the risk increases with the dose of radiation. This immediately gives rise to the question of what the ICRP considers "*acceptable*". In Publication 26, it pursued the concept of comparing the radiation-induced stochastic effects against the risks in other occupations regarded as "safe": *"comparing this risk with that for other occupations recognised as having high standards of safety"*. The ICRP thus concluded in Publication 26, while also considering various other assumptions, that the risk associated with the equivalent dose of 50 mSv per year would be "acceptable" for occupational radiation exposure. This concept was aligned with the approach taken in other professions and was explained in detail in ICRP publications 27 (ICRP 1977b) and 45 (ICRP 1985).

In paragraph 15 of Publication 26, the ICRP introduced the "detriment", a fundamental concept that it has used ever since; refer also to (SSK 2018). The LNT model was updated in ICRP Publication 26. It was described in paragraph 24 as "a cautious assumption", and the DDREF was considered (paragraph 30), with a view to recommending a dose limit, as a means of counteracting what at the time was suspected to be an overestimation of the radiation risk at low doses.

It should be noted that, when setting the dose limits in Publication 26, the ICRP also considered the experience available at the time that in a large group of occupationally exposed workers a logarithmic normal distribution of annual doses resulted with an arithmetic mean of approx. 5 mSv per year. In Germany, the level today is much lower than 5 mSv per year. Only in very few individuals does the annual dose approximate the current annual dose limit of 20 mSv.

For the general public, the ICRP recommended a dose-equivalent limit of 5 mSv per year in paragraph 117 of Publication 26 for the critical group[12]. It was assumed that due to the principle of optimisation the actual doses would be ten times lower. This was formulated by the ICRP as follows: *"(119) The assumption of a total risk of the order of 10^{-2} Sv^{-1} (see paragraph 60) would imply the restriction of the lifetime dose to the individual member of the public to a value that would correspond to 1 mSv per year of life-long whole-body exposure. For the reasons given in the following paragraphs, the Commission's recommended whole-body dose-equivalent limit of 5 mSv (0.5 rem) in a year, as applied to critical groups, has been found to provide this degree of safety and the Commission recommends its continued use under the conditions specified in paragraphs 120-128."*

To justify the limits for occupational radiation exposure, the ICRP discussed a cost-benefit analysis in Publication 26 It raised doubts, however, as to the applicability of this approach to the entire population (ICRP 1977a, paragraph 70, 71). A different approach was therefore used, i. e. the radiological risks were compared against the other risks of everyday life: *"(117) Radiation risks are a very minor fraction of the total number of environmental hazards to which members of the public are exposed. It seems reasonable therefore to consider the magnitude of*

[12] A critical group should be representative of those individuals in the population in whom the highest level of exposure is expected. (ICRP 26 (1977a) Para. 85: "… *be representative of those individuals in the population expected to receive the highest dose equivalent."*)

radiation risks to the general public in the light of the public acceptance of other risks of everyday life. This acceptance (when related to risks that could not be reduced or avoided entirely) is motivated by the benefits that would not otherwise be received, by an assessment of the social cost of achieving a possible reduction of risk, or by an implicit judgement that the risk is negligible."

The ICRP considered the comparison with the risks of using public transport to be a suitable criterion for establishing a radiation exposure limit for the general public and states in paragraph 118: *"… On this basis, a risk in the range of 10^{-6} to $l0^{-5}$ per year would be likely to be acceptable to any individual member of the public."*[13]

2.1.3 ICRP Publication 60

In Publication 60 (ICRP 1991), the ICRP no longer applied the aforementioned approach of comparing against risks in other occupations or everyday risks. Greater emphasis was placed on defining the terms *unacceptable, tolerable* and *acceptable. Unacceptable* (not tolerable) implies that, under standard working conditions, a risk is not acceptable; this can change following accidents or disasters. *Tolerable* refers to situations that are unwelcome but can be tolerated, while *acceptable* implies that such risks can be accepted after optimisation. The ICRP drew the line between "*unacceptable*" and "*tolerable*" for occupational radiation exposure at one radiation-induced occupational death per year per 1,000 people. In the rationale (ICRP 1991, Annex C, ch. C14), reference was made to a British study in which an annual risk of death of 1 in 100 was deemed unacceptable in relation to occupational activities. However, according to this study, a risk of 1 in 1,000 could hardly be deemed completely unacceptable if everything had been done to minimise the risk.

In paragraph 124 of Publication 60, the ICRP drew attention to the fact that limits do not represent a demarcation line between safe and dangerous. Nor are they used, moreover, to minimise radiation exposure and demand technical improvements. Thirdly, limits are not to be regarded as the sole instrument of protection against radiation. In many cases in which regulators use limits as tools, the better solution would be to optimise protection.

In paragraph 24 of Publication 60, the ICRP reinforced the assumption of an LNT model for the comparative description of the radiation risk for stochastic effects (detriment) and in (74) the application of a DDREF of 2. However, it also pointed out that the LNT model is not suitable for calculating the number of cases of illness and death.

The assessment of radiation risks was modified significantly in ICRP Publication 60 with the introduction of a multiplicative model to replace the additive model that had previously been used. "*(76) … This model, the multiplicative risk projection model, is probably too simple, even for the exposure of adults. The Japanese data show that neither it nor the additive risk projection model (see below) adequately fits the pattern of mortality following the exposure of young children. The model does not necessarily imply a multiplicative biological process - it may only be a convenient description of the way in which the probability of an attributable cancer varies with time after exposure.*"

Based on this consideration and more recent epidemiological data on the risk of cancer in Hiroshima and Nagasaki, and the application of a multiplicative risk projection model, an average annual limit of 20 mSv resulted for occupationally exposed workers, expressed as 100 mSv every five years whereby 50 mSv may not be exceeded in any one year. In the

[13] The risk assumed here by the ICRP (1977a) is very low. In the 1970s, the number of road deaths per year per 100,000 inhabitants in the Federal Republic of Germany was 20 to 30. By 2020, it was still around 3.

following, however, occupational radiation exposure is not examined further. The SSK has already commented on this and on the principles for justifying the limits applicable therein (SSK 2018). In the following, attention is focused on the limits for the general public.

In Publication 60, the ICRP recommended an effective dose limit of 1 mSv per year for the general public. In special, albeit unspecified situations, it allowed for up to 5 mSv per year provided an average of 1 mSv per year was not exceeded in a five-year period.

It stressed that there are two approaches for selecting this limit: firstly, the selection of a limit between tolerable and no longer tolerable risks in the same way as for occupational radiation exposure, and secondly the comparison with the variability of natural radiation exposure on the other. The ICRP regarded the first option as extremely difficult in that it requires "*social judgement*", but the second option as more feasible. The ICRP noted: "*This natural background may not be harmless, but it makes only a small contribution to the health detriment which society experiences. It may not be welcome, but the variations from place to place (excluding the large variations in the dose from radon in dwellings) can hardly be called unacceptable."*

In addition, limits of 15 mSv per year for the lens of the eye and 50 mSv per year for the skin were recommended in paragraph (194) of ICRP Publication 60 to prevent deterministic effects in the general population, as the effective dose did not take the eye lenses and skin into consideration. *"(194) Limits are also needed for the lens of the eye and localized areas of the skin since these tissues will not necessarily be protected against deterministic effects by the limit of effective dose. Because the total period of exposure may be nearly twice as long as for occupational exposure, and because the exposed individuals may show a wider range of sensitivity than the more limited population of workers, the recommended annual limits (non-occupational) for the equivalent dose in these tissues are lower than those for workers. The Commission has adopted an arbitrary reduction factor of 10, leading to annual limits of 15 mSv for the lens and 50 mSv averaged over any 1 cm^2 area of skin, regardless of the area exposed."*

2.1.4 ICRP Publication 103

Publication 103 of the ICRP (ICRP 2007a), which formed the basis for the EURATOM Basic Radiation Protection Standards of 2013 (Euratom 2014) and the German Radiation Protection Act (StrlSchG) of 2017 (StrlSchG 2017), generally updated but also restructured the radiation protection system as defined in ICRP Publication 60 (ICRP 1991). In particular, the categories of radiation exposure were reorganised by distinguishing between planned, existing and emergency exposure situations, while for existing and emergency exposure situations ranges of reference levels were introduced. For the general public, the annual limit of 1 mSv for planned exposure situations remained in place. The regulations for existing and emergency exposure situations recommended in ICR Publication 103 are not addressed in more detail here. The ICRP stated: *"(243) Dose limits apply only to planned exposure situations, not to the medical exposure of patients. The Commission has concluded that the existing dose limits as recommended in ICRP 60 (ICRP, 1991b) continue to guarantee an appropriate level of protection.* […] *Within one exposure category – whether exposure of workers or members of the general public – dose limits apply to the sum of exposures from sources relating to activities that are already justified."*

Exposure to sources of radiation occurring naturally at the site, which can amount to many times the limit of 1 mSv per year, remains unaffected by the ICRP system. Exposure to radon and derived products in dwellings and to materials from human activities that contain natural radionuclides (naturally occurring radioactive material, NORM) is the exception here. Separate reference levels will be introduced for such cases.

The ICRP recommended the following basic limits for protecting the general public: annual effective dose of 1 mSv, annual dose of 15 mSv for the eye lens and 50 mSv for the skin. The ICRP notes that higher levels may also be permitted for the annual effective dose provided that the average over five years does not exceed 1 mSv per year. In addition to these limits, various other levels are given as criteria for practical radiation protection but are not examined more closely here; see Table 8 in ICRP Publication 103 (ICRP 2007a).

In planned exposure situations, optimisation is required below the limit; however, no lower level for optimisation is expressed in relation to quantity or time. Optimisation should take social and economic aspects in all exposure situations into account.

The system presented in ICRP Publication 103 was adopted in the 2013 EURATOM Basic Safety Standards for Radiation Protection. The new limit for occupational radiation exposure of the lens of the eye recommended in 2011 (20 mSv a^{-1} instead of 150 mSv a^{-1}) (ICRP 2011) and the new reference level for radon (ICRP 2010, Part 2) were incorporated into the EURATOM Basic Safety Standards (EURATOM 2014) and the German Radiation Protection Act (StrlSchG 2017). The new dose coefficients for radon were not adopted (ICRP 2017). Protection against radon in buildings was formulated using a reference value of 300 Bq per m^3 and reference levels were introduced for radionuclides occurring naturally in building materials.

2.2 German legal framework

In 1959, the Basic Radiation Protection Standards (EAG 1959) established a cumulative limit for the entire population of 5 rem ≅ 50 mSv in those up to the 30 years of age, with an annual limit of 0.5 rem ≅ 5 mSv for special groups. Roughly the same limit was adopted in Section 29 of the first StrlSchV (StrlSchV 1960). An annual limit of 0.5 rem ≅ 5 mSv was specified for individuals only occasionally spending time in a monitored area [14]. For those occasionally spending time in a controlled area, an annual limit of 1.5 rem ≅ 15 mSv was set.

The Basic Radiation Protection Standards of 1980 (Euratom 1980) were implemented by way of StrlSchV 1989 (StrlSchV 1989). In doing so, the limitation of radiation exposure in the general population was addressed in more detail: Section 44(1) specified a limit of 1.5 mSv per year from direct radiation; Section 44(2) allowed for 5 mSv per year subject to an official exemption. In Section 45, the "30 mrem per year concept" was established, i. e. limits for airborne emissions and waterborne emissions of in each case 0.3 mSv per year. At the same time, partial-body dose limits of 1.8 mSv per calendar year were introduced for the bone surface and skin, as well as partial body dose limits of 0.9 mSv per calendar year for all other organs and tissues.

The recommendations of ICRP Publication 60 (ICRP 1991) and the amended Basic Radiation Protection Standards (Euratom 1984) were implemented with the amendment of StrlSchV 2011 (StrlSchV 2001). The recommendations of StrlSchV 1989 regarding the limits for the effective dose of 1 mSv per year, 15 mSv per year for the lens of the eye and 50 mSv per year for the skin, were upheld.

One special feature of the German regulations must be mentioned here since it is relevant above all to the risk comparison of radiation protection against that in other areas of environmental and health protection. The system for protecting the public from radiological risks in planned exposure situations extends far beyond mere limitation. In conjunction with an unlimited

[14] The current regulations define the monitored area as one in which those working there may receive more than 1 mSv but less than 6 mSv per year. Could they receive more than 6 mSv in a year, a controlled area must be established.

obligation for optimisation and extremely conservative calculation methods in the general calculation principles (BMI 1979), the AVV to Section 47 StrlSchV (2001)[15] (BMU 2012) and the AVV Activities (BMU 2020b), the exposure of the general public to radiation in planned exposure situations for the representative person is kept at least two powers of ten below the limit; refer to the Parliamentary Report of the Federal Government (BMU 2020a).

Even the specification in the Parliamentary Report of < 10 µSv per year for civilian exposure to radiation from nuclear installations and facilities or from research, technology and households, respectively, is extremely conservative. In its statement, the SSK established that realistic dose estimates for the representative person are lower than 1 µSv per year in the case of nuclear installations and facilities (SSK 2008).

Regulations for exposure to radiation from natural radioactivity were first established in StrlSchV 2001. Section 97 StrlSchV specified an effective dose constraint of 1 mSv per year for increased exposure to residual natural radioactivity and radiation; this was also taken as a criterion for release of residues from regulatory control. It should be pointed out again here that a dose constraint (according to German law) effectively defines an acceptance threshold.

The recommendations of ICRP Publication 103 and the new European Basic Radiation Protection Standards (EURATOM 2014) which are based on these recommendations were implemented by the Radiation Protection Act (StrlSchG 2017) and underpinned by the Radiation Protection Ordinance (StrlSchV 2018). A detailed system of dose limits, reference levels and dose constraints was thus introduced for the various exposure situations as defined by ICRP Publication 103 for occupational radiation exposure, medical radiation exposure and public radiation exposure, as well as radiation exposure for non-medical imaging purposes.

Figure 2-2 illustrates the development of the essential limits for restricting the exposure of the general population to radiation according to German radiation protection laws.

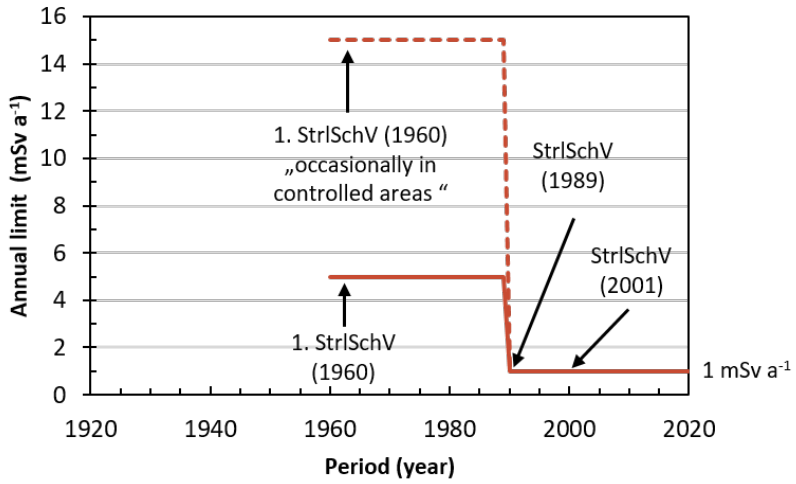

Figure 2-2: Development over time of the annual limits for the population in Germany with respect to the effective dose. The dashed line indicates the limit for special population groups, i. e. for individuals only occasionally spending time in controlled areas.

With a view to planned exposure situations, an effective dose limit of 1 mSv per calendar year is set in Section 80 StrlSchG (StrlSchG 2017) based on the sum of licensed activities; see also (SSK 2015). In addition, organ equivalent dose limits are set at 15 mSv and 50 mSv per

[15] In the version valid up to 31 December 2018

calendar year for the lens of the eye and for the skin, respectively. No other organ dose limits were included in StrlSchG; see also (SSK 2020).

In Section 62 StrlSchG (StrlSchG 2017), an effective dose limit of 1 mSv per year is specified as the criterion for release of residues from regulatory control; in Section 64 StrlSchG, a dose constraint of 1 mSv per year is specified for the removal of contamination (natural radionuclides) from land.

Whereas the term "limit" is not used with respect to the post-closure phase in the safety requirements for final disposal of heat-generating radioactive waste (BMU 2010), the following is stated:

"*6.2 For the post-closure phase, it shall be demonstrated that in the case of probable developments due to the release of radionuclides originating from stored radioactive waste, individual members of the public may be exposed to an additional effective dose in the range of 10 microsieverts only per year. To be considered here are individuals alive today who will be exposed throughout their lifetime.*

6.3 For less likely developments in the post-closure phase, it must be demonstrated that the additional effective dose caused by the release of radionuclides originating from stored radioactive waste does not exceed 0.1 millisieverts per year for the individuals thus affected. Likewise to be considered here are individuals alive today who will be exposed throughout their lifetime."

In paragraph 6.2, the BMU refers to the trivial dose according to ICRP Publication 104 (ICRP 2007b). An annual risk of less than 10^{-5} is given in paragraph 6.3, based on ICRP Publication 81 (ICRP 1998). However, according to ICRP Publication 81 a dose of 0.3 mSv per year corresponds to an annual risk of approximately 10^{-5}. The dose limit given by the BMU is three times lower. The BMU limits do not confer with the recommendations of (RSK und SSK 2002), in which levels of 0.3 mSv per year for normal development and 1 mSv per year for rare developments are proposed. In ICRP Publication 103, 0.3 mSv per year is again recommended by the ICRP.

Concerning the addition of radioactive substances to consumer products and their activation, Section 40 StrlSchG (StrlSchG 2017) specifies an admissibility criterion in the range of 10 µSv per year. The same criterion in the range of 10 µSv per year is the basis for the exemption levels and clearance values as per Annex 4 StrlSchV (StrlSchV 2018).

Different standards are applied by the StrlSchG to natural radioactivity. This results in a different approach to radiation protection as regards exposure to natural and artificial radioactivity and radiation. Exposure to natural radioactivity is treated as an existing exposure situation. For existing exposure situations, Section 118 StrlSchG sets a lower reference level for the effective dose for a representative person of 1 mSv per year as the target for protection and specifies that an upper reference level of 20 mSv per year must not be exceeded.

Reference levels for the effective dose of 1 mSv per year apply to legacy sites, according to Section 136 StrlSchG. According to Section 133 StrlSchG, reference levels for the effective dose of 1 mSv per year apply to radioactivity in building materials in addition to external radiation exposure outdoors.

In the case of radon, the concept of a reference level of 1 mSv per year for existing exposure situations reaches its limits. Section 124 StrlSchG sets a reference level of 300 Bq m^{-3}, which

in light of the dose coefficients of 9 nSv/(Bq EEC h m^{-3})[16] (UNSCEAR 2019) and an exposure time of 8,760 h corresponds to an effective dose of approximately 10 mSv per year.

For emergency exposure situations, Section 93 StrlSchG sets a reference level for the effective dose for the representative person of 100 mSv per year; in Section 118 StrlSchG, 20 mSv per year is defined as the reference level for the transition to an existing exposure situation.

3 Natural radiation exposure

The majority of the radiation to which the population is exposed worldwide results from natural radioactivity and the ionising radiation emanating from it (Cinelli et al. 2019). Exceptions to this are only found in areas that are heavily contaminated due to anthropogenic influences or due to medical use in individuals (Siehl 1996, Eisenbud und Gesell 1997). Natural radioactivity and natural ionising radiation emanate primarily from high-energy cosmic rays that interact with the upper atmosphere, and from long-lived (primordial) radionuclides in the earth's crust and their decay products (terrestrial radiation). These components and the resultant dose due to external radiation exposure, ingestion and inhalation, are described and discussed below. Where the annual effective dose or dose rates are specified as numerical values, it should be noted that there are often large variations. The specification of an average value, whether for Germany or the world as a whole, only serves the purpose of classifying the respective component relative to the others. Overarching frequency distributions are required for a meaningful discussion but are not always available; discussing them here would exceed the scope of this statement. Figure 3-1 offers an impression of the variability of the annual effective dose from natural radiation sources for the populations of 15 countries.[17]

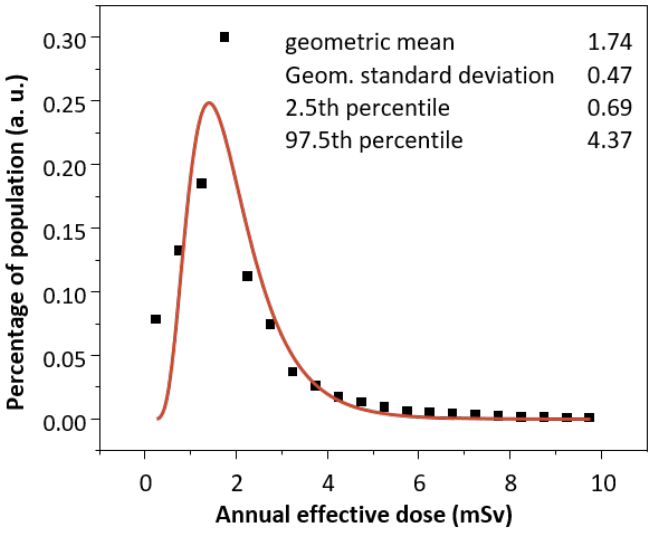

Figure 3-1: Distribution of the population in 15 countries by annual effective dose from natural radiation exposure (compiled according to (UNSCEAR 2000)). The red curve illustrates the fit of a log normal distribution to the data. This results in the parameters listed in the figure.

[16] EEC: equilibrium equivalent concentration

[17] China, Japan, Malaysia, Denmark, Finland, Lithuania, Belgium, Netherlands, Bulgaria, Hungary, Romania, Russia, Albania, Italy, Portugal (UNSCEAR 2000)

Reference is made in sections 3.1 to 3.2 to the global situation and average values are considered without weighting according to the size of the affected population. Radon is treated as a special case in section 3.3. Values are then given for Germany (section 3.4) and examples of the frequency distributions for dose values are given based on the example of northern Germany.

3.1 Cosmic radiation and cosmogenic radionuclides

3.1.1 External exposure from cosmic radiation

Depending on its origin, cosmic radiation is classified as galactic or solar. Galactic radiation consists of approximately 88 % protons and 10 % helium nuclei and electrons (UNSCEAR 2008a). The energy of these particles ranges from 10^8 eV to over 10^{20} eV. The second component of cosmic radiation originates from solar particle events. Protons are mainly produced here too, but with much lower energy levels. Cosmic gamma radiation is absorbed almost completely in the atmosphere and has little significance at sea level. The sun's influence on cosmic radiation is most significant during the eleven-year period of its activity (solar cycle). Solar wind (plasma that generates a magnetic field) increases and decreases to the same extent as its flow of particles. When the activity is high, it shields the galactic component so efficiently that the resulting cosmic radiation (i. e. the sum of galactic and solar components) decreases. A high level of solar activity therefore leads to lower radiation exposure due to cosmic rays. The Earth's magnetic field also contributes significantly to shielding. At low latitudes (near the equator), the charged particles strike the field lines vertically and are deflected due to the Lorentz force. At high latitudes, i. e. near the poles, the particles enter parallel to the field lines and thus can penetrate lower atmospheric layers.

However, the dose for humans at sea level is not determined by the primary particles but rather by the secondary products resulting from nuclear reactions with the atoms of the atmosphere. Those most relevant at ground level are muons and photons. An annual effective dose of 270 µSv of direct ionising radiation is the global average for people living at sea level. This portion of the dose rate, generated by photons and direct ionising radiation, is estimated using the formula

$$\dot{E}_1 = \dot{E}_1(0)[0{,}21e^{-1{,}649z} + 0{,}79e^{0{,}4528z}]$$

(Bouville and Lowder 1988), where z is the height above sea level in metres and $\dot{E}_1(0)$ is the annual effective dose at sea level as per (UNSCEAR 2008a). Neutrons contribute another 48 µSv. The neutron contribution increases as the altitude rises in the mountains. Including the contribution of the neutrons, this results in an annual effective dose of 380 µSv as the global population-weighted average (UNSCEAR 2008a). During air travel at altitudes of ten to twelve kilometres, electrons, positrons and protons contribute to the effective dose in addition to muons, photons and neutrons. This results in effective dose rates of approx. 2 µSv h^{-1} to 8 µSv h^{-1} depending on the latitude.

3.1.2 Internal exposure from cosmogenic radionuclides

Atoms in the atmosphere (mainly in the stratosphere) interact with cosmic protons and with the neutrons which are formed as secondary products. Cosmogenic radionuclides thus result. Worthy of mention here are ^{3}H, ^{7}Be, ^{10}Be, ^{14}C, ^{22}Na and ^{129}I. The only products of radiological relevance here are the isotopes, which are not only produced in significant quantities but are also incorporated into the metabolism of the human body. Ingestion leads to annual averaged age-class effective doses of approx. 12 µSv from ^{14}C, 0.15 µSv from ^{22}Na, 0.03 µSv from ^{7}Be and 0.01 µSv from ^{3}H (UNSCEAR 2000). Considerable quantities of ^{3}H and ^{14}C in particular were additionally released into the atmosphere during nuclear weapons testing, so that the

influence of the latter during the 1960s and 1970s significantly exceeded the dose from cosmogenically produced quantities.

3.2 Terrestrial radionuclides

Some naturally occurring radionuclides have such long half-lives that they have not yet decayed since the formation of the solar system. These are called primordial radionuclides. They include, for example, ^{40}K, ^{87}Rb, ^{138}La, ^{147}Sm and ^{176}Lu, whereby ^{40}K plays by far the most important role: potassium is an essential element for humans and radioactive ^{40}K thus always accounts for approx. 0.01 % of the potassium content in the body. Unlike the nuclides mentioned above, nuclides ^{238}U, ^{235}U and ^{232}Th, which are likewise primordial, do not disintegrate to become stable daughters. They form long decay chains of radioactive nuclei, known as radiogenic nuclides. A number of these are alpha emitters with correspondingly high relative biological efficacy. Some of these nuclides decay within seconds while others have half-lives in the range of several years. The decay series only end with the stable lead isotopes: ^{206}Pb, ^{207}Pb and ^{208}Pb.

A full overview of the series and the role of radioactive equilibria can be found in (Kratz und Lieser 2013) and (Magill et al. 2018), for example. Only the radiologically relevant nuclides are discussed below.

The radionuclides mentioned above are omnipresent in soil and rock but vary considerably in their concentration (and mobility) (Atwood 2010). In dried topsoil (Wiechen 1998, DIN ISO 18589-2), the global average is 370 Bq kg^{-1} ^{40}K, for example, and 35 Bq kg^{-1} each for ^{232}Th and ^{238}U (UNSCEAR 2000). The latter corresponds to approx. 3 g of uranium per ton of soil. In some rocks, such as granite, these specific activities may be many times higher; chemical leaching, separation and transport processes can lead to local accumulation of certain elements that occur in the decay series. This applies to the ^{238}U decay series, e. g. ^{226}Ra, which dissolves much more readily and is therefore more mobile than its parent, ^{230}Th. The daughter of ^{226}Ra is the gaseous ^{222}Rn, which is discussed in section 3.3.

3.2.1 External radiation exposure

Only isotopes that emit gamma radiation or produce short-lived daughter nuclei that emit gamma radiation contribute to external radiation exposure. The most important primordial nuclide in this case is ^{40}K, which emits gamma radiation of almost 11 % after electron capture. Numerous members of the uranium and thorium series are also gamma emitters but are not usually considered individually for external radiation exposure. The variable to be measured here is the air kerma rate or energy dose rate at an altitude of one metre. Due to the specific activity in soil as mentioned above, the contributions of ^{40}K and the ^{232}Th and ^{238}U series of 17 nGy h^{-1}, 16 nGy h^{-1} and 18 nGy h^{-1}, respectively, result in a global average outdoors of 51 nGy h^{-1}. The variation is significant and ranges from approx. 1 nGy h^{-1} to over 1,200 nGy h^{-1}, e. g. in parts of Norway or India (UNSCEAR 2000), or even higher in other uninhabited or only sparsely populated areas (Ghiassi-nejad et al. 2002). The gamma dose rate not only fluctuates spatially but is also time-dependent, e. g. due to fluctuations in the radon activity concentrations (and therefore also their gamma ray-emitting daughter nuclides), as well as to precipitation and shielding through moisture (or snow) on the ground. These time-dependent fluctuations can amount to a factor of 2, but are usually much smaller.

Building materials are the main contributor to gamma exposure indoors. The dose rate inside buildings is usually higher than outdoors. The most obvious reason is the change in geometry from a half-space in the open (radiation only from below) to an enclosed setting in rooms where the radiation emanates from all directions. Globally, the average dose rate is 84 nGy h^{-1}, with extreme values of 2 nGy h^{-1} and 2,000 nGy h^{-1}. In some countries the dose rate in dwellings is

comparable or even lower than outdoors. This is the case in countries such as Thailand or the USA, where houses are largely constructed from wood. Wood contains far fewer radionuclides than mineral-based building materials.

The effective dose is calculated using the conversion coefficients of energy dose (air) to effective dose (0.7 Sv Gy^{-1} (UNSCEAR 1993)) and the proportion of time spent outdoors (0.2) and indoors (0.8). Due to the slightly higher dose rate on the one hand and the considerably longer periods spent indoors on the other, an average annual effective dose of 0.41 mSv (5th and 95th percentiles of 0.2 mSv and 1.0 mSv, respectively) results. Another 0.07 mSv can be added from time spent outdoors (5th and 95th percentiles of 0.03 mSv and 0.12 mSv, respectively). This adds up to an effective dose of 0.48 mSv due to external radiation exposure. It should be noted with respect to the ranges that this data represents only approx. 40 % of the world's population. The conversion factor for children and adolescents is approx. 10 % to 30 % higher due to the difference in body proportions from adults. This results in a similarly increased effective dose for these age groups.

3.2.2 Internal radiation exposure through ingestion and inhalation (except radon)

Internal radiation exposure results from the absorption of terrestrial radionuclides through ingestion and inhalation.

The majority of the ingested dose stems from the radionuclides of the uranium and thorium decay series and ^{40}K, which are present in food and drinking water. A very small proportion also originates from cosmogenic radionuclides.

Just as the content of terrestrial radionuclides varies greatly in different locations (see Introduction, section 3.2), so does that of (ground) water and food. In addition to the specific activities, assumptions about eating habits are also included in the estimation of an ingested dose. These vary considerably not only from country to country but in some cases also interindividually (FAO 1984, ICRP 1975,WHO 1988).

Potassium is an essential and at the same time omnipresent element. The primordial radioactive isotope ^{40}K therefore plays a significant role. Food often contains rather high levels of potassium and, in turn, high specific activities of ^{40}K. In healthy individuals, however, the potassium concentration remains consistently within relatively narrow limits (almost 0.2 % in all tissues). A likewise very consistent specific activity of approx. 60 Bq kg^{-1} thus results in the human body. Additional ingestion of natural ^{40}K with food will not alter this specific activity. Taking 3 µSv per Bq kg^{-1} (NCRP 1987) as the conversion coefficient, an annual effective dose of approx. 180 µSv results; 170 µSv a^{-1} is given by (UNSCEAR 2008a).

Of the remaining radionuclides, ^{210}Pb, ^{210}Po, ^{226}Ra, ^{228}Ra, ^{238}U, ^{230}Th, ^{228}Th, ^{232}Th and ^{235}U are those with the highest ingestion rates worldwide, on average, from the diet as a whole. Considering the annual ingested activity for many countries, logarithmic distributions with a width of more than one order of magnitude result. It is therefore difficult to formulate statements concerning global mean values. Medians for the radionuclides mentioned above range from approx. 0.2 Bq for ^{235}U and ^{232}Th to 30 Bq or over 50 Bq for ^{210}Pb and ^{210}Po, respectively (UNSCEAR 2000).

Seafood is a significant source of natural radionuclide ingestion in humans. Specific activities of ^{210}Po of 2.4 Bq kg^{-1}, 15 Bq kg^{-1} and 6 Bq kg^{-1} are typically found in fish, mussels and crustaceans, respectively. The consumption of seafood is highly specific on a national (and regional) level, moreover. Consumption of approx. 13 kg per year leads to an average uptake of approx. 30 Bq of ^{210}Po (UNSCEAR 2000). Drinking water is often the main source of uranium and radium.

Once incorporated into the human body, the radionuclides accumulate – sometimes very specifically – in certain organs or tissues. Both radium, a calcium homologue, and lead thus tend to target the bones, while uranium is additionally found in the kidneys. Polonium undergoes transfer mainly in the liver and kidneys, thorium in the bones (surface and marrow), liver and gonads. Potassium is found in muscle tissue and therefore spreads relatively evenly throughout the body (IAEA 2004, Volkmer 2012). Using biokinetic and dosimetric models, an effective dose of 140 µSv per year due to the radionuclides of the uranium and thorium decay series is derived from this data. (UNSCEAR 2008a) specifies a global mean value of 120 µSv per year. Combined with the dose owing to the content of ^{40}K in human tissue, a value of 290 µSv per year is derived by (UNSCEAR 2008a) for the effective dose from ingestion.

In the case of inhalation, consideration should be given to radionuclides of the thorium and uranium decay series which are present in respirable particles. This proportion is greater inland than by the sea where the concentration of activity in the air is much lower. The burning of coal (fly ash) makes a significant contribution here that is difficult to distinguish from purely natural substrate.

On the other hand, consideration should be given to the decay products of the radon isotopes ^{220}Rn and ^{222}Rn, which mostly dominate. They accumulate on aerosols and thus enter the lungs. These radionuclides also belong to the uranium and thorium decay series but are listed separately due to their differing genesis. Radon and its daughters are considered separately in the following section (3.3).

The highest concentrations of activity (medians) are found with ^{210}Pb (500 µBq m^{-3}) and ^{210}Po (50 µBq m^{-3}). Approx. 1 µBq m^{-3} is contributed by the nuclides ^{238}U, ^{230}Th, ^{226}Ra, ^{232}Th, ^{228}Ra and ^{228}Th. With all these values, the spread for the different regions of the world amounts to one order of magnitude.

Adding these figures together, a global median of 6 µSv is obtained for the annual effective dose from inhalation of all nuclides, except radon and its decay products (UNSCEAR 2000).

3.3 Internal exposure to radiation from radon

The inhalation of radon and its decay products (DPs) makes the greatest contribution to the effective dose in the global population. This applies not only to the inhaled dose but also to the effective dose from natural sources in general. At the same time, however, the calculation is rather complicated and fraught with uncertainties.

The radiation exposure mainly entails ^{222}Rn and its short-lived decay products and, to a lesser extent, ^{220}Rn/DP. While the direct alpha decays of ^{222}Rn make a contribution, the radioactive progenies of ^{222}Rn accumulate and decay on the walls of the respiratory tracts. Both radon isotopes also have beta- and gamma-emitting daughters, but the alpha decays are largely responsible for the tissue damage due to their high LET value. The radon decay products can also accumulate on aerosols and will be more or less mobile or respirable depending on their size. Consideration is therefore given to the "Factor", which is defined as the ratio of the equilibrium-equivalent radon activity concentration to the actual radon activity concentration and can assume values between 0 and 1 (SSK 2000). The factor typically ranges from 0.4 indoors to 0.6 outdoors.

Radon emanates wherever uranium or thorium is present. Typical values for the concentration of radon activity (activity per cubic metre of air) in soil air range from a few kBq m^{-3} to 1,000 kBq m^{-3}, whereby the values are mostly below 20 kBq m^{-3} in approx. 30 % of Germany's surface and levels exceeding 100 kBq m^{-3} are only to be expected in some highly confined areas. In outdoor air, radon is strongly diluted. Hence, values of 1 Bq m^{-3} and in rare cases up to

50 Bq m^{-3} are measured at a height of 1.5 m. The concentration of the activity of radon decay products likewise varies considerably. Only few reliable studies are available on this subject. In dwellings, radon can pass through floor slabs that are not intact or may be exhaled from building materials, for example. If dissolved in water, moreover, radon can enter a building via the drinking water supply; this is only significant in the case of very fresh water from a spring, not after dwelling for a long period in a storage tank or after treatment. Depending on the degree of air exchange, radon will accumulate in rooms. Activity concentrations may reach several thousand Bq m^{-3}, but typically the values are much lower. Exposure to radiation from radon in buildings in Germany has been studied thoroughly. According to (BMU 2021), the mean annual radon activity concentration in indoor spaces in Germany is 50 Bq m^{-3}. However, the activity concentrations in Germany even in buildings are very heterogeneous due to the different geological conditions. In areas with radon activity concentrations in soil air of up to 20 kBq m^{-3}, it is rare to find radon activity concentrations of more than 100 Bq m^{-3} in indoor spaces. However, increased radon concentrations can be expected more frequently in buildings where the concentrations of radon activity in soil air exceed 20 kBq m^{-3} and depending on the design and state of the construction. Another source of radiation exposure is radon released from handled NORMs, or from stockpiles and residues.

The given radon concentrations in indoor air are determined with direct-reading or accumulating dosimeters, or the total radon concentration is recorded without subtracting a geogenic substrate value, i. e. the value in the open uninfluenced by housing.

Evaluation of radon exposure is a special feature since dose limits and constraints are otherwise oriented to the effective dose. However, due to the variability of the equilibrium factor and also different living habits (e. g. respiratory rate depending on physical exertion at work), this method is fraught with huge uncertainties.

The biological efficacy of radon is still the subject of ongoing research, moreover. Typical values for the effective dose from radon inhalation are proposed by (UNSCEAR 2000) as follows:

Indoors 40 Bq m^{-3} · 0.4 · 7,000 h · 9 mSv per MBq h m^{-3} = 1.0 mSv

Outdoors 10 Bq m^{-3} · 0.6 · 7,000 h · 9 mSv per MBq h m^{-3} = 0.095 mSv

Equilibrium factors between ^{222}Rn and its decay products of F = 0.4 indoors and at F = 0.6 outdoors were thus assumed by (UNSCEAR 2000).

The ICRP suggests that the dose coefficient be revised (ICRP 2017). The SSK recommendation on radon dose coefficients (SSK 2017a) suggests retaining the dose coefficient of 9 mSv per MBq h m^{-3} until new and reliable evidence is available.

In industrialised nations, the majority of people spend most of their time indoors (typically 7,000 h per year). Combined with the radon activity concentrations indoors mentioned above, this accounts for the highest contributions to the inhaled dose. The estimation provided in (BMU 2021) suggests that the radon activity concentrations in room air amount to > 100 Bq m^{-3} for 1.3 to 1.6 million dwellings and > 1,000 Bq m^{-3} only for 4,000 to 25,000 dwellings. Using the dose coefficient of 9 mSv per MBq m^{-3} h while assuming a respiratory rate of 0.6 m^3 h^{-1}, 100 Bq m^{-3} of an effective dose corresponds to approx. 2 mSv a^{-1} and 1,000 Bqm^{-3} to approx. 20 mSv a^{-1} (see also section 3.4).

Sections 121-132 StrlSchV (StrlSchV 2018) provide regulations for protection against radon in common spaces and at workplaces (indoors). Based on Section 121 StrlSchG (StrlSchG 2017), areas in Germany were studied and defined where the mean annual ^{222}radon activity concentration in air is expected to exceed the reference level of 300 Bq m^{-3} (mean annual

concentration in respiratory air) in a significant number of buildings with shared indoor spaces or workplaces.

3.4 Dose estimation, variability of activity concentrations and frequency distributions in Germany

The average level of natural radiation exposure (effective dose) in Germany per year, with low temporal variability, is 2.1 mSv. This has been derived from the regular reports submitted to the Federal Government since 1958 which cover radiation exposure from both natural and anthropogenic sources. At the time of compiling this document, the latest available edition of (BMU 2021) is that which reflects the status of the year 2018. Cosmic radiation (sea level) accounts for approx. 300 µSv and terrestrial radiation approx. 400 µSv, of which approx. 100 µSv results from staying outdoors and approx. 300 µSv from staying indoors. Ingestion of natural radionuclides results in an annual effective dose of approx. 300 µSv. Inhalation of radon and decay products results in an annual effective dose of 1,100 µSv, divided into approx. 200 µSv and approx. 900 µSv from staying outdoors and indoors, respectively. The following should be underlined: "*It should be noted that the values for the entire population represent averaged effective doses. The actual annual dose in one person greatly depends on individual circumstances.*" Furthermore, "*In the light of variances in the individual components, especially in radon exposure and the six age groups to be considered according to Directive 96/29 Euratom, an effective dose of between 2 and 3 mSv results under average conditions.*"

Some examples of the natural variability in Germany are provided below, initially based on the activity concentrations of certain important natural radionuclides in the compartments of soil, air and water. This list does not claim to be exhaustive, nor do the values represent coverage intervals or 95th percentiles. They are merely intended as insights into the variation found in Germany. This variation causes marked variability in the effective doses for people in Germany. Living and eating habits are additionally considered, which differ from person to person. The following overview was therefore designed to firstly present the radionuclide activity concentrations for all compartments and then give the dose range that thus results. Unless specified otherwise, the source is (BMU 2021):

Depending on type, the soil typically contains

- ^{40}K (100 Bq kg^{-1} to 650 Bq kg^{-1})
- ^{232}Th (7 Bq kg^{-1} to 50 Bq kg^{-1})
- ^{238}U (7 Bq kg^{-1} to 35 Bq kg^{-1})

and their daughter nuclides.

In (BMU 2021), local concentrations are given for ^{226}Ra

- of 30 Bq kg^{-1} to 500 Bq kg^{-1} in granite
- of only 1 Bq kg^{-1} to 39 Bq kg^{-1} in sand

Isotope ^{232}Th was detected at levels of

- 17 Bq kg^{-1} to 311 Bq kg^{-1} in granite
- 1 Bq kg^{-1} to 64 Bq kg^{-1} in sand

According to (BMU 2021), the specific activity of ^{226}Ra in soil varies between 8 Bq kg^{-1} in Mecklenburg-West Pomerania and 170 Bq kg^{-1} in the former uranium mining regions of Thuringia.

Due to the varying content of gamma-emitting nuclides in the soil, the local dose rate outdoors also fluctuates. Between 0.5 $\mu R\ h^{-1}$ and 40.5 $\mu R\ h^{-1}$ are given by (Czempiel und Schmier 1981) as the dose rates for the former West German federal states. By adapting a log-normal distribution to the data, a geometric mean of 5.9 $\mu R\ h^{-1}$ is obtained with lower and upper 2.5th percentiles of 3.2 $\mu R\ h^{-1}$ and 10.8 $\mu R\ h^{-1}$, respectively. Spending a total of 1,760 h outdoors per calendar year results in an effective dose[18] for adults of 56 $\mu Sv\ a^{-1}$ to 190 $\mu Sv\ a^{-1}$. A mean of 100 $\mu Sv\ a^{-1}$ is given in (BMU 2021) for external radiation exposure outdoors due to terrestrial radiation.

In (Czempiel und Schmier 1981), a dose range of 2 $\mu R\ h^{-1}$ to 30 $\mu R\ h^{-1}$ per hour is given for dwellings due to external radiation exposure. By adapting a log-normal distribution to the data, a geometric mean of 8.0 $\mu R\ h^{-1}$ is obtained with lower and upper 2.5th percentiles of 4.0 $\mu R\ h^{-1}$ and 16 $\mu R\ h^{-1}$, respectively. Spending a total of 7,000 h indoors per calendar year results in an effective dose for adults of approx. 280 $\mu Sv\ a^{-1}$ to approx. 1,100 $\mu Sv\ a^{-1}$. Radionuclides in building materials are the cause. Radiation exposure in a house built from natural stone is three times higher on average than in a wooden house. Regional fluctuations between the federal states, also due to the preference for certain building materials, account for a factor of up to 3. The data published in (Czempiel und Schmier 1981) is not representative of the population-weighted situation in Germany: though only collected in the old federal states of West Germany, it reflects the entire spectrum of possible living situations with respect to the influence of dwellings, regions and building materials. A range of 20 $nSv\ h^{-1}$ to 700 $nSv\ h^{-1}$ is given in (BMU 2021), with a mean value of 80 $nSv\ h^{-1}$, which is highly consistent with the geometric mean of the data from (Czempiel und Schmier 1981). The average annual effective dose given by (BMU 2021) is approx. 300 $\mu Sv\ a^{-1}$ indoors in Germany due to external (gamma) radiation. Added to this is cosmic radiation at sea level of approx. 300 $\mu Sv\ a^{-1}$. This contribution doubles with every increase in altitude of about 1,500 m. This must be considered in high mountain regions, but an assumption of 300 $\mu Sv\ a^{-1}$ is correct as an approximation for the majority of the population of Germany. Thus, the variability of the dose due to cosmic radiation in Germany is quite low.

[18] To achieve the rough estimate given here, a factor of 0.01 $Sv\ R^{-1}$ was used for conversion to the photon dose equivalent in accordance with the "Procedures manual for monitoring radioactive substances in the environment and external radiation" of the BMU (https://www.bmuv.de/en/themen/atomenergie-strahlenschutz/strahlenschutz/ionisierende-strahlung/ueberwachung-der-radioaktivitaet-in-der-umwelt/procedures-manuals). The effective dose was estimated by assuming a weighting factor of 1 for gamma radiation. It is not possible to make a more accurate calculation using $H^*(10)$ or $H_P(10)$ without knowledge of the radiation field.

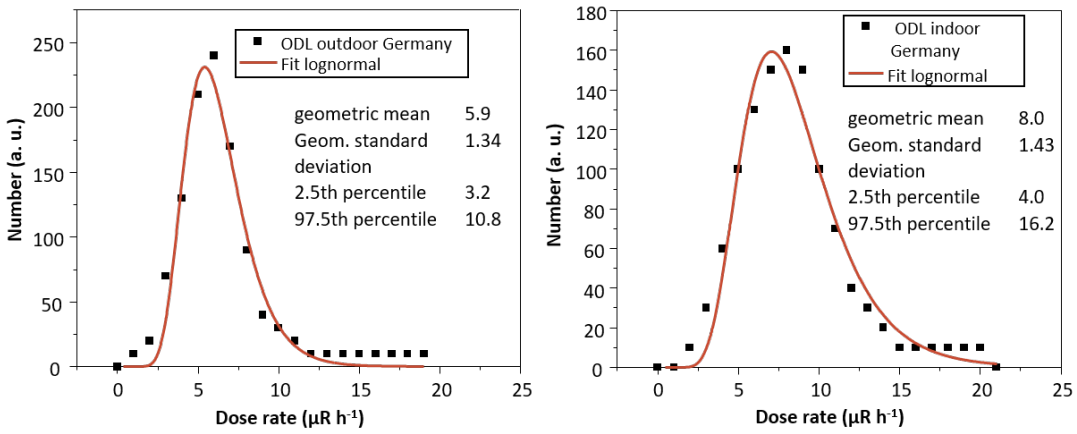

Figure 3-2: Local dose rates (ODL) outdoors (left) and indoor (right) (from Czempiel und Schmier 1981)

In *ground-level air*, radon – as already discussed in section 3.3 – predominates. In addition, ranges are given in (BMU 2021) for the following naturally occurring radionuclides:

- ^{238}U (0.8 µBq m^{-3} to 2.0 µBq m^{-3})
- ^{234}U (1.4 µBq m^{-3} to 2.0 µBq m^{-3})
- ^{230}Th (0.6 µBq m^{-3} to 1.7 µBq m^{-3})
- ^{226}Ra (1.3 µBq m^{-3} to 6.3 µBq m^{-3})
- ^{210}Pb (200 µBq m^{-3} to 670 µBq m^{-3})
- ^{210}Po (26 µBq m^{-3} to 48 µBq m^{-3})
- ^{232}Th (0.4 µBq m^{-3} to 1.2 µBq m^{-3})
- ^{228}Th (1.0 µBq m^{-3} to 1.2 µBq m^{-3})
- ^{228}Ra (0.6 µBq m^{-3} to 1.7 µBq m^{-3})

The following are found in *groundwater*:

- ^{3}H (40 mBq l^{-1} to 400 mBq l^{-1})
- ^{40}K (11 mBq l^{-1} to 15,000 mBq l^{-1})
- ^{232}Th (0.4 mBq l^{-1} to 70 mBq l^{-1})
- ^{238}U (1 mBq l^{-1} to 200 mBq l^{-1})
- ^{226}Ra (4 mBq l^{-1} to 400 mBq l^{-1})
- ^{222}Rn (2,000 mBq l^{-1} to 1,500,000 mBq l^{-1})

The following predominate in *inland surface waters*:

- ^{3}H (up to 1,000 mBq l^{-1})
- ^{7}Be (up to 500 mBq l^{-1})
- ^{40}K (30 mBq l^{-1} to 1,000 mBq l^{-1})
- ^{232}Th (10 mBq l^{-1} to 100 mBq l^{-1})
- ^{238}U (10 mBq l^{-1} to 100 mBq l^{-1})

In *seawater*, the levels are in some cases much lower:

- ^{3}H (20 mBq l^{-1} to 100 mBq l^{-1})

- ^{40}K (11,800 mBq l^{-1} to 12,300 mBq l^{-1})
- ^{238}U (40 mBq l^{-1} to 41 mBq l^{-1})
- ^{226}Ra (0.8 mBq l^{-1} to 8 mBq l^{-1})
- ^{210}Pb (0.4 mBq l^{-1} to 2 mBq l^{-1})
- ^{210}Po (0.6 mBq l^{-1} to 1.9 mBq l^{-1})
- ^{232}Th (0.0004 mBq l^{-1} to 0.029 mBq l^{-1})
- ^{228}Th (0.004 mBq l^{-1} to 0.29 mBq l^{-1})
- ^{228}Ra (0.8 mBq l^{-1} to 8 mBq l^{-1})

The levels in seawater do not contribute to the dose through direct ingestion, but mainly through the consumption of seafood. As already mentioned in section 3.2.2, the alpha emitter ^{210}Po makes the largest contribution to human radiation exposure due to the consumption of seafood.

Given its volatility in surface waters and in the sea, radon plays no part. Suspended matter and sediment must also be considered in the compartments mentioned above. They can contain up to 1 Bq g^{-1} of ^{7}Be and ^{40}K, for example. With respect to radiation exposure of the general public in Germany, these compartments likewise play their part, though to a lesser extent.

In *drinking water*, the ranges of activity are as follows:

- ^{40}K (3 mBq l^{-1} to 800 mBq l^{-1})
- ^{238}U (0.5 mBq l^{-1} to 100 mBq l^{-1})
- ^{234}U (0.5 mBq l^{-1} to 170 mBq l^{-1})
- ^{226}Ra (0.5 mBq l^{-1} to 33 mBq l^{-1})
- ^{222}Rn (1,000 mBq l^{-1} to 122,000 mBq l^{-1})
- ^{210}Pb (0.2 mBq l^{-1} to 24 mBq l^{-1})
- ^{210}Po (0 mBq l^{-1} to 10 mBq l^{-1})
- ^{232}Th (0.1 mBq l^{-1} to 4 mBq l^{-1})
- ^{228}Ra (0.5 mBq l^{-1} to 26 mBq l^{-1})
- ^{228}Th (0.2 mBq l^{-1} to 6 mBq l^{-1})

In *mineral water*, the levels can be much higher:

- ^{40}K (30 mBq l^{-1} to 1,600 mBq l^{-1})
- ^{226}Ra (0.5 mBq l^{-1} to 310 mBq l^{-1})

The estimates for the *diet as a whole* are

- ^{238}U (0.001 Bq kg^{-1} to 0.02 Bq kg^{-1})
- ^{234}U (0.004 Bq kg^{-1} to 0.036 Bq kg^{-1})
- ^{230}Th (0.001 Bq kg^{-1} to 0.004 Bq kg^{-1})
- ^{226}Ra (0.006 Bq kg^{-1} to 0.042 Bq kg^{-1})
- ^{210}Po (0.01 Bq kg^{-1} to 0.15 Bq kg^{-1})
- ^{232}Th (0.001 Bq kg^{-1} to 0.004 Bq kg^{-1})
- ^{228}Ra (0.019 Bq kg^{-1} to 0.069 Bq kg^{-1})

The isotope ^{40}K, while accounting for the largest proportion of activity in food, does not appear in this list given that its variability is not reflected by a variability in the dose: Potassium is an element that naturally contains a constant level of 0.0117 % ^{40}K with a specific activity of approx. 31 Bq g^{-1} potassium. The proportion of this isotope in the human body always remains constant, moreover. The proportion of the essential element potassium is regulated by the metabolism and kept constant within very narrow limits. Therefore, the specific activity of ^{40}K in the body likewise remains constant.

In (BMU 2021), the following conclusion is drawn: *"The uptake of natural radionuclides depends on their content in food and their metabolic activity. Ingestion of K-40 with food results in a mean specific activity of 40-60 Bq/kg body weight. From the uranium and thorium decay series, Pb-210 and Po-210 are the major contributors to radiation exposure with a mean annual age-weighted intake of 30 Bq and 58 Bq, respectively (figures according to UNSCEAR 2000)."*

In the human body, the mean levels of activity are approx.

- ^{3}H (20 Bq)
- ^{14}C (4,000 Bq)
- ^{40}K (4,000 Bq)
- ^{87}Rb (600 Bq)
- ^{238} U (0.5 Bq)
- ^{226} Ra (1.2 Bq)
- ^{210}Pb (18 Bq)
- ^{210}Po (15 Bq)
- ^{232}Th (0.2 Bq)
- ^{228} Ra (0.4 Bq)
- ^{228}Th (0.4 Bq)

Due to markedly varied biological effects (e. g. alpha versus beta and gamma emitters, but also distributions in the different organs of the human body), the activity ratios are not on a direct scale with the respective contributions to the effective dose and therefore must be calculated from these, e. g. using the respective dose coefficients from ICRP 103 (ICRP 2007a). The content of ^{40}K alone in the human body – which is unavoidable and barely influenceable – leads to an annual effective dose in adults of approx. 165 µSv (BMU 2021). There is little variation in this value, as already mentioned above, due to the constancy of the potassium concentration in the human body.

The dose from inhalation is dominated by ^{222}Rn and its decay products. According to the BfS, the ^{222}Rn activity concentration outdoors in Germany is between 3 Bq m^{-3} and 31 Bq m^{-3} and can be approximated by a logarithmic normal distribution with a geometric mean of 8.2 Bq m^{-3} and geometric standard deviation of 1.9 (Kümmel et al. 2014). In contrast, the geometric mean for radon in dwellings, averaged over the year and adjusted for standard living conditions, is 45 Bq m^{-3} i. e. six times higher (Petermann und Bossew 2021). The 25th and 75th percentiles are 27 Bq m^{-3} and 68 Bq m^{-3}, respectively. Using the fit parameters of the log-normal distribution specified therein, results in a 97.5th percentile of 230 Bq m^{-3}.

Based on the conversion factors given in section 3.3, levels of 0.02 mSv to 0.29 mSv per year outdoors and 0.68 mSv to 1.7 mSv per year indoors are obtained for the values listed above. Assuming that areas with the highest activity concentrations of ^{222}Rn in outdoor air also have the highest activity concentrations in indoor air, the resulting range for the 25th percentile and

75th percentile is approx. 0.7 mSv to 2 mSv per year. The value for the 97.5th percentile corresponds to 5.7 $mSva^{-1}$.

The variability of radiation exposure from inhalation of ^{222}Rn and its short-lived decay products is thus much larger than that from all other components of natural radiation collectively. The variability ranges from the 2.5th to the 97.5th percentile of the dose. In the case of external radiation indoors, this variability amounts to approx. 700 µSv per year. Outdoors, it is 150 µSv per year. In contrast, fluctuations in the cosmic radiation dose can be ignored up to an altitude of 500 m, which thus applies to the majority of the population in Germany. The fluctuation in the ingested dose very much depends on individual eating habits. A variation of no more than 200 µSv per year can be assumed, however. The exposure of smokers to radiation from inhaling ^{210}Pb and ^{210}Po in tobacco is not considered here[19]. Cosmic radiation thus contributes 0.3 mSv to the annual effective dose, ingestion approx. 0.3 mSv to 0.5 mSv and external radiation exposure 0.35 mSv to 1.2 mSv. Under these circumstances, the assumption of a maximum variation in radiation exposure without radon in Germany of 1 mSv per year is realistic.

Both the variability of radionuclide concentrations and differences in people's eating and living habits make it difficult to realistically determine the levels of radiation exposure from natural sources and adequately account for their variability: "*Due to the high variability of natural radioactivity concentrations in the environment that is untouched by humans, both external and internal natural radiation exposure are subject to considerable fluctuations. It cannot be assumed to be constant, as suggested (...) with mean values, but must be taken as a random variable.*" (Michel et al. 2006).

Details, including the influence of age and sex averaging, are likewise presented in (Michel et al. 2006). In many cases, the logarithmic normal distribution can be taken as a useful working hypothesis for radiation exposure of a group or population. Logarithmic normal distributions are skewed to the right, with high probabilities of low realisations and low probabilities of high realisations.

In (Michel et al. 2006) , the distributions of all components of natural radiation exposure were determined in Lower Saxony. The distribution of the age-weighted annual effective dose in Lower Saxony is shown in Figure 3-3. The weighting according to age was based on the formula provided by (UNSCEAR 2000):

$$E_{\text{gesamt, Mittel}} = 0{,}05 \times E_{\text{gesamt, } 1<a\leq 2} + 0{,}03 \times E_{\text{gesamt, } 7<a\leq 12} + 0{,}65 \times E_{a>17}.$$

A comprehensive data set for Lower Saxony can be found in (Vahlbruch 2004).

[19] One cigarette contains approx. 9 mBq to15 mBq ^{210}Po in equilibrium with ^{210}Pb. Smoking 20 cigarettes per day results in an estimated annual organ equivalent dose in the lungs of more than 0.8 mSv (Steiner et al. 2017)

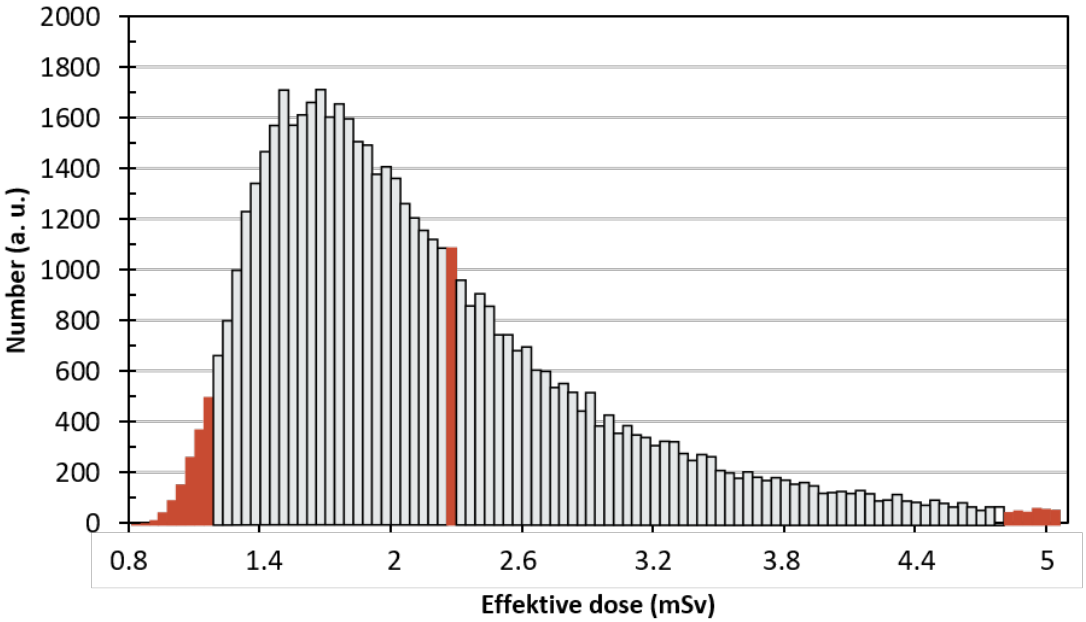

Figure 3-3: Frequency distribution of age-weighted annual effective doses from natural radioactivity and radiation in Lower Saxony. The expected level of 2.24 mSv is highlighted, as are the upper and lower 2.5th percentiles of 1.2 mSv and 4.7 mSv (Michel et al. 2006). These involve simulated exposures (Monte Carlo) based on distributions of different exposure pathways and their summation. The y axis has arbitrary units.

In terms of inhalation and ingestion, there are clear differences in the radiation exposures among various age classes. Two opposing factors need to be considered with inhalation and ingestion: the increasing intake and respiratory rate from infancy to adulthood and the higher dose coefficients at a younger age. It should be noted here that the calculation of the 70-year follow-up dose can result in artefacts (Michel 2016). Long-lived radionuclides do not release their 70-year follow-up dose to (young) people during the first year; nevertheless, the entire follow-up dose is allocated to the year of ingestion. Such modelling is only useful if there is a "radiological" balance between humans and their environment. This is not the case during the first years of life and results in doses that appear to be especially high.

In the various German federal states, the expected levels for natural radiation exposure differ only slightly. The distributions for the individual federal states (Table 3-1) do not differ significantly in terms of geometric means and standard deviations (Ritzel 2008). The 97.5th percentiles are shifted in some cases significantly, however, depending on geological and structural conditions. The 95 % coverage interval of 1.2 mSv a^{-1} to 4.6 mSv a^{-1} given in (Ritzel 2008) for Germany contrasts with the statement in (BMU 2021) that "*for average conditions an effective dose between 2 and 3 mSv results*" (per year). For members of the public in Germany, the BfS states that "*depending on the place of residence, dietary and life habits, it sometimes adds up from 1 millisievert to 10 millisieverts*"[20] per year.

[20] https://www.bfs.de/EN/topics/ion/environment/natural-radiation/natural-radiation_node.html;jsessionid=89B3DBDBD7F71593CDA960A32449AC21.2_cid391, last accessed 21.01.2022

Table 3-1: Statistical parameters of the total age-weighted natural annual effective dose in mSv in Germany and selected federal states and locations using the conversion factor for radon from UNSCEAR 1993 (from Ritzel 2008)

	Mean	**Typical range**	
World (UNSCEAR 2008)	2.4	1.0	13
	Expected level	2.5th percentile	97.5th percentile
Germany	2.2	1.2	4.6
Lower Saxony	2.2	1.2	4.7
Saxony	2.6	1.2	6.3
Rhineland-Palatinate	2.8	1.2	6.2
Aue (Ore Mountains)	2.6	1.2	6.3

To achieve a realistic model, every effort must be made to quantify the total distributions. They must be given as fully descriptive variables, e. g. geometric means and geometric standard deviations.

The levels specified by the Federal Environment Ministry for Germany are summarised in Table 3-2 (BMU 2021).

Table 3-2: Mean effective dose in Germany from natural radiation or natural radioactive materials via different exposure pathways (BMU 2021)

	Mean effective dose in millisieverts per year	
From cosmic radiation (at sea level)	Approx. 0.3	
From external terrestrial radiation	Approx. 0.4	
of which outdoors (5 hours/day)		Approx. 0.1
of which indoors (19 hours/day)		Approx. 0.3
From inhalation of radon decay products	Approx. 1.1	
of which outdoors (5 hours/day)		Approx. 0.2
of which indoors (19 hours/day)		Approx. 0.9
From ingestion of naturally occurring radioactive materials	Approx. 0.3	
Total natural radiation exposure	Approx. 2.1	

3.5 Concluding remarks

As already mentioned several times, mean and median values are to be interpreted with caution due to the immense variability in natural radioactivity and radiation. They should only be used to give an indication of the approximate level and distribution of the annual effective dose across the various components. In this light, the following values should also be understood as applicable to the global situation (UNSCEAR 2008). Cosmic radiation contributes 390 µSv (section 3.1). Terrestrial sources (section 3.2) contribute 480 µSv to external radiation exposure (section 3.2.1), 290 µSv to internal radiation exposure due to ingestion and an additional 6 µSv due to inhalation (except radon) (section 3.2.2). Inhalation of radon and its short-lived decay

products makes the largest contribution to the effective dose with 1,300 µSv per year (section 3.3). This adds up to approximately 2.4 mSv per year. In different regions of the world, the individual contributions can vary by more than one order of magnitude. The following typical ranges are given by (UNSCEAR 2008); values from (UNSCEAR 2000) are in brackets:

- Cosmic radiation 0.3 mSv to 1.0 mSv (0.3 mSv to 2.0 mSv)[21]
- External terrestrial radiation 0.3 mSv to 1.0 mSv (0.2 mSv to 1.0 mSv)[22]
- Inhalation 0.2 mSv to 10.0 mSv
- Ingestion 0.3 mSv to 1.0 mSv (0.2 mSv to 0.8 mSv)[23]

A "typical range" of only 1.0 mSv to 13.0 mSv is likewise given by (UNSCEAR 2008) for the annual effective doses. The 95th percentile is given in (UNSCEAR 2000) as 4.0 mSv a^{-1}. Extreme values amount to almost 1 mSv on the South Pacific Islands and more than 50 mSv in parts of India, Brazil and Iran.

Exposure to radiation from natural sources is often altered due to human activities. These include mining activities and the resultant tailings. Buildings provide shielding against terrestrial radiation; at the same time, natural radioactivity in building materials leads to additional radiation exposure when indoors. This category can also include air travel, as already mentioned in section 3.1, which exposes both workers and members of the general public to radiation. The occupational radiation exposure resulting from all the activities mentioned above is not covered by this statement. Please refer in this case to (SSK 2018).

4 Anthropogenic radiation exposure in planned exposure situations

4.1 Overview and dose limits

The exposure of individual members of the public to radiation can in principle arise from various anthropogenic sources. These include radionuclides of both artificial origin (e. g. from the use of nuclear fission) and natural origin which result from technological processes (e. g. the NORM[24] field). Various regulations can be found in StrlSchG and StrlSchV, accordingly, which place limitations on such radiation exposure and medical radiation exposure in various situations and make a distinction from occupational radiation exposure, respectively. The central regulations for limiting radiation exposure in the general population are laid down in Section 80 StrlSchG (StrlSchG 2017). According to Section 80(1) StrlSchG, "*the limit of the sum of the effective doses for individual members of the public is 1 millisievert per calendar year*[25] *for exposure from 1. activities requiring approval or notification under this law or the Atomic Energy Act.*"

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21 The lower value applies to sea level, the upper value to people living at altitudes above 3,000 m. This means 2% of the population receives 10 % of the collective dose due to cosmic radiation (UNSCEAR 2000).

22 Ranges reflect the difference between the 5th and 95th percentile of the values from (UNSCEAR 2000). It should be noted that only approx. 25% of countries and 40 % of the world's population are represented by this data.

23 UNSCEAR 2000 gives this as a "typical range" and refers to the composition of food and drinking water. Immensely varied country-specific and individual eating habits further complicate the specification of more precise values.

24 NORM = naturally occurring radioactive material (radionuclides from the decay series of ^{238}U, ^{235}U, ^{232}Th and ^{40}K)

25 The unit of measurement "millisievert per calendar year" is abbreviated below as "mSv a^{-1}".

Below, section 4.2 firstly provides an overview of how to determine radiation exposure with a model for the "representative person". Section 4.3 then discusses the distinction between occupational and medical radiation exposure. Section 4.4 addresses the individual causes of real or potential radiation exposure in members of the public from anthropogenic and anthropogenically modified natural sources. A brief overview of the radionuclides involved is provided in section 4.5. Lastly, section 4.6 presents a comparison with the UNSCEAR recommendations.

The exposure of patients to radiation in the medical setting is not discussed in more detail in this chapter.

4.2 Determination of radiation exposure by modelling for the "representative person"

Almost all radiation to which members of the general public can generally be exposed from anthropogenic sources outside the medical setting are so low that they cannot be detected by means of direct measurement. Radioecological and dosimetric models are therefore used to estimate the levels of radiation exposure. From any given source (for example the discharge of radionuclides), modelling the dispersion of radionuclides in environmental media (air, water, soil) permits the potential uptake of these radionuclides by humans via different radioecological pathways to be calculated. Using dose coefficients, the potential radiation exposure of the individuals considered in the model can be calculated from this potential uptake of nuclide-specific activities. Depending on the exposure situation, moreover, the model includes direct radiation and, if applicable, gamma and beta submersion and gamma radiation in soil.

Radiological models are used rather than direct measurements since the radiation exposure levels in Germany from anthropogenic sources outside the medical setting are extremely low and because, in particular, the dose rates of photon fields resulting from additional contamination of environmental media and food are far lower than the doses generated by ubiquitous natural background radiation. This applies to emissions from NORM-processing plants (from stockpiles, residues and processes such as conditioning treatment etc.) and to discharges of radioactive materials from nuclear installations.

To establish a suitable model, it is essential to make appropriate assumptions about the living habits of the people exposed and include them in the model in an appropriate way. To this end, the ICRP introduced the term "representative person" in Recommendation 101a (ICRP 2006), which replaced the term "critical group" that had previously been used. The representative person is "an individual receiving a dose that is representative of the more highly exposed individuals in the population" (ICRP 2006). The representative person is not characterised by special living and eating habits that differ from normal standards. A discussion of the role of the representative person can be found in (SSK 2013). In this regard, the ICRP states:

- The representative person should represent a group of individuals who, under the given circumstances (as the basis for the model) receive a dose that is higher than that in most other groups.
- Exposure pathways must be considered in full, assumptions of the spatial distribution of radionucludes must be included in the considerations, and dose coefficients must be selected for the respective age groups accordingly.

- The chosen description of the living habits must be reasonable, sustainable and homogeneous[26].
- Parameters must be defined (besides other living habits) which describe the eating habits of the representative person.
- These parameters are to be selected in such a way that they are representative of the small group of exposed individuals under consideration and do not correspond to the extreme habits of one individual.
- If no location-related data is available, the 95th percentile for the distributions of the consumption levels of essential foods in the population can represent a conservative assumption for defining precisely these consumption levels.

Furthermore, the ICRP states in (ICRP 2006) that considering uncertainties is a necessary part of any radiological assessment. Parameters (such as consumption levels) as per (ICRP 2006) must be regarded as subject to uncertainties – not, however, fixed values such as dose coefficients, the uncertainties and variabilities of which are not taken into account. The uncertainties can be considered probabilistically in the light of distributions for individual parameters or deterministically with an appropriate selection of parameter values.

The models used in Germany in this context and their results are discussed in detail in section 4.4.

4.3 Differentiation from occupational radiation exposure and from medical radiation exposure

Radiation exposure of the general public, according to Section 2(6) StrlSchG, is the exposure of individuals to radiation that does not include occupational or medical radiation exposure. The terms “occupational exposure” (Section 2(7) StrlSchG) and “medical exposure” (Section 2(8) StrlSchG) must therefore be used for the purpose of differentiation.

Occupational radiation exposure includes, among other things, the “exposure of an individual who is in an employment relationship with a view to carrying out work” (Section 2(7)(1) StrlSchG). It therefore suffices that the individual is employed e. g. by the operator or licence holder of a plant or facility, irrespective of the level of radiation exposure. The individual must not necessarily be an “occupationally exposed person”[27] as defined by Section 5(7) StrlSchG.

Reference is made at various points of the StrlSchG to the dose criterion of 1 mSv a^{-1}, e. g. in the definition of the term “occupationally exposed person” in Section 5(7) StrlSchG and in the various regulations of Sections 25, 26, 50 and 52 StrlSchG. In these regulations, however, the focus is not on fulfilling, but on the possibility of exceeding the dose criterion of 1 mSv a^{-1}. Hence, the regulations relating to occupational radiation exposure are not discussed in more detail below.

Medical radiation exposure refers to the exposure of patients (or asymptomatic individuals) as part of examinations and treatments, and subjects involved in medical research (Section 2(8)(1) and (2) StrlSchG). Medical radiation exposure also includes exposure to radiation among caregivers and companions capable of giving consent who are knowingly and willingly exposed

[26] “Homogeneous” refers to the composition of the group of individuals represented by the representative person. The size of the group should be selected in such a way that the differences between its members do not prove too great and the spread of the values for the parameters that describe the living conditions is not too large.

[27] An occupationally exposed person is an individual who is exposed as part of their occupational activities and whose exposure exceeds any of the dose criteria specified in Section 5(7) StrlSchG.

to ionising radiation (Section 2(8)(3) StrlSchG). Caregivers and companions must therefore be adequately informed about the radiation exposure and knowingly accept it. Anyone accompanying the patient who is not informed or is inadequately informed about being exposed to radiation, e. g. in the waiting room, is not exposed to medical radiation exposure and is considered a member of the general public.

4.4 Causes for anthropogenic radiation exposure of the general public

4.4.1 Overview

In Germany, the general public is mainly exposed to the following real or potential causes of radiation from anthropogenic sources:

- Radionuclides discharged with exhaust air or wastewater from nuclear power plants and other nuclear installations or facilities where radionuclides are handled as part of normal operations – see section 4.4.2
- Direct radiation from installations or facilities where radionuclides are handled, accelerator systems are operated or ionising radiation is used as part of normal operations – see section 4.4.3
- Clearance of radioactive materials, buildings or floor areas of the site for reuse, recycling or removal – see section 4.4.4
- Handling materials exempted from the licensing obligation, consumer goods, finding and assuming actual control over radioactive materials – see section 4.4.5
- Application of mobile gamma radiography – see section 4.4.6
- Discharges of iodine – see section 4.4.7
- Transporting radioactive materials – see section 4.4.8
- Patient excretions and exposure of individuals to external radiation from patients after the use of unsealed radioactive substances – see section 4.4.9
- Activities involving NORM – see section 4.4.10
- Legacies and residues from mining and industry – see section 4.4.11

The nature and extent of such exposure to radiation is discussed in the sections mentioned, while an overview is provided in section 4.6. This chapter does not address the release of radionuclides from nuclear installations or facilities where radionuclides are handled, in design-basis accidents, beyond design-basis accidents or accidents, since such exposure to radiation is not part of planned radiation exposure situations. There is likewise no discussion of potential radiation exposure from stockpiled nuclear weapons.

4.4.2 Discharges from nuclear installations and authorised handling

The operation of nuclear power plants and other nuclear installations and facilities where radionuclides are handled potentially leads to the release of radionuclides with exhaust air and also with wastewater. The term is defined in Section 1(1) StrlSchV (StrlSchV 2018) as the “release of liquid, airborne particulate or gaseous radioactive substances by intended pathways”. The radionuclides thus released can contribute to human radiation exposure through different radioecological pathways.

In this regard, Section 81(5) StrlSchG confers the power to issue a statutory order to protect the population and the environment, enabling a legal decree to stipulate “which dose limits apply to discharges with air or water when planning, constructing, operating, decommissioning, safely

containing and dismantling nuclear installations, installations within the meaning of Section 9a(3)(1) clause 2 of the Atomic Energy Act, installations for generating ionising radiation and facilities". This statutory order is fulfilled in Sections 99 to 103 StrlSchV, wherein the aspects of limiting the discharge of radioactive substances (Section 99), establishing the radiation exposure to be expected among members the public (Section 101), the permissibility of radioactive substance discharges (Section 102) and, lastly, the monitoring of emissions and immissions (Section 103) are regulated.

According to Section 99(1) StrlSchV, "the limits of the effective dose of exposure for members of the public due to discharges of radioactive substances into the air or water from such installations or facilities shall be 0.3 millisieverts per calendar year". Thus, in contrast to Section 47 StrlSchV (2001), organ dose limits are no longer defined. Section 99(2) StrlSchV regulates the case where discharges from several sources can overlap in one place: "*If several activities are taken into account for compliance with the dose level in accordance with Section 80 subsection (1) of the Radiation Protection Act, the competent authority shall endeavour to ensure that the totality of discharges of radioactive substances from these practices into the air or water also complies with the dose levels stipulated in subsection (1).*" Superpositions and pre-loads must therefore be considered.

4.4.2.1 Elaboration in a general administrative provision (AVV)

The technical elaboration of the exposure calculation is regulated in a general administrative provision (Allgemeine Verwaltungsvorschrift, AVV) as defined in Section 100(3) StrlSchV. A provision of this kind was introduced in Germany in 1990 and its content has remained consistent ever since. Whereas the AVV to Section 47 StrlSchV (2001) (BMU 2012a) previously had to be used on account of transitional provisions of the StrlSchV, the "AVV Tätigkeiten" (activities) now applies (BMU 2020a).

In general, when estimating the radiation exposure of the general public from radioactive substances discharged into the air or water from an installation or facility, all justified exposure pathways need to be considered based on local conditions at the site or due to the nature of the installation. The radiation exposure at the receiving points (site of use or place of exposure) which are influenced most unfavourably by the discharges of the installation in question and by any potential preliminary loads, including exposure to direct radiation, is to be calculated. According to the AVV, these are the sites in the vicinity of the installation where, due to the distribution of the discharged radionuclides and under consideration of various possible uses from spending time or consuming food that was produced there, as well as from direct radiation, the reference person[28] is exposed in each case to the highest level of radiation. To implement these requirements, the previous AVV to Section 47 StrlSchV (2001) (BMU 2012a) and the AVV Activities (BMU 2020a) contain model parts that describe the dispersion of radionuclides in the environment and the uptake of radionuclides via different radioecological pathways.

4.4.2.2 Dispersion

Both the previous AVV to Section 47 StrlSchV (2001) (BMU 2012a) and the AVV Activities (BMU 2020a) contain model parts that describe the dispersion of radioactive substances in the atmosphere and the dispersion of radioactive substances in surface water. While the latter consist of simple mixture assumptions while accounting for the discharge point and widening

[28] For discharges with air and water, there may be different locations with the highest level of exposure that need to be considered separately.

of the plume in the flowing water, the models for dispersion in the atmosphere are more complex.

To date, the Gaussian plume model to be applied in accordance with (BMU 2012a) was used in the dispersion calculations for airborne discharges. The atmospheric dispersion is thus parameterised with the aid of an analytical three-dimensional Gaussian function. The calculation is performed in a horizontal polar coordinate system. In the direction of dispersion, integration takes place via the time-variable concentration (plume model). For long-term dispersions, the calculation results are sectorally averaged (taking 12 sectors into account), thus reflecting the horizontal atmospheric dispersion. Vertically, dispersion factors that depend on distance and dispersion class are used. The dispersion velocity refers to the effective dispersion height; vertical velocity distribution is not considered.

The AVV Activities (BMU 2020a), on the other hand, proposes the use of a Lagrangian particle model with upstream wind field model[29]. The dispersion is thereby calculated using stochastic modelling of the dispersion trajectories of very many model particles. The dispersion trajectories are formed using the deterministic velocity vectors of a three-dimensional wind field and the stochastic vectors of a dispersion field.

In both cases, the models can be used to determine the distance- and direction-dependent radionuclide concentration in the air and wet and dry deposition in soil. This data represents the input data for the following dose calculation. Initial comparisons for sites where calculations of the radiation exposure according to the AVV to Section 47 StrlSchV (2001) (BMU 2012a) are available based on the Gaussian plume model show that the differences in the results of both models are small, since the Gaussian plume model also considered extensive correction factors for adaptation to the local conditions (orography, building development, etc.).

4.4.2.3 Exposure pathways

According to (BMU 2012a) and (BMU 2020a), the following exposure pathways are to be considered for airborne discharges:

- External radiation exposure through gamma radiation in exhaust air plume (gamma submersion)
- External radiation exposure through gamma radiation from radioactive substances deposited in soil (terrestrial gamma radiation)
- External radiation exposure through beta radiation in exhaust air plume (beta submersion)
- Intake of radioactive substances with respiratory air (inhalation)
- Intake of radioactive substances with food (ingestion) through their deposition on plant parts and their transfer from soil to plant

  The following exposure subpathways are to be considered for ingestion:

  - Air – plant
  - Air – fodder crop – cow – milk
  - Air – fodder crop – animal – meat
  - Air – breast milk
- Air – food – breast milk

[29] The freely available ARTM computer model can be used for the calculations.

According to (BMU 2012a) and (BMU 2020a), the following exposure pathways are to be considered for waterborne discharges:

- Periods spent on sediment (terrestrial gamma radiation on riverbank sediment, silt deposit sites or floodplains) (“riverbank sediment” for short)
- Intake of radioactive substances with food (ingestion)

  The following exposure subpathways are to be considered for ingestion:

  - Consumption of drinking water
  - Consumption of fish from the water
  - Cattle trough with the subpathways of cow – milk consumption and animal – meat consumption
  - Irrigation of agricultural land with the subpathways of fodder crop – cow – milk consumption, fodder crop – animal – meat consumption, consumption of leafy vegetables, consumption of plant products without leafy vegetables

  Breast milk due to intake of radioactive substances by the mother via the ingestion pathways listed above
- Agricultural use of river and sewage sludge from the target system for cultivation of agricultural products with the subpathways: dwelling time, fodder crop – cow – milk consumption, fodder crop – animal – meat consumption, consumption of leafy vegetables, consumption of plant products without leafy vegetables are to be considered.

The considerations of the listed exposure pathways and their modelling, both in the AVV to Section 47 StrlSchV (2001) (BMU 2012a) and in the AVV Activities (BMU 2020), are conservative; the true level of exposure is therefore overestimated. This also includes the assumption of a similar type of discharge lasting over 50 years at the site and the calculation of follow-up doses over 50 years in adults, or up to and including the age of 70 years for all age groups, and the inclusion of previous exposure (or the superposition of multiple causes) for the site in question.

Parameters and assumptions to be used as a basis for the calculations are given in Annex 11 Parts A, B and C StrlSchV.

4.4.2.4 Prospective calculation of exposure and retrospective estimation of exposure

The models according to the AVV to Section 47 StrlSchV (2001) in the version valid until the end of 2018 (BMU 2012a) were primarily used for prospective calculations. They help determine the amount of activity discharged into air or water which in each case is compatible with the dose limit of 0.3 mSv per calendar year. The models were and are used directly or in the same way for retrospective calculations to estimate the radiation exposure that would be calculated from the amount of activity actually discharged in a given year.

The AVV Activities (BMU 2020a), while containing identical models for prospectively calculating and retrospectively estimating the exposure, contains different sets of values for the parameters to be used in the calculation. The set of parameters for retrospectively estimating the exposure is in this case less conservative than that for prospectively calculating the exposure.

The two calculations differ in that prospective calculations are based on the maximum permissible discharges combined with very conservative assumptions about radiation exposure (including factors specific to the exposure pathway and generic radionuclide-specific factors

for iodine isotopes), whereas retrospective calculations take the actual discharges occurring during a specific period (according to data from discharge monitoring) combined with more realistic assumptions of radiation exposure. Thus, depending on the installation, operational state and proposed discharge levels, the calculated prospective values for the effective dose range from several $\mu Sv\,a^{-1}$ to a few hundred $\mu Sv\,a^{-1}$, but the retrospective calculation for the same installations is in the range of $nSv\,a^{-1}$ to values in the order of 1 $\mu Sv\,a^{-1}$.

4.4.2.5 Specification of activity concentrations for discharges from radiation protection areas

In addition to the complex calculation of the permissible activity concentrations from discharges discussed in sections 4.4.2.1 to 4.4.2.4, a simplified procedure may be applied as per Section 102(2) StrlSchV for installations or facilities according to Section 102(1) StrlSchV which require neither a licence as per Sections 6, 7, 9 or 9b of the Atomic Energy Act nor a planning licence as per Section 9b of the Atomic Energy Act. In such a case, no explicit calculation of permissible discharge quantities is necessary; instead, predefined values for the volume-related activity concentration in exhaust air and wastewater can be used. These values are specified in Annex 11 Part D Table 6 StrlSchV and give the maximum permissible activity concentrations to be observed on average over a calendar year in relation to discharges from radiation protection areas.

The values according to Annex 11 Part D Table 6 StrlSchV were derived from simple, generic model assumptions for the description of inhalation, beta submersion and gamma submersion, the validity and conservativity of which were verified on the basis of the AVV to Section 45 StrlSchV (1989), with various amendments which largely correspond to the AVV to Section 47 StrlSchV (2001) (BMU 2012a). The scenarios, assumptions and parameters used to obtain these values were summarised and explained in a statement from the SSK (SSK 2002).

4.4.2.6 Retrospective determination of radiation exposure

Retrospective calculations have been carried out for various nuclear installations to determine the radiation exposure for different calendar years from their operation. The radiation exposure via the air and water pathways is thus determined which results if the real discharges from the site and the real discharges from the other installations, which each represent pre-exposure for the site in question, are included in the dispersion models according to the AVV to Section 47 StrlSchV (2001) (BMU 2012a).

It is therefore possible to determine the radiation exposure via the air and water pathways from the Isar Nuclear Power Plant (Kernkraftwerk Isar, KKI), for example. The actual, balanced discharges of the two reactors are thus applied individually in the dispersion models while accounting for the characteristics of the site, and the concentrations produced by these discharges at the least favourable receiving points are calculated in water and air, including any deposits. The radioecological pathways (food production and consumption) are then determined, as defined in the AVV to Section 47 StrlSchV (2001) (BMU 2012a).

In some cases, the actual discharges from reactor KKI 1, now decommissioned, are orders of magnitude below the approved levels which were defined on the basis of prospective calculations (cf. section 4.4.2.5). Whereas the licence (SMUV 2017) foresees, for example, the "*discharge of radioactive substances with air up to $1.0 \cdot 10^{15}$ Bq per calendar year for radioactive gases and up to $3.0 \cdot 10^{10}$ Bq per calendar year for radioactive aerosols (half-life of more than 8 days) without ^{131}I*", in 2018 only $1.4 \cdot 10^{9}$ Bq ^{85}Kr, $2.4 \cdot 10^{10}$ Bq ^{3}H and $4.4 \cdot 10^{8}$ Bq ^{14}C were discharged, while radioactive aerosols discharged with exhaust air were below the limits of detection.

Results from the calculations for the Isar Nuclear Power Plant based on retrospective modelling and on actual quantities discharged can be found in Table 4-1.

Table 4-1: Radiation exposure determined retrospectively for the population per calendar year around nuclear sites using the example of the Isar nuclear reactors (KKI) 1 and 2 in Germany (potential effective dose for adults with data of Hoppe and Nitzsche 2012 to 2019[30] while applying AVV to Section 47 StrlSchV (2001))

Year	**Radiation exposure water pathway**		**Radiation exposure air pathway**		**Status of installations**	
	KKI 1	KKI 2	KKI 1	KKI 2	KKI 1	KKI 2
2011	0.01 µSv	0.74 µSv	1.4 µSv	0.47 µSv	Operation until 17/03/2011	In operation
2012	0.01 µSv	0.71 µSv	0.02 µSv	0.49 µSv	post-shutdown	In operation
2013	0.005 µSv	0.68 µSv	0.02 µSv	1.4 µSv	post-shutdown	In operation
2014	0.005 µSv	0.78 µSv	0.01 µSv	1.0 µSv	post-shutdown	In operation
2015	0.007 µSv	0.55 µSv	0.06 µSv	0.28 µSv	post-shutdown	In operation
2016	0.02 µSv	0.34 µSv	0.03 µSv	0.19 µSv	Decommissioned	In operation
2017	0.02 µSv	0.40 µSv	0.03 µSv	0.30 µSv	in decommissioning	In operation
2018	0.02 µSv	0.68 µSv	0.005 µSv	0.28 µSv	in decommissioning	In operation

[30] Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2011; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2011. Aachen, 26.03.2012 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2012; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2012. Aachen, 26.03.2013 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2013; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2013. Aachen, 26.03.2014 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2014; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2014. Aachen, 26.03.2015 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2015; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2015. Aachen, 26.03.2016 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2016; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2016. Aachen, 26.03.2017 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2017; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2017. Aachen, 26.03.2018 (nicht veröffentlicht)

Hoppe G, Nitzsche O (Brenk Systemplanung GmbH). Strahlenexposition in der Umgebung des Kernkraftwerks Isar 1 (KKI 1) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2018; Strahlenexposition in der Umgebung des Kernkraftwerks Isar 2 (KKI 2) durch die Ableitung radioaktiver Stoffe mit Luft und Wasser im Jahr 2018. Aachen, 26.03.2019 (nicht veröffentlicht)

In the case of the Isar (KKI) 2 nuclear reactor, which is in operation, the values reported for the potential effective dose are mainly caused by radionuclide ^{14}C (as CO_2), which accounts for approx. 95 %. The impact of shutting down KKI 1 in 2011 is clear to see from the comparison of the calculated exposure to airborne radioactivity.

The actual activity concentration of radionuclides in environmental media, sewage sludge, residues from incinerators, plants and food continues to be monitored as part of the Integrated Measurement and Information System for Surveillance of Environmental Radioactivity (IMIS) and in comparable local environmental monitoring programmes run by the operators of nuclear installations. The results of these measurements can be found in the BMU reports on environmental radioactivity (cf. e. g. BMUB 2018). The activities detected in the environmental media are significantly lower than the values calculated in the models.

When interpreting the calculated potential radiation exposure, it should also be noted that the true living habits of individual members of the public were not taken as the basis, but rather the living and eating habits of the reference person as per AVV to Section 47 StrlSchV (2001) (BMU 2012a). Consequently, the consumption of food produced in the vicinity of the nuclear site and the periods spent there were significantly overestimated. The actual radiation exposure of members of the general public is therefore significantly lower than the effective dose levels stated in Table 4-1.

Based on similar calculations, comparable levels for the potential effective dose are obtained for other nuclear installations in Germany. An overview of retrospective calculations for all nuclear installations in Germany for 2016 can be found in (BMUB 2018b). Superposition may result from the discharges of several nuclear installations into water along the course of a river or through tributaries (example: Main-Rhein/Neckar-Rhein), whereas only the doses discharged by neighbouring installations (e. g. nuclear reactors at the same site) into air approximately add up. In total, the actual effective dose from discharges by nuclear installations in Germany is significantly lower than 1 $\mu Sv\,a^{-1}$.

4.4.3 Direct radiation

4.4.3.1 Data and radiological modelling

Consideration must be given to exposure of the general public to direct radiation from artificial sources wherever larger amounts of radioactive substances accumulate, nuclear fission processes take place, or accelerator systems are in operation (concerning NORM, see sections 4.4.10 and 4.4.11). This may be the case with nuclear installations or facilities where radionuclides are handled, storage facilities or buffer storage areas at such installations or facilities, the operation of nuclear power plants and research reactors, and other situations.

Exposure to direct radiation is limited – as for discharges in air and water – based on the dose limitation according to Section 99(1) StrlSchV. Since the limit for the effective dose according to Section 80(1) StrlSchG is 1 $mSv\,a^{-1}$ (see section 4.1), and the doses of radioactive substances discharged with air or water are limited in each case to 0.3 $mSv\,a^{-1}$ according to Section 99(1) StrlSchV, the remaining difference of 1 $mSv\,a^{-1}$ – while accounting for multiple cases of exposure (superposition) – is to be attributed to direct radiation. This approach is justified given that both the AVV to Section 47 StrlSchV (2001) (BMU 2012a), which is still applicable for a transitional period, and the AVV Activities (cf. section 4.4.2.1) have designed the respective exposure model to ensure that, in addition to the modelled radiation exposure, there is no further realistic possibility of additional radiation exposure of the reference person or representative person.

Chapter 10 of AVV Activities (BMU 2020a), "Exposure of humans to ionising radiation from installations and facilities", contains specifications for calculating radiation exposure from the operation of a plant. Emphasis is placed here on the fact that there are no generally valid, simplified procedures for estimating direct radiation exposure and that the dose rate must be calculated individually in each case. The following is stated: *"The radiation fields (gamma radiation, X-rays, neutron radiation) in areas accessible to the public are to be calculated with the aid of generally accepted simulation methods (e. g. MCNP, SCALE, PENELOPE)."* For simple geometries (source, shield) in the case of photon fields, methods with sufficient accuracy that are based on point kernel integration can also be used.

While the methods mentioned are to be used to prospectively calculate the radiation exposure, the actual exposure can be determined retrospectively not only with calculations but also by analysing measurements (such as dosimeters or dose rate sensor attached to the perimeter fence).

4.4.3.2 Estimation of the effective dose

The actual pattern of the dose rate along the perimeter fence of a nuclear installation varies by orders of magnitude depending on the distribution of the sources and shields. Measurements and calculations based on activity inventories that are current and chosen to be overarchingly high show that the hypothetical radiation exposure from spending time permanently at the least favourable point of the perimeter fence does not exceed the several hundred $\mu Sv\ a^{-1}$. Since such a point does not correspond to the location where a single member of the public actually resides, and the dose rate decreases rapidly as the distance from the nuclear site increases, realistic values for the effective dose from direct radiation are found to be in the range of $1\ \mu Sv\ a^{-1}$ or lower (SSK 2008).

4.4.4 Clearance

Clearance of radioactive substances[31] from nuclear installations has been taking place in Germany for about three decades. Corresponding SSK recommendations in the 1990s, and since 2001 the Radiation Protection Ordinance (StrlSchV) in force, have formed the basis for this process. The current StrlSchV (2018) regulates such clearance in Sections 31 to 42 and accompanying annexes.

As a result of formal clearance, materials, buildings and sites in which only minimal radioactivity is found (in the form of contamination or activation) are thus no longer classified legally as radioactive. In this case, however, the minimal radioactivity must be lower than predefined limits (clearance levels[32]) which are designed to ensure that any radiation to which an individual is exposed due to such minimal radioactivity is negligible, i. e. may amount to a maximum individual effective dose of 10 µSv. The clearance concept can be traced back to the definition of the term "radioactive substance" found in Section 3 (1) of the Radiation Protection Act, according to which any substance containing radionuclides is initially declared radioactive. The reverse exception, i. e. disregarding the activity that is still physically present, is regulated in Section 3 (2) StrlSchG among others by clearance levels that must not be exceeded.

For practical application of the clearance concept, clearance levels are specified for the mass- or surface-related activity of the relevant radionuclides; compliance with these levels must be

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[31] As defined by the Atomic Energy Act (AtG 1985) and Radiation Protection ACt (StrlSchG 2017)

[32] The clearance levels must be distinguished from exemption levels, which among other regulate the handling of radioactive substances without the need for a licence. The exemption levels can be found in Annex 4 Table 1 column 2 and 3 StrlSchV.

demonstrated by measuring the material, building or floor area to be cleared. The clearance levels depend on the clearance option in question (unrestricted clearance, specific clearance, e. g. disposal of the cleared substance on a landfill site) and are differentiated, accordingly, in StrlSchV. The German clearance levels for unrestricted clearance are based on Safety Guide RS-G-1.7 of the IAEA (IAEA 2004b) and Safety Report 44 of the IAEA (IAEA 2005a), in which values are derived that can be applied as exemption levels and as clearance levels for unrestricted clearance. These values have been derived by taking the dose criterion for negligible exposures into consideration according to which the individual effective dose is in the range of 10 $\mu Sv\ a^{-1}$. The exposure situations necessary for deriving such values are described in detail in Safety Report 44 and are of a generic nature, i. e. they define abstract rather than concrete exposure situations.

The German clearance levels for the options of specific clearance were derived from diverse radiological studies and by applying the same dose criterion of 10 $\mu Sv\ a^{-1}$. In this case, however, the radiological models account for specific marginal conditions of the respective material cycle (example: clearance of metallic radioactive materials for recycling) and the respective destination (example: clearance of waste for disposal at a landfill site or an incineration plant). Restrictions then arise as to the continued use of the cleared substances.

A complete overview of the models and clearance options can be found for example in (Thierfeldt et al. 2016a) and (Thierfeldt et al. 2016b).

All radiological models for determining the clearance levels appear to be rather, and in some cases very, conservative. The definitions described with respect to clearance and the practice of clearance procedures ensure that the actual exposure of individual members of the public to radiation via the respective release pathway remains below the dose of 10 $\mu Sv\ a^{-1}$ [33]. Consideration is given in (Thierfeldt et al. 2003) to the collective doses (and thus also the distribution of the individual doses) that could result from all clearances in Germany. The 2003 findings are still representative of the current situation. They demonstrate that the total collective dose caused by clearance is significantly below 1 $person \cdot Sv\ a^{-1}$.

4.4.5 Handling exempted substances, consumer goods, finding and assuming actual control over radioactive substances

4.4.5.1 Data and radiological modelling

Section 12(3) StrlSchG regulates any activities subject to a licence that involve the handling other radioactive substances. The respective definition can be found in section 4.4.4. If a licence is required, the statements in section 4.1 apply. No licence is required for handling substances that fall below the exemption levels. These exemption levels are set out in Annex 4 Table 1 columns 2 and 3 StrlSchV as values for the total activity and/or mass-related activity. The total activity values are based on Recommendation RP 65 (CEC 1993) and those for mass-related activity on Recommendation RS-G-1.7 (IAEA 2004b), which were already discussed in section 4.4.4. These sets of values are legally regulated in Annex VII Table A Part 1 and Table B of the European basic radiation protection standards (EURATOM 2014) and have been adopted as such in the German Radiation Protection Ordinance. Both sets of values were derived from the dose criterion for the individual effective dose of 10 $\mu Sv\ a^{-1}$. Regulations for consumer goods are based on the same or stricter requirements.

[33] It should be noted here that the dose criterion of 10 $\mu Sv\ a^{-1}$ as per Section 31 StrlSchV applies per clearance option according to Section 35 and Section 36(1)(1) to (7) StrlSchV.

Various other regulations in StrlSchV are based on the given exemption levels – especially those for mass-related activity. This also includes Section 168 StrlSchV, which regulates the matter of finding and assuming control over radioactive substances.

Such an approach serves to ensure that control is maintained over radioactive substances whose handling would usually be subject to a licence.

4.4.5.2 Estimation of the effective dose

In general, the approach adopted in StrlSchV in association with the definition of "radioactive substance" as per StrlSchG is a formal means of ensuring that exposure of members of the general public to radiation from substances that are not subject to a licence does not exceed 10 $\mu Sv\ a^{-1}$. A more detailed estimate of the actual effective doses for members of the public in Germany cannot be made since the activities of the substances that could cause such radiation exposure have not been systematically documented.

4.4.6 Use of gamma radiography for non-destructive testing of materials

The use of radiation sources in mobile radiography for the non-destructive testing of materials can likewise cause radiation exposure in members of the public. Mobile radiography is used for example to check welds on buildings (e. g. bridges, steel structures), boilers, pipelines and similar structures. When radiating the test object, the source is extended out of the shielding container and causes a dose rate in the environment. To prevent unnecessary radiation exposure among the personnel exposed to the radiation and members of the general public who are or may be present in the vicinity of the sources, temporary control zones are created. However, if the activities take place for example under bridges or comparable structures, radiation exposure (e. g. of road users on the bridge) can nevertheless result.

The anticipated dose among members of the public is very low due to the shielding offered by the building and the time-limited duration of the radiation exposure. The number of people exposed is also low, moreover, due to the efforts made to shield the gamma radiation and the distance from the source. A research project currently underway at the Federal Office for Radiation Protection aims to address this aspect, among other things (Kummer et al. 2019).

4.4.7 Radiation exposure of the general public from discharges of iodine in Germany

The operation of nuclear power plants and the production of ^{131}I for radioiodine therapy by companies specialised in the manufacture of radionuclides contribute significantly to iodine discharges in Germany. Both types of discharge differ fundamentally from one another in terms of activity concentrations and release circumstances, meaning that the potential radiation exposure for the population in the surrounding residential districts varies considerably. In addition, iodine is released into the environment by being discharged with wastewater or excreted by patients following radioiodine therapy. These various release and exposure pathways are briefly compared below.

In the case of nuclear power plants, most gaseous iodine is produced mainly as a vapour in the form of elementary and organically bound iodine. Iodine sorption filters help to reduce the release of iodine in exhaust air. At a large nuclear power plant, the authorised discharge levels during the operational phase are in the range of several GBq ^{131}I per year, for example, while the actual discharges usually amount to only a few MBq per year, i. e. in the per mille range of the authorised discharge quantity. The release heights for most discharges are around 130 m above ground level (stack). The radiological assessment of these discharges is as follows: Using the model of the AVV to Section 47 StrlSchV (2001) (BMU 2012a), a thyroid dose in the range

of approx. 300 µSv a^{-1} was calculated from the authorised release quantity for the age group of small children across all sources and exposure pathways. This represents a calculated exhaustion of the limit for the thyroid gland of 900 µSv a^{-1} according to Section 47(1) StrlSchV (2001) by the potential discharges of approx. 30 %. Using the same model assumptions, thyroid doses of 1 µSv a^{-1} or less are calculated based on the actual discharges. The current version of StrlSchV offers no dose limit for the thyroid gland.

The authorised discharge quantities in the production of radionuclides are in the range of 10^{10} Bq a^{-1} for ^{123}I, 10^{8} Bq a^{-1} for ^{125}I and 10^{9} Bq a^{-1} for ^{131}I. In contrast to nuclear power plants, the height of release is roughly equivalent to the heights of the production plant buildings, i. e. approx. 15 m above ground level. The radiological assessment of these discharges is as follows: Using the model of the AVV to Section 47 StrlSchV (2001) (BMU 2012a), a thyroid dose for small children was calculated from the authorised release quantity, exhausting the limit of 900 µSv a^{-1} as per Section 47(1) StrlSchV (BMU 2012a) by approx. 90 %. The authorised quantities were also exhausted by about 1/3 in the case of adults. The authorised limits are exhausted by the actual discharges to the extent of some 10 %.

With respect to exposure of the general public to radiation from ^{131}I, the quantities excreted by patients who have undergone radioiodine therapy must also be considered. On this subject, the SSK published the recommendation in 2004 titled “Determination of the contribution to radiation exposure at a nuclear facility due to radionuclide excretion from patients following nuclear medical treatments” (SSK 2004). The following statements are made therein:

“*Based on the iodine-131 excretions determined per inhabitant and year for the application categories and the treatment and diagnosis figures, the total amount of iodine-131 released into the environment due to patient excretions after discharge from treatment can be estimated at 3,149 GBq per year... This by far exceeds the quantities discharged by nuclear installations. In 2001, between 0.00004 and 0.2 GBq of iodine-131 was discharged with exhaust air from nuclear power plants in Germany [BMU, 2001]. The fission and activation products discharged by German nuclear power plants with wastewater in 2001 totalled 0.0001 to 0.5 GBq [BMU, 2001].*

The iodine-131 discharged by nuclear medicine facilities with wastewater can be estimated at less than 2 GBq per year for the whole of Germany [Eschner, 2002]. The iodine-131 excreted by patients into the environment after discharge from treatment thus also exceeds the quantities of iodine-131 released into the environment from this source.

[…]

In relation to the volumes of water from waterworks and precipitation, a concentration of < 0.1 Bq/litre of iodine-131 results for Germany based on the calculated amounts of iodine-131 excreted by patients following treatment. In the vicinity of conurbations with high population density, the value can reach up to 0.15 Bq/litre.

Pre-exposure to iodine-131 excreted by patients after treatment is relevant in licensing procedures in the case of conurbations with high population density and receiving watercourses with low water flow.”

Based on the model calculations with the AVV to Section 47 StrlSchV (2001) (BMU 2012a), a dose of 153 µSv a^{-1} was calculated for the thyroid and 18 µSv a^{-1} for the effective dose (considering breast milk as the exposure pathway in each case) in small children, as the age group with potentially the highest exposure around the Isar river north of Munich, relating to the annual discharge of 22 GBq ^{131}I into the Isar with wastewater.

The SSK thus concludes in its recommendation, “Determination of the contribution to radiation exposure at a nuclear facility due to radionuclide excretion from patients following nuclear

medical treatments" (SSK 2004), that "*this comparison confirms … that patient excretions as a source of environmental radioactivity must not be ignored when determining pre-exposure.*"

The three listed contributions to the release of radioiodine, namely through exhaust air from nuclear power plants and radionuclide production facilities, and through patient excretions in wastewater, demonstrate that exposure situations can exist in Germany in which members of the public are exposed to radiation largely from radioiodine, and especially ^{131}I. Irrespective of the source of such discharges, the extent of the radiation exposure still always remains clearly below the limits of the Radiation Protection Ordinance.

4.4.8 Transport of radioactive material

4.4.8.1 Data and radiological modelling

The transport of radioactive material can likewise contribute to a small extent to the exposure of members of the public to radiation from artificial[34] sources. These "transport limits", known as activity limits (classed as A_1 and A_2), which may be contained in various transport packages, are set out in Table 2 of the IAEA Transport Regulations (IAEA 2018) as limits for the total activity and mass-related activity. These limits have also been adopted in transport regulations such as the ADR[35] and the Hazardous Goods Transport Ordinance – Road, Rail and Inland Waterways.

The values below are based on radiological models. Annex 1 of the Advisory Material on the IAEA Transport Regulations (IAEA 2012) presents the Q System for calculating the activity that may be contained in transport items such that radiation exposure is suitably limited in the event of transport accidents. The models of the Q System consider various routes of exposure from a transport item involved in a serious traffic accident (type A), each of which can result in external or internal radiation exposure of individuals. These five exposure pathways are classified as Q_A (for external photon irradiation), Q_B (for external beta-particle irradiation), Q_C (for inhalation), Q_D (for skin contamination) and Q_E (for inhalation due to contamination transfer and submersion). Limits for alpha-emitting radionuclides, neutron emitters and tritium are addressed separately.

Limits A_1 and A_2 are calculated on the basis of the following reference doses:

- The effective dose for an individual exposed to a type A package that has been involved in a serious traffic accident should not exceed the reference dose of 50 mSv.
- The equivalent dose for individual organs, including the skin, should not exceed 0.5 Sv, or 0.15 Sv for the lens of the eye, respectively, in this individual.
- It is thereby assumed that the individual in question is very unlikely to spend more than 30 minutes within one metre of the damaged transport item.

In the event of an accident in which a transport item is damaged and, in particular, the shielding effect of the outer packaging is compromised, a hypothetical radiation exposure is considered which does not contribute to the usual exposure of members of the public to radiation. Exposure to radiation from the transport of radioactive substances is limited to external exposure to photons from the transport items. In this respect, the following limits are placed on the dose rate relative to the distance from the transport vehicle:

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[34] In addition, naturally occurring radioactive materials (NORM) are also transported. The transport regulations contain far less restrictive exemptions for such goods, however.

[35] Accord européen relatif au transport international des marchandises dangereuses par route (European Convention on the International Carriage of Dangerous Goods by Road)

- 10 mSv h^{-1} at a distance of 3 m from unshielded transport goods (without packaging) in the case of material with low specific activity (LSA) or surface-contaminated objects (SCO), which are being transported in individual type IP-1, IP-2 or IP-3 packaging
- 2 mSv h^{-1} anywhere on the surface of a transport package, except for those under exclusive use where 10 mSv a^{-1} applies to the surface
- 2 mSv h^{-1} anywhere on the surface of the transport vehicle (including load) and 0.1 mSv a^{-1} at a distance of 2 m
- Various other limits for different types of transport packages, special circumstances, interruption of transport etc.
- Special limits on the dose rate for uranium and thorium ores and concentrates derived from these ores

4.4.8.2 Estimation of the effective dose

The regular reports by the Federal Government on environmental radioactivity and radiation exposure do not include the evaluation of transport-related dose distribution. Few measurement-based radiological examinations have been performed to this end. In (SSK 1998) and (SSK 1999), for example, the radiation exposure associated with police operations during the 1997 and 1998 CASTOR transports was evaluated on the basis of dose-rate measurements on the CASTOR containers, analysis of the official dosimeters of the police and federal border control forces and incorporation measurements of some of these operational forces. The SSK thus draws the following conclusions: "*The contamination determined from these transport activities does not increase the radiation exposure of the general public and thus does not pose a health risk. There is also no increase in the radiation exposure among the personnel accompanying the transport from such contamination; health risks are therefore ruled out.*" Given that the limit of detection of the official dosimeters ranged from 0.05 to 0.2 mSv, only a limited statement could be made concerning the actual effective dose, which was below these values. Additional incorporation measurements taken from a total of 24 members of the operational forces with a whole-body counter did not deliver any measurements above the limits of detection for ^{60}Co and ^{137}Cs. A dose estimate based on the incorporated activity at precisely these limits of detection, calculated back to the time of deployment, resulted in maximum individual effective doses in the range of 30 µSv.

Various studies have been conducted on the basis of radiological models, on the other hand, three of which are listed below.

- An overview in particular of the radiation exposure potentially caused by surface contamination of transport items can be found, for example, in (IAEA 2005b). Limits for surface contamination were determined as part of this coordinated research project. They were designed to replace the limits currently applicable based on the Fairbairn model (Fairbairn 1961). The Fairbairn model applied 50 mSv a^{-1} as the primary dose limit for the individual effective dose. The dose limits for surface contamination thus determined still apply today.
- The radiation exposure of the population in Germany from the standard road and rail transportation of products from the nuclear fuel cycle, large radioactive sources, radioactive waste from scientific, medical and technological applications, radiographic and other radiation sources and radioisotopes for scientific, medical and technological applications was investigated (Sentuc and Schwarz 2008). Based on scenarios that can be regarded as realistic to comprehensive in terms of transport frequency, the distance

of individuals from transport vehicles and exposure times, individual effective doses were estimated in the range of 10 µSv a^{-1} or orders of magnitude lower.

– The Konrad transport study (Sentuc et al. 2010), which considers the transport of radioactive waste to the Konrad repository only, estimates that individual effective doses of max. 20 µSv a^{-1} can be expected from spending time outdoors, based on a realistic transport frequency for year-round residents near transport routes with high volumes of waste. The modelling was carried out for both adults and infants.

4.4.9 Patient excretions and external radiation exposure of individuals from patients after the use of unsealed radioactive substances or sources of radiation

The SSK evaluated the exposure of individual members of the public to radiation via the water pathway due to patient excretions in recommendation (SSK 2004). The very conservative dose estimation for ^{131}I based on model calculations, which resulted in effective doses in the range of 10 µSv a^{-1} depending on age group, was already addressed in section 4.4.7. No comparable estimates were made in (SSK 2004) for other radionuclides used for diagnostic or therapeutic purposes.

The discharge of patients after the use of unsealed radioactive substances and the residual radioactive substances (radiation sources) enclosed in the body are regulated in the Radiation Protection in Medicine directive (BMU 2011). One condition for discharge is that, by considering the anticipated contacts, the exposure of other individuals to radiation due to discharging the patient must be estimated and, consequently, individual members of the public are not to be exposed to more than 1 mSv per calendar year.

4.4.10 Activities involving NORM

4.4.10.1 Radiation exposure of the general public

Exposure to radiation from NORM, i. e. materials as defined by Section 5(22) StrlSchG, in the sense of planned exposure situations, arises on the one hand from discharges and on the other hand from residues that have been cleared from regulatory control. In the study by (Kunze et al. 2015), a large number of industrial sectors in which NORMs are processed were examined in this respect for their emissions in the form of discharges with wastewater and as aerosols, gaseous discharges and radon. Examples for such industries include rare earth extraction, the manufacture of thorium-containing products, processing of niobium and tantalum ores, oil and natural gas production, geothermal energy extraction, phosphorus production, primary production of iron and much more. The dose calculations performed with similar models and similar parameter assumptions as in sections 4.4.2 and 4.4.4 reveal potential radiation exposures that can reach doses in the range of some 100 µSv a^{-1} in certain industries and, in particular, small children.

In addition to the discharges, exposure to radiation from residues cleared from regulatory control as per Section 62 StrlSchG or retained under regulatory control as per Section 63 StrlSchG is also relevant. Conservative modelling of the potential radiation exposure of the population ensures that the dose to members of the public is significantly below the limit of 1 mSv per year provided the monitoring limits are observed.

4.4.10.2 Differentiation from occupational radiation exposure to NORM

The distinction between radiation exposure of the general public as outlined in section 4.4.10.1 and occupational radiation exposure differs from the approach to nuclear installations and the handling of anthropogenic radioactive substances (cf. section 4.3). The handling of NORM is

defined in Section 4(10) StrlSchG and the respective requirements are regulated in Sections 55 to 67 StrlSchG. According to Section 55 StrlSchG, an estimation of the whole body dose relating to the workplace must be carried out for individuals employed at a facility that handles NORM in such a way and belongs to one of the fields of activity listed in Annex 3 StrlSchG prior to commencing the activity and must be repeated in the event of significant changes in the working conditions. If the estimation reveals that an individual employed there is to be graded as an occupationally exposed person (see section 4.3), the authority must be notified of the activity.

The list of activities in Annex 3 StrlSchG is based on the studies of anthropogenic substances and products containing natural radionuclides which began in the 1990s and have continued ever since (TÜV 1991). Various activities were preselected in these studies, whereby the effective dose levels of 1 mSv a^{-1} and 6 mSv a^{-1} can in principle be exceeded in Germany. The positive list in Annex 3 StrlSchG was thus compiled and is regularly reviewed and updated.

A guideline (BMU 2003) pertaining to the determination of exposures from natural radiation is available which can be used to estimate the exposure to ^{222}Rn and the whole body dose of individuals working in the fields mentioned.

Studies have shown that radiation exposure from radon is the main contributor to the dose in these fields of activity. The exposure pathway for radon inhalation is at the same time also the only one that is recorded systematically over a wide dose range for NORM workplaces. The listing in the annual report on environmental radioactivity and radiation exposure (BMUB 2018) shows that in 2016 dose values for 374 people were reported to the National Dose Register at the BfS. Furthermore, 53 people were reported to the registry who were carrying out renovation works in underground mines belonging to the Wismut GmbH company. The mean annual personal dose for all 374 individuals was 3.2 mSv. Values lower than 1 mSv a^{-1} were found in approx. 1/3 of the individuals registered. On average, Wismut GmbH employees had received doses of 1.4 mSv, with the maximum reaching 5.2 mSv. Based on these distributions, however, no conclusions can be drawn as to the number of those employees working with NORMs in whom an estimation of the exposure revealed no signs of radiation exposure above 1 mSv a^{-1} and for whom, therefore, no report was submitted to the National Dose Register. From previous studies (such as (TÜV 1991)), summarised in the statement of the SSK of 1997 (SSK 1997), for example, it can be concluded that some 100,000 people in Germany at least work in the fields listed in Annex 3 StrlSchG, but receive annual doses of less than 1 mSv and are therefore not classified as occupationally exposed, i. e. they are regarded as members of the general public.

4.4.11 Remediation of legacies and residues from mining and industry

A distinction must be made between the legacies of former mining operations, such as those at the uranium mines in Thuringia and Saxony, and the residues from mines that are currently in operation (i. e. planned) and industry. The term “residue” is defined in Section 5(32) StrlSchG; Annex 1 StrlSchG specifies the residues within the meaning of the law.

Legacies and residues can contain radionuclides of natural origin and thus result in exposure of the general public to radiation from naturally occurring radionuclides. As with discharges from nuclear installations (section 4.4.2), the individual dose arising from legacies and residues of mining and industry cannot be measured directly or can only be partly measured directly. It must instead be determined with model calculations based on the activity of the deposited substances, the airborne and water-borne discharge of nuclides and external radiation. To calculate the radiation exposure caused by mining, the “Calculation bases for the determination of radiation exposure resulting from mining-related environmental radioactivity” (calculation bases – mining) (BfS 2010) apply.

Legacies of former uranium mines represent an existing exposure situation which is evaluated by applying reference levels. To date, the legacies in Saxony and Thuringia still result in effective doses in the population locally that exceed the reference level of 1 mSv per calendar year (up to approx. 4 mSv a^{-1}). This is mainly due to the increased ^{222}Rn activity concentrations arising from stockpiles in the vicinity of residential areas where remediation has not taken place or is still to be finalised.

In addition to the existing radiation exposures from the legacies themselves, radiation exposure of the general public resulting from remediation must also be considered, including exposure from remediation-related residues, e. g. water treatment. These can be regarded as planned radiation exposures. The radiation exposure levels of the population in the vicinity of the Wismut GmbH remediation sites compiled for the year 2016 show that effective doses in excess of 1 mSv a^{-1} do not result from the remediation itself or the residues arising from remediation (BMUB 2018).

- With respect to airborne remediation-related discharges of radioactive dusts and radon from foul-air systems, radiation exposure of the local population of up to 0.5 mSv has been calculated.
- The discharge of radioactive substances with wastewater (surface water, leachate and floodwater) likewise results in exposure of the population to radiation from the Wismut sites. Floodwaters are purified, as are larger quantities of captured leachate. However, they contain residual concentrations of radionuclides after the purification process that are much lower than the authorised limits but still exceed the natural background levels and therefore contribute to a small extent to radiation exposure of the population. (BMU 2018a) indicates that the level of radiation exposure from discharges with water at former uranium mining sites peaks at 0.25 mSv a^{-1}.
- The two exposure fractions are not to be regarded as additive due to the spatial distance between each of the least favourable points of exposure for which the estimates were made.

For all other mining sites and operations with mining and industrial residues in Germany, the radiation exposure of the population can be assumed to be much lower, since the residues arising there contain significantly lower amounts of mobilisable natural radionuclides than the extensive legacies of the Wismut GmbH uranium mining sites.

4.5 Radionuclides

The radionuclides involved in the exposure situations described in sections 4.4.2 to 4.4.8 cover a wide range of artificially produced radioisotopes. In the case of nuclear installations, they include not only ^{60}Co and ^{137}Cs but also diverse fission products of the uranium isotopes as well as alpha-emitting radionuclides Np, Pu, Am and Cm isotopes.

Gaseous fission products are also found in the discharges from nuclear power plants and research reactors, especially the radioactive isotopes of Kr and Xe, and iodine isotopes.

This list gives only an overview of the most relevant radionuclides and is not to be considered exhaustive. Clearance values and exemption levels are provided for almost 800 radionuclides in Annex 4 Table 1 Column 3 StrlSchV.

In the exposure situations described in sections 4.4.10 and 4.4.11, on the other hand, only those radionuclides are involved which also occur naturally and whose activity concentration has been modified purely by technical processes. These are:

- radionuclides of the decay series of ^{238}U und ^{235}U.

- radionuclides of the decay series of ^{232}Th.
- ^{40}K.

The various radon isotopes included in the three decay series mentioned (^{222}Rn, ^{220}Rn and ^{219}Rn) may give rise to a special radiation exposure situation. This was discussed in section 3.3.

4.6 Summary and comparison with the 2016 UNSCEAR report

4.6.1 Level of radiation exposure in the population in Germany from anthropogenic sources in planned exposure situations

The values presented in this section with respect to radiation exposure of the general population in Germany from artificial sources in the context of planned exposure situations (i. e. excepting medical radiation exposure) can be summarised in accordance with Table 4-2. The type of radiation exposure in individual members of the public in Germany from artificial sources discussed in this chapter together with the corresponding section, the associated dose limit or constraint as per the regulations, and the range within which the individual effective dose typically lies, are stated.

Table 4-2: *Overview of the extent of the actual effective dose for individual members of the public in Germany from artificial sources*

Type of radiation exposure	Section	Dose limit/constraint/ criterion	Typical dose range
Discharges with exhaust air or wastewater from nuclear power plants, other installations or facilities	4.4.2	0.3 mSv a^{-1} per pathway	<< 10 µSv a^{-1}
Direct radiation from installations or facilities	4.4.3	1 mSv a^{-1} *	< 100 µSv a^{-1}
Clearance of radioactive substances, buildings or floor areas of the site, depending on the clearance option	4.4.4	10 µSv a^{-1}	< 10 µSv a^{-1}
Handling exempted substances, consumer goods, finding and assuming actual control over radioactive substances	4.4.5	1 mSv a^{-1}	< 10 µSv a^{-1}
Application of mobile gamma radiography	4.4.6	1 mSv a^{-1}	< 10 µSv a^{-1}
Iodine discharges	4.4.7	1 mSv a^{-1}	< 10 µSv a^{-1}
Transport of radioactive material	4.4.8	1 mSv a^{-1}	≤ 10 µSv a^{-1}
Patient excretions	4.4.9	1 mSv a^{-1}	< 10 µSv a^{-1}
External radiation exposure from patients discharged after the use of radioactive substances	4.4.9	1 mSv a^{-1}	< 1 mSv a^{-1}

*) 1 mSv a^{-1} reduced by the contribution from discharges with exhaust air or wastewater

This overview shows that, with the exception of external radiation exposure from patients discharged after the use of radioactive substances,

- the exposure to radiation is so low that it can be determined only by means of model calculations and not from measurements of the dose rate or incorporated activity.
- the individual effective doses calculated in this way are in the range of some 10 µSv per calendar or significantly lower.

– the limit of 1 mSv per year applicable in this case to the individual effective dose according to Section 80 StrlSchG is in each case exhausted only by fractions or is undershot by several orders of magnitude.

4.6.2 Extent of radiation exposure of the general public in Germany from sources of natural origin

The exposure of the general public in Germany to radiation from sources of natural origin in the context of planned exposure situations is caused by the naturally occurring radionuclides contained in NORMs, which contribute at the workplace to radiation exposure of – with the corresponding result of the requisite dose estimation for non-occupationally exposed – personnel, and by deposits of large quantities (residues) via different pathways to the exposure of members of the public to radiation, as well by radon from ground air. Dose levels at the workplace and doses for members of the public caused by residues can reach several 100 $\mu Sv\ a^{-1}$; the annual radiation exposure for individual members of the public from radon, on the other hand, is in the millisievert range, though the range is large. Exposure to radiation in Germany from sources of natural origin is therefore some orders of magnitude higher than that from various types of artificial source (with the exception of medical radiation exposure). This is to be distinguished from existing exposure situations, such as legacies from uranium mining, mining stockpiles etc., which are not considered in the overview provided here.

4.6.3 Comparison with the 2016 UNSCEAR report concerning discharges from nuclear installations

In its 2016 report, UNSCEAR (UNSCEAR 2016) makes recommendations for the calculation of discharges from nuclear installations (Annex A of (UNSCEAR 2016)) and lists estimates for the actual radiation exposure of the general public from all types of energy production (Annex B of (UNSCEAR 2016)). The model provided in Annex A of (UNSCEAR 2016) for the dispersion of radionuclides released through aqueous and gaseous discharges is of a similar complexity and describes largely identical exposure pathways to those also included in the assessments in Germany (cf. section 4.4.1). This is also evident from a comparison with similar international recommendations for calculating radiation exposure from discharges, such as IAEA Safety Report 19 (IAEA 2001).

The individual effective doses given in Annex B of (UNSCEAR 2016) for electricity generated at nuclear power plants are given as approx. 1 $\mu Sv\ a^{-1}$ for European nations. This retrospective assessment is based on a comparable analysis of the exposure pathways to be considered while referring to actual discharges and is therefore methodologically identical to the approach described in section 4.4.2.5. This figure is to be regarded as an upper estimate given that it is based on large-scale averaging and accounts for the discharges from numerous types of nuclear power plant which in part discharge significantly larger quantities per amount of energy generated around the globe. The result confers with the data obtained for German installations, as presented above.

5 Carcinogenic modes of action of ionising radiation

Cancer is a very common disease, the cause of which is not usually clearly identifiable in a specific case. Nevertheless, many biological, chemical and physical toxins are known to increase the incidence of cancer in individuals having been exposed accordingly. This chapter provides an overview of the basic mechanisms of carcinogenesis and potential modes of action of ionising radiation. An outline of the biological experiments with exposure levels below

50 mGy is designed to provide information on the lowest doses that lead to cellular changes and – if possible – the dose-response relationship.

The term cancer is a collective term for a variety of diseases with one common denominator: a group of cells that can be traced back to a progenitor cell, whereby the cells reveal increased growth compared to the neighbouring cells. The resulting tumour can displace or destroy the surrounding tissue. This is often accompanied by a loss of function, and the degenerated cells can no longer fulfil their original tissue function. In addition, tumour cells can acquire the ability to metastasise, i. e. to detach from the primary tumour and settle elsewhere. The mechanisms of increased growth and displacement of normal cells are also similar in the case of leukaemia. In this document, the term cancer is used as a collective term for malignant tumours and haematological neoplasms (leukaemia, lymphoma, multiple myeloma, etc.).

Compared to their normal progenitor cells, cancer cells exhibit various functional changes which were summarised by (Hanahan and Weinberg 2011) under the *hallmarks of cancer*: sustained growth-promoting (proliferative) signalling; non-response to growth inhibitors; resistance to cell death; replicative immortality; deregulation of the cellular energy balance; circumvention of attacks by the immune system; induction of angiogenesis (formation of new blood vessels); activation of invasiveness and metastasis. Mutations and chromosomal changes that result in the alteration or modified regulation of gene products are largely responsible for these functional changes. Genomic instability and mutations are listed by (Hanahan and Weinberg 2011) as characteristics that facilitate cancer, in the same way as persistent inflammation. Modified gene regulation can also result from epigenetic changes.

5.1 The role of DNA damage and mutations in carcinogenesis

A mutation is a change in the nucleotide sequence in the genetic substance, DNA, entailing the modification of individual bases, incorporation or deletion of individual nucleotides or larger sections of a sequence, or the rearrangement of whole sections of chromosomes. Mutations are genetically stable and can be passed on to subsequent cell generations. Not every mutation results in modified gene products and thus a change in cell function. Mutations frequently result from the incorporation of incorrect nucleotides during replication, i. e. duplication of the genetic material prior to cell division; hence, a certain correlation is noted between the division activity of a tissue and the frequency with which cancer develops in this tissue (Tomasetti and Vogelstein 2015). Mutations also occur, however, as a result of the failed repair or non-repair of DNA damage, meaning that every DNA-damaging agent can be regarded as potentially carcinogenic. In an analysis of biological mechanisms of the carcinogenicity of 109 group I carcinogenic agents according to the IARC (International Agency for Research on Cancer), a very large proportion (including ionising radiation) exhibit DNA reactivity and genotoxicity (Birkett et al. 2019). In addition, many of the non-DNA-reactive carcinogenic agents lead indirectly to genotoxicity, e. g. by means of inhibiting processes in DNA metabolism, hormonal stimulation of proliferation, generation of oxidative stress. It should be noted that in the case of chemical DNA-reactive genotoxic agents, as with ionising radiation, it is assumed that there is no safe exposure threshold, whereas thresholds are assumed for non-DNA-reactive agents even if they are associated with genotoxicity (Nohmi 2018).

Considering DNA damage as the primary event in the development of cancer, the assumption that there is no threshold results from the fact that even the smallest doses can lead to DNA damage. If the dose is so small that not every cell is affected, there may still be hits – at a correspondingly low probability – in relevant cells.

Attempts to measure the different types of radiation-induced DNA damage experimentally are hampered by the fact that many methods of detection are not very sensitive and/or the

relationship between damage frequency and measured variable is not clear (e. g. detection of DNA strand breaks with gel electrophoresis, including single-cell gel electrophoresis (COMET assay) or elution). Other methods of measurement do not detect the primary damage but rather an intermediate product after a cellular reaction, e. g. the highly sensitive detection of double-strand breaks (DSB) from γH2AX foci or foci of proteins that bind DSB regions, such as 53BP1. In the case of radiation, a linear dependency on the dose can be theoretically assumed for types of DNA damage occurring from individual ionisation events, such as base damage or single strand breaks. With other types of damage, e. g. double-strand breaks and complex DNA damage, the interplay of independent ionisations is conceivable, at least in part, and can possibly lead to a quadratic component in dose dependency. A recent evaluation of literature on the dose dependency of DNA damage after irradiation (UNSCEAR 2021) established that in most studies the induction of DNA damage was consistent with linear dose dependency. However, very little data is available for the dose range well below 100 mGy (see Table 5-1).

5.1.1 Cellular responses to DNA damage

In addition to such primary damage that occurs from the direct interaction of radiation or radiation-generated radicals with DNA, there are various mechanisms that further damage the DNA due to the cellular response to DNA damage: these include a persistent increase in oxidative stress in affected cells and non-targeted effects that lead to DNA damage in cells that are spatially and/or temporally separated but not directly affected (bystander effect, genomic instability). In these cases, non-linear dependencies on the dose are to be expected.

In response to the presence of damage in the DNA, the cells pursue an exhaustive process involving different response mechanisms (DNA damage response). These include the activation of repair mechanisms and the change in the balance between different mechanisms that can repair the same type of damage, halting the cell cycle, changes to metabolism, alterations in epigenetic patterns and RNA and protein expression, induction of regulated mechanisms for cell death or cell ageing and differentiation. The complex interaction of these processes determines whether a cell will survive and can proliferate after DNA damage has been induced or whether it will die or remain in a non-proliferating state. The nature of the repair, moreover, determines whether the DNA damage can be removed without error such that the original DNA state is restored, or whether a mutation becomes permanent. With many of these response mechanisms, non-linear dose dependencies or qualitative differences between low (≤ 100 mGy) and higher doses were observed – at least in individual experiments (UNSCEAR 2021). Both sublinear (including threshold dose or hormesis) and supralinear dependencies, as well as isolated multiphasic dose-effect curves, have been reported (see Table 5-1).

5.1.2 Mutation enrichment and evolutionary processes in carcinogensis

If the DNA damage occurs in DNA segments that are responsible for cancer-relevant processes and gene products (e. g. oncogenes, tumour suppressor genes) and the affected cell, as a stem or progenitor cell, largely possesses the ability to divide, the response mechanisms can therefore cause the affected cell to proliferate further with genetic changes in relevant DNA segments. The DNA damage may then be associated with the later onset of cancer. It should be noted, however, that the development of cancer is a multistage process. Recent estimates, following an analysis of the DNA sequence in different tumour types, assume that clinically detectable tumours have an average of four mutations in cancer-relevant genes (driver genes), whereby the values vary quite considerably between the different tumour entities (Alexandrov et al. 2013, Martincorena et al. 2017). In addition, tumour tissue contains many (hundreds to hundreds of thousands) further mutations that are probably not causally involved in carcinogenesis and are referred to as passenger mutations.

The new analytical techniques make it increasingly possible to draw conclusions from the distribution of mutations within a tumour about the individual steps in the development of the tumour. Tumour evolution thereby follows principles that are known from population genetics. Mutations that offer a strong selection advantage can cause the cells that carry them to multiply at the expense of other cells in the tumour. The dynamics of tumorigenesis are not yet fully understood. Though a gradual increase in changes and iterative cycles of mutation and selection are usually assumed, thus reflecting the long period over which a tumour develops, there is also evidence of isolated major events which simultaneously lead to a larger number of changes – mostly rearrangements of larger DNA segments (Davis et al. 2017). As a result of mutations in certain genes that are required for genomic stability, mutations can also occur in clusters although the relative importance of this mutator phenotype is contentious (Roberts and Gordenin 2014). Nevertheless, it can be assumed that the relevant changes in the development of cancer usually occur sequentially and as independent events. Individual changes are thereby attributable to replication errors, others to exposure to genotoxic agents or lifestyle factors. Hence, in the multifactorial and multistep process of carcinogenesis with a cancer causally related to radiation exposure, the radiation may be responsible for only one or a few of the driver mutation events.

5.1.3 Adverse outcome pathways (AOPs)

The indicated reaction pathway from DNA damage via mutagenesis and functional changes in the affected gene also plays a central role in adverse outcome pathways (AOPs) for exposures to genotoxic agents, including ionising irradiation. AOPs are modular constructs that represent the information available on the pathway from a molecular initiating event (MIE) through several key events (KEs) to an adverse outcome (AO) (Ankley et al. 2010). AOPs are established according to specified rules and stored in a database (https://aopwiki.org/). The modular structure allows predictions to be made for hitherto uncharacterised or inadequately characterised substances provided they induce the same MIE as substances with known mechanisms of action. Toxicology is therefore an important field of application. The first AOPs for exposures to ionising radiation were recently described (Helm and Rudel 2020, Stainforth et al. 2021, Chauhan et al. 2021a,b). For example, Chauhan et al. 2021a have established an AOP for the development of lung cancer after exposure to radiation involving the following steps (see Figure 5-1): Direct deposition of energy (= MIE) → DNA damage (KE1) → inadequate repair (KE2) → mutation/chromosomal aberration (KE3 and KE4) → hyperplasia (KE5) → lung cancer (AO). The long-term goal of using AOPs in the field of radiation research is to include quantitative data and examine dose-response relationships for the individual KEs so as to identify critical thresholds that must be exceeded in order to further advance the path towards the AO (Chauhan et al. 2021b).

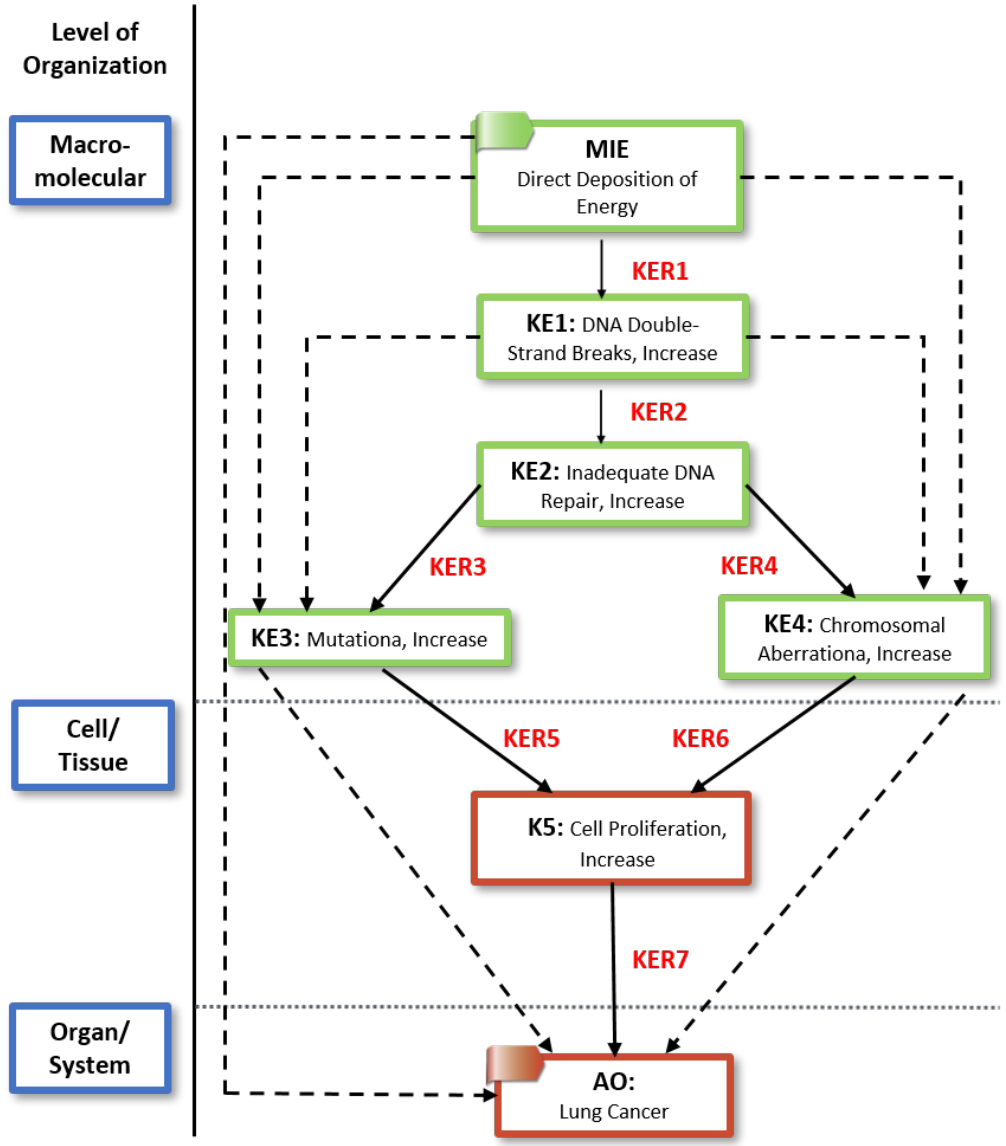


Figure 5-1: Adverse outcome pathways (AOP) from directed energy deposition (MIE) that leads to DNA damage (KE1) and ends in AO lung cancer. Individual key events (KEs) are linked directly by key event relationships (KERs) (solid lines). Indirect relationships (dashed lines) are not considered further in this example. Modified after (Chauhan et al. 2021a)

5.2 The significance of the cell environment, cell communication and immune system in carcinogenesis

It is becoming increasingly clear that genetic (and epigenetic) changes and selection may be necessary but insufficient factors in carcinogenesis. Driver mutations, for example, were also found in the elderly in various normal tissues (e. g. skin, oesophagus) in clones of cells ((Martincorena et al. 2015), (Martincorena et al. 2018), (Martincorena 2019), (Risques and Kennedy 2018)). These clones could represent early stages of a multistage process that remain stuck at this stage due to the low probability that the still “missing” mutations will occur in these very cells. Any mechanism that limits the growth of these clones simultaneously reduces the probability of further relevant mutations in these cells. Competition with normal neighbouring cells is an example of such a mechanism. If neighbouring cells are killed or prevented from dividing as a result of radiation exposure, repopulation with derivatives of the

mutation-bearing clone may occur, especially if the existing mutation renders the cells more resistant to radiation exposure. (Fernandez-Antoran et al. 2019) observed such a process in a mouse model for oesophageal cancer after irradiation with only 50 mGy. Increased division of the repopulating cells then increases the probability of generating further mutations. However, intercellular interactions can also have the opposite effect. For example, at very low doses (2 mGy) irradiation in normal cells has been seen to cause apoptosis in preneoplastic cells (Portess et al. 2007).

It is becoming increasingly clear that the mutations alone do not suffice for clinically detectable cancer to develop, and that the tumour microenvironment (TME) plays a pivotal role (Weaver and Gilbert 2004). Malignant tumours contain not only tumour cells, but also various normal tissue cells such as stromal cells (connective tissue cells), blood vessels and immune cell infiltrates embedded in extracellular matrix molecules such as collagens, other adhesive proteins and polysaccharides. The composition of the TME and secreted factors can promote or inhibit tumour growth. Radiation can induce tumour-promoting responses by acting directly on the cells of the TME, or by the cells of the TME responding to signals from the irradiated tumour cells (Barcellos-Hoff and Ravani 2000, Barker et al. 2015, Monjazeb et al. 2020, McLaughlin et al. 2020). These mechanisms were mainly studied in connection with radiation doses relevant to radiotherapy. However, some studies in the low dose range (50 mSv to 100 mSv) revealed tumour-promoting reactions after injecting non-tumorigenic or low-tumorigenic cells into irradiated target organs ((Nguyen et al. 2011), (Omene 2020)).

The immune system also plays an important role in terms of the ability (or inability) of (pre)malignant cell clones to proliferate further. In general, the immune system should recognise and attack cancer cells due to the expression of neo-antigens (immunosurveillance). Various mechanisms permit the tumour cells to evade such an attack from the immune system. After irradiation with higher doses, restoration of immune responses aimed at the tumour is often observed (Gaipl et al 2014). The influence of low doses that generally tend to have an anti-inflammatory effect (Frey et al. 2015) has not been fully investigated with respect to immunosurveillance. An AOP for ionising irradiation and breast cancer considers, as key events, not only the increase in reactive oxygen and nitrogen species (KE 1), the increase in DNA damage, genomic instability and mutations (KE 2) and increased proliferation and hyperplasia (KE 3), but also the increase in inflammatory reactions (KE 4), but rates the materiality of this KE as only moderate, whereas the materiality of KE 1 to KE 3 is rated as high (Helm und Rudel 2020).

5.3 Conclusions on dose thresholds and dose-response relationships from biological experiments

In contrast to the data on biological effects at higher doses, the data available on low radiation doses is generally still limited. In many of the experiments reviewed in (UNSCEAR 2021), only one dose point was in the low dose range. Concerning the question of a threshold, it may be of interest to consider the lowest doses for which effects have been described. Table 5-1 shows that changes in various cancer-relevant processes may already be observed at very low doses of about 1 mGy to 10 mGy, and in the pKZ1 test system at just 0.005 mGy. This is well below the dose range within which statements can be made based on epidemiological studies in humans and indicates that the cells can also recognise and react to very low additional doses despite the constant background radiation.

Dose dependencies observed with in vitro and in vivo biological experiments with at least one data point at ≤ 50 mGy, are also listed in Table 5-1. While the induction of primary DNA damage exhibits largely linear dose dependency, non-linear dependencies in the range of small doses and qualitative differences between small and larger doses are described for the cellular

responses. Sublinear and supralinear dependencies were noted among the nonlinear dose dependencies. In some cases, multiphase dose and time dependencies were observed, but the changes were statistically significant only at some individual dose and time points. It is mostly unclear whether and to what extent these sporadically observed changes, which are considered statistically significant, are random findings or possess biological relevance. In the future, it would be desirable to substantiate the assumed multiphase dependencies with experiments covering a larger number of dose and time points. Overall, the published data is largely heterogeneous in the case of many endpoints, depending among others on the types of cell, tissue and animal. In general, the degree of independent confirmation from observations in the literature is rather low. For these reasons, and because the significance of the examined individual responses to the overall process of carcinogenesis has not been adequately explained to date, it is not yet possible to determine the dose dependency of the resulting overall response from evaluating the individual steps in the entire process.

Studies into the induction of cancer in animal models could deliver important insights into the dose dependency of the resulting overall response. In doing so, it should be noted that the transferability of the results to humans is limited, e. g. due to variability in spontaneous tumour incidences and spectra or the shorter life span (Anisimov et al. 2005). Studies into the induction of cancer frequently involve animals that have an increased susceptibility to certain cancers due to specific genetic changes (e. g. in oncogenes or tumour suppressor genes). Sublinear dose dependencies and hormetic effects are sometimes reported in relation to the induction of cancer in animal models, but the number of studies with doses significantly below 100 mGy is limited (Table 5-1 and Paunesku et al. 2020). As with epidemiological studies in humans, the failure to observe effects at low or very low doses may be attributable to an insufficiently large study cohort. A meta-analysis of 262 experimental data sets with respect to the induction of cancer in mice, rats and dogs after irradiation found no reliable evidence of hormesis (Crump et al. 2012). The authors discuss various issues with the experimental design which can lead to the apparent development of hormetic effects.

Closer harmonisation of biological and epidemiological studies should in the future deliver further data on very low to low doses, e. g. through the use of molecular epidemiology or the application of biological modelling in epidemiology.

Table 5-1: Selected effects at doses in the range of < 50 mGy[36]

Reference	Dose range	Biological system	Endpoint	Lowest effective dose	Dose-response relationship	Comment
Rothkamm and Löbrich 2003	1.2 mGy – 2,000 mGy	Primary human fibroblasts (confluent) (in vitro)	γH2AX foci	1.2 mGy	Linear at 1.2 mGy – 2,000 mGy	Repair defect (decrease in γH2AX foci) at very low doses
Suzuki et al. 2006	10 mGy – 1,000 mGy	Normal human cells (in vitro)	Phospho-ATM foci	10 mGy	Linear 10 mGy – 1,000 mGy	No dose-dependent differences in repair
Ojima et al. 2008	1.2 mGy – 200 mGy	Primary human fibroblasts (in vitro)	Phospho-ATM foci	1.2 mGy	Linear at 1.2 mGy – 100 mGy	Lindane treatment for prevention of a bystander response (noticeable as supralinear induction above 1.2 mGy)
Saha et al. 2014	10 mGy – 100 mGy in utero irradiation	Mouse neuronal cells after in vivo irradiation	53BP1 foci	10 mGy	Linear at 10 mGy – 100 mGy	No decrease in foci after 6 h at 10 mGy – 50 mGy
Osipov et al. 2015	20 mGy – 250 mGy	Human mesenchymal stem cells (in vitro)	γH2AX foci and phospho-ATM foci	20 mGy	Linear at 20 mGy – 250 mGy	Reduced decrease in γH2AX foci at 20 mGy – 80 mGy; no dose-dependent differences in the decrease in phosphoATM foci
Virag et al. 2019	5.4 – 107.7 mGy	Human dental pulp stem cells (in vitro)	Phosphorylation of H2AX	5.4 mGy	Supralinear	Phosphorylation after 24 h at all doses as with non-irradiated control
Grudzenski et al. 2010	2.5 mGy – 200 mGy	Primary human fibroblasts (confluent) (in vitro)	γH2AX foci and phospho-ATM foci	2.5 mGy	Linear at 2.5 mGy – 200 mGy	Reduced decrease in γH2AX foci at 2.5 mGy – 20 mGy
Grudzenski et al. 2010	10 mGy – 1,000 mGy Total-body irradiation	Various organs in the mouse after in vivo irradiation	γH2AX foci and 53BP1 foci	10 mGy	Linear at 10 mGy – 1,000 mGy	Reduced decrease in γH2AX foci at 10 mGy versus 100 mGy
Asaithamby and Chen 2009	5 mGy – 1,000 mGy	Human cancer cell line and immortalised epithelial cell line (in vitro)	53BP1 foci (live-cell imaging)	5 mGy	Linear at 5 mGy – 1,000 mGy	Efficiency of the decrease in 53BP1 foci not reduced at 5 mGy – 50 mGy
Boei et al. 2012	50 mGy – 500 mGy	Human lymphoblastoid cells (in vitro)	LOH mutation	Stat. sign. above 50 mGy	Linear at 50 mGy – 500 mGy	LOH as a measure for non-repair or failed repair of DSB
Boei et al. 2012	2 mGy – 100 mGy	Human primary fibroblasts (in vitro)	Micronuclei	Stat. sign. above 20 mGy	Linear at 10 mGy – 100 mGy; threshold also possible at < 10 mGy	Micronuclei as a measure of unrepaired DSB; poss. trigger for immune system

[36] The references listed here were largely extracted from the summary by UNSCEAR (UNSCEAR 2021) of biological mechanisms at low doses.

Reference	Dose range	Biological system	Endpoint	Lowest effective dose	Dose-response relationship	Comment
Manning et al. 2014	25 mGy – 300 mGy Total-body irradiation	Mouse reticulocytes after in vivo irradiation	Micronuclei	Stat. sign. above 25 mGy	Linear at 25 mGy – 300 mGy	Micronuclei as a measure of unrepaired DSB; poss. trigger for immune system
Khattab et al. 2017	8.3 mGy – 1,333 mGy	Mouse reticulocytes after in vivo irradiation	Micronuclei	Stat. sign. above 8.3 mGy	Linear at 8.3 mGy – 300 mGy	Micronuclei as a measure of unrepaired DSB; poss. trigger for immune system
Young et al. 2012	10 mGy – 5,000 mGy	Mouse embryonic fibroblasts (in vitro)	G2/M arrest	No induction at 0 mGy - 100 mGy; induction at >= 500 mGy	Threshold assumed between 100 mGy and 500 mGy	
Xue et al. 2016	50 mGy, 300 mGy, 500 mGy, 2,000 mGy	Human cancer cell line (in vitro)	G2/M arrest	No arrest at 50 mGy; arrest noticeable at 300 mGy	Threshold between 50 mGy and 300 mGy	Correlation of missing G2/M arrest with hyper-radiosensitivity (HRS)
Pretazzoli et al. 2000	20 mGy and 300 mGy	Human lymphocytes from various donors (in vitro)	G2/M arrest	At just 20 mGy in some donors; only at 300 mGy in most	n. a.	Donor-specific variation
Saintigny et al. 2016	50 mGy – 10,000 mGy per nucleus after 3H-thymidine incorporation	Hamster cell line (CHO) (in vitro)	Mutations	50 mGy	Triphasic curve; peak at 50–500 mGy (mutation from oxidative stress) followed by a decrease	The peak is not noticeable after γ irradiation;
Tanaka and Furuta 2020	20 mGy – 7,000 mGy	Drosophila larvae (in vivo)	Mutations	20 mGy/50 mGy increase (female/male)	Multiphasic	Sex-specific differences
Zelensky et al. 2020	10 mGy – 1,000 mGy	Mouse embryonic stem cells (in vitro)	Insertional mutagenesis	10 mGy	Linear 10 mGy – 200 mGy, then plateau; supralinear 0–10 mGy	Model for failed DSB repair
Ormsby et al. 2016 Zeng et al. 2006	0.001 mGy – 1,000 mGy in vivo	Mouse spleen after in vivo irradiation	pKZ1 inversion test	0.005 mGy	Triphasic: increase at 0.01 mGy, decrease versus background at 1 mGy – 10 mGy, followed by another increase	Depends on time of analysis
Iwasaki et al. 2011	10 mGy, 20 mGy, 40 mGy, 1,000 mGy	Human lymphocytes (in vitro)	Unstable chromosomal aberrations (dicentric chromosomes and centric rings)	Stat. sign. above 20 mGy	Linear at 0 mGy – 40 mGy	
Grdina et al. 2015	5 mGy – 100 mGy	Mouse cancer cell line (in vitro)	Induction of adaptive response; NF-kB activation	5 mGy	n. a.	
Park et al. 2015	10 mGy	Human lymphoblastoids/ lymphoma cells (in vitro)	Induction of adaptive response	10 mGy	n. a.	

Reference	Dose range	Biological system	Endpoint	Lowest effective dose	Dose-response relationship	Comment
Rodrigues-Moreira et al. 2017	20 mGy	Human haematopoietic stem cells (in vitro)	Transient (0–2 h) oxidative stress and post-translational activation of the Keap1/Nrf2 pathway; persistent (> 6d) oxidative stress	20 mGy	n. a.	Activation of Keap1/Nrf2 pathway leads to autophagy and mitophagy
Bernal et al. 2013	Mouse in utero irradiation 4 mGy, 7 mGy, 14 mGy, 30 mGy, 76 mGy	Locus-specific promoter methylation after mouse irradiation in vivo	Hypermethylation	7 mGy	Max. at 14 mGy – 30 mGy; same as control at 76 mGy	
Song et al. 2015	1 mGy, 10 mGy, 100 mGy total-body irradiation	Mouse splenocytes after in vivo irradiation	Modified cytokine gene expression	1 mGy	Complex	
Azimian et al. 2015	20 mGy, 50 mGy, 100 mGy	Human mononuclear cells (in vitro)	Expression of pro- and anti-apoptotic genes	20 mGy	Complex	
Saha et al. 2014	10 mGy – 200 mGy in utero irradiation	Mouse neuronal cells after in vivo irradiation	Apoptotic cells	10 mGy	Linear at 10 mGy – 200 mGy	
Portess et al. 2007	0.5 mGy – 500 mGy	Rat fibroblasts (in vitro)	Intercellular induction of apoptosis	2 mGy	Plateau above 50 mGy	
Hong et al. 2014	5 mGy – 20 mGy	Primary rabbit chondrocytes (in vitro)	Inhibition of IL-1β-induced chondrocyte dedifferentiation	5 mGy	n. a.	
Joo et al. 2012, 2015	1 mGy, 5 mGy, 10 mGy, 50 mGy, 1,000 mGy, 1,000 mGy, 2,000 mGy	Human mast cell lines (in vitro)	Inhibition of the release of inflammatory mediators	10 mGy	Effect at 10 mGy – 100 mGy	
Song et al. 2019	10 mGy, 50 mGy, 100 mGy, 500 mGy	Rat mast cells (in vitro)	Reduction of mast cell migration and gene expression alterations	10 mGy	Complex	
Fernandez-Antoran et al. 2019	50 mGy total-body irradiation	P53-mutated mosaic mouse after in vivo irradiation	Induction of differentiation and proliferation stop in WT cells, compensated by the increased proliferation of p53-mutated cells	50 mGy	n. a.	Model for promoting the expansion of mutated cells through irradiation
Braga-Tanaka et al. 2018, Paunesku et al. 2021, and the references listed therein	Chronic irradiation daily for approx. 400 days with approx. 0.05 mGy d^{-1} to approx. 20 mGy d^{-1}, total dose 20 mGy – 8 Gy	Wild-type mice with different genetic backgrounds (in vivo)	Development of cancer	20 mGy	Complex	Incidence only of non-fatal liver tumours increased at a total dose of 20 mGy, incidence of various tumour types increased at 400 mGy, but not the overall frequency of neoplasia
Braga-Tanaka et al. 2018, Paunesku et al. 2021, and the references listed therein	Chronic irradiation daily for approx. 400 days with approx. 0.05 mGy d^{-1} to approx. 20 mGy d^{-1}, total dose 20 mGy – 8 Gy	Wild-type mice with different genetic backgrounds (in vivo)	Shortened lifespan	400 mGy (significant in females)		

Reference	Dose range	Biological system	Endpoint	Lowest effective dose	Dose-response relationship	Comment
Mitchel et al. 2008	48 mGy, 97 mGy, 148 mGy as chronic exposure (0.33 mGy d^{-1})	C57BL/6 wild-type mouse (in vivo)	Shortened lifespan and induction of cancer	48 mGy	Shortened lifespan at 48 mGy, but not at 97 mGy or 197 mGy	No difference in the total cancer incidence versus the non-irradiated control at any dose, but at 48 mGy the frequency of T-cell lymphomas increased significantly, and the latency of B-cell lymphomas decreased
Mitchel et al. 2008	48 mGy, 97 mGy, 148 mGy as chronic exposure (0.33 mGy d^{-1})	C57BL/6 p53+/- heterozygous mouse (in vivo)	Shortened lifespan and induction of cancer	n. a.	n. a.	Lifespan not shortened and no lymphomas or other tumours induced by the tested doses
Lemon et al. 2017	10 mGy CT scan	P53+/- mouse after in vivo irradiation	Prolonged lifespan and tumour latency	10 mGy	n. a.	Hypothesis: upregulation of (suboptimal) p53 conc. (Paunesku et al. 2020)
Munley et al. 2011	4 fractions at 5 mGy, 15 mGy, 25 mGy in 4 weeks + 2 CT scans at 30 mGy for monitoring (i. e. total doses of 80 mGy, 120 mGy, 160 mGy as total-body irradiation)	Mouse in vivo irradiation after induced lung-specific expression of the human Ki-ras (G12C) oncogene	Number and size of lung tumours	80 mGy	No dose dependency	Increase in the number of tumours per animal, but not the size. According to the authors, the lack of dose dependency indicates tumour promotion
Miller et al. 2013	4 fractions at 10 mGy, 30 mGy, 50 mGy in 4 weeks as total-body irradiation	Mouse in vivo irradiation after treatment with carcinogenic noxious agents (NKK)	Number and size of lung tumours	40 mGy	No dose dependency	Increase in the number of tumours per animal and tumour size

6 Cancer risk due to in utero exposure

Radiation exposure during prenatal development can induce malignant tumours or leukaemias that manifest after a few years in childhood or even later in adulthood. The permitted statutory limit for the uterine dose due to occupational exposure is 1 mSv during the entire pregnancy. In section 6.1, this chapter first contains an overview of the latest scientific findings concerning the risks of malignant tumours and leukaemia following in utero exposure during childhood, and then discusses the risks in adulthood in section 6.2.

The note below relating to the nomenclature concerns not only this chapter, but also the statement and the scientific background as a whole, in particular the following three chapters. One main outcome of many radiation epidemiology investigations is the ratio of an excess incidence or mortality rate and the background rate (i. e. a quotient of the total rate and the background rate minus one). In this document, like in the Recommendation of the basic principles of determining dose limits for occupationally exposed persons (SSK 2018) and in the glossary of the UNSCEAR 2012 Report (UNSCEAR 2012), this rate is referred to as the excess relative rate (ERR). In the literature on radiation epidemiology, this rate is frequently termed excess relative risk. Strictly speaking, however, this is not correct, as most epidemiological studies set out to estimate a rate and not a risk. A risk is the combination of a probability of an outcome weighted with a severity of the damage. In frequentist statistics, probability distributions are interpreted as the limit of an infinite number of similar trials, in Bayesian inference as a convolution of an a priori probability distribution with the result of a new trial. UNSCEAR additionally emphasises the difference of a rate based on observations within a study group from risks that are projected onto a study group from other observations (UNSCEAR 2012). The design of a prospective cohort study can thus be based on power calculations with projected risks, while the data obtained in the study can be used to extrapolate rates or excess rates.

In this scientific background, risk assumptions are based on narrative deductions, for example comparative assessments of the results of various radiation epidemiology investigations. The excess relative risk as the outcome of an appraisal of the current scientific knowledge is an analogue to the excess relative rate in individual radiation epidemiology studies.

Where the authors have used the coefficient as the “excess relative risk” for the outcome of a specific study, this is indicated accordingly.

6.1 Cancer risk in childhood

Many case control studies and cohort studies show an increased risk of developing malignant tumours and leukaemia in childhood following in utero exposure to ionising radiation. By far the largest case control study is the Oxford Survey of Childhood Cancer (OSCC) study. This study recorded deaths in England starting in 1953 and evaluated the deaths in relation to diagnostic X-ray imaging of the abdomen. Parents were interviewed and medical records were obtained from the clinics. Among the cohort studies, the study of Japanese atomic bomb survivors (Life Span Study, LSS) is the most significant study. The SSK studied this topic more in-depth in an earlier recommendation (SSK 2008). Therefore, only a brief outline of this topic will be provided in the following.

In the OSCC, Stewart et al. (1956, 1958) were the first to report a correlation between childhood cancer deaths and prenatal radiation exposure. The dependence of the risk on the number of radiation exposures was significant and consistent with the linear dose-response relationship. An analysis of cancer mortality between 1953 and 1967 by Bithell and Stewart (1975) showed

a relative risk of 1.47 (95 % CI: 1.34–1.62); in other words: cancer-related death was 47 % more common among children exposed to X-rays in utero than among those not exposed in utero.

A later analysis of this study for the period 1953 to 1981 (with birth years as of 1943) included a total of 15,276 cancer-related deaths in individuals aged up to 15 years and a corresponding number of control persons (Doll and Wakeford 1997). Approximately 16 % of the cases and 12 % of the control persons had been exposed to X-ray imaging in utero (Mole 1990a). More than 90 % of the X-ray examinations had taken place in the third trimester of pregnancy, so that the results of the OSCC essentially relate to radiation exposure in this period. The analysis by Doll and Wakeford (1997) revealed a (non-adjusted) relative cancer risk for children with in utero exposure to X-rays of 1.39 (95 % CI: 1.30–1.49) compared with children not exposed to X-rays. Separate estimations of the relative risk of malignant tumours and leukaemia produced very similar results. It was maintained that the OSCC represents approximately 75 % of the worldwide statistical information on childhood cancer following in utero exposure, despite the large number of other case control studies (Doll and Wakeford 1997).

To be able to determine a risk coefficient for the radiation risk on the basis of the relative risks, an estimation of radiation doses is necessary. Extensive investigations were carried out in the OSCC in an effort to reconstruct the doses associated with the X-ray examinations in the different years. The radiation doses per image decreased as the calendar years increased. For the year 1958 a mean whole-body dose of the foetus of 6.1 mGy was calculated (Mole 1990a, 1990b). Based on the OSCC data for the study population born between 1940 and 1976 and the estimated uterine doses, the coefficient – with a linear dose-response relationship of the excess relative cancer mortality rate[37] – was found to be 51 Gy^{-1} (95 % CI: 28–76) for malignant tumours and leukaemia combined (Bithell 1993, Wakeford and Little 2003). In line with the decrease in the radiation doses, the relative rate also declined with each birth year from 1947 to 1967. However, the years following 1967 saw an increase in the relative rates despite a decrease in radiation doses. This increase in the rates has yet to be explained and may be related to a decrease in the proportion of deaths recorded by the OSCC from 80 % in the early years of the study to 55 % towards the end of the study. Assuming that the increase in the rates after 1967 is an artefact of the data, Wakeford and Little (2003) estimated a four-fold lower coefficient of 13 Gy^{-1}. Table 6-1 provides a summary of different coefficients from the OSCC. There are no explicit estimates of coefficients for childhood leukaemia following in utero exposure. However, as the relative rates for leukaemia and all cancers together are similar, the coefficients for leukaemia and cancer can also be assumed to be similar (SSK 2008).

[37] The authors use the term “excess relative risk”.

Table 6-1: *Excess relative mortality rate[38] per foetal dose in different analyses of the OSCC data with 95 % confidence intervals for cancer in children under the age of 15 (radiation doses in the order of 10 mGy) according to (SSK 2008)*

Period of mortality data	Reference for relative rate	Reference for dosimetry	Coefficient (Gy^{-1})	Reference for coefficient
1953–1972[a]	Bithell and Stiller 1988	UNSCEAR 1972	29 (17–44)	Bithell and Stiller 1988
1953–1978[b]	Bithell 1993	Mole 1990b	51 (28–76)	Doll and Wakeford 1997
1958–1961	Mole 1990b	Mole 1990b	38 (7–79)	Wakeford and Little 2003
1953–1972[a]	Bithell and Stiller 1988	Mole 1990a	13[c]	Wakeford and Little 2003

[a]: Limited to birth cohort 1943–1972
[b]: Limited to birth cohort 1940–1976
[c]: No confidence interval indicated

The second largest study after the OSCC on cancer following in utero exposure assessed the mortality due to malignant tumours and leukaemia during the first ten years of life of children who were born between 1947 and 1960 in 42 maternity hospitals in the northeastern USA and discharged from the hospitals alive (Monson and MacMahon 1984). In this study, the radiographic examinations were reconstructed on the basis of medical records. The study showed a relative risk of 1.27 (95 % CI: 0.95–1.70) for malignant tumours and of 1.52 (95 % CI: 1.18–1.95) for leukaemia. Both results are consistent with the findings of the OSCC and are compatible with the assumption of a similar relative risk of malignant tumours and leukaemia.

Wakeford and Bithell (2021) recently carried out a review of different types of childhood cancer following in utero exposure. Here, the relative risks of the OSCC were compared with other case control studies and cohort studies, for which a meta-analysis was carried out. For all cancers together, the OSCC showed a relative risk of 1.39 (95 % CI: 1.30–1.49), which was very similar to the relative risk of 1.30 (95 % CI: 1.18–1.43) found in the meta-analysis of all other case control studies. For leukaemia alone, the relative risk was 1.51 in the OSCC (95 % CI: 1.35–1.69) and 1.28 (95 % CI: 1.16–1.41) in the meta-analysis. For all cancers except leukaemia the relative rate was 1.46 (95 % CI: 1.31–1.62) in the OSCC, compared to 1.31 (95 % CI: 1.13–1.53) in the meta-analysis. Various other endpoints were also compared. Overall, despite the wide confidence intervals for more specific types of cancer, the results are generally consistent. In general, the risks found in the OSCC are slightly higher than those calculated in the other studies combined. However, it must be noted that the advances in medicine led to a reduction in radiation doses with each subsequent birth year. In the OSCC more than one third of the children were born between 1939 and 1955. Compared to later years, the doses in this period were relatively high. Many of the other studies included later birth years than the OSCC, so that the relative risks can be expected to be lower. The methodical diversity of the studies included, along with the agreement of the results of the OSCC with those of other studies, provides strong evidence of a direct causal relationship between in utero radiation exposure and an increased risk of childhood cancer.

Having said this, the OSCC remains the only study in which the foetal doses were precisely reconstructed while at the same time being large enough to derive a reliable risk coefficient (Wakeford 2013). In order to preserve the OSCC data and make it available for future scientific

[38] The authors use the term “excess relative risk”.

research, efforts are currently underway to reprocess this data and archive it digitally (Bithell et al. 2018, Draper et al. 2018, Kendall et al. 2018).

Among the cohort studies, the study of Japanese atomic bomb survivors is the largest study on childhood cancer (Yoshimoto et al. 1988). The LSS followed up 1,263 children with in utero exposure up to their 15th birthday. Among this population only two cases of malignant tumours were reported, at doses of 0.56 Gy and 1.39 Gy, and not a single case of leukaemia. It must, however, be considered that, owing to the limited size and low spontaneous cancer rates in childhood, less than one case of cancer is to be expected (Yoshimoto et al. 1988, Wakeford and Little 2003). Therefore, the risk evaluation depends largely on individual cases. A comparison of the excess absolute risks shows that the values in the LSS are significantly lower than in the OSCC.

This difference in the LSS and in some other cohort studies compared with the OSCC has led to discussions as to whether the risk was systematically overestimated in the case control studies (Boice and Miller 1999). To assess the compatibility, Wakeford and Little (2003) calculated the excess relative and absolute risks per dose for the LSS together with the confidence intervals for all types of cancer, as well as separately for leukaemia and for malignant tumours. While lower risks were found for the LSS, they were compatible with those of the OSCC given the uncertainties. The authors concluded that, considering the uncertainties, the results of the two studies were not inconsistent.

Further criticisms of the results of the OSCC were brought forward (Boice and Miller 1999), such as a possible recall bias of the mothers, the similarity in the risks for different types of cancer or the big difference in the risks between radiation exposure in utero and in early childhood. These criticisms are reviewed and discussed, for example, in (Wakeford 2008), (Wakeford and Bithell 2021) and (SSK 2008). A detailed investigation of the strengths and weaknesses of the OSCC and LSS was also carried out by the ICRP (2003). The ICRP concluded that, in spite of some methodical shortcomings, the OSCC suggests a marked radiation risk of childhood cancer, which is also confirmed by other case control studies. It further noted that the risks estimated in the OSCC must be interpreted with caution against the backdrop of the lower risks observed in the LSS and other cohort studies. The National Council on Radiation Protection and Measurements (NCRP 2013) also compiled and discussed the various case control and cohort studies. Further studies relating to risk estimations after X-ray imaging in utero that were published between 1990 and 2006 were summarised in (Schulze-Rath et al. 2008).

In view of the scientific evidence, the SSK came to the following conclusion in an earlier study: "*The relative risks observed in the OSCC study are altogether consistent with a large number of case control studies of the risk of childhood leukaemia and cancer following X-ray examinations in utero. Cohort studies, particularly the study among a group of Japanese children who were in utero at the time of the bombings and who were already observed from birth onwards, point towards lower risks. However, given the very small number of cases, the results of cohort studies are of limited significance.*" (SSK 2008). For this reason, based on the OSCC results, an excess relative risk per uterine dose of 40 Gy^{-1} was assumed. As a difference in the proportional increase of the risk of childhood leukaemia and malignant tumours was not discernible, the same risk coefficient was used for both endpoints. The following was concluded: "*As the results of other case control studies for relative risks due to X-ray examinations in utero essentially confirm the OSCC results, but cohort studies have reported lower results, the Commission on Radiological Protection assumes that, based on current knowledge, the risk coefficients indicated above adequately reflect the risk situation or are a little too high.*" (SSK 2008). There have been no robust quantitative results since this publication that reveal the need for a reassessment of the risk estimates. Therefore, the SSK

confirms its previous statement and uses an excess relative risk per dose of 40 Gy^{-1} for malignant tumours and leukaemia in its calculation of lifetime risks. Based on the analyses of the OSCC, the excess relative risk per dose was found to range between 13 Gy^{-1} and 51 Gy^{-1}, although this estimation of the range is subject to considerable uncertainties.

6.2 Cancer risk in adulthood

The Japanese atomic bomb survivors represent the main source of information relating to cancer in adulthood following in utero exposure. Further studies were carried out among the Mayak workers and residents of the Techa river that drains from the contaminated waters around the Mayak production facilities.

The incidence of malignant tumours between the ages of 12 and 55 years was assessed by Preston et al. (2008). In the follow-up up to the year 1999, 94 cases of cancer were observed among 2,452 persons exposed in utero. In 40 cases of cancer, the uterine dose was greater than 5 mSv. The excess relative rate[39] declined with increasing attained age. At an exposure of 1 Sv and an age of 50 years, the excess relative rate was 1.0 (95 % CI: 0.2–2.3). No difference in the excess relative rate was found for different trimesters of pregnancy at the time of exposure.

The mortality due to malignant tumours and leukaemia among atomic bomb survivors was studied by (Delongchamp et al. 1997). The study included 807 persons exposed in utero to doses greater than 10 mSv. Cancer cases occurring between the ages of 17 and 46 years were recorded. Only ten cancer-related deaths were observed, eight of which due to malignant tumours and two due to leukaemia. There were nine cancer cases in women, compared to only one case of leukaemia and no case of malignant tumours in men. The mortality rate due to malignant tumours was significantly increased, with an excess relative rate[39] per dose of 2.4 Sv^{-1} (90 % CI: 0.3–6.7) for both sexes combined. The extent of this increase was similar to that in persons exposed in the first six years of life, for whom an excess relative rate per dose of 1.4 Sv^{-1} (90 % CI: 0.4–3.1) was determined. An estimation of the excess relative rate for women alone revealed an excess relative rate per dose of 6.7 Sv^{-1} (90 % CI: 1.6–16.9). The number of leukaemia cases was too small to estimate an excess relative rate.

In the most recent and largest study on the risk of cancer in adulthood following exposure in utero, (Sugiyama et al. 2021) analysed the mortality among atomic bomb survivors. Given the longer observation period until 2012, significantly more cancer-related deaths were recorded than by (Delongchamp et al. 1997). Furthermore, individuals exposed to a very low dose < 5 mGy were included to better characterise the background risk. Among 2,463 individuals exposed in utero there were 137 deaths from malignant tumours and 8 deaths from leukaemia or lymphoma. Eighty of the 137 cases of malignant tumours occurred in men, 24 of whom were exposed to doses greater than 5 mGy. There were 57 deaths in women, 21 of whom were exposed to doses greater than 5 mGy. For leukaemia or lymphoma there were two deaths in men, both of whom had been exposed to doses greater than 5 mGy, and six deaths in women, four of whom received doses greater than 5 mGy. Owing to the low number of deaths due to leukaemia or lymphoma, no risks were determined for these endpoints. Therefore, only the deaths due to malignant tumours are discussed in the following. A marked difference between the sexes was found. In adults with an attained age of > 20 years, an excess relative rate[40] per uterine dose of 1.84 Gy^{-1} (95 % CI: 0.18–4.98) was found for women. In contrast, no increased risk was observed in men, and the best estimate was an excess relative rate per uterine dose

[39] The authors use the term “excess relative risk”.

[40] The authors use the term “excess relative risk”.

of -0.18 Gy^{-1} (95 % CI: <-0.77–0.94). The upper 95 % confidence interval for men is thus considerably lower than the best estimate for women. An investigation of excess relative mortality rates of sex-specific cancers produced no evidence that would explain the differences between men and women. It was assessed whether a low birth weight, a small head size or the loss of a parent may have an impact on the risk of radiation-induced malignant tumours, but no verifiable impact of these factors was found. Similarly, the excess relative rate was not dependent on the trimester of pregnancy at the time of exposure.

(Schonfeld et al. 2012) assessed the mortality among 8,000 offspring of Mayak workers with a follow-up to the year 2008. Of these, 3,226 individuals had been exposed in utero to a mean cumulative uterine dose of 54 mGy during pregnancy. There were 75 deaths from malignant tumours, 28 of which occurred in exposed individuals. Twelve cases of leukaemia were reported, six of which in exposed individuals. No association was found between cancer and radiation. The excess relative rate[40] per uterine dose was -0.1 Gy^{-1} (95 % CI: <-0.1–4.1) for malignant tumours and -0.8 Gy^{-1} (95 % CI: <-0.8–46.9) for leukaemia. There was no evidence suggesting that the risks were dependent on attained age or sex; however, the statistical power for this was very limited. In a follow-up study on the incidence of malignant tumours among the offspring of the Mayak workers, Tsareva et al. (2016) identified 177 cancer cases up to 2009, including 66 with radiation exposure. No increased incidence rate was found, with an excess relative rate[40] per dose of -1.0 Gy^{-1} (95 % CI: not determinable – 0.5). The lower confidence interval could not be determined.

The incidence of malignant tumours and leukaemia among the offspring of the Techa river residents was studied by (Krestinina et al. 2017). The follow-up lasted until the end of 2009, and the oldest person at this time was 59 years. 242 malignant tumours and 26 cases of leukaemia were observed among roughly 11,000 persons. Of these, 56 (29) patients with malignant tumours had received a dose greater than 5 (10) mGy, and ten (eight) leukaemia patients had received a bone marrow dose greater than 5 (10) mGy. The analysis showed no increase in the incidence rate, with an excess relative rate[40] per dose of -0.7 Gy^{-1} (95 % CI: <-10.7–14.8) for malignant tumours and of -1.1 Gy^{-1} (95 % CI: -1.5–9.9) for leukaemia. It must be noted, however, that the confidence intervals are very wide; therefore, no conclusion could be drawn as to potential differences between the sexes or a change in the risk with attained age.

The offspring of the Mayak workers and of the Techa river residents were combined in a joint cohort (Urals Prenatally Exposed Cohort, UPEC) and analysed with regard to the incidence and mortality of malignant tumours (Akleyev et al. 2016). As already observed in the separate analyses of the two cohorts, no increased risk due to radiation was found. (Schüz et al. 2017) analysed the incidence and mortality rates of haematological malignancies in the combined UPEC cohort with a follow-up until 2009. The incidence dataset showed an excess relative rate[41] per dose of 7.7 Gy^{-1} (95 % CI: 0.2–25.6) for leukaemia and lymphoma, while an excess relative risk per dose of 1.6 Gy^{-1} (95 % CI: -0.9–11.9) was found for mortality. The differences between the two datasets and the wide confidence intervals currently do not allow definitive conclusions to be drawn as to the risk of haematological malignancies.

In summary, it can be said that the LSS is the only study that enables a quantification of the cancer risk in adults following radiation exposure in utero. The latest and largest study of the LSS by Sugiyama et al. (2021) assessing the mortality of all malignant tumours combined showed an increased cancer mortality among women aged > 20 years with an excess relative rate per dose of 1.84 Gy^{-1}. This finding was statistically significant with a 95 % confidence

[41] The authors use the term “excess relative risk”.

interval. For men, on the other hand, no increase in mortality was found. This difference in the risk between men and women is not yet understood. The level of increase in mortality per uterine dose among women is similar to the results of prior analyses of the LSS (Delongchamp et al. 1997, Preston et al. 2008). No impact of the trimester of pregnancy at the time of exposure on the increase in mortality was observed. While the studies among the Mayak workers and the Techa river residents – which have a markedly lower statistical power than the LSS – found no increase in the incidence and mortality rates, the confidence intervals are compatible with the results of the LSS. Compared to the high values for the excess relative rate, as found in the OSCC for childhood cancer following in utero exposure, the increases in cancer rates in adulthood are substantially lower in all studies. Furthermore, the confidence intervals are also not compatible with the risks of the OSCC. This shows that the mortality increases per uterine dose observed in the OSCC must not be applied to risks in adulthood. However, the risks in adulthood following exposure in utero are of a similar magnitude as the risks in adulthood following exposure in early childhood. For leukaemia, the number of cases was not large enough to determine an increase in mortality. To estimate the level of lifetime risks for leukaemia in adulthood, an excess relative risk per uterine dose of 1.84 Gy^{-1} is therefore also assumed for women.

When estimating the lifetime risks for cancer and leukaemia following in utero exposure, the result of the latest and largest study conducted by Sugiyama et al. (2021) is used in this report. For women the dose response is linear with an excess relative risk per uterine dose of 1.84 Gy^{-1}, whereas no risk is assumed for men.

7 Cancer risk due to exposure during childhood and adolescence

The risk of cancer, especially that of leukaemia, due to childhood exposure to ionising radiation is of particular interest, as children are known to have an increased risk compared to adults, which persists into old age. The Life Span Study (LSS) of Japanese atomic bomb survivors continues to be an important source of epidemiological evidence relating to the risks of ionising radiation. The acute exposure of the LSS cohort differs from the exposure of children to radiation today, who tend to be repeatedly exposed to low doses, such as those associated with radiographic or CT imaging.

The extrapolation of the cancer risk following childhood exposure into old age requires reliable and well described models. This report will therefore focus solely on publications that provide this type of information. For the scenarios studied in this recommendation, i. e. “homogeneous external radiation exposure” and “incorporation of ^{131}I”, this implies a restriction to the following endpoints: (a) all malignant tumours, (b) all leukaemias with and without CLL, (c) myelodysplastic syndromes and (d) thyroid cancers.

An overview of the relevant literature identified is provided below. The summary is provided in a table in Annex C and includes a description of the strategy for the systematic literature search. This is followed by a description of the relevant individual publications and the risk models used in these publications, separately for each of the above endpoints. Finally, a summary of and motivation for the results used in this statement is provided.

7.1 Overview of literature results

Studies that relate to the endpoints (a) all malignant tumours, (b) all leukaemias with and without CLL and (c) thyroid cancer, which were used as a basis for the subsequent calculations, are outlined below.

In addition, a study on myelodysplastic syndrome (MDS) is described separately. MDS was not diagnosed specifically prior to the 1980s and not systematically prior to 2000. It is likely that some cases that were identified as acute myeloid leukaemia (AML) in the early years would have been classified as MDS based on present-day criteria (Hsu et al. 2013). To ensure consistency when comparing the study observations, leukaemia and MDS were grouped into one category in many reports. For this reason, no separate lifetime risks are calculated for MDS in this publication.

The majority of original papers identified have already been used and/or summarised in one of the four evaluations of pooled data or five reviews (Tab. 7-1). It is worthwhile noting that, with regard to the original papers included, there is hardly any overlap between the summarising publications. Essentially, the studied populations include the following cohorts: atomic bomb survivors (n=13 publications), residents of areas contaminated by the Chornobyl accident (n=4), residents of the Techa river that drains from the contaminated waters around the Mayak production facilities (n=1), individuals exposed to increased radon or terrestrial gamma radiation in previous dwellings (n=4), radiotherapy patients (n=31), the majority of which were haemangioma patients (n=9), tinea capitis (n=6), thymus (n=6), mostly from the 1940s and 1950s, patients exposed to diagnostic X-ray imaging (TBC, scoliosis, thyroid gland) (n=9) and to diagnostic CT imaging (n=7).

In the relevant studies, the most frequently studied endpoints are: all cancers or malignant tumours (“solid tumours”) (n=28), thyroid cancer (n=26), all leukaemias or leukaemias and myelodysplastic syndromes (MDS) (n=20). These are also the cancer entities for which (UNSCEAR 2019) found an increased risk with radiation exposure during childhood compared to during adulthood. Providing a quantitative summary of the individual studies is exceedingly difficult. The study cohorts vary considerably, as does the type of data recorded. Due to the study design, the differing length of the observation period, the nature of the data recorded in the respective studies, as well as the size of the studied cohorts, different models that are mutually incompatible with one another were used, which generally cannot be summarised in a meta-analysis. In some cases, a re-evaluation of original data in pooling studies is possible, which allows some of these issues to be circumvented. Dosimetry is a common weakness of many studies; however, the increases in cancer rates per dose are generally in line with those found in the studies among atomic bomb survivors.

Studies among atomic bomb survivors still provide an important basis for estimating the risks of radiation exposure during childhood, not least because of the good dosimetry and the long observation period. For this reason, the text below focuses on the results of the LSS and on the risk models that are needed to estimate lifetime risks.

Table 7-1: Pooled analyses, reviews and individual studies

Summaries (topic)	**Individual studies included**
Pooled analyses	
Exposure to external radiation during childhood and thyroid cancer (Veiga and Lubin continued this research) (Ron et al. 1995)	Favus et al. 1976; Hempelmann et al. 1967; Hempelmann et al. 1975; Modan et al. 1977; Pottern et al. 1990; Ron et al. 1989; Ron and Modan 1980; Schneider et al. 1986; Schneider et al. 1993; Shore et al. 1985; Shore et al. 1993; Thompson et al. 1994; Tucker et al. 1991
Cohort studies on exposure to external radiation during childhood and leukaemia and thyroid cancer (Veiga et al. 2016)	Adams et al. 2010; Bhatti et al. 2010; de Vathaire et al. 1999; Eidemüller et al. 2011; Furukawa et al. 2013; Haddy et al. 2009; Lindberg 2001; Mihailescu et al. 2002; Pottern et al. 1990; Preston et al. 2007; Sadetzki et al. 2006; Svahn-Tapper et al. 2006; Tucker et al. 1991
Follow-up of Veiga et al. 2016 (Lubin et al. 2017)	Adams et al. 2010; Bhatti et al. 2010; de Vathaire et al. 1999; Eidemüller et al. 2011; Furukawa et al. 2013; Haddy et al. 2009; Lindberg 2001; Mihailescu et al. 2002; Preston et al. 2007; Sadetzki et al. 2006
Cohort studies on leukaemia in radiotherapy patients exposed to < 100 mSv during childhood. Comparison of leukaemia mortality with atomic bomb survivors (Little et al. 2018)	Adams et al. 2010; Davis et al. 1989; Dondon et al. 2004; Hsu et al. 2013; Lindberg et al. 1995; Little 2008; Pearce et al. 2012; Ronckers et al. 2010; Zablotska et al. 2014
Reviews	
Cohort studies on exposure to external radiation during childhood and leukaemia and myelodysplastic syndromes (Little 2008)	Delongchamp et al. 1997; Haddy et al. 2006; Kleinerman et al. 2005; Lindberg et al. 1995; Lundell and Holm 1996; Preston et al. 1994; Preston et al. 2004; Ron et al. 1988; Ronckers et al. 2001; Shore et al. 2003
Pre- and postnatal diagnostic X-ray imaging and childhood cancer (Schulze-Rath et al. 2008)	Bunin et al. 1994; Hahn et al. 2001; McLaughlin et al. 1993; Meinert et al. 1999; Modan et al. 2000; Morin Doody et al. 2000
Pre- and postnatal diagnostic X-ray imaging and childhood cancer (Wakeford 2008)	Ager et al. 1965; Graham et al. 1966; Gunz and Atkinson 1964; Meinert et al. 1999; Murray et al. 1959
Head/neck CT and childhood cancer (Chen et al. 2014)	Mathews et al. 2013; Pearce et al. 2012
Natural radiation and childhood cancer (Mazzei-Abba et al. 2019)	Evrard et al. 2006; Hauri et al. 2013; Kendall et al. 2013; Meulepas et al. 2019; Nikkilä et al. 2016; Nikkilä et al. 2018; Pearce et al. 2012; Raaschou-Nielsen et al. 2008; Spycher et al. 2015; UKCCS 2002
Not included in a pooled analysis or in a review	Berrington de González et al. 2016; Berrington de González et al. 2017; Cardis et al. 2005; de Vathaire et al. 1993; Del Risco Kollerud et al. 2014; Hammer et al. 2009; Holmberg et al. 2002; Huang et al. 2014; Imaizumi et al. 2006; Ivanov et al. 2006; Iwanaga et al. 2011; Journy et al. 2016; Kaiser and Walsh 2013; 2016; Kaiser et al. 2016; Karlsson et al. 1998; Kopecky et al. 2006; Krestinina et al. 2013; Little et al. 2014; Little et al. 2015; Lubin et al. 2004; Lundell et al. 1994; Noshchenko et al. 2010; Preston et al. 2008; Ronckers et al. 2006; Sadetzki et al. 2005; Smoll et al. 2016; Walsh and Kaiser 2011; Zablotska et al. 2011; Zupunski et al. 2019

7.2 Results

7.2.1 All cancers and/or malignant tumours

7.2.1.1 Natural external radiation exposure

In a cohort study, (Spycher et al. 2015) investigated whether the incidence of childhood cancer is associated with exposure to terrestrial and cosmic radiation. The cohort consisted of 2,093,660 children under the age of 16 years included in the Swiss census in 1990 and 2000. Data relating to cancer diagnosed in the cohort up to the end of 2008 was identified from the Swiss Childhood Cancer Registry. A total of 1,782 cancer cases were registered, including 530 with leukaemia and 423 with a tumour of the central nervous system. The ambient dose rate at the children's places of residence was estimated with a model based on 161 in-situ gamma-ray spectrometry measurements by helicopter, 837 ambient dose rate measurements and 612 laboratory measurements of rock and soil samples by gamma-ray spectrometry (Rybach et al. 2002). The cumulative ambient doses over the follow-up period ranged from 0.03 mSv to 49.4 mSv, with a mean value of 9.06 mSv and a median of 9.12 mSv. In a linear dose-response model, the hazard ratios per cumulative ambient dose were 1.03 mSv^{-1} (95 % CI: 1.01; 1.05) for all cancers and 1.04 mSv^{-1} (95 % CI: 1.00; 1.08) for leukaemia and also for tumours of the central nervous system. Adjustment for potential confounding factors had an only minor impact on the results. When restricting the analysis to children who resided in the same place (or in the same municipality) at least 5 years before entry into the cohort, there was a trend towards a stronger association of cancer incidence and cumulative ambient dose. The results are consistent with studies on cancer in childhood, adolescents and young adults following CT scans during childhood (see sections 7.2.2 and 9.1.1).

Various case control studies on the incidence of childhood cancer and external background radiation have produced contradictory results. The dose range in the studies is lower than in the cohort study of (Spycher et al. 2015). (Mazzei-Abba et al. 2019) discuss methodical aspects, strengths and weaknesses of the individual studies.

7.2.1.2 Life Span Study (LSS) of atomic bomb survivors

Grant et al. evaluated the incidence of malignant tumours in adulthood, diagnosed from 1958 through 2009, among atomic bomb survivors who were exposed during childhood and adolescence. They placed particular emphasis on adjusting for smoking (Grant et al. 2017). This publication is discussed in detail in section 8.3, therefore only a short summary is provided here: the cohort included approx. 105,000 individuals, including 80,000 members with dose estimates and 25,000 persons who were not exposed, with a total of 22,528 incident primary cancers. Around 45 % were aged under 20 years at the time of exposure, 89 % of those exposed had weighted colon doses of up to 0.2 Gy. The authors offer a detailed description of the models and model selection. A significant increase in the incidence of malignant tumours was observed at the dose range up to 0.1 Gy. A linear dose-response model provides the best description of the data in women, compared to a linear-quadratic model in men, whereby the reasons for this difference are currently not understood. The recorded tumours included 22 cases of melanoma and 516 cases of non-melanoma skin cancer. In this regard, Preston et al. (2008) note that participation in the Adult Health Study of the Radiation Effects Research Foundation has little impact on cancer registration, with the exception of selective screening for thyroid and skin cancer.

In an earlier publication, Preston et al. analysed atomic bomb survivors (2,452 exposed in utero and 15,388 in early childhood, i. e. below five years) for whom incident cancer data was available for the period 1958 to 1999 (Preston et al. 2008). The proportion of cohort members

with a radiation exposure below 100 mSv (colon dose) was 82 % in early childhood and 74 % in utero. Only eight cases of cancer were diagnosed prior to the age of 20 years. Cancer of the breast and of the reproductive organs accounted for 48 % of the malignancies in women. Thyroid cancer accounted for 3 % of cancers in men and 11 % in women. No melanoma and eleven non-melanoma skin cancer were observed in the cohort. The estimates for a linear-quadratic dose-response model were associated with wide confidence intervals, so that the authors report the results of the linear method (Tab. 7-2). The evidence for an effect of sex on the relative increase in the incidence rate was not statistically significant (p = 0.13). The excess relative rate[42] (ERR) per dose was 1.7 (95 % CI: 1.1−2.5) to the power -1.1 for individuals exposed up to the age of five years (Tab. 7-3) and 0.42 for those exposed in utero (95 % CI: 0.0−2.0) to the power -2.8 of attained age. The difference between the powers -1.1 and -2.8 was not significant (p = 0.30). According to the authors, the respective EAR models describe the data just as well as the ERR models.

The ERR models of (Grant et al. 2017) and (Preston et al. 2008) show major uncertainties in early childhood owing to the limited number of cases, whereas the models of (Grant et al. 2017) show considerably stronger increases in the incidence rates than those of (Preston et al. 2008) (Figure 7-1), but with a more rapid decrease with increasing age (Table 7-2). For cancers in old age, the study of (Preston et al. 2008) contributes little evidence owing to the shorter follow-up. Since the models of (Preston et al. 2008) and (Grant et al. 2017) provide consistent results for malignancies in young and middle-aged adults (Figure 7-2), and the latter models also include radiation exposure during adulthood, lifetime risk for cancer in childhood and adulthood are estimated below using a standardised calculation based on the ERR model of (Grant et al. 2017). The table below additionally shows the EAR model of (Preston et al. 2008) (Table 7-2).

Table 7-2: *ERR models in the publications of (Preston et al. 2008) and (Grant et al. 2017) as a function of the dose d, attained age a, age at radiation exposure e, and sex (s or specifically f or m)*

Preston et al. 2008 − early childhood	Grant et al. 2017
$\mathrm{ERR} = \beta_{1s} \cdot d \cdot \exp\left[\delta_{1s} \ln\left(\frac{\alpha}{50}\right)\right]$	$\mathrm{ERR} = \beta_{1s} \cdot d \cdot \exp\left[\delta_{1s} \ln\left(\frac{a}{70}\right) + \delta_{2s} \frac{e-30}{10}\right]$
$\beta_{1f} = 2{,}2\ \mathrm{Gy}^{-1}$ $\beta_{1m} = 1{,}3\ \mathrm{Gy}^{-1}$ $\delta_{1f} = \delta_{1m} = -1{,}1$	$\beta_{1f} = 0{,}60\ \mathrm{Gy}^{-1}$ $\beta_{1m} = 0{,}33\ \mathrm{Gy}^{-1}$ $\delta_{1f} = \delta_{1m} = -1{,}66$ $\delta_{2f} = \delta_{2m} = -0.236$
$\mathrm{EAR} = \beta_{1s} \cdot d \cdot \exp\left[\delta_{1s} \ln\left(\frac{\alpha}{50}\right)\right]$ (per 100,000 person − years) $\beta_{1f} = 76\ \mathrm{Gy}^{-1}$ $\beta_{1m} = 36\ \mathrm{Gy}^{-1}$ $\delta_{1f} = \delta_{1m} = 2{,}9$	

[42] The authors use the term “excess relative risk”.

Table 7-1: Estimates of the excess relative incidence rate per dose for malignant tumours at age 50 in childhood exposure cohorts and respective 95 % confidence intervals (according to Preston et al. 2008)

Excess relative rate per dose	Model with attained age dependence for radiation exposure in early childhood, with sex effect [Sv^{-1}]	Model with common attained age dependence for radiation exposure in utero and in early childhood, with no sex effect (Sv^{-1})
sex-averaged*	1.7 (0.9−3.8)	1.7 (1.1−2.5)
male	1.3 (0.6−2.2)	
female	2.2 (1.3−3.4)	
Power of attained age in the respective model †	-1.1 (-2.3 − 0.2)	-1.3 (-2.4−-0.06)

* The sex effect in the regression model is not statistically significant (p = 0.13)

† In the regression model used, the change in the excess relative risk is taken to be proportional to a power of attained age, which was estimated as the coefficient of the logarithmic age in the model.

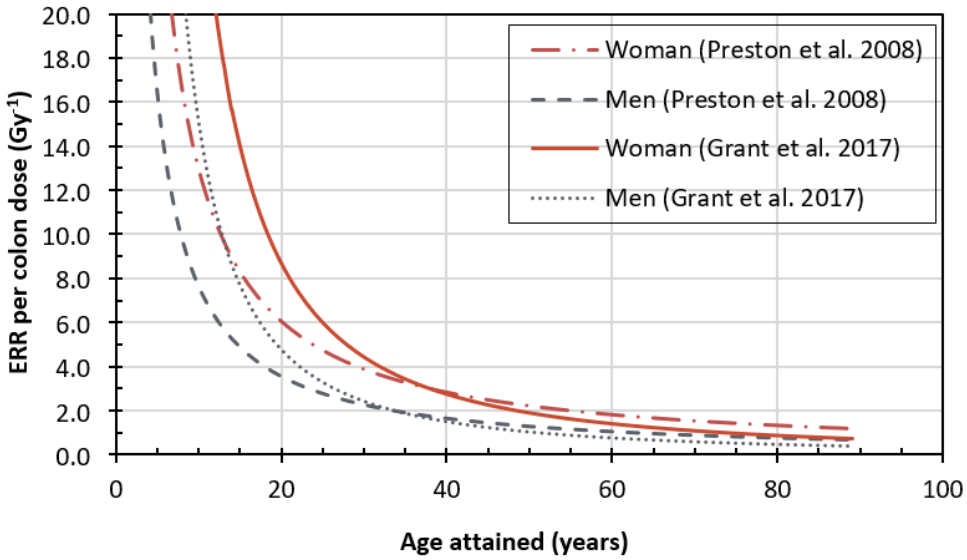


Figure 7-1: Excess relative rate[43] (ERR) per colon dose (Gy^{-1}) from the models of (Preston et al. 2008) and (Grant et al. 2017) for children exposed at age five

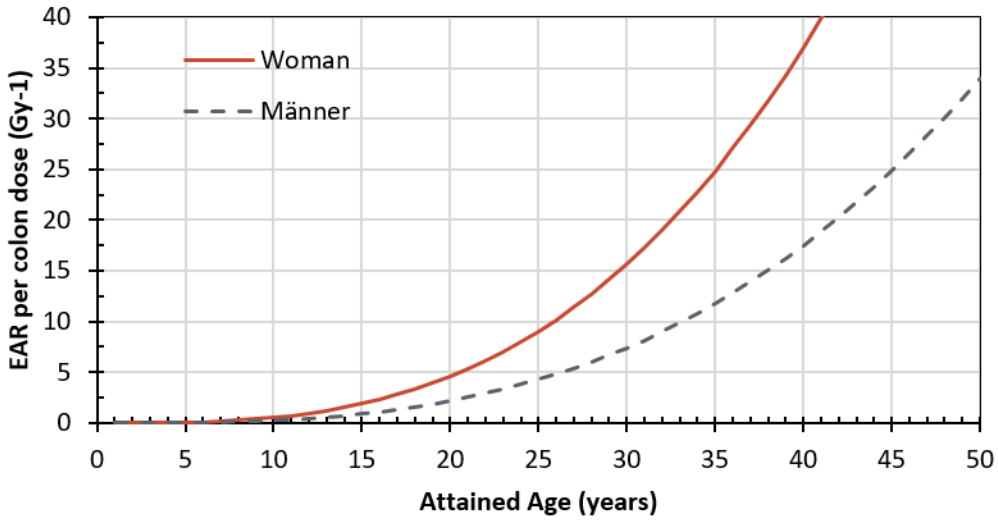


Figure 7-2: *Excess absolute rate (EAR) per 100 000 person-years and per colon dose (Gy^{-1}) from the model of (Preston et al. 2008) for children exposed at age five*

7.2.2 Haematological malignancies (leukaemia, lymphoma)

Hsu et al. modelled the incidence of leukaemia, lymphoma and multiple myeloma in a cohort of approx. 113,000 atomic bomb survivors with a dose estimate for the roughly 94,000 exposed individuals and around 27,000 non-exposed individuals who were alive in 1950 (Hsu et al. 2013). About 41 % were under 20 years of age at the time of exposure. Between 1950 and 2001, 944 of the subjects included in the analyses were diagnosed with a malignancy. To estimate the excess relative rate [43] (ERR) and the excess absolute rate (EAR), the authors fitted a pure quadratic model, a spline model and a categorical model in addition to a linear and a linear-quadratic model for the dose. In the tables they report the preferred linear-quadratic model, separately for leukaemia other than chronic lymphocytic leukaemia (CLL) and adult T-cell leukaemia (ATL, a viral disease) as well as for individual subtypes of leukaemia, lymphoma and multiple myeloma. The dose-response relationship for leukaemia without CLL and ATL was non-linear, with strong effects of attained age and time since exposure, whereby approx. 47 % of leukaemia cases were AML. Like in earlier analyses, there was a weak suggestion of a dose-response relationship for non-Hodgkin's lymphoma in men, but not in women. There was no evidence of radiation-related increased risks for Hodgkin's lymphoma or multiple myeloma. A comprehensive list of the parameter estimates for the models is provided in Annex 2 of the publication. The preferred model for leukaemia other than CLL and ATL does not distinguish by sex, city or age at exposure, but contains terms for attained age and time since exposure; the linear coefficient for the ERR at 1 Gy is 0.79 (95 % CI: 0.03−1.93), the quadratic coefficient is 0.95 (95 % CI: 0.34−1.80).

[43] The authors use the term "excess relative risk".

Table 7-4: *Model with a linear-quadratic dose response and dependence on time since exposure (from (Hsu et al. 2013))*

$$\mathrm{ERR} = (\beta_1 d + \beta_2 d^2) \cdot \exp\left[\alpha \cdot \ln\left(\frac{a}{70}\right) + \gamma \cdot \ln\left(\frac{TSE}{40}\right)\right]$$

$$\beta_1 = 0{,}79\ \mathrm{Gy}^{-1}$$

$$\beta_2 = 0{,}95\ \mathrm{Gy}^{-2}$$

$$\alpha = -1{,}09$$

$$\gamma = -0{,}81$$

In a pooled analysis of mortality and incidence studies on low-dose exposure during childhood, Little et al. estimated the increase in the rate of leukaemia following childhood exposure (Little et al. 2018). To this end, they pooled cohorts with an age at first exposure below 21 years and limited the analysis to cohort members with < 100 mSv and excluding cancer patients. The analysis included nine cohorts (from France, Japan, Canada, Sweden, the USA and the United Kingdom) with exposure to diagnostic or therapeutic medical radiation, as well as atomic bomb survivors. The cohorts consisted of 262,573 persons with radiation exposure < 100 mSv, of which 154 developped myeloid malignancies (including 79 acute myeloid leukaemias, 8 myelodysplastic syndromes and 36 chronic lymphocytic leukaemias) and 40 acute lymphocytic leukaemias. The estimated relative rates per 100 mSv were 3.09 (95 % CI: 1.41−5.92, p-trend < 0.01) for acute myeloid leukaemia and myelodysplastic syndromes, 2.56 (95 % CI: 1.09−5.06, p-trend = 0.03) for acute myeloid leukaemia alone, and 5.66 (95 % CI: 1.35−19.71, p-trend = 0.02) for acute lymphocytic leukaemia. No clear dose response was observed for chronic myeloid leukaemia (p = 0.39). The individual cohorts are slightly heterogeneous, and evidence suggesting a deviation from a linear dose response was weak. When restricting the cohorts to individuals exposed to < 50 mSv, the above trends remained statistically significant (p < 0.05). The EAR at 100 mSv were in the order of 0.1 to 0.4 deaths per 10,000 person-years. The authors conclude that the risk estimates from studies of medically exposed cohorts were generally slightly higher, but statistically compatible with those of the LSS.

A meta-analysis on cancers following low-dose exposure (< 100 mGy) during adulthood and childhood recently published in the monographs of the National Cancer Institute (NCI) (Hauptmann et al. 2020) has been prepared with great care: accompanying articles published in the same volume highlight strengths and weakness of the studies, examine sources of bias and discuss difficulties in interpreting the data (see also section 8.2.1). Six studies assessing the incidence of leukaemia after childhood exposure were evaluated jointly: two paediatric CT scan studies and four ecological studies on background radiation. The meta-ERR[44] at 100 mGy was 2.84 (95 % CI: 0.37−5.32), similar to that of the pooling analysis of (Little et al. 2018). The publication contains no information on age dependencies, which is indispensable when estimating lifetime risks. It also does not contain evaluations by leukaemia subtypes. However, the authors noted that their results are consistent with those of the studies on atomic bomb survivors.

[44] The authors use the term “excess relative risk”.

The first publications relating to studies on leukaemia after childhood CT examinations were based on studies conducted in Germany (Krille et al. 2015), France (Journy et al. 2016), the Netherlands (Meulepas et al. 2019), Great Britain (Berrington de González et al. 2016; Berrington de González et al. 2017; Pearce et al. 2012), Australia (Mathews et al. 2013) and Taiwan (Huang et al. 2014). Even though the increases in the incidence rate varied slightly and different assumptions about latency periods were made, and different in- and exclusion criteria were applied, the risk estimates are relatively similar (Table 7-5). They provide evidence for an increased incident risk of leukaemia and MDS, whereas the evidence for leukaemia alone (without MDS) is much weaker. Only few publications contain information about the range of the organ doses and/or effective doses in the cohorts. Meulepas et al. (2019) and Mathews et al. (2013) indicate bone marrow doses ranging from around 4 mGy to 6 mGy; the organ doses reported by Pearce et al. (2012) are in the order of 50 mGy and 400 mGy. Providing a summary is not possible due to the heterogeneous modelling of the relationship of the increase in the leukaemia rate with age and time. The anticipated pooled analyses could offer some clarity here.

Table 7-5: Increase in the incidence of leukaemia after CT exposure

Author	**Dose***	**Measure of relative leukaemia rate**	**Endpoint**	**Cases**	**Coefficient (mGy^{-1})**
Pearce et al. 2012	**	ERR per dose	Leukaemia+MDS	74	0.036 (0.005–0.120)
			Leukaemia without MDS	65	0.019 (-0.012–0.079)
			MDS	9	6.098 (>0 -145.4)†
Mathews et al. 2013	5.9 mGy	ERR per dose / here with 1 year latency	Leukaemia+MDS	246	0.039 (0.014–0.070)
			Leukaemia without MDS	211	-0.03 (-0.31–0.24)
			MDS	35	0.21 (0.03–0.39)
Huang et al. 2014	-	HR *** exposed yes/no	Leukaemia+MDS	25	1.90 (0.82–4.40)
Krille et al. 2015	11.7 mGy	HR per dose	Leukaemia	17	1.009 (0.981–1.037)
Journy et al. 2016	-	HR per dose	Leukaemia+MDS	12	1.015 (0.974–1.024)
Meulepas et al. 2019	4.5 mGy	ERR per dose	Leukaemia+MDS	13	0.0004 (-0.0012–0.0161)
			Leukaemia without MDS	9	0.0021 (-0.0012–0.0240)

* estimated mean dose

** (detailed table in the publication, no mean dose indicated)

*** HR: Hazard Ratio

† Uncertain estimates due to algorithm convergence issues

A chapter of the report (UNSCEAR 2019) examines the risk of leukaemia due to repeated exposure to low doses of ionising radiation. Here it is postulated that most of the evidence on the risk of leukaemia originates from studies on exposure situations with acute exposure to medium to high doses, but that exposure to (sometimes repeated) computed tomography (CT) scans is far more relevant today, as these examinations account for a large proportion of overall

exposure within the scope of medical procedures. Childhood CT-scan studies generally have the advantage that they provide information on relevant increases in the leukaemia rate per bone marrow dose that are not based on extrapolation from other exposure scenarios. Owing to the relatively short follow-up period, current analyses do not provide any insights on age dependencies. In the future, analysis of larger cohorts, longer follow-up periods, higher case numbers and better control of potential confounding factors (such as the indication for the scans) are expected to provide better insights on individual tumour types and age dependencies. For the purposes of the report (UNSCEAR 2019) lifetime risks were calculated on the basis of the UK childhood CT-scan study (Berrington de González et al. 2016) and the LSS cohort, and the increase in the leukaemia rate per bone marrow dose (< 10 % difference) was found to be in good agreement for the exposure scenario of the CT study population (low dose, exposure at a young age, brief follow-up period up to the maximum age of 30 years). This increases the confidence in methods that transfer the LSS models to other populations and exposure conditions. Currently, the models derived from the LSS appear to be the method of choice for risk estimations for an entire lifetime, not least because of the long follow-up of the LSS.

Therefore, this statement uses the formula derived by Hsu et al. (2013) for calculating the increase in the leukaemia rate per bone marrow dose to estimate the lifetime risks for leukaemia. Since the basis of evidence for the development of lymphoma is weak at best, lymphoma will not be considered further here.

7.2.3 Myelodysplastic syndrome (MDS)

In a historic cohort study, Iwanaga et al. assessed the incidence of MDS from 1985 to 2004 in two sub-cohorts of atomic bomb survivors from Nagasaki (Iwanaga et al. 2011). The first sub-cohort included 64,026 people with a known distance to the epicentre from the database of the Nagasaki University Atomic-Bomb Disease Institute (ABDI), the second sub-cohort included 22,245 persons with an estimated radiation dose from the Radiation Effects Research Foundation Life Span Study (LSS). Details relating to the incidence of MDS were obtained through a comparison with the local cancer registry. Following earlier studies of leukaemia, linear and linear-quadratic models were fit for the dose-response relationship, with continuous values and/or categorical indicators for dose (d) and distance (r) in the formula

$$\lambda = \lambda_0(a,s) \cdot [1 + \beta_1 d + \beta_1 d^2] \text{ or } \lambda = \lambda_0(a,s)\left[1 + \gamma^{-\beta r}\right].$$

In contrast to other studies, attained age and age at exposure were not included in the models as modifiers of the excess relative rate[45]. In the ABDI cohort, 30 % and 63 % were under the age of ten and 20 years, respectively, at exposure; in the LSS cohort it was 35 % and 68 %. In both cohorts, MDS incidence rates decreased with the (categorical) age at exposure and significantly with distance. In the LSS cohort, a linear model provided the best fit, with an excess relative rate per 1 Gy dose of 4.3 (95 % CI: 1.6–9.5); a linear-quadratic model (like for AML) did not improve the fit (p = 0.43). As data on MDS is only available from 1985 onwards, i. e. 40 years after exposure, the study does not provide any information about incidence rates in the first 40 years. The authors conclude that radiation-induced increases in MDS incidence rates can still be observed 40 years after exposure; this is in contrast to the leukaemia rates, which level off after an initial increase. In this regard it must be noted that their models do not include attained age as a modifier of the excess relative rate.

[45] The authors use the term “excess relative risk”.

7.2.4 Thyroid cancer

The risk of radiation-induced thyroid cancer is highest in childhood. Key insights on thyroid cancer originate from studies in patients undergoing radiotherapy of the head and neck (particularly for Hodgkin's lymphoma), from the study in atomic bomb survivors and from investigations on radioiodine exposure resulting from the Chrnobyl accident (UNSCEAR 2013). The most recent summary of UNSCEAR (2019) takes into account these studies as well as more recent studies.

The latest publication on thyroid cancer in the cohort of Japanese atomic bomb survivors was written by (Furukawa et al. 2013). Between 1958 and 2005 the authors identified 371 primary thyroid cancers with a diameter > 10 mm among the 105,401 cohort members. The estimated median and mean organ dose was 0.009 Gy and 0.142 Gy, respectively. For an exposure of 1 Gy at the age of ten years and an attained age of 60 years, they estimated the excess relative rate[46] as being 1.28 (95 % CI: 0.59–2.70) using a linear dose-response model with modification by attained age and age at exposure. The risk rapidly decreased by 53 % (p = 0.03) with each decade increase in age at exposure (Figure 7-3). The difference in the excess relative rate between the sexes was not significant (p = 0.30), but the best estimate for women was higher than for men by a factor of 2. The authors found no evidence of a non-linear dose response or of a threshold dose. The applied model is not reported explicitly in the publication, but can be found in (UNSCEAR 2019):

Table 7-6: *Risk model for thyroid cancer after exposure (according to UNSCEAR 2019) as a function of the dose d, sex m, attained age a, and age at exposure e.*

$$\mathrm{ERR} = (\beta \cdot d) \cdot (1 + \alpha \cdot m_s) \cdot \exp\left[\delta_1 \cdot \ln\left(\frac{a}{60}\right) + \delta_2 \frac{e - 10}{10}\right]$$

$$\beta = 1{,}28$$

$$\alpha = 0{,}327$$

$$\delta_1 = -1{,}27$$

$$\delta_2 = -0{,}769$$

$$m_{\mathrm{sex}} = -1 \text{ for men}, +1 \text{ for women}$$

[46] The authors use the term "excess relative risk".

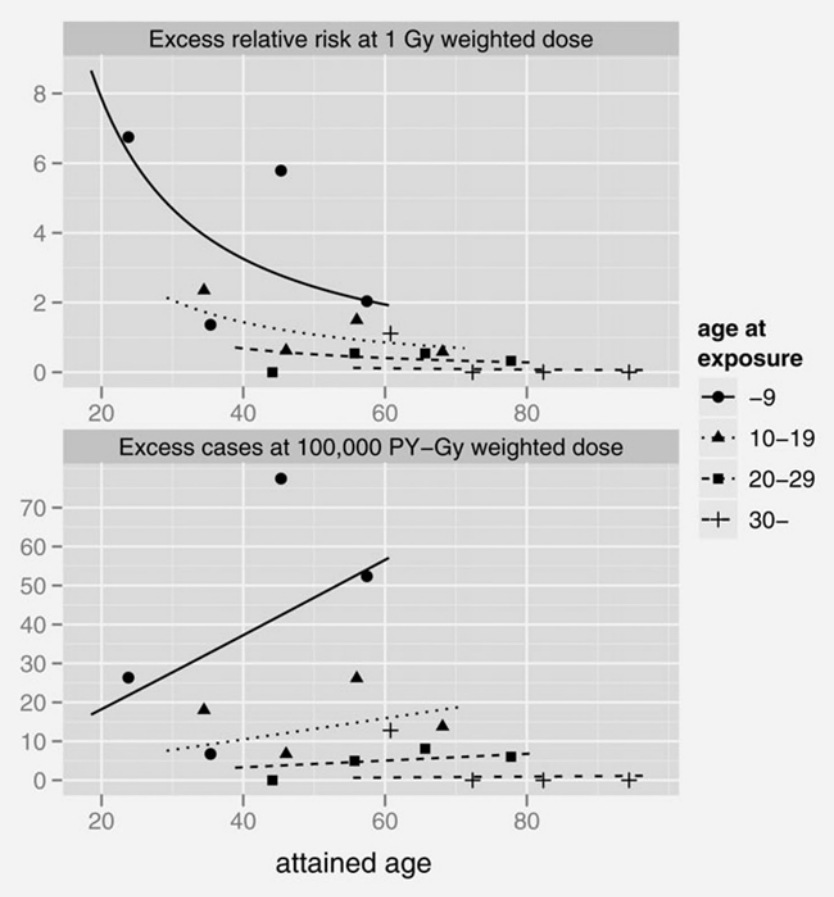


Figure 7-3: *Fitted values of the excess relative rate[47] for thyroid cancer at 1 Gy (Furukawa et al. 2013)*

For a subgroup of 292 thyroid cancers with a papillary histology in the LSS, (Kaiser et al. 2020) assessed the increase in the incidence rate using biologically based models. For exposure at the age > 30 years, they found no radiation-related increase in the incidence rate. The root cause was reported to be a rapidly decreasing sensitivity to radiation with onset of puberty, which could be related to the disappearance of foetal stem cells in the thyroid.

Numerous studies of the cohorts from Russia (Ivanov et al. 2006), the Ukraine (Little et al. 2014) and Belarus (Zablotska et al. 2011, Little et al. 2015) who were exposed to radiation as children after the Chornobyl accident have been published, among which modelling approaches that include biomarkers for radiation (Kaiser et al. 2016) and take into account dosimetry measurement errors (Little et al. 2014, Little et al. 2015). The dosimetry is based on interviews on post-accident behaviour, in combination with estimations of iodine uptake and thyroid mass, to determine the dose due to internal radiation. The dose distribution ranges from organ doses of 0.5 mGy up to 40 Gy. Little et al. describe in detail the models applied for estimating the excess odds ratio (EOR) per dose, including the estimated effect of age at exposure (Little et al. 2014, Little et al. 2015).

For the Ukrainian-American cohort study initiated by the National Cancer Institute (UkrAm cohort, (Tronko et al. 2006), (Brenner et al. 2011), (Tronko et al. 2017)), (Little et al. 2014) used three models to take into account the uncertainties in the estimations of thyroid exposure and thyroid mass: two types of regression calibration and a Monte Carlo method. The EORs

[47] The authors use the term “excess relative risk”.

estimated using these models are 5.79 Gy^{-1} (95 % CI: 1.92–27.04), 4.78 Gy^{-1} (95 % CI: 1.64–19.69) and 4.93 Gy^{-1} (95 % CI: 1.67–19.90); the adjusted risk estimates are thus 7 % higher than or 11 % and 8 % lower than the unadjusted estimates.

For the Belarusian population, (Little et al. 2015) used a regression calibration method, a Monte Carlo maximum likelihood method and a Bayesian Markov Chain method. The EORs estimated using these models are 1.31 Gy^{-1} (95 % CI: 0.47–3.31), 1.48 Gy^{-1} (95 % CI: 0.53–3.87) and 1.16 Gy^{-1} (95 % CI: 0.20–4.32), and are thus 13 %, 2 % and 23 % lower than the unadjusted estimate of 1.51 Gy^{-1} (95 % CI: 0.53–3.86). The estimated EORs are thus considerably lower than those of the Ukrainian cohort, which could be explained by a far better individual estimation of the thyroid mass and thus of the thyroid dose in the Belarusian cohort.

Based on the review of (Ron et al. 1995), a pooled analysis of cohort studies on exposure to external radiation during childhood and thyroid cancer was carried out (Lubin et al. 2017, Veiga et al. 2016). The study aimed to evaluate the incidence rate ratio (RR) for thyroid radiation doses < 0.2 Gy, to provide evidence of a threshold dose, and to identify possible modifiers of the dose response, e. g. sex, age at exposure, time since exposure. To this end, data from nine cohort studies of childhood external radiation exposure and thyroid cancer with individualised dose estimates was pooled; the studies included ≥ 1,000 irradiated subjects or at least ≥ 10 thyroid cancer cases, with data limited to persons exposed to doses < 0.2 Gy (Lubin et al. 2017). The cohorts included: childhood cancer survivors (n = 2), children treated for benign diseases (n = 6), and atomic bomb survivors (n = 1). They identified 252 cases in exposed individuals in 2,588,559 person-years and a further 142 cases in non-exposed individuals in 1,865,957 person-years. For both < 0.2 Gy and < 0.1 Gy, the RRs increased with the thyroid dose ($p < 0.01$), without a significant departure from linearity ($p = 0.77$ and $p = 0.66$. respectively). Estimates of the threshold dose ranged from 0.0 Gy to 0.03 Gy, with an upper 95 % confidence limit of 0.04 Gy. The estimates of the relative incidence rate at 0.2 Gy and 0.1 Gy, limiting exposure data to < 0.2 Gy and < 0.1 Gy, are RR = 3.0 (95 % CI: 2.1–4.9) and RR = 2.9 (95 % CI: 1.7–6.6). Lubin et al. 2017 observed no departure from a linear dose response and estimated an excess relative rate[48] at 0.2 Gy of 2.2 (95 % CI: 1.3–3.3). The positive dose-response relationship persisted > 45 years after exposure (similar to the results reported by (Furukawa et al. 2013) for the LSS), it was greater at a younger age at exposure and a younger attained age and did not differ significantly by sex or number of radiation treatments. As the studies on tinea capitis and atomic bomb survivors accounted for 52 % and 28 % of exposed cases, a sensitivity analysis was carried out in which one study was omitted from the analysis each time. Omission of the tinea capitis study resulted in a 31 % decrease in RR at 0.2 Gy, omission of the atomic bomb survivors study in a 25 % increase in RR. With $p = 0.89$ for Cochrans Q-statistics, the heterogeneity analysis indicated homogeneity of the risk estimates. However, the authors note that it is difficult to draw definitive conclusions from the increases in the incidence rates per thyroid dose for cohorts with substantial differences in exposure, such as medically exposed persons, atomic bomb survivors and those exposed after the Chornobyl accident with mild to moderate iodine deficiency and/or intensive screening.

7.3 Conclusions

The choice of publications considered here is greatly restricted by the requirement that they must include sufficiently described and reliable models that enable an extrapolation of the cancer risk following exposure during childhood all the way into old age.

[48] The authors use the term “excess relative risk”.

Evaluations of the LSS meeting these requirements are available for all groups of cancer described above, and with restrictions also for the myelodysplastic syndrome. Despite the many differences in radiation exposure, the analyses of dose-response relationships reported in the single studies reviewed here are statistically compatible with those of the LSS. However, they refer largely to childhood cancer only, because – unlike the LSS – no models were fit that quantify the age dependency of the risk over a long period of time.

Therefore, the risk estimations carried out for the present statement are based on the models for malignant tumours derived for the LSS by (Grant et al. 2017), for leukaemia by (Hsu et al. 2013) and for thyroid cancer by (Furukawa et al. 2013).

8 Cancer risk due to exposure during adulthood

8.1 Overview

Two fundamental reviews on the risk of cancer after exposure to ionising radiation and its uncertainties were recently published. Section 8.2 provides a brief summary of the aspects relevant to radiation exposure during adulthood, comments on their applicability for estimating the cancer risk after continuous exposure and offers a rationale for selecting the Life Span Study (LSS) as a basis for calculating lifetime risks in the present scientific background. Sections 8.3 and 8.4 present the key findings of the LSS for the radiation-induced incidence of all malignant tumours (Grant et al. 2017) and leukaemia (Hsu et al. 2013). The two subsequent sections refer to chapter 7 with regard to the state of knowledge concerning the radiation risk for myelodysplastic syndromes and for thyroid cancer. Finally, section 8.7 briefly summarises the current state of knowledge concerning the predisposition to an increased cancer risk after exposure.

8.2 Recent fundamental reviews

8.2.1 National Cancer Institute (NCI) monograph on epidemiological studies on the cancer risk after exposure to ionising radiation

In a series of articles in the Journal of the National Cancer Institute Monographs, a comprehensive analysis of epidemiological studies on the risk of cancer after exposure to ionising radiation was published in 2020 (JNCI 2020)[49]. The analysis considers studies with predominantly low-LET radiation in which the mean dose of the subjects was smaller than 100 mGy. The studies calculated exposure-related increases in cancer rates using a linear no-threshold dose-response model. Key priorities of the analysis included a discussion of the impact of errors and, based on this, meta-analyses of studies in which the errors did not bias the result for the excess relative rate per dose in a potentially significant manner. The analysis was published in a series of six publications. The first study (Berrington de González et al. 2020) describes the design of the analysis of the errors and provides a summary of the 26 epidemiological studies included in the analysis. The key results of other studies of the series are summarised briefly and partly commented on below.

(Daniels et al. 2020) investigated the possible impact of dosimetry errors on the estimated excess relative rate per dose. Eight of the studies investigated exposure due to environmental contamination, four addressed exposure within the scope of medical procedures and fourteen dealt with occupational exposure. (Daniels et al. 2020) identified three case control studies in

[49] The authors of this monograph use the term “excess relative risk”.

which dose determination errors may have led to overestimation of the risk of radiation. In these studies, the dose determination was based on interviews conducted after case ascertainment. For the remaining 23 studies, the authors rated the impact of dosimetry errors on the radiation risk outcome as low.

(Schubauer-Berigan et al. 2020) analysed the possible impact of confounding and selection bias on the result of the 26 studies. They identified lifestyle-related risk factors as one of the primary causes of a possible distortion of the study results. For occupational exposure studies, other risk factors in the workplace and the often better health status of the working population compared to the general population (known as "healthy worker effect") were additionally considered. The available data suggests that the impact of confounding and selection bias in 22 of the studies is expected to be low. (Schubauer-Berigan et al. 2020) found evidence of selection bias in one study, and identified a possible impact due to lifestyle-related factors and the healthy worker effect in three occupational exposure studies.

(Linet et al. 2020) evaluated the impact of loss to follow-up, misclassification as well as over- or underascertainment of diseases/causes of death, and of changes in classification systems over the course of the study. Based on their analysis, they conclude that the vast majority of studies do not contain sufficient information to assess the impact of strengths or errors in case ascertainment on the risk estimation. However, the limited data available suggests that – with the exception of four studies – the effects on the estimated relative rate are low.

The review conducted by (Gilbert et al. 2020) provides a summary of epidemiological studies of cohorts exposed to medium and high doses and of radiobiological studies which, viewed collectively, show a clear correlation between exposure to ionising radiation and increases in cancer risks. They discuss the use of a linear dose-response model both for low- and moderate-dose studies and for high-dose studies. They estimate the statistical power of studies with mean doses below 100 mGy. Finally, they discuss the interpretation of confidence intervals and the applicability of the Bradford Hill criteria for deriving causal relationships.

Hauptmann et al. (2020) summarised the results of error analyses and carried out meta-analyses of the studies showing no major potential for a significant impact of errors on the estimated excess relative rate per dose. For exposure during adulthood, the excess relative rate per dose was estimated as 0.29 Gy^{-1} (95 % CI: 0.11−0.47) for malignant tumours and 1.6 Gy^{-1} (95 % CI: 0.7–2.5) for leukaemia. The results are in line with the LSS of the atomic bomb survivors of Hiroshima and Nagasaki without application of a dose and dose-rate effectiveness factor.

The following should be taken into account when evaluating the findings of (Hauptmann et al. 2020):

- The excess relative rate per dose for malignant tumours is noticeably lower than 0.47 Gy^{-1} (90 % CI: 0.18−0.79), the key finding of INWORKS (Richardson et al. 2015), whose pooled analyses of American, English and French studies contributed significantly to the meta-analysis of (Hauptmann et al. 2020). The difference lies in the relation of the cancer rate to the personal dose, while the key finding of INWORKS, like the results of the LSS, relates to an adjusted colon dose[50], which was adjusted to account for potential bias in historical dosimeter measurements[51]. When related to the personal dose, INWORKS found an excess relative rate per dose of 0.33 Gy^{-1} (90 % CI:

[50] INWORKS only considers photon radiation in the dose calculations

[51] The estimation of adjusted doses in the regression analysis includes an assumption about the true dose distribution in the studied cohort.

0.12−0.56) (Richardson et al. 2015), in line with the findings of Hauptmann et al. (2020).

- The studies with a mean dose lower than 100 mGy are considered by (Berrington de González et al. 2020) to be low-dose studies. They relate the estimate for the excess relative rate per dose to a value of 100 mGy (Hauptmann et al. 2020). In the studies considered, however, a considerable number of cohort members received medium and high doses. For leukaemia, for example, the highest bone marrow dose reported in the most relevant studies (based on the weight in the meta-analysis) was 2,363 mGy in Taiwanese people exposed to contaminated construction materials (Hsieh et al. 2017), 1,217.5 mGy in occupationally exposed workers in the United Kingdom (Muirhead et al. 2009) and 820.2 mGy in US nuclear workers (Schubauer-Berigan et al. 2015). The INWORKS analyses illustrate that estimates for the cohort as a whole are of only limited significance for low doses. (Leuraud et al. 2015) reported a significant result of 15.9 mGy for leukaemia and for the whole cohort with a mean adjusted bone marrow dose by photon radiation, but no significance when restricting the analysis to cohort members receiving a maximum of 100 mGy.

8.2.2 UNSCEAR 2019 Report

In two chapters of Annex A *Evaluation of selected health effects and inference of risk due to radiation exposure* of the report (UNSCEAR 2019), selected scenarios are used to estimate lifetime risks of mortality due to malignant tumours and leukaemia after exposure during adulthood, discuss as far as possible the impact of errors and draw conclusions on the transferability the results of the LSS and of INWORKS to other scenarios (UNSCEAR 2019). This section is based on the UNSCEAR 2019 Report and particularly on its general conclusions without discussing the individual studies again in detail.

Based on a review of studies on the cancer risk after exposure during adulthood, Annex A of the UNSCEAR 2019 Report uses the INWORKS study (Leuraud et al. 2015, Richardson et al. 2015) for an estimation of lifetime risks and their uncertainties. The estimations are made on the basis of an exposure period of 15 years with a colon dose of 100 mGy for malignant tumours and a bone marrow dose of 200 mGy for the risk of leukaemia. After comparing the calculated risks with risk estimates based on the LSS of survivors of the atomic bombings of Hiroshima and Nagasaki, UNSCEAR draws the following conclusions:

- For special scenarios that simulate the exposure scenarios and the follow-up in INWORKS in a simplified manner, the risk estimates are in line with those calculated on the basis of INWORKS and LSS without application of a dose and dose-rate effectiveness factor. This is regarded as confirmation that the results of the LSS can be transferred to other scenarios.
- For the special scenarios mentioned, the calculations based on INWORKS provide a higher reliability and lower uncertainties than those based on the LSS.
- For scenarios with a follow-up to a high age (90 years), there are greater differences in the calculations. Essentially, this is due to the limited observation period of INWORKS.

In this scientific background, lifetime risks up to the age of 90 years are calculated. According to the UNSCEAR analysis, the existing studies on cancer risks after prolonged or repeated exposure are of only limited suitability for a follow-up to high age. On the other hand, the UNSCEAR report has boosted confidence in the transferability of the results of the LSS to scenarios with prolonged exposure. For this reason, the calculation of lifetime risks in this report is based on the transfer of risk estimates from the LSS to the scenario of continuous exposure

during adulthood in Germany. The key results of the LSS on the incidence of malignant tumours and leukaemia are summarised in the two following sections.

8.3 All malignant tumours

In their study, (Grant et al. 2017) analyse the incidence of malignant tumours in the LSS cohort in the calendar years 1958 to 2009. The cohort includes not only residents of Hiroshima and Nagasaki who were within a 10-kilometre distance from the hypocentres at the time of the bombings, but also residents who were outside the two cities. The data for the second group is used only to better capture dependencies of the spontaneous incidence of malignant tumours on birth year, sex and age.

Regular queries were sent to the national family registry (*koseki*) to ascertain whether the cohort members were still alive. The follow-up of the incidence of malignant tumours started on 1 January 1958 and ended at one of the following events, whichever occurred first: i) cancer diagnosis, ii) death, iii) person no longer registered in *koseki* and iv) 31 December 2009.

The study is based on data for 105,444 members of the LSS cohort for whom kerma and colon dose estimates were available in the *Dosimetry System 2002 Revision 1*. In the calculations, the neutron dose contribution is weighted with a factor of ten. Kerma values greater than 4 Gy were truncated to 4 Gy, as it is assumed that such high dose estimates are most likely overestimated (Cullings et al. 2017). To correct for classical dose-estimation errors, the estimated doses were replaced by an adjusted dose, i. e. an expected dose estimate that takes into account the uncertainties of the dose estimates (Pierce et al. 1991). In this report, the truncated and adjusted dose used in the LSS is termed “adjusted dose” in short.

The data on the incidence of malignant tumours originates from comparisons of the data of the cohort members with the cancer registers of the cities and prefectures of Hiroshima and Nagasaki, with the Adult Health Study and with clinical and autopsy programs of the Radiation Effects Research Foundation (RERF) (Grant et al. 2017). Diagnoses based solely on a postmortem examination were excluded. Furthermore, in situ cancers and cancers in the intestinal mucose were not included in the study. A total of 22,538 cases of first primary malignant tumours were identified among the cohort members. Stomach cancer was the most common type of cancer and accounted for 29.5 % of incident cancer cases among males and 21.3 % among females.

The authors assessed the shape of the dose-response curve and its dependence on sex, age at exposure, time since exposure and attained age using Poisson regression methods. To this end, the data was organised into a very large number of groups, stratified among other things by sex, place of residence at the time of exposure, age at exposure, attained age, adjusted colon dose, calendar year and smoking habits. Data on smoking habits corresponds to the data used in an earlier study on lung cancer (Furukawa et al. 2010). For each group the data includes, among other things, the number of person-years and malignant tumour cases, mean values of the adjusted colon dose, age at exposure, time since exposure and attained age.

An additive model for the effects of smoking and radiation provides a slightly better fit than a multiplicative model (Grant et al. 2017). However, to enable comparability with earlier studies, the latter model is preferred. The model is a product of the spontaneous incidence rate for non-smokers, the relative rate for smokers and the relative rate $(1 + ERR_{rad})$ for exposed persons.

The dependence of the excess relative rate[52] for exposed persons (ERR_{rad}) on the adjusted colon dose, *d*, age at exposure, *e*, and attained age, *a*, is given by

$$ERR_{rad} = (\beta_{1s} d + \beta_{2s} d^2) \cdot \exp\left[\delta_1 \ln\left(\frac{\alpha}{70}\right) + \delta_{2s} \cdot \frac{e-30}{10}\right]$$

where the index *s* indicates the sex.

The key results of the model preferred by (Grant et al. 2017) are:

- The spontaneous incidence of malignant tumours increases roughly to the fifth power of attained age in males and to the third power in females (Figure 8-1). This increase is lessened somewhat at older ages, especially among males. The female-to-male incidence rate ratio decreases from 3 at age 30 to 1 at age 50 and to below 1 at older ages. The cancer incidence rate increases by approximately 15 % for males and 6.5 % for females per decade increase in birth year.
- For women, the ERR_{rad} shows linearity with the adjusted colon dose with a coefficient β_{1f}, of 0.64 Gy^{-1} and a 95 % confidence interval of 0.52 Gy^{-1} to 0.77 Gy^{-1}. For men, there is a linear-quadratic dependence on the adjusted colon dose with β_{1m} = 0.094 Gy^{-1} (95 % CI: <0.02−0.23) and β_{2m} = 0.11 Gy^{-2} (95 % CI: 0.04−0.19). The radiation effect is significantly greater among women than among men, particularly at low doses.
- The curvature of the dose response for males is characterised largely by a flat radiation response in the range of 0.20 Gy to 0.75 Gy (Figure 8-2); in the lower dose range of 0 Gy to 0.1 Gy a linear dose response model showed a coefficient of 0.33 Gy^{-1} (95 % CI: <-0.10−0.89).
- ERR_{rad} decreases with age at exposure. The model shows no evidence of a difference between the sexes; the decrease for both sexes is 22 % (95 % CI: 13 %−30 %) per decade.
- ERR_{rad} decreases with attained age, the decrease being more pronounced for males (δ_{1m} = -2.70 (95 % CI: -3.58−-1.81)) than for females (δ_{1f} = -1.36 (95 % CI: -1.86−-0.84)).
- In the dose category from 0.005 Gy to 0.2 Gy, slightly more than 2 % of the 6,891 cases are associated with exposure.

[52] The authors use the term “excess relative risk”.

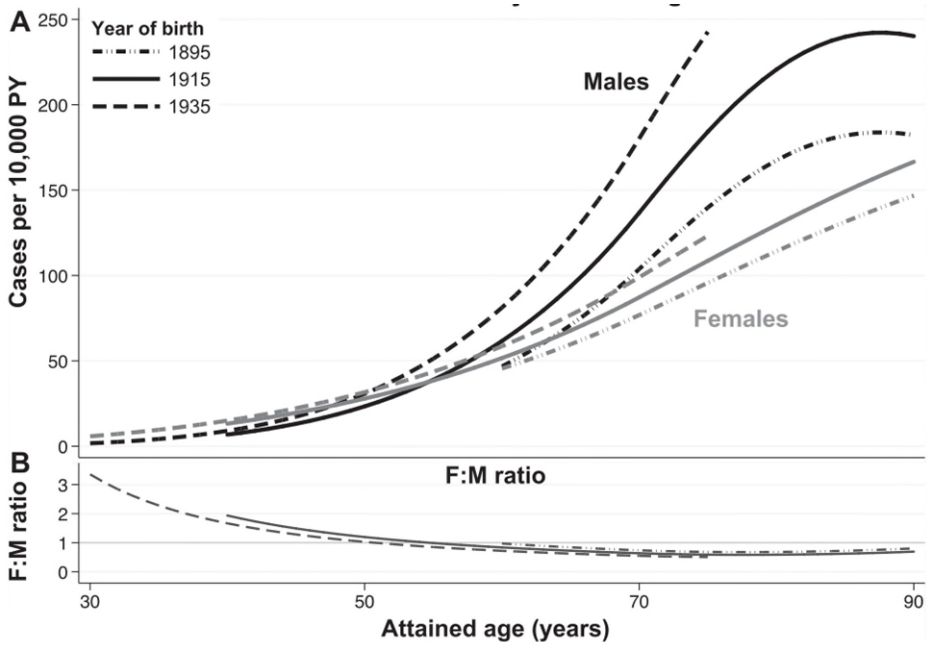


Figure 8-1: *Spontaneous incidence of malignant tumours among non-smokers in the LSS (A), and the female-to-male incidence rate ratio (B) (Grant et al. 2017).*

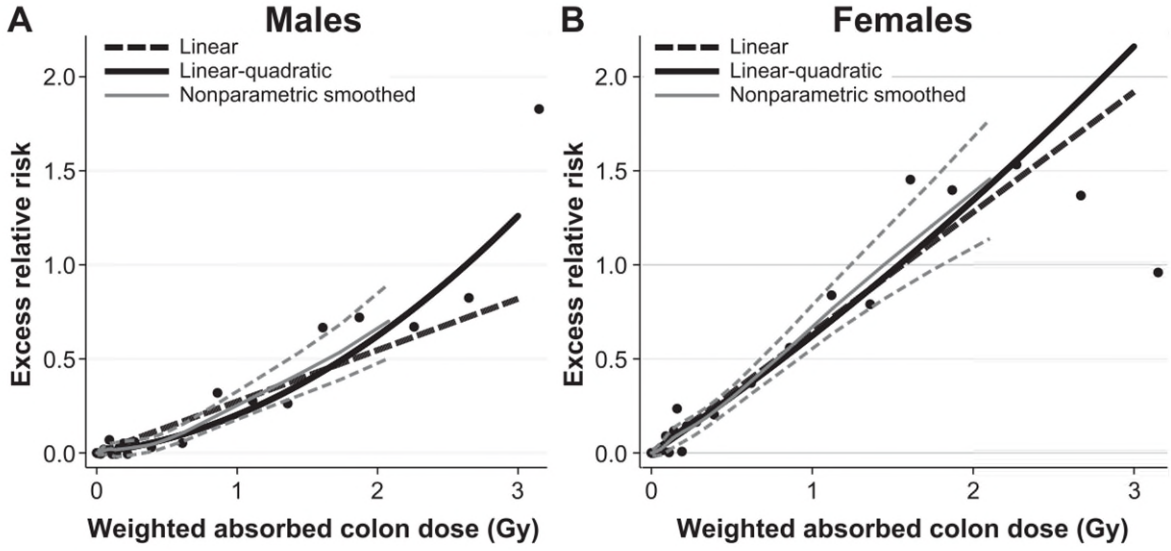


Figure 8-2: *Dose dependence of the ERR_{rad} in the linear and linear-quadratic model (black solid curves), in the analysis of the categories (points) and their smoothed curves with the respective 95 % confidence interval (solid grey curves) (Grant et al. 2017).*

(Grant et al. 2017) also analyse the incidence data for malignant tumours using a linear dose-response model in which the decrease in the ERR_{rad} is dependent on attained age but not on sex. For women with an age at exposure of 30 years and an attained age of 70 years, the ERR_{rad} per adjusted colon dose, β_{1f}, is 0.60 Gy^{-1} (95 % CI: 0.49−0.72); for men it is β_{1m} = 0.33 Gy^{-1} (95 % CI: 0.25−0.42). ERR_{rad} decreases with age at exposure, by 21 % (95 % CI: 12 %−29 %) per decade. In this model the coefficient for the decrease with attained age is $\delta_{1f} = \delta_{1m}$ = -1.66 (95 % CI: -2.11−-1.20).

With the extended follow-up of the cancer incidence dataset of the LSS cohort, (Grant et al. 2017) for the first time identified a non-linear dose response for males, while the dose response

for females remained linear. The reasons for the change in the dose response in males compared to earlier analyses are not currently understood. Since (Grant et al. 2017), several specific cancers have been analysed in detail, including lung cancer and colorectal cancer (Cahoon 2017, Sugiyama 2020), the two most common types of cancer among men. For both types of cancer, the dose response was linear in both men and women. Furthermore, it must be considered that Grant et al. performed a joint analysis of many types of cancer, for which age dependencies may differ. It cannot be ruled out that the use of a common model to describe these differing age dependencies has an impact on the dose response. Therefore, due to a current lack of scientific understanding, this report uses the linear model, which is also consistent with earlier analysis of the LSS.

8.4 Leukaemia

In their study, Hsu et al. (2013) analyse the leukaemia incidence in the LSS cohort in the calendar years 1950 to 2001. The cohort includes not only residents of Hiroshima and Nagasaki who were within a 10-kilometre distance from the hypocentres at the time of the bombings, but also residents who were outside the two cities. The data for the second group is used only to better capture dependencies of the spontaneous leukaemia incidence rates on birth year, sex and age.

Queries were sent to the national family registry (*koseki*) on a three-year basis to ascertain whether the cohort members were still alive. Given the completeness of the register, it was possible to record the vital status of more than 99 % of the cohort members up to the end of the follow-up. The follow-up of the leukaemia incidence started on 1 October 1950 and ended at one of the following events, whichever occurred first: i) cancer diagnosis, ii) death, iii) person no longer registered in *koseki* and iv) 31 December 2001.

The leukaemia incidence data stems from a special register for Hiroshima and Nagasaki, which was established in the early 1950s, and starting in the late 1980s from the city and prefecture cancer registers. The information was supplemented by records of the hospitals in both cities and their surroundings. In addition, death certificates were evaluated and clinical information relating to the leukaemia cases was obtained as far as possible. If information on a leukaemia case was contradictory, the data source with the highest quality (e. g. clinical records) was selected.

The study is based on data for 113,011 members of the LSS cohort for whom bone marrow dose estimates were available in the *DS02* dosimetry system. The adjusted and truncated bone marrow dose is used. The indicated adjusted bone marrow dose is the sum of the absorbed dose from photon radiation plus ten times the absorbed dose from neutron radiation.

The authors assessed the shape of the dose-response curve and its dependence on sex, age at exposure, time since exposure and attained age using Poisson regression methods. To this end, the data was organised into a very large number of groups, stratified among other things by sex, place of residence at the time of exposure, age at exposure, attained age, adjusted bone marrow dose and calendar year. For each group, the data includes the number of person-years and leukaemia cases, mean values of the adjusted bone marrow dose, age at exposure, time since exposure and attained age.

It was found that models for excess relative rates generally described the data better than models for excess absolute rates (EAR).

For the rates of chronic lymphocytic leukaemia and adult T-cell leukaemia, Hsu et al. (2013) found no associated with radiation exposure. For all other types of leukaemia together (hereafter “leukaemia” in short), they identified a total of 312 individuals who were in the Hiroshima or

Nagasaki prefecture at the time of the diagnosis. More than half of these cases (176) were classified as acute myeloid leukaemia (AML).

The preferred model for leukaemia is a linear-quadratic dose-response model of the excess relative rate [53] (ERR) with a dependence on attained age, a, and on time since exposure, TSE, with no dependence on city and sex:

$$ERR = (\beta_1 d + \beta_2 d^2) \cdot \exp\left[\alpha \ln\frac{a}{70} + \gamma \ln\frac{\mathrm{TSE}}{40}\right].$$

Figure 8-3 presents the results of the preferred model graphically. The key results of the model are:

- From an age of 10 years, the spontaneous incidence increases in a superlinear fashion with attained age. The incidence in women is only half that in men. The rate in Nagasaki is around 35 % lower than in Hiroshima. The incidence was highest for those born in 1920. For cohort members born in 1900 or 1940, it is about 30 % lower.
- The excess relative rate exhibits a linear-quadratic response to the adjusted bone marrow dose. For an age at exposure of 30 years and an attained age of 70 years, the dose coefficient of the linear term is $\beta_1 = 0.79\ \mathrm{Gy}^{-1}$ and that of the quadratic term is $\beta_2 = 0.95\ \mathrm{Gy}^{-2}$. Non-linearity of the ERR for leukaemia is driven by AML.
- The excess relative rate decreases with attained age and time since exposure ($\alpha = -1.09$; $\gamma = -0.81$); at any given time since exposure the excess relative rate decreases with the age at exposure. At any given attained age, on the other hand, it increases with the age at exposure. This is due to the fact that, at any given attained age, older age at exposure implies a shorter time since exposure. The highest excess relative rate was found for those exposed early in life and shortly after exposure (the follow-up started around 5 years after exposure).
- In the dose category 5 mGy to 200 mGy with a mean of 50 mGy, approximately 10 % of leukaemia cases (8.1 of 79) were associated with radiation exposure.

[53] The authors use the term “excess relative risk”.

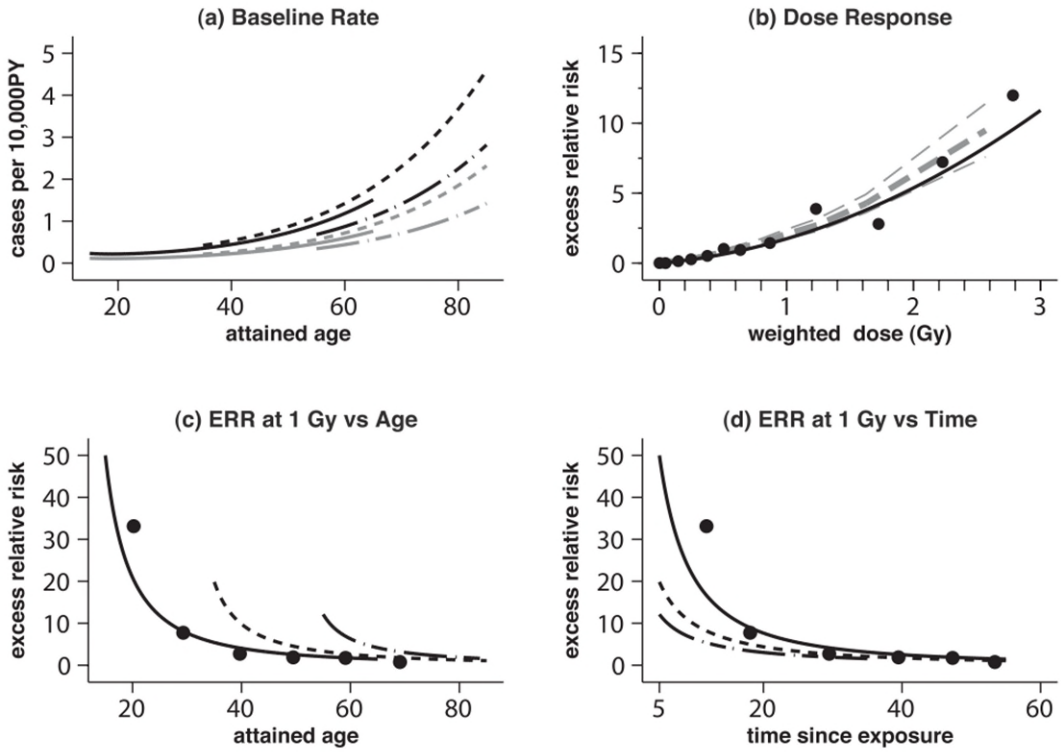


Figure 8-3: *Results of the Poisson regression for the risk of leukaemia other than chronic lymphocytic leukaemia and adult T-cell leukaemia in the LSS (from (Hsu et al. 2013)). Plot (a): Age dependence of the baseline rates in Hiroshima for men (black lines) and women (grey) born in 1895 (dash-dot), 1915 (dash) and 1935 (solid); (b) dose response of the excess relative rate[54] for a person exposed at age 30 and an attained age 70: linear-quadratic fit (solid black line), and in the individual dose categories (dots) including a smoothed curve with a plus/minus 1 standard deviation confidence interval (dashed grey line); (c) and (d) time dependence of the excess relative rate (curves for the three birth cohorts, dots for birth year 1935).*

(Hsu et al. 2013) additionally analyse the leukaemia incidence overall and for individual categories of age at exposure using a linear dose-response model with no further age dependencies. The results for the excess relative rate per bone marrow dose are summarised in Table 8-1.

Table 8-1: *Linear dose estimates for the excess relative rate of leukaemia in individual categories of age at exposure and in total (data from (Hsu et al. 2013)).*

Age at exposure (years)	Leukaemia cases	Excess relative rate per bone marrow dose (Gy^{-1})
0–19	106	6.5 (95 % CI: 4.0; 10.3)
20 – 39	122	3.9 (95 % CI: 2.3; 6.1)
40+	84	4.0 (95 % CI: 2.1; 6.9)
All	312	4.7 (95 % CI: 3.3; 6.5)

[54] The authors use the term “excess relative risk”.

8.5 Myelodysplastic syndrome

The literature on the risk of myelodysplastic syndrome (MDS) related to exposure to ionising radiation is described in chapter 7. Information on the coefficient in a linear dose response for exposure during adulthood was only provided by (Iwanaga et al. 2011). In this study, the excess relative rate for MDS after exposure at age ≥ 20 years is a factor of 2 smaller than after exposure at age < 20 years.

8.6 Thyroid cancer

The literature relating to the incident risk of thyroid cancer after exposure to ionising radiation is described in chapter 7. While there is clear evidence for an increased risk after exposure at a young age to thyroid radiation doses below 1 Gy, there is no such evidence for exposure during adulthood. However, the age-dependent risk function described in chapter 7 for thyroid cancer in the LSS is also based on extensive data on exposure during adulthood; for this reason, it is also used below for the calculation of lifetime risks after exposure during adulthood.

8.7 Predisposition to an excess cancer risk after exposure

In addition to age at exposure and sex, both of which have been well characterised as effect modifiers for cancer induction due to radiation, other individual characteristics may influence the risk of cancer after exposure. These include, for example, lifestyle factors such as diet or exposure to other genotoxic substances (overview in (Averbeck et al. 2020)). In some epidemiological studies of corresponding tumour entities (e. g. lung cancer after radon exposure), the factor smoking habits is considered as an effect modifier, while the impact of other lifestyle factors has not been well characterised thus far.

Genetic variations may also have an impact on the risk of cancer after exposure. An increase in the risk of breast cancer due to radiation is of particular interest, e. g. as a consequence of regular mammograms, in women with an increased family history of breast cancer or women with BRCA1 and BRCA2 gene mutations (overview in (Seibold et al. 2020)).

Using smokers and women predisposed to breast cancer by way of example, it is shown below how an increased risk after radiation in comparison with persons to whom these factors do not apply can be estimated. In both cases the radiation-induced absolute risk is expected to be increased.

Lung cancer accounts for about 15 % of all malignant tumours in men; in women it is 9 % (Barnes et al. 2016). The vast majority of these cases are attributable to smoking. Around 20 % of all women and 26 % of all men in Germany are active smokers (Seitz et al. 2019). Compared to non-smokers, the risk of lung cancer in men is increased by a factor of about 20, in women by a factor of about 10 (Pesch et al. 2012). In order to assess the effect of smoking on radiation effect, consideration must be given to the interaction between radiation and smoking. The largest study of external radiation exposure is the LSS (Furukawa 2010, Cahoon 2017). The dependency of the radiation-induced increase in lung cancer rate on smoking intensity is complex: compared with non-smokers, the excess relative rate[55] increases with increasing smoking intensity, at first up to a maximum of around seven cigarettes per day. For high smoking intensities, it then decreases significantly; however, the extent of this decrease is accompanied by great uncertainties (Ulanowski et al. 2020). With regard to lifetime risks this means that at least smokers with a low and medium smoking intensity have a radiation risk that

[55] The authors use the term “excess relative risk”.

increases proportionally with increasing smoking intensity, or even disproportionally, with the risk not attributable to radiation, i. e. the risk with smoking but without radiation exposure. For radiation-induced lifetime risks, as illustrated further down in Table 9-2, this means that at least the proportion of cases that is attributable to lung cancer will be considerably lower in non-smokers, but higher in smokers. For former smokers, who account for about 25 % of all persons in Germany (Seitz et al. 2019), the risk of lung cancer declines as the time since cessation of smoking increases, but remains higher than in non-smokers (Pesch et al. 2012).

Breast cancer is the most common type of cancer in women, contributing about a third of all malignant tumours (Barnes et al. 2016). Compared to women with no history of familial breast cancer, women with breast cancer in the family (in this study mothers, sisters or daughters with breast cancer) have a nearly two-fold risk of developing breast cancer (Hemminki and Vaittinen 1998). The Swedish Hemangioma Cohort, in which women were exposed to radiation for haemangioma treatment in early childhood, showed an increased incidence of breast cancer. In this study, the authors were also able to obtain data on familial breast cancer and analyse it together with the radiation effect (Eidemüller et al. 2021). It was found that the radiation-induced excess breast cancer rate in women with a family history of breast cancer was increased by a factor of around 3 compared to women with no history of familial breast cancer. Since all women had been exposed during early childhood, it is not sure whether the factor applies equally for radiation exposure in adulthood. It does, however, also seem plausible to assume an increased absolute risk following radiation exposure during adulthood. The proportion of radiation-induced lifetime risks that is attributable to breast cancer may therefore be increased by a factor of around three for women with breast cancer in the family.

9 Lifetime risks

9.1 Basic principles

9.1.1 Exposure scenarios

In order to estimate lifetime risks for specified annual effective doses, two exposure scenarios are assumed in this chapter, namely external photon radiation and incorporation of iodine-131. It is further assumed that the annual dose remains constant throughout a lifetime. The intrauterine dose is put on par with the annual dose after parturition.

For the three life phases i) in utero, ii) childhood and adolescence and iii) adulthood, chapters 6 to 8 provide a summary – based on the literature reviews – of the cumulative doses for which there is evidence of an excess cancer risk after protracted/repeated radiation exposure. This summary is meant to serve as guidance when determining which annual effective dose will be used to estimate lifetime risks in this statement. The connection to a risk due to an annual effective dose of 1 mSv is made in the main text of the statement.

- Lifetime risks are calculated up to the 90th birthday, i. e. including an attained age of 89 years. With an assumed minimum latency period of two years for leukaemia and five years for malignant tumours, this takes into consideration an effect of radiation over a lifespan including the age of 87 years and 84 years, respectively.

9.1.1.1 External radiation exposure

Evidence of an increased risk of malignant tumours exists for radiation exposure in utero for an absorbed uterine dose in the order of 6 mGy (SSK 2008), and for protracted/repeated radiation exposure during adulthood for absorbed colon doses of 100 mGy (UNSCEAR 2019, Haylock et al. 2018). To improve the comparability with the Life Span Study (LSS) of the survivors of

the atomic bombings of Hiroshima and Nagasaki, the studies relate the excess mortality rate due to malignant tumours attributable to radiation exposure to the colon dose. For protracted/repeated exposure during childhood or adolescence, there exists one study on background radiation that provides evidence of a radiation-induced increase in CNS tumours (tumours of the central nervous system) for cumulative doses of around < 50 mSv (Spycher et al. 2015). In a linear dose-response model, the hazard ratio per cumulative ambient dose was 1.04 mSv^{-1} (95 % CI: 1.00–1.08) for CNS tumours, which is consistent with the key finding for the excess relative rate per dose in the brain of 0.016 mGy^{-1} (95 % CI: 0.006–0.037) in a study of the relationship between cancer in children, adolescents and young adults and paediatric CT scans in the United Kingdom (Berrington de Gonzalez et al. 2016).

The conversion of an effective dose due to external photon radiation into absorbed organ doses depends on the radiation geometry and the photon energy. For the calculations made here, isotropic exposure to photons with an energy of 1 MeV is assumed. Consequently, the ratio of both the effective dose and the absorbed dose in the colon to the ambient equivalent dose $H^*(10)$ is approx. 0.6 (SSK 2017c). The numerical values of the effective dose and the absorbed dose in the colon can therefore be considered equal for a good approximation for the type of exposure.

For in utero or annual effective doses of 1 mSv, the cumulative colon doses for all three life phases considered are lower than the lowest doses for which there is evidence of an increased risk of any malignant tumours. For an estimation of lifetime risks of malignant tumours, it would therefore have to be assumed that evidence for increased risks at higher dose rates can be transferred to 1 $mSva^{-1}$. This is avoided in the present scientific background. Instead, the calculations are carried out for an annual effective dose for which the colon dose is covered by evidence of an increased risk of malignant tumours.

At an annual effective dose of 3 mSv, the cumulative colon dose for exposure during adulthood is within the evidence for an excess risk of malignant tumours and for exposure during childhood and adolescence within the evidence for CNS tumours. For exposure in utero, there is only evidence for a dose that is at least twice as high. However, the calculations show that the excess lifetime risk for malignant tumours due to exposure in utero to 3 mSv is very small compared to the risk of radiation exposure cumulated during adulthood, so that the considerable uncertainty of the risk assessment of 3 mSv prior to birth has a negligible impact on the overall lifetime risk.

Evidence of an increased risk of leukaemia exists for exposure in utero for an absorbed uterine dose in the order of 6 mGy (SSK 2008), for repeated and/or prolonged exposure during childhood and adolescence in a pooled analysis of studies with mean bone marrow doses of < 100 mGy (Hauptmann et al. 2020), and for protracted/repeated radiation exposure during adulthood for bone marrow doses in the order of 300 mGy (Leuraud et al. 2015).

As with the colon, the numerical values of the absorbed dose in the bone marrow and of the effective dose can, in good approximation, be considered equal.

For in utero or annual effective doses of 1 mSv, the estimated bone marrow doses for all three life phases considered are lower than the lowest doses for which there is evidence of an increased risk of leukaemia. For an estimation of lifetime risks, it would therefore have to be assumed that evidence for increased risks of leukaemia at higher dose rates can be transferred to 1 mSv/a. This is avoided in the present scientific background. Instead, the calculations are carried out for an annual effective dose for which the bone marrow dose comes at least close to the range for which there is evidence of an increased risk of leukaemia.

At 3 $mSv\,a^{-1}$ the cumulative bone marrow dose of 210 mGy for radiation exposure during adulthood is below a cumulative bone marrow dose of 300 mGy, for which there is evidence of

an increased risk of leukaemia with repeated exposure. Based on an evaluation of all the information available, however, UNSCEAR decided to carry out modelling of lifetime risks using a comparable dose, namely 200 mGy (UNSCEAR 2019). The SSK decided to follow this approach.

For exposure during childhood and adolescence to 3 mSv per year, the cumulative dose to the bone marrow is covered by the evidence of an increased risk of leukaemia. For exposure in utero, there is only evidence for a dose that is at least twice as high. However, the calculations show that the excess lifetime risk for leukaemia due to in utero exposure to 3 mSv is very small compared to exposure to 3 mSv per year, both during childhood and adolescence as well as during adulthood, both of which have a cumulative dose considerably higher than 3 mSv. Since the excess risk due to radiation exposure throughout an entire lifetime is decisive for the estimations made in this report, the calculations are carried out for annual effective doses of 3 mSv and the uncertainty resulting from extrapolation of the relatively small contribution of in utero exposure is accepted.

Table 9-1 provides a summary of the

- lowest values of absorbed organ doses for which there is evidence of an increased cancer risk due to protracted/repeated exposure to external photon radiation, and
- cumulative absorbed doses in the uterus or in the bone marrow and colon due to external photon radiation with an effective dose of 1 mSv in utero and 3 mSv annually.

Table 9-1: *Lowest absorbed dose in the uterus, colon and bone marrow with evidence of an increased cancer risk due to protracted/repeated exposure to external radiation and cumulative doses at different age intervals for a specified annual effective dose.*

Cancer type/exposure period	**Lowest dose with evidence of an increased cancer risk**			**Absorbed doses at an annual effective dose of**	
	Evaluating reference	Study	Absorbed dose (mGy)	1 mSv a^{-1}	3 mSv a^{-1}
Malignant tumours				Colon dose (mGy)	
In utero	SSK 2008	OSCC[a]	6	1[b]	3[b]
Childhood and adolescence	Hauptmann et al. 2020	Swiss BG[c]	< 50[g]	18 (age 0–17)	54 (age 0–17)
Adulthood	UNSCEAR 2019	INWORKS[d]	100	72 (age 18–89)	216 (age 18–89)
Leukaemia				Bone marrow dose (mGy)	
In utero	SSK 2008	OSCC[a]	6	1[b]	3[b]
Childhood and adolescence	Hauptmann et al. 2020	Pooled data[e]	< 100	18 (age 0–17)	54 (age 0–17)
Adulthood	UNSCEAR 2019	INWORKS[f]	300	72 (age 18–89)	216 (age 18–89)

a Oxford Survey of Childhood Cancer (Bithell and Stiller 1988; Doll and Wakeford 1997; Wakeford and Little 2003)
b Uterine dose
c Background ionizing radiation and the risk of childhood cancer: A census-based nationwide cohort study (Spycher et al. 2015)
d International Nuclear Workers Study (Richardson et al. 2015)
e Six studies of the risk of leukaemia with mean bone marrow doses < 100 mGy (four for natural background radiation and two for CT scans)
f International Nuclear Workers Study (Leuraud et al. 2015)
g Cumulative ambient dose (mSv)

9.1.1.2 Incorporation of ^{131}I

Evidence of an increased risk of thyroid cancer after incorporation of ^{131}I during childhood and adolescence was found in the Ukraine, in Belarus and in the affected regions of Russia following the Chornobyl nuclear accident. Owing to the half life of eight days, thyroid exposure after incorporation of ^{131}I is, per se, protracted.

For incorporation of ^{131}I, the risk of cancer is determined largely by the thyroid dose. Given the tissue weighting factor of 0.04 for the thyroid, an absorbed dose in the thyroid of 25 mGy corresponds to an effective dose of 1 mSv. With an annual effective dose of 1 mSv, the thyroid dose accumulated during childhood and adolescence is 450 mGy (18 × 25 mGy).

This value is below the mean thyroid dose of 570 mGy in the Ukrainian-American cohort, the cohort with the strongest evidence for an increased risk of thyroid cancer after incorporation of ^{131}I during childhood and adolescence (Tronko et al. 2006, Brenner et al. 2011, Tronko et al. 2017). By contrast, an annual effective dose of 3 mSv during childhood and adolescence due to incorporation of ^{131}I results in a thyroid dose of 1,350 mGy for which the existing evidence indicates an increased risk of thyroid cancer.

There is no evidence to support an increased risk of thyroid cancer after incorporation of ^{131}I during adulthood or by mothers during pregnancy.

9.1.2 Lifetime risk calculation methods

Based on the two exposure scenarios, lifetime risks are calculated for radiation exposure in utero, during childhood and adolescence, and during adulthood separately for women and men. A possible dependence of the risk coefficient on the dose or the dose rate is not considered; i. e. a DDREF of 1 is used in this report. Important factors that must be considered when calculating the lifetime risks include the cancer incidence and all-cause mortality in the German population as well as the excess relative risk of cancer after exposure. As illustrated in chapters 5 to 9, in most calculations it is assumed that the excess relative rate of cancer incidence or mortality (abbreviated as ERR) observed in the LSS offers an adequate description of the excess relative risk of incident cancer. One exception to this is the calculation of the incident cancer risk in childhood and adolescence after exposure in utero. Here, the excess relative rate of incident cancer derived by the SSK in an earlier report (SSK 2008) based on various analyses of the OSCC is used. A rationale for exclusively using ERR models is provided in section 9.4.

Lifetime risks are calculated using the definition of lifetime attributable risk (LAR). For exposures that have an only minor impact on overall mortality, the LAR is a good approximation for the excess incidence probability (UNSCEAR 2019). In the calculation of the lifetimes risks, the functions of the excess relative rate per dose estimated in the various studies are transferred to the German population, multiplied with the current incident cancer rates, and integrated with an adjustment for relative survival over the corresponding period of time:

$$\mathrm{LAR}\left(a_f, e, d\right) = \sum_i \int_{e_i + t_{\mathrm{Lat}}}^{a_f} \mathrm{ERR}(a, e_i, d_i) \cdot I_D(a) \cdot \frac{S_D(a)}{S_D(e_i)} da$$

I_D and S_D represent the spontaneous incidence rate and the survival in Germany. Both functions are dependent on age. The exposure scenario is characterised via the different ages at exposure, summarised in e, and the corresponding doses d. Here, the dose d_i is totalled for all annual radiation exposures i. Integration takes place from the age at the respective exposure, e_i, plus a minimum latency period, t_{Lat}, up to the desired final age, a_f.

For incident cancer rates in Germany, 2017 data from the Robert Koch-Institute is used (RKI and GEKID 2021). This data is grouped in 5-year intervals (0-4, 5–9, ..., 80–84, 85+). The data

does not contain skin cancer covered by the ICD-10 category C44 "other malignant neoplasms of skin". The RKI justifies this as follows: "*Incidence of all cancers combined does not include non-melanoma skin cancer, as is customary internationally"*.

The survival rates in Germany are based on data of the Federal Statistical Office for the year 2017 (Destatis 2020).

To enable a comparison, the spontaneous cases that are expected without radiation exposure in the respective time periods are also calculated. The data sources used in the calculations are shown in Annex A

9.1.3 Endpoints

Lifetime risks are calculated for the incidence of malignant tumours and leukaemia in the scenario external radiation exposure, and thyroid cancer (ICD-10: C73) in the scenario incorporation of ^{131}I.

For malignant tumours, all endpoints with the ICD-10 classifications from C00 to C80 are considered. Other malignant neoplasms of the skin (ICD-10: C44) are not considered. These neoplasms have a very high spontaneous incidence. There is, however, barely any epidemiological evidence of an increased risk of squamous cell carcinomas due to exposure to low skin doses (UNSCEAR 2000). (Preston et al. 2007) analysed the incidence of non-melanoma skin cancer in the LSS. A total of 330 cancers were identified, including 166 basal cell carcinomas and 131 squamous cell carcinomas. A categorical analysis showed no continuous increase in the excess relative rate with the dose, but it did show a very slight increase in the incidence rate below 1 Gy and a sharp increase in the highest dose category (skin dose ranging from 1 Gy to 4 Gy). A spline function for the dose dependency of the excess relative rate describes the data better than a linear function. The fit showed coefficients of 0.17 Gy^{-1} (with no indication of the confidence interval) for skin doses below 1 Gy and 1.2 Gy^{-1} (90 % CI: 057–2.3) for skin doses higher than or equal to 1 Gy. In their more recent study on cancer incidence in the LSS, (Grant et al. 2017) found no dose dependency of skin cancers. In their analyses, (Ulanowski et al. 2020) found that the estimated radiation-attributed incidence rate in the LSS below 1 Gy is close to zero. The SSK is currently working on a separate recommendation that focuses more closely on the risk of radiation for skin cancer.

For leukaemia, the endpoints C91 to C95 are included. Lymphoma including multiple myeloma are thus not included in the risk assessment. For lymphoma and multiple myeloma, the risk estimates are associated with major uncertainties. In addition, the best risk estimates for these endpoints suggest significantly lower risks than for leukaemia. They would therefore only play a minor role in the risk assessment. The selection of the endpoints C91 to C95 also follows the approach of international organisations (UNSCEAR 2019).

9.2 Models for the excess relative risk per dose

This section summarises the main characteristics of the models used for estimating the excess relative risk of cancer in the German population. As outlined in the previous chapters, these are generally models used to estimate the excess relative cancer rates[56] in the LSS. For cancer risks due to in utero exposure, incidence data is limited. For this reason, the models used here for in utero exposure are based on mortality data: the cancer risks in childhood and adolescence are based on an estimation of the SSK from 2008 and the cancer risks in adulthood on a model for

[56] The authors use the term "excess relative risk".

the excess relative rate of leukaemia mortality in the LSS. Annex B provides an overview of the mathematical functions used, along with the parametric values.

9.2.1 External radiation exposure

9.2.1.1 Radiation exposure in utero

For cancer risks in childhood and adolescence, the main model is based on the OSCC. It is a linear dose-response model with no further age dependencies. The excess relative cancer mortality rate is high. The excess relative risk per uterine dose was estimated as 40 Gy^{-1} (SSK 2008). This excess relative cancer rate is used equally for the risk in men and in women, as well as for malignant tumours and leukaemia. In this regard it must be considered, though, that the spontaneous background rates in childhood and adolescence are lower than those in adulthood.

For risks in adulthood after exposure in utero, the preferred model is based on the LSS, which is is also a linear dose-response model with no further age dependencies. For women, an excess relative risk per uterine dose of 1.84 Gy^{-1} is used both for malignant tumours and for leukaemia (Sugiyama et al. 2021). The risk coefficient is thus considerably lower than for cancer in childhood and adolescence. For men, as the epidemiological data shows no evidence indicative of a risk, a zero risk is assumed. A minimum latency period of five years for malignant tumours and of two years for leukaemia is assumed.

9.2.1.2 Radiation exposure during childhood and adolescence and during adulthood

As discussed in the previous chapters, the same risk models are used for radiation exposure during childhood and adolescence and for radiation exposure during adulthood. For radiation exposure during childhood and adolescence, these models are used to calculate the risks both in childhood and adolescence as well as in adulthood. In addition to the preferred risk models identified, comparison models are calculated. Concerning the lifetime risks, the differences between the models are a reflection of the uncertainties associated with the models chosen.

Malignant tumours. In the preferred model for malignant tumours – based on Grant et al. (2017), – the excess relative risk is linear in the adjusted colon dose and dependent on attained age and age at exposure. For men and women, the excess relative risk decreases with increasing attained age and increasing age at exposure. The risk coefficient is higher for women than for men; in the lifetime risk calculation this is partly compensated by the higher spontaneous risk in men. Two comparison models are additionally calculated. One model is structurally similar to the preferred model, but shows a linear-quadratic dose response for men. As outlined above, in (Grant et al. 2017) this model shows a better fit for the data, but the reasons for a possible change in the dose response in men compared to earlier analyses is currently not understood. A linear dose-response model with no age dependencies is additionally calculated. A minimum latency period of five years is assumed.

Leukaemia. The preferred model for leukaemia is based on (Hsu et al. 2013) and is dependent on time since exposure and attained age. The excess relative risk shows a linear-quadratic dependence on the adjusted bone marrow dose. The excess relative risk decreases with increasing attained age and with increasing time since exposure. The excess relative risk is assumed to be identical for men and women. In addition, two comparison models with a linear dose-response relationship are calculated. The first comparison model is dependent on age at exposure, the second has no further dependency on age. These simplified models were also adjusted to the data of the LSS in (Hsu et al. 2013). For leukaemia, a minimum latency period of two years is assumed.

In the LSS the follow-up for the incidence of leukaemia starts only in 1950 (Hsu et al. 2013), i. e. five years after exposure. The preferred model shows a strong dependency on age, and

extrapolation of the model to short times after exposure results in very high values for the excess relative risk at a young age. This may be the result of the extrapolation of the function beyond the data range. Therefore, for times since exposure that amount to less than five years, the value of excess relative risk for a time since exposure of five years is used. This avoids the use of very high risk values for which there is no epidemiological evidence. This is also consistent with the ProZES approach for estimating the probability of a causal relationship between cancer and preceding radiation exposure (Ulanowski et al. 2020). For times since exposure that amount to less than two years, the risk disappears owing to the assumed minimum latency period.

9.2.2 Incorporation of ^{131}I

The preferred model for the dependence of the thyroid cancer rate on the adjusted thyroid dose exhibits a linear dose response, with different risk coefficients for women and men (Furukawa et al. 2013). The risk coefficient is higher for women than for men. The excess relative risk decreases with increasing attained age and with increasing age at exposure. A minimum latency period of five years is assumed.

9.3 Results

9.3.1 External radiation exposure

9.3.1.1 Malignant tumours

Table 9-2 shows the probabilities for excess malignant tumours in the respective sex and age groups and in different lifetime periods due to radiation exposure and the spontaneous incidence. The estimations are based on an annual exposure of 3 mSv. The risks in adulthood are calculated with a cumulative dose of 216 mSv up to and including the age of 89 years. The radiation exposure during childhood from birth up to and including the age of 17 years is 54 mSv. The minimum latency period is five years. Therefore, when looking at exposure during adulthood, only exposure up to and including the age of 84 years plays a role. When calculating the risks in childhood, only exposure in the first 13 years, i. e. up to and including the age of 12, is relevant. For radiation exposure in utero, a value of 3 mSv is assumed.

Table 9-2: Estimated incidence probability of malignant tumours in different lifetime periods due to external exposure with an effective dose of 3 mSv a^{-1} and spontaneous incidence

Model	**Cumulative colon dose/ period of exposure**	**Excess or spontaneous incidence[a] of developing[a, b] a malignant tumour[b]**			
		Girls (0–17 years)	**Boys (0–17 years)**	**Women (18–89 years)**	**Men (18–89 years)**
Exposure during adulthood					
MT_1 (preferred)	216 mSv in 72 years	-	-	$260 \cdot 10^{-4}$	$165 \cdot 10^{-4}$
MT_2	216 mSv in 72 years	-	-	$269 \cdot 10^{-4}$	$49 \cdot 10^{-4}$
MT_3	216 mSv in 72 years	-	-	$327 \cdot 10^{-4}$	$174 \cdot 10^{-4}$
Exposure during childhood and adolescence					
MT_1 (preferred)	54 mSv in 18 years	$4.2 \cdot 10^{-4}$	$2.2 \cdot 10^{-4}$	$244 \cdot 10^{-4}$	$140 \cdot 10^{-4}$
MT_2	54 mSv in 18 years	$2.7 \cdot 10^{-4}$	$4.3 \cdot 10^{-4}$	$253 \cdot 10^{-4}$	$49 \cdot 10^{-4}$
MT_3	54 mSv in 18 years	$0.15 \cdot 10^{-4}$	$0.06 \cdot 10^{-4}$	$127 \cdot 10^{-4}$	$62 \cdot 10^{-4}$

Model	Cumulative colon dose/ period of exposure	Excess or spontaneous incidence[a] of developing[a, b] a malignant tumour[b]			
		Girls (0–17 years)	Boys (0–17 years)	Women (18–89 years)	Men (18–89 years)
Exposure in the uterus					
U_1	3 mSv	$1.2 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$	-	-
U_2	3 mSv	-	-	$20 \cdot 10^{-4}$	0
Spontaneous risk					
Incidence in Germany		$15 \cdot 10^{-4}$	$16 \cdot 10^{-4}$	$3{,}675 \cdot 10^{-4}$	$4{,}269 \cdot 10^{-4}$

[a] in the respective sex and age group

[b] without other malignant neoplasms of skin (according to ICD10: C44)

For women exposed to an annual dose of 3 mSv during adulthood, i. e. who received a total dose of 216 mSv, the preferred model MT_1 predicts an excess incidence of $260 \cdot 10^{-4}$ for radiation-induced malignant tumours. For exposed men, the model estimates an excess incidence of $165 \cdot 10^{-4}$. The comparison model MT_2 differs from the model MT_1 especially by the linear-quadratic dose response for men. For protracted exposure, the proportion of the risk that is attributable to the quadratic dose part is suppressed, resulting in a considerable decrease in the risk. For exposure during adulthood the model MT_3, with no age dependencies, yields similar risk values as the model MT_1.

For the models MT_1 and MT_2, the risks in adulthood after radiation exposure during childhood and adolescence are similar to the risks after exposure during adulthood despite the lower dose. This is due to the fact that the excess relative risk for a younger age at exposure increases in both models. The model MT_3 is independent of age at exposure and thus results in lower risks than after exposure during adulthood. The risks in adulthood after exposure in utero is considerably lower than after exposure during childhood and during adulthood.

For the risks in childhood after exposure during childhood and adolescence, the model MT_1 estimates an excess incidence of $4.2 \cdot 10^{-4}$ for females and an excess incidence of $2.2 \cdot 10^{-4}$ for males. The model MT_2 yields similar risk coefficients. The risks of the model MT_3 are considerably lower, as the models MT_1 and MT_2 lead to high values for the excess relative risk in a young attained age. Exposure to 3 mSv in utero results in an estimated excess incidence of $1.2 \cdot 10^{-4}$ in girls and $1.1 \cdot 10^{-4}$ in boys.

Overall, using the preferred models MT_1 and U_2 the risks in adulthood from the different exposure periods add up to an excess incidence of $524 \cdot 10^{-4}$ for women and $305 \cdot 10^{-4}$ for men. Without exposure to radiation, spontaneous incidences in these periods are estimated to be $3{,}675 \cdot 10^{-4}$ for women and $4{,}269 \cdot 10^{-4}$ for men. In childhood and adolescence, overall radiation-induced incidences of $5.4\ 10^{-4}$ for girls and of $3.3 \cdot 10^{-4}$ for boys can be expected with the models MT_1 and U_1. In this period, the spontaneous incidence in Germany is $15 \cdot 10^{-4}$ for girls and $16 \cdot 10^{-4}$ for boys.

9.3.1.2 Leukaemia

Table 9-3 shows the probabilities of developing leukaemia in different lifetime periods for an annual exposure of 3 mSv. The minimum latency period for leukaemia is two years. Consequently, for exposure during adulthood, exposure up to and including the age of 87 years is relevant, and for risks in childhood the period up to and including the age of 15 years is relevant.

Table 9-3: *Estimated incidence probability of leukaemia in different lifetime periods due to external exposure with an effective dose of 3 mSv per year and spontaneous incidence*

Model	**Cumulative bone marrow dose/ period of exposure**	**Excess or spontaneous incidence probability[a] of developing leukaemia [a]**			
		Girls (0–17 years)	**Boys (0–17 years)**	**Women (18–89 years)**	**Men (18–89 years)**
Exposure during adulthood					
L_1 (preferred)	216 mSv in 72 years	-	-	$24 \cdot 10^{-4}$	$36 \cdot 10^{-4}$
L_2	216 mSv in 72 years	-	-	$64 \cdot 10^{-4}$	$94 \cdot 10^{-4}$
L_3	216 mSv in 72 years	-	-	$74 \cdot 10^{-4}$	$108 \cdot 10^{-4}$
Exposure during childhood and adolescence					
L_1 (preferred)	54 mSv in 18 years	$3.4 \cdot 10^{-4}$	$4.6 \cdot 10^{-4}$	$4.0 \cdot 10^{-4}$	$5.9 \cdot 10^{-4}$
L_2	54 mSv in 18 years	$0.71 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$	$34 \cdot 10^{-4}$	$49 \cdot 10^{-4}$
L_3	54 mSv in 18 years	$0.51 \cdot 10^{-4}$	$0.78 \cdot 10^{-4}$	$25 \cdot 10^{-4}$	$36 \cdot 10^{-4}$
Exposure in the uterus					
U_1	3 mSv	$0.70 \cdot 10^{-4}$	$0.93 \cdot 10^{-4}$	-	-
U_2	3 mSv	-	-	$0.54 \cdot 10^{-4}$	0
Spontaneous risk					
Incidence in Germany		$7.3 \cdot 10^{-4}$	$9.4 \cdot 10^{-4}$	$98 \cdot 10^{-4}$	$140 \cdot 10^{-4}$

[a] in the respective sex and age group

For exposure during adulthood with a total of 216 mSv in 72 years, the preferred model L_1 estimates an excess incidence of $24 \cdot 10^{-4}$ for women and $36 \cdot 10^{-4}$ for men. The excess relative risk calculated with the model L_1 decreases with increasing attained age and increasing time since exposure; therefore, the risks in adulthood are lower than in the comparison models L_2 and L_3, which do not show such a drop in the excess relative risk. The analyses performed by (Hsu et al. 2013) showed that the dependence of the risk on age and time since exposure plays an important role for leukaemia. It can therefore be assumed that the models L_2 and L_3 overestimate the risks. By the same token, the risks estimated by the model L_1 for adulthood are also lower than those estimated in the comparison models for exposure during childhood and adolescence. This effect is reversed for risks in childhood and adolescence, where the model L_1 estimates the greatest risks. The risk after exposure to 3 mSv in utero plays a minor role for the risks in adulthood, but is somewhat more significant for the risks in childhood and adolescence.

Overall, using the models L_1 and U_2, the excess leukaemia risks in adulthood from the different exposure periods add up to an incidence of $29.0 \cdot 10^{-4}$ for women and $41.9 \cdot 10^{-4}$ for men. Without exposure to radiation, the spontaneous incidence in this period is $98 \cdot 10^{-4}$ for women and $140 \cdot 10^{-4}$ for men. In childhood and adolescence, overall radiation-induced incidences of $4.1 \cdot 10^{-4}$ for girls and of $5.5 \cdot 10^{-4}$ for boys can be expected with the models L_1 and U_1. In the same period, the spontaneous incidence in Germany is $7.3 \cdot 10^{-4}$ for girls and $9.4 \cdot 10^{-4}$ for boys.

9.3.1.3 Uncertainties

The uncertainty of the calculated lifetime risks cannot be accurately estimated with the current state of knowledge.

For the special case of the risk of malignant tumours among male workers with a follow-up to 60 years of age after occupational radiation exposure between the ages of 30 to 45 years with a cumulative colon dose of 100 mGy, UNSCEAR indicated an uncertainty range of

approximately one fifth to double the best estimate (UNSCEAR 2019). This value applies for a representative group of occupationally exposed male workers in the United Kingdom (scenario population) and is based on

- the transfer of the ERR per adjusted colon dose estimated in INWORKS (Richardson et al. 2015) to the scenario group chosen by UNSCEAR; the investigation of a cohort of occupationally exposed men in the United Kingdom (Muirhead et al. 2009) represents the main contribution to INWORKS, so that it was assumed that this transfer does not contribute significantly to the overall uncertainty;
- the assumption that the spontaneous cancer risks in the scenario population correspond to those in INWORKS;
- a discussion of all known sources of error and a semi-quantitative estimation of the impact of these sources on the overall uncertainty of the indicated risk: a probability of $10 \cdot 10^{-4}$ with a credible interval of $2 \cdot 10^{-4}$ to $20 \cdot 10^{-4}$. This credible interval is influenced significantly by the uncertainty of the ERR per colon dose. The scenario was selected to minimise other sources of uncertainty. The more significant of these sources of uncertainty include i) the difference in the sex distribution in INWORKS and in the scenario population, ii) dose contributions that were not considered in INWORKS (neutrons, unrecorded exposure at the workplace and occupational x-ray examinations), iii) possible differences in risk factors such as alcohol consumption and smoking, iv) the assumption of a minimum latency period of five years and v) a difference in the healthy worker effect.

For the leukaemia risk in a scenario population with a bone marrow dose of 200 mGy, UNSCEAR reports a similar result: a probability of $5 \cdot 10^{-4}$ with a credible interval of $1 \cdot 10^{-4}$ to $10 \cdot 10^{-4}$ (UNSCEAR 2019).

The above scenarios are closely related to parameters of INWORKS (Richardson et al. 2015, Leuraud et al. 2015), such as mean age at exposure, mean duration of exposure and mean duration of follow-up. As the power of INWORKS is not sufficient to estimate the dependence of the excess relative rate (ERR) on time parameters, INWORKS is of only limited validity for other scenarios. UNSCEAR (2019) bases its consideration of other scenarios on the transfer of risk estimates from the LSS, but does not attempt to quantify the uncertainty of such a transfer.

In the LSS, due to the small case numbers, the excess relative risk estimates for leukaemia (Hsu et al. 2013) have a greater uncertainty than for all malignant tumours combined (Grant et al. 2017). Furthermore, the excess relative risk estimates for cancer after exposure in utero or during childhood (Preston et al. 2008) exhibit significantly greater uncertainties than for exposure during adulthood.

9.3.1.4 Myelodysplastic syndrome

Myelodysplastic syndrome (MDS) is a clonal disorder affecting the haematopoietic stem cells in the bone marrow. An accumulation of genetic damages such as chromosomal aberrations or point mutations and proliferation lead to the formation of malignant cells that increasingly disrupt normal haematopoiesis. The malignant stem cells no longer produce fully mature and fully functional blood cells. The uncontrolled proliferation of these malignant stem cells leads to a quantitative deficiency of mature blood cells. The resulting symptoms are attributable primarily to leukopenia, anaemia and thrombocytopenia. MDS can progress to acute myeloid leukaemia (AML).

Using data from the Düsseldorf-based MDS register, (Neukirchen et al. 2011) calculated an age-adjusted MDS incidence of $4.15 \cdot 10^{-4}$ per year. The risk of developing MDS increases

significantly with age and begins primarily from an age of 60 years. The mean age is above 70 years. The incidence is higher in men than in women. Based on registry data from the USA, (Cogle 2015) calculated an age-adjusted incidence of $3.3 \cdot 10^{-4}$ per year for the period 2001 to 2003 and of $4.9 \cdot 10^{-4}$ per year for the period 2007 to 2011. Cogle points out that the registry is incomplete with regard to MDS and estimates the true incidence to be between $5.3 \cdot 10^{-4}$ and $13.1 \cdot 10^{-4}$ per year. In comparison, the age-adjusted incidence probability of leukaemia in Germany for the period 1999 to 2016 remained more or less constant, at $13.9 \cdot 10^{-4}$ per year for men and $9.0 \cdot 10^{-4}$ per year for women (RKI and GEKID 2021).

For MDS in a cohort of atomic bomb survivors from Nagasaki, (Iwanaga et al. 2011) report an excess relative rate[57] per adjusted bone marrow dose of $4.3\ \mathrm{Gy}^{-1}$ (95 % CI: 1.6–9.5). In comparison, in the LSS Hsu et al. (2013) found a linear-quadratic dependence of the excess relative rate on the adjusted bone marrow dose with a linear coefficient of $0.79\ \mathrm{Gy}^{-1}$ (95 % CI: 0.03−1.93) and a quadratic coefficient of $0.95\ \mathrm{Gy}^{-1}$ (95 % CI: 0.34−1.80) for leukaemia at the age of 70 years after exposure at the age of 30 years.

As a general comparison, the product of age-adjusted incidence and ERR per bone marrow dose is comparable for MDS and leukaemia. Therefore, a similar radiation risk can be expected. However, if the two risks were added to one another, MDS cases that have progressed to AML would be counted twice. It can thus be assumed that the contribution of MDS to the overall risk of radiation-induced malignancies would not be greater than that of leukaemia.

9.3.2 Incorporation of ^{131}I

When estimating the risks after incorporation of ^{131}I, only thyroid cancer is considered as an endpoint. No comparison models are used for this endpoint, and no risks after in utero exposure are calculated either. Table 9-4 shows the probabilities of developing thyroid cancer in different lifetime periods. With a tissue weighting factor of 0.04 for the thyroid and a thyroid dose of 75 mGy per year, the effective dose per year is 3 mSv. Even if there is evidence to support a shorter latency period of three years for thyroid cancer following exposure during childhood (Heidenreich et al. 1999), a latency period of five years – like for all malignant tumours – is assumed here. In numeric terms, the difference for the cumulative incidences up to the age of 90 years is very small.

[57] The authors use the term “excess relative risk”.

Table 9-4: *Estimated incidence probability of thyroid cancer (ICD-10: C73) in different lifetime periods due to a constant exposure with a thyroid dose of 75 mGy a^{-1} per year and spontaneous incidence*

Model	**Cumulative thyroid dose / period of exposure**	**Excess or spontaneous incidence probability[a] of developing thyroid cancer**			
		Girls (0–17 years)	**Boys (0–17 years)**	**Women (18–89 years)**	**Men (18–89 years)**
Exposure during adulthood					
Thyroid (TH)	5,400 mSv in 72 years	-	-	$80 \cdot 10^{-4}$	$17 \cdot 10^{-4}$
Exposure during childhood and adolescence					
Thyroid (TH)	1,350 mSv in 18 years	$10.4 \cdot 10^{-4}$	$2.3 \cdot 10^{-4}$	$353 \cdot 10^{-4}$	$69 \cdot 10^{-4}$
Spontaneous risk					
Incidence in Germany		$0.91 \cdot 10^{-4}$	$0.40 \cdot 10^{-4}$	$89 \cdot 10^{-4}$	$38 \cdot 10^{-4}$

[a] Cases per 10,000 persons in the respective sex and age group

For exposure during adulthood (cohort 18 to 89 years), the thyroid model (TH) estimates a total excess incidence of $80 \cdot 10^{-4}$ for women and $17 \cdot 10^{-4}$ for men. The risk depends strongly on the age at exposure. For this reason, the calculations yield higher incidences in adulthood after exposure during childhood and adolescence of $353 \cdot 10^{-4}$ for women and $69 \cdot 10^{-4}$ for men, despite the lower doses.

Overall, using the TH model, the excess incidences in adulthood from the different exposure periods add up to $433 \cdot 10^{-4}$ for women and $86 \cdot 10^{-4}$ for men. Without exposure to radiation, the spontaneous incidence in this period is $89 \cdot 10^{-4}$ for women and $38 \cdot 10^{-4}$ for men. In childhood and adolescence, overall radiation-induced incidences of $10.4 \cdot 10^{-4}$ for girls and of $2.3 \cdot 10^{-4}$ for boys can be expected. In the same period, the spontaneous incidence in Germany is $0.9 \cdot 10^{-4}$ for girls and $0.4 \cdot 10^{-4}$ for boys.

9.4 Comparison with ICRP 103

The International Commission on Radiological Protection published the basic calculations used to justify its recommendation of an effective dose limit for the population through planned activities in Annex A of ICRP Publication 103 (ICRP 2007a). The starting point was the calculation of cancer incidence risks with an averaging of results obtained through the use of ERR and EAR models. The results of the individual models were not published. In calculations of lifetime risks due to prolonged exposure, UNSCEAR (2019) found differences of less than a factor of 2 between the two models. For example: the ERR model used estimated a cumulative excess risk of malignant tumours due to prolonged exposure from ages 30 to 45 years to a total colon dose of 100 mGy of $39 \cdot 10^{-4}$ up to the age of 90, compared to $52 \cdot 10^{-4}$ with an EAR model. For leukaemia and a total bone marrow dose of 200 mGy the excess relative risk model estimated a cumulative excess risk of $15 \cdot 10^{-4}$ up to the age of 90, compared to $20 \cdot 10^{-4}$ with an EAR model. This statement deals with orders of magnitude of risks, not with differences of less than a factor of 2. Therefore, in order to minimise unnecessary work, only models to estimate the excess relative risk were used; EAR models were not included.

Table 9-5 offers a comparison of the lifetime incidence risks calculated for this statement with the results of the ICRP Publication 103 (ICRP 2007a).

Table 9-5: *Cancer incidence risks after continuous life-long exposure to ionising radiation with an effective dose of 3 mSv per year.*

Scenario	Endpoint	Source / ratio	Probability		
			Women	Men	averaged
External radiation exposure	Malignant tumours without skin cancer	This statement	$508 \cdot 10^{-4}$	$307 \cdot 10^{-4}$	$408 \cdot 10^{-4}$
		ICRP 103[a]	$203 \cdot 10^{-4}$	$131 \cdot 10^{-4}$	$167 \cdot 10^{-4}$
		Ratio	2.5	2.4	2.4
	Leukaemia	This statement	$31 \cdot 10^{-4}$	$47 \cdot 10^{-4}$	$39 \cdot 10^{-4}$
		ICRP 103[a]	$9 \cdot 10^{-4}$	$12 \cdot 10^{-4}$	$11 \cdot 10^{-4}$
		Ratio	3.4	3.8	3.6
	Sum	This statement	$540 \cdot 10^{-4}$	$354 \cdot 10^{-4}$	$447 \cdot 10^{-4}$
		ICRP 103[a]	$212 \cdot 10^{-4}$	$143 \cdot 10^{-4}$	$177 \cdot 10^{-4}$
		Ratio	2.5	2.5	2.5
Incorporation of ^{131}I	Thyroid cancer	This statement	$443 \cdot 10^{-4}$	$88 \cdot 10^{-4}$	$266 \cdot 10^{-4}$
		ICRP 103[b]	$338 \cdot 10^{-4}$	$77 \cdot 10^{-4}$	$207 \cdot 10^{-4}$
		Ratio	1.3	1.1	1.3

[a] Nominal risk coefficients from Table A.4.18 multiplied by 0.255 (85 age groups with 3 mSv per year yields a cumulative effective dose of 0.255 Sv)

[b] Nominal risk coefficients from Table A.4.18 multiplied by 6.375 (85 age groups with an effective dose of 3 mSv per year and a thyroid weighting factor of 0.04 corresponds to a cumulative thyroid dose of 6.375 Sv)

In the scenario “external radiation exposure”, the results of the sex-averaged risk calculations for malignant tumours outlined here are higher than those of the ICRP by a factor of 2.4. This is essentially due to the use of a DDREF of 2.0 by the ICRP. By contrast, the SSK sees no evidence for a lower risk per dose at exposure to low doses and low dose rates in comparison with the LSS. The remaining difference of around 20 % is attributable to the use of different risk models (newer LSS results in the current calculations, the transfer of the excess relative cancer incidence rates[58] in the LSS versus averaging of the transfer of the excess relative rates and the transfer of the excess absolute rates) and background risks (Germany 2017 versus averaging of Western and Asian countries at the start of the century). The difference is greater for leukaemia. This is essentially due to the modelling. The ICRP calculations are based on LSS data up to the year 1987, for which a sharp decrease in the risk was found with increasing time since exposure (Preston et al. 1994). The calculation model used in this report takes into account data up to the year 2001, which did not confirm this sharp decrease (Hsu et al. 2013), resulting in a considerably higher risk for longer times after exposure. For the sum of malignant tumours and leukaemia, the current calculations and the calculations of the ICRP differ from one another by a factor of 2.5.

In the scenario “incorporation of ^{131}I” the radiation-induced lifetime risk for thyroid cancer for women as well as the sex-averaged risk calculated by the ICRP are 30 % lower than in this statement. Given the uncertainties, this finding is consistent. The risks calculated for men, however, only differ by around 10 %, even though the ICRP used a DDREF of 2.0. In the calculations, the excess relative risk for women is twice as high as for men, both in the study on which the present statement is based (Furukawa et al. 2013, Annex B Section 1.3) and in the pooling analysis of seven studies used by the ICRP (Ron et al. 1995). However, the calculations

[58] TheICRP uses the term “excess relative risk”.

differ from one another in terms of the age dependency of the excess relative risk and the background risk. Owing to the higher background risk for women, the radiation-induced lifetime risk is higher than for men by a factor of 5 in this statement and by a factor of 4.4 in the calculations of the ICRP. A sex difference in the excess relative risk by a factor of 2 in the data of the LSS was confirmed by an analysis using mechanistic models (Kaiser et al. 2021). However, an update of the pooling found no significant differences between the sexes (Veiga et al. 2016, Lubin et al. 2017).

10 Approaches to protect the population from carcinogenic substances

Risk assessment of chemical carcinogens presents a major challenge in the field of toxicology. Even though exposures have been decreased effectively in the past decades, small amounts of carcinogenic substances in the environment, in food and at the workplace are often still present and cannot be fully avoided. These include, for example, products of combustion, carcinogenic metal compounds and chemicals, but also natural bioactive food ingredients as well as substances that occur during the storage and preparation of food, including mycotoxins, acrylamide, nitrosamines, heterocyclic aromatic amines and polycyclic aromatic hydrocarbons (e. g. benzo[a]pyrene). Thanks to increasingly sensitive trace analyses, these types of contaminants can be detected with increasing accuracy. Therefore, a scientific evaluation of carcinogenic substances in the low dose range will also be relevant in the future.

A distinction between genotoxic and non-genotoxic carcinogens was traditionally regarded as particularly relevant for such a risk assessment. For the latter substances, which are frequently classified as “tumour promoters”, the existence of no observed adverse effect levels (threshold values) is frequently postulated, irrespective of different underlying mechanisms. In contrast, genotoxic carcinogens, their metabolic precursors and DNA-reactive metabolites are considered risk factors at all concentrations, since even one or a small number of DNA lesions may lead to mutations and thus increase the risk of cancer.

Various approaches to assess and decrease exposure to genotoxic carcinogens exist; these concepts can be divided into pragmatic risk-reduction approaches, risk-based assessments and scientific approaches including a detailed consideration of the mode of action. Different approaches and reference values for excess cancer risks apply for exposure of the general public and exposure at the workplace. A tolerable lifetime risk of 4:1,000 and an acceptable lifetime risk of 4:10,000 or 4:100,000 (from 2018) are specified explicitly for hazardous substances in the workplace; this kind of “traffic light system” does not apply to the general public. Here, the aim is to achieve an excess cancer risk of < 1:1,000,000 for substances that are suspected to be carcinogenic. If, on the other hand, data from carcinogenicity studies in animals is available, the “margin of exposure” (MOE) approach is used to prioritise risk management. If the actual exposure is lower by a factor of 10,000 or more than the dose that causes tumours in 10 % of animals in animal studies (lower confidence bound), this substance is given a low priority for further risk management actions; this corresponds to an excess cancer risk of 1:100,000. These approaches are explained in more detail in the following. It must be emphasised that the respective risks are always assigned to individual substances, which means that the overall risk due to exposure to multiple chemical carcinogens may be higher. A comprehensive consideration of all substances, exposure pathways and all cancer types comparable to the field of radiation protection, does not exist for chemical-genotoxic agents.

10.1 Protection of the population against excess cancer risks due to chemicals and food ingredients

As mentioned previously, genotoxic carcinogens such as the heat-induced contaminants acrylamide, furan, nitrosamines or polycyclic aromatic hydrocarbons in food, cannot be fully avoided, and establishing approaches for a scientifically based risk assessment plays a crucial role (see, among others, WHO and FAO 2009). In general, a minimisation rule applies at first, i. e. an approach to minimise the concentration of a substance in a food as far as reasonably possible (as low as reasonably achievable – ALARA); this consideration also takes into account socio-economic considerations. This is a pragmatic approach that does not take account the carcinogenic potential of a substance, the mode of action, or the actual exposure of a person, i. e. the amount ingested per kg bodyweight per time unit. Furthermore, there is no prioritisation of the various genotoxic substances in terms of risk minimisation.

The "threshold of toxicological concern" (TTC) approach is yet another assessment approach. It is a screening and prioritisation tool to assess the safety of substances of unknown toxicity in food (EFSA 2019). The tool was developed to review and prioritise, based on their chemical structure, the risk assessment of several tens of thousands of substances that are not specifically regulated, where human oral exposure can be estimated to be relatively low. The TTC approach is used when substance-specific toxicity data is limited and applies to many thousand substances with or without structural alerts for genotoxicity as well as for cancer and non-cancer endpoints. The TTC values follow what is known as the Cramer classification; for substances that may be DNA-reactive mutagens and/or carcinogens, the relevant TTC value is 0.0025 $\mu g\,kg^{-1}$ body weight per day. This value is based on an analysis of the carcinogenic potency (TD_{50}) of 730 chemical carcinogens in animal testing. Based on a linear extrapolation, for the majority of genotoxic carcinogens this exposure represents an estimated life-long cancer risk of < 1:1,000,000 as the target for protection. However, three groups of carcinogens were omitted here, namely aflatoxin-like substances and azoxy- or N-nitroso compounds, as these classes include numerous compounds with high genotoxic potency (Kroes et al. 2004). The Cramer classification is meanwhile also based in particular on models using computer-based (quantitative) structure-activity relationships ((Q)SAR models). The TTC approach is not suitable for substances for which European legislation requires the submission of toxicity data, or when sufficient toxicity data is available; in these cases, substance-specific risk assessments must be carried out (EFSA 2019).

In addition to the ALARA principle and the TTC approach, in 2005 the European Food Safety Authority (EFSA) implemented the "Margin of Exposure" (MOE) approach , which applies for substances that are both genotoxic and carcinogenic (EFSA 2005) and for which substance-specific toxicity and carcinogenicity data is available. The MOE is calculated on the basis of the estimated exposure of humans and the effect dose established or estimated in animal testing. A benchmark dose (BMD) is typically used for this, calculated as an excess tumour incidence of 10 %. Taking into consideration uncertainties in sample collections and measurements, the lower value of the 95 % confidence interval is used (Benchmark Dose Lower Bound, $BMDL_{10}$) (EPA 2012, EFSA 2017, Cléro et al. 2021). The magnitude of a risk is inversely proportional to the MOE: if the MOE (as the ratio between $BMDL_{10}$ in animal testing or the corresponding human tumour incidence derived from epidemiological studies and the measured or estimated exposure in humans) is 10,000 or higher, the EFSA rates the carcinogenic risk as being on the low side and recommends assigning a low priority to these substances. In contrast, the further the MOE is below 10,000, the greater the risk appears, and the more urgent minimisation measures become. This approach thus takes into account a consumer's exposure to a genotoxic substances and relates it to the carcinogenic effect of a defined dose in animal testing (EFSA

2005). In 2012 this approach was also expanded to impurities in food; in this context it is also important to consider the uncertainties in deriving and interpreting the dose response (Benford et al. 2010, EFSA 2012). The risk is not precisely quantified.

The MOE approach presupposes that more or less extensive toxicology data is available for the substance in question.

10.2 Risk assessment of chemical carcinogens at the workplace

Even if this document deals with exposure of the general public, this section considers at the regulations governing chemical carcinogens at the workplace, since here a concept existsthat distinguishes between tolerable and acceptable risks using a traffic light model. In the past, values known as technical reference concentrations (TRC values), which were based on the state of the art in production, treatment and processing, were used for carcinogenic substances at the workplace; starting in early 2005, the German Hazardous Substances Regulation requires the establishment of health- or risk-based occupational exposure limits also for carcinogenic substances based on the results of toxicology studies.

The Committee on Hazardous Substances (AGS) of the Federal Ministry of Labour and Social Affairs follows a risk-based approach using exposure-risk relationships (ERB) (TRGS 910). The ERB of a carcinogenic substance describes the relationship between the concentration of the substance after inhalation and the statistical probability of developing cancer. The ERB derived from experimental or epidemiological studies forms the basis for the extrapolation to the lower risk range, which generally cannot be verified in animal testing or observed epidemiologically in practice. The reference period for the risk is an entire lifetime (lifetime risk). The boundary between a high risk (red area) and a medium risk (yellow area) is referred to as tolerable risk. The tolerable risk corresponds to a statistical additional cancer risk of 4:1,000, meaning that, statistically, four out of 1,000 persons exposed to the substance throughout their working life will develop cancer. This value was derived from comparative risks, e. g. the risk of an agricultural worker being killed in an accident or the risk of a non-smoker who is not exposed to hazardous substances at work developing lung cancer.

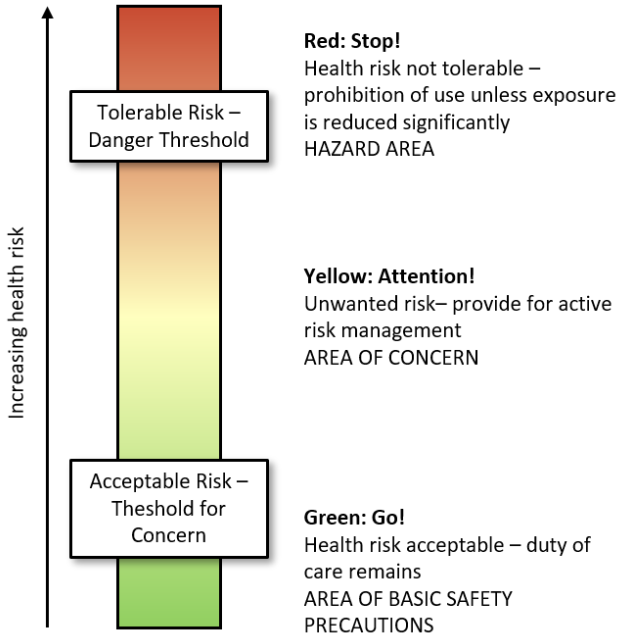


Figure 10-1: *The risk-based concept of the AGS (BAuA 2012)*

Above the tolerance risk, employees should generally not be exposed, or only for a short period of time, as this constitutes an unacceptable risk. The boundary between a medium risk (yellow area) and a low risk (green area) is referred to as an acceptable risk. During the introductory phase (until 2013), the acceptable risk corresponded to a statistical additional cancer risk of 4:10,000, meaning that, statistically, four out of 10,000 persons exposed to the substance aimed to be reduced to four out of 100,000 persons. Both the tolerable and the acceptable risk are thus general parameters, i. e. not substance-specific. Depending on whether the substance is classified as having direct or indirect genotoxic effects, linear or sublinear extrapolation takes place. If the threshold of an acceptable risk is passed, this is associated with a low acceptable risk (for a more detailed description, see (SSK 2018)).

The Permanent Senate Commission of the German Research Foundation (DFG) for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) pursues a different, complementary approach for evaluating and setting threshold limits for carcinogens at the workplace.

In order to differentiate carcinogenic substances based on the existing evidence on the one hand, but also according to their potency under workplace conditions in consideration of the mode of action on the other hand, already in 1998 the MAK Commission established five categories of carcinogenic substances. Substances that cause cancer in humans and that can be assumed to contribute to the risk of cancer (sufficient evidence of a correlation between exposure of humans and the occurrence of cancer in epidemiological studies) are classified in category 1. Category 2 is reserved for substances that are considered carcinogenic for humans because sufficient data from long-term animal studies or evidence from animal studies and epidemiological studies and substantiated by information on the mode of action from short-term in-vitro assays indicates that they can contribute to the risk of cancer. As long as no quantitative data is available to derive an effect threshold, in either case it is not possible to establish a health-based MAK and/or BAT value that protects against an additional cancer risk. In these cases, where data permits, the AGS carries out exposure-risk assessments that assess and/or reduce the exposure based on tolerable and acceptable risks. Substances that cause concern that they are or could be carcinogenic but cannot be assessed conclusively due to insufficient data are classified in category 3. The classification in category 3 is provisional (DFG 2020). Categories 4 and 5 for carcinogens, which were newly established in 1998, were an important step towards differentiating carcinogenic substances according to their carcinogenic risk at low doses (Neumann et al. 1998). Carcinogens that are either not genotoxic or for which genotoxicity is not a primary concern are classified in category 4. For these substances, provided the MAK or Biological Tolerance (BAT) value is observed, no increased cancer risk is expected. Examples are substances that are expected to contribute to an increased risk of cancer only if irritation occurs (e. g. formaldehyde, see below) or in the presence of chronic inflammation, as in the case of chronic irritation of the lungs with biopersistent, alveolar dusts following a decreased clearance of the particles by macrophages. Category 5 includes genotoxic carcinogens which, provided the MAK or BAT value is observed, contribute only slightly – if at all – to an increased cancer risk or for which dose-dependent risk assessments can be carried out. Categories 4 and 5 require extensive data that allows a MAK or BAT value to be classified or established or, for category 5, a data-based risk assessment. A similar concept was later also adopted at the EU level by the Scientific Committee on Occupational Exposure Limits (SCOEL) (Bolt and Huici-Montagud 2008) and, following its dissolution, by the European Chemicals Agency (ECHA) (ECHA 2019). This approach has meanwhile been accepted worldwide in the scientific community and will certainly gain in importance as the scientific knowledge on mechanisms of action increases.

10.3 Mode-of-action (MOA)-based limits for genotoxic carcinogens

The differentiation between genotoxic and non-genotoxic carcinogens was a decisive step towards a scientifically based assessment of carcinogenic substances. It is generally accepted that a concentration at which no adverse effects are observed (known as no observed adverse effect level, NOAEL) exists for non-genotoxic carcinogens, frequently classified as tumour promoters, irrespective of the different underlying mechanisms, which consequently allows the derivation of a health-based limit value (e. g. carcinogens of MAK category 4).

By contrast, genotoxic carcinogens, their metabolic precursors and DNA-reactive metabolites are traditionally viewed as risk factors at all concentrations, as even one or few DNA lesions can theoretically lead to mutations and thus increase the risk of cancer. For substances that directly react with DNA, risk managers have followed the minimisation rule (ALARA) for a long time. The plausibility of the linear no-threshold hypothesis, i. e. the linear extrapolation of cancer risks from high exposure to the low dose range, has been and is still being increasingly questioned when it comes to cancer risk assessments (e. g. Kobets und Williams 2019, Cohen et al. 2019, Greim und Albertini 2015, Thomas et al. 2015). As the majority of key events in chemical carcinogenesis exhibit a non-linear dose response, it can be assumed that tumour development also does not have a linear dose response in most cases. Here, depending on the effects profile of a substance, a sublinear but in some cases also a supralinear dose-response curve can often be expected in the low dose range (Figure 10-2; Figure 10-3).

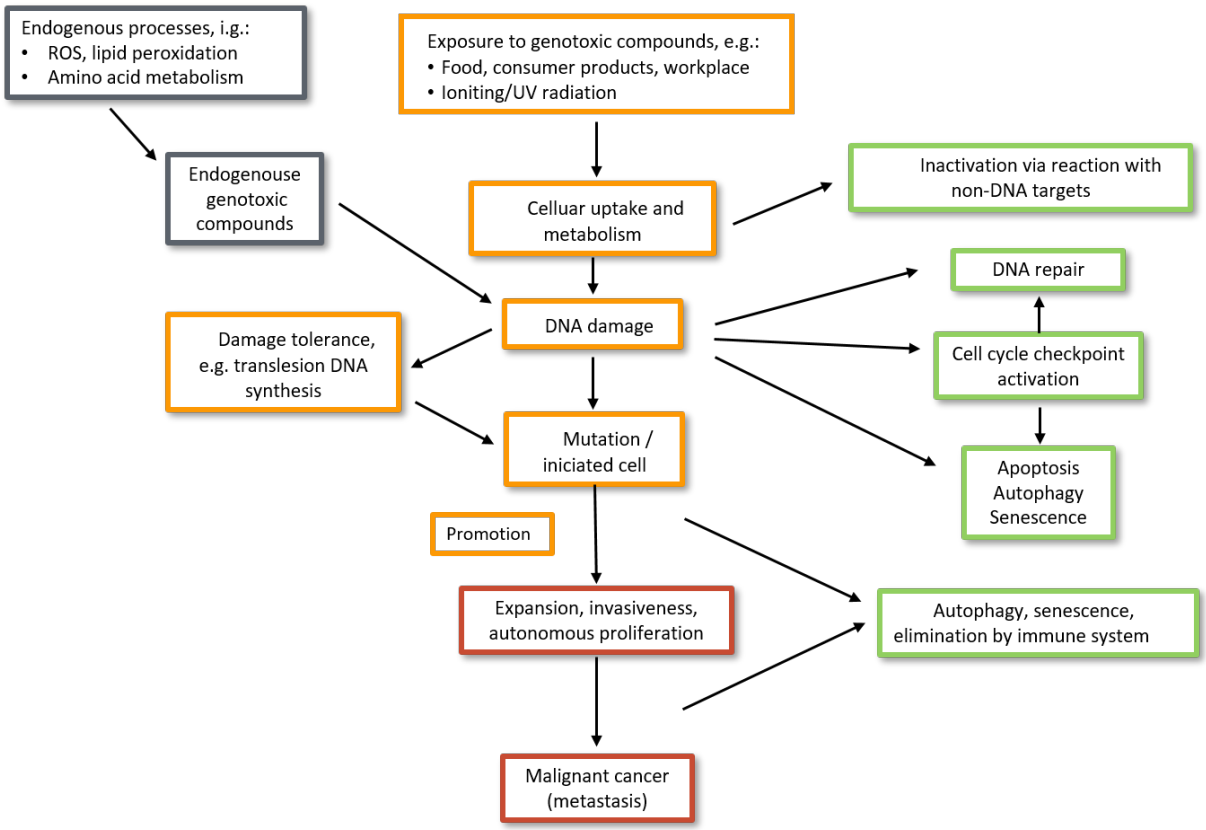


Figure 10-2: *Diagram of the causes and consequences of DNA damage.*

Left: Endogenous and exogenous factors and cellular processes that lead to DNA damage and increase the risk of tumour development. Right: Processes that decrease the extent of DNA damage, mutation induction and tumour development (according to Hartwig et al. 2020)

A first critical event is the induction of DNA damage, which interferes with DNA transcription and replication and can lead to base mispairing at the time of DNA replication. Possible consequences include mutations and genomic instability which may lead to cancer in somatic cells, but also to reproductive toxicity if sperm or egg cells are affected. In an effort to maintain the integrity of the genome and to keep the mutation rate low, a complex response network to DNA damage has evolved (summarised in Hartwig et al. 2020). It includes various DNA repair systems for different types of DNA damage, cell cycle control mechanisms to prevent replication of damaged DNA as well as the induction of apoptosis in case of severe DNA damage. Mutations arise through direct integration of incorrect DNA bases in the course of replication or by activation of DNA polymerases with an increased error tolerance, depending on the nature of the DNA damage. Initiated cells and cell clones can also be eliminated by the immune system. Therefore, an overall distinction must be made between DNA damage that can potentially be repaired and mutations, as irreversible changes in the genetic information, and it can be assumed that by far not every DNA lesion will lead to a tumour. In addition to DNA damage, epigenetic alterations can also contribute to the carcinogenicity of substances if they occur at relevant concentrations for human exposure.

Threshold values have also been postulated for multiple carcinogens in animal testing (Kobets and Williams 2019). However, it must be considered that effect thresholds for carcinogenicity derived from long-term animal testing inevitably represent approximations, as reliable tumour incidences in the low dose range cannot be estimated from animal testing simply due to the limited number of animals. Increased tumour incidences in animal testing are generally observed at higher concentrations that are often already moderately toxic. The shape of the dose-response curve in the lower dose range, which is generally relevant for human exposure, cannot, however, be derived from these studies (Figure 10-3). At present it is not possible to specify a general range for which a risk of cancer can be safely excluded, in particular for directly DNA-reactive, genotoxic carcinogens, and in the absence of substance-specific data, linear extrapolation is carried out.

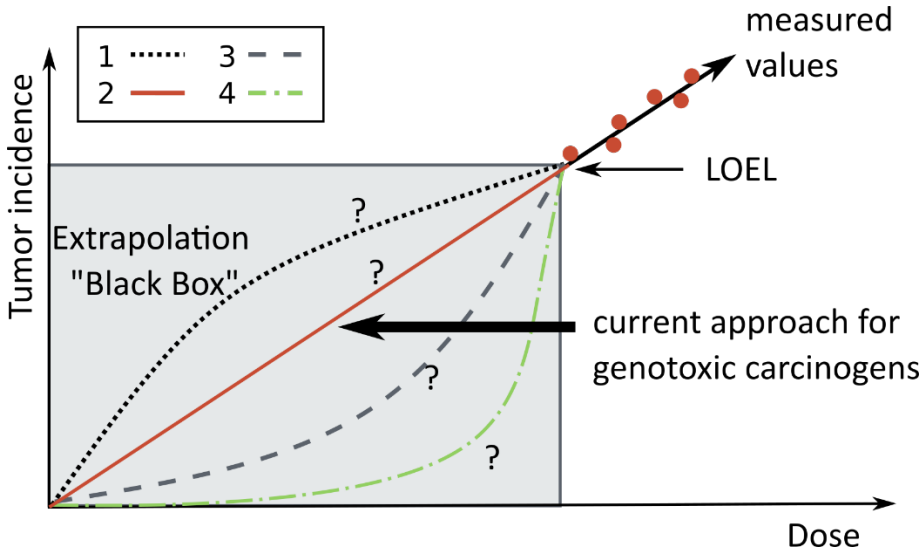


Figure 10-3: *The problem of deriving a dose-response relationship from experimental animal data. LOEL: lowest observed effect level; 1: supralinear response; 2: linear response; 3: sublinear response; 4: threshold response)*

Advances in both the analytics and our understanding of cellular processes involved in tumour development have contributed significantly to a more differentiated risk assessment, also of genotoxic carcinogens. This applies, for example, to the detection and quantification of DNA

lesions and mutations, but also to transcriptomic and other cellular responses which, viewed together, contribute to a deeper mechanistic understanding of the key processes in what is known as the adverse outcome pathway (AOP). Scientific findings show that the dose response for genotoxic carcinogens in the low dose range and thus the existence of a mode of action-based practical or actual threshold is substance-specific and dependent on the specific modes of action (see examples 10.3.1 to 10.3.3). Based on this, and using numerous examples, the approach for evaluating carcinogens was further discussed, refined and published (Hartwig et al. 2020) by a joint working group of the two Permanent Senate Commissions of the DFG for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK) and on Food Safety (SKLM). Key aspects relate to the comparison of induced DNA lesions by exogenous exposure with endogenously induced DNA lesions, for example in the course of metabolic processes, as well as sensitive methods for the quantification of DNA lesions that may be used for a quantitative estimation of the cancer risk in the lower dose range, which is difficult to access in carcinogenicity studies. A general outline is given in Figure 10-4.

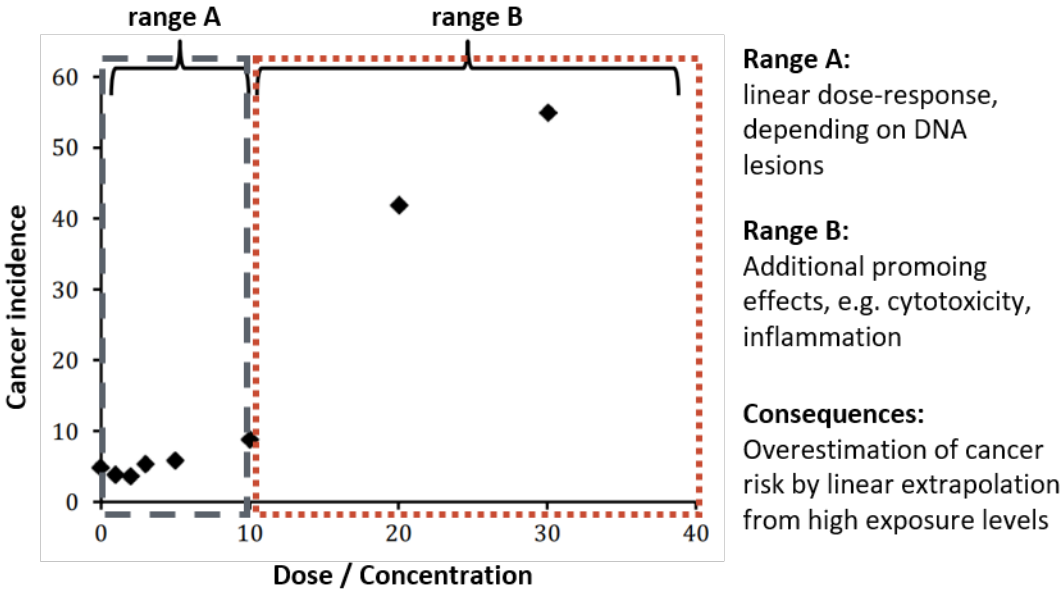


Figure 10-4: Diagram of a non-linear dose response as observed in many cancer risk studies (modified according to Hartwig et al. 2020).

For many chemical carcinogens (both genotoxic and non-genotoxic), the dose-response curves are not linear across the entire dose range. In fact, they often exhibit at least two phases, in the sense that a range with a flat slope is followed by a steep increase, as shown in the diagram in Figure 10-4. While the flat slope of range A is determined by the induction of DNA damage and its conversion into mutations, the steep increase in range B can be explained mechanistically by the saturation of detoxifying or repair mechanisms and/or by the induction of any type of tumour promotion mechanism, which generally follow a non-linear (often threshold-like) dose response. A measurable (frequently steep) increase of the cancer incidence is observed in the high dose range (B) due to the onset of tumour promotion and/or saturation effects. If the slope of range B is used for a risk assessment by (linear) extrapolation, the cancer risk in range A is likely to be overestimated (Hartwig et al. 2020).

Other substances can increase the genomic instability through indirect genotoxic mechanisms, not by reacting directly with the DNA themselves, but rather by interfering with DNA repair processes and other cellular responses to DNA damage at low concentrations. As these effects are mediated through interaction with proteins, no linear dose-response relationship would be

expected here either, and no adverse effects levels (NOAEL) can theoretically be derived. However, this presupposes that the concentrations above which cellular protection mechanisms are inactivated are also known for humans.

10.3.1 Example formaldehyde

Formaldehyde exposure is attributed to both exogenous (environment, indoor air, cosmetics, workplace) and endogenous sources (metabolic intermediate in the amino acid metabolism). Due to the high chemical reactivity, formaldehyde causes local irritation as well as acute and chronic toxicity after direct contact in the target tissue. Furthermore, formaldehyde is considered carcinogenic and induces squamous cell carcinoma of the nose in experimental animals and – with less convincing evidence – nasopharyngeal carcinomas in humans. Also, there is limited evidence for an increased occurrence of leukaemia in humans, albeit without mechanistic or experimental support. Formaldehyde induces DNA base damage, DNA-protein cross-links and DNA-DNA cross-links. This genotoxicity, along with an increased cell proliferation, are considered relevant causal events. While the International Agency for Research on Cancer (IARC) classified it in category 1 (human carcinogen), the MAK Commission classified formaldehyde in carcinogenicity category 4, under the assumption that an increase in the cancer risk is not expected as long as the MAK value is complied with. In spite of the induction of DNA lesions down to the low dose range, this decision is based on the assumption that an increase in mutagenicity and carcinogenicity is prevented as long as irritation and accelerated cell proliferation in the target cells of the nose can be excluded. Therefore, a MAK value of 0.3 ppm (0.37 mg/m^{-3}) was established in 2000 (Greim 2000). Since then a number of publications have appeared that deal with the quantification of DNA lesions in the target tissues and the relationship of endogenously induced DNA lesions compared with the same DNA lesions caused by exogenous exposure. Advanced analytical methods allow to distinguishbetween DNA lesions caused by endogenous formaldehyde formed within the amino acid metabolism and lesions caused by exogenous formaldehyde exposure (Swenberg et al. 2011). With regard to a risk assessment of exposure via food, e. g. from natural sources such as fruit and vegetables or from food contact materials, among other things, the EFSA calculated that formaldehyde intake accounts for only 0.1 % compared with the endogenous metabolic turnover of formaldehyde (EFSA 2014b). For inhalation exposure typical at the workplace, investigations performed among others by Swenberg et al. (Swenberg et al. 2011) showed that exposure by inhalation of up to 10 ppm for one day did not lead to a measurable increase in endogenously induced DNA adducts in the blood or bone marrow. Even in the nasal epithelium, inhalation exposure of more than 10 ppm was necessary in order to exceed the level of endogenous DNA lesions (Figure 10-5).

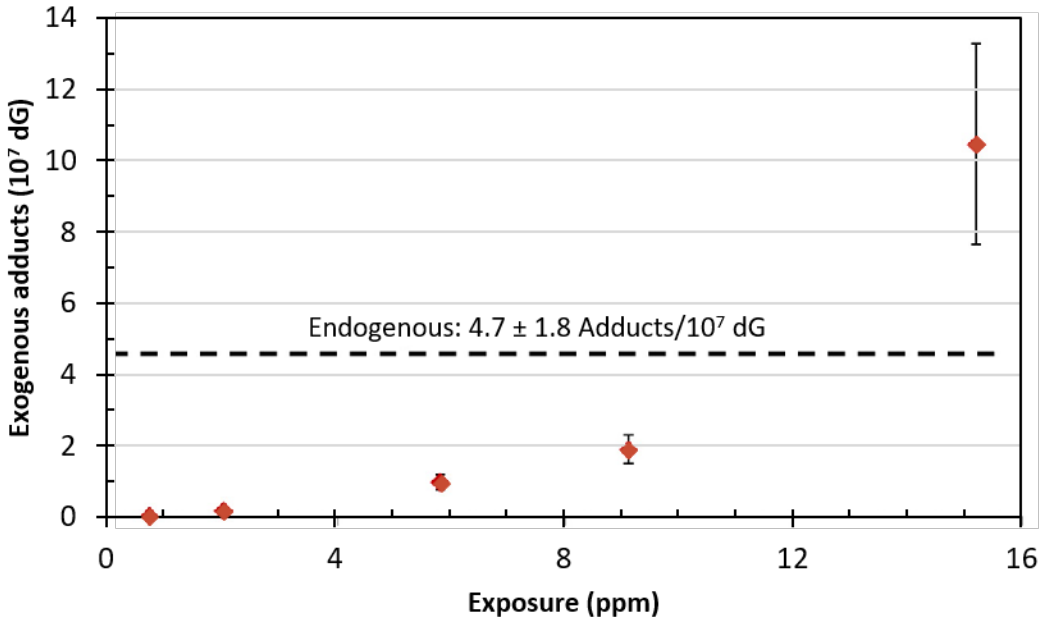


Figure 10-5: Degree of DNA damage in rat nasal epithelium caused by exogenous inhalation exposure to formaldehyde over 6 hours. Measurements were performed after 6 hours of inhalation of 0 ppm, 0.7 ppm, 2 ppm, 9.1 ppm and 15.2 ppm (Swenberg et al. 2011).

A relevant conversion of DNA lesions into mutations requires accelerated cell proliferation in addition to DNA damage; in this regard, local formaldehyde levels in particular are decisive. Results from animal experiments to analyse gene expression profiles have also produced evidence of a possible threshold for irritation. At the level of transcription, a benchmark dose of 1 ppm was identified for significant alterations in sensitive genes which are associated with cellular stress, inflammation and cell proliferation; 2 ppm induced transcriptional changes that affect the immune system, inflammation and apoptosis as well as increased proliferation (Andersen et al. 2010). This data is consistent with the irritation of the eyes, nose and throat observed in human volunteer studies at 0.5 ppm or 1 ppm. In view of the presently available data, it can therefore be assumed that there is no additional risk for nasal tumours at low doses below the level of irritation, thus confirming the sublinear dose-response curve and the MAK value of 0.3 ppm.

Overall, while formaldehyde has been shown to be carcinogenic after inhalation, an additional cancer risk is expected neither for the general population nor for occupationally exposed persons, provided the workplace limits are observed.

10.3.2 Example benzo[*a*]pyrene

Benzo[*a*]pyrene (BaP) belongs to the group of polycyclic aromatic hydrocarbons (PAH), which are common environmental and food contaminants. PAH are formed continuously with incomplete combustionor pyrolysis of organic material and are thus present in the ambient air, in water, soils and sediments. Sources of considerable exposure of the population also include tobacco smoke and food, for example grilled meat. In workplace settings, highest exposure levels are observed during aluminium production. As BaP is only one component of PAH mixtures of varying composition, there are no epidemiological carcinogenicity data for BaP alone. Due to strong and consistent evidence of the carcinogenicity of BaP in many animal species for practically all exposure pathways, which is further substantiated by consistent and coherent mechanistic information, BaP was classified by the IARC as carcinogenic to humans

(group 1) (IARC 2010) and by the MAK Commission in carcinogenicity category 2 (Hartwig 2013b). The carcinogenic effect of BaP is attributed to the formation of DNA adducts. The formation of stable DNA adducts at the N2 position of guanine by *syn*- and *anti*-benzo[*a*]pyrene-7,8-dihydrodiol-9,10-epoxide (BPDE) is assumed to be the most relevant metabolic pathway. These lesions can in principle be repaired by the nucleotide excision repair (NER) pathway (Camenisch and Naegeli 2009, Hess et al. 1997). In case of incomplete repair prior to replication, the DNA lesions can lead to mutations and cancer (Melendez-Colon et al. 1999).

The question on the dose-response relationship for BPDE-induced DNA adducts at the N2 position of guanine in the low dose range, the correlation with mutations, the DNA repair capacity and the onset of a transcriptional DNA damage response was assessed in TK6 cell cultures (Piberger et al. 2018). The results show a linear dose response for DNA adducts, which were already detected at concentrations as low as 10 nM BPDE. Furthermore, in the same dose range, a linear increase in mutations was observed, along with a linear correlation between the number of DNA adducts and mutations also in the lowest concentration range (Figure 10-6).

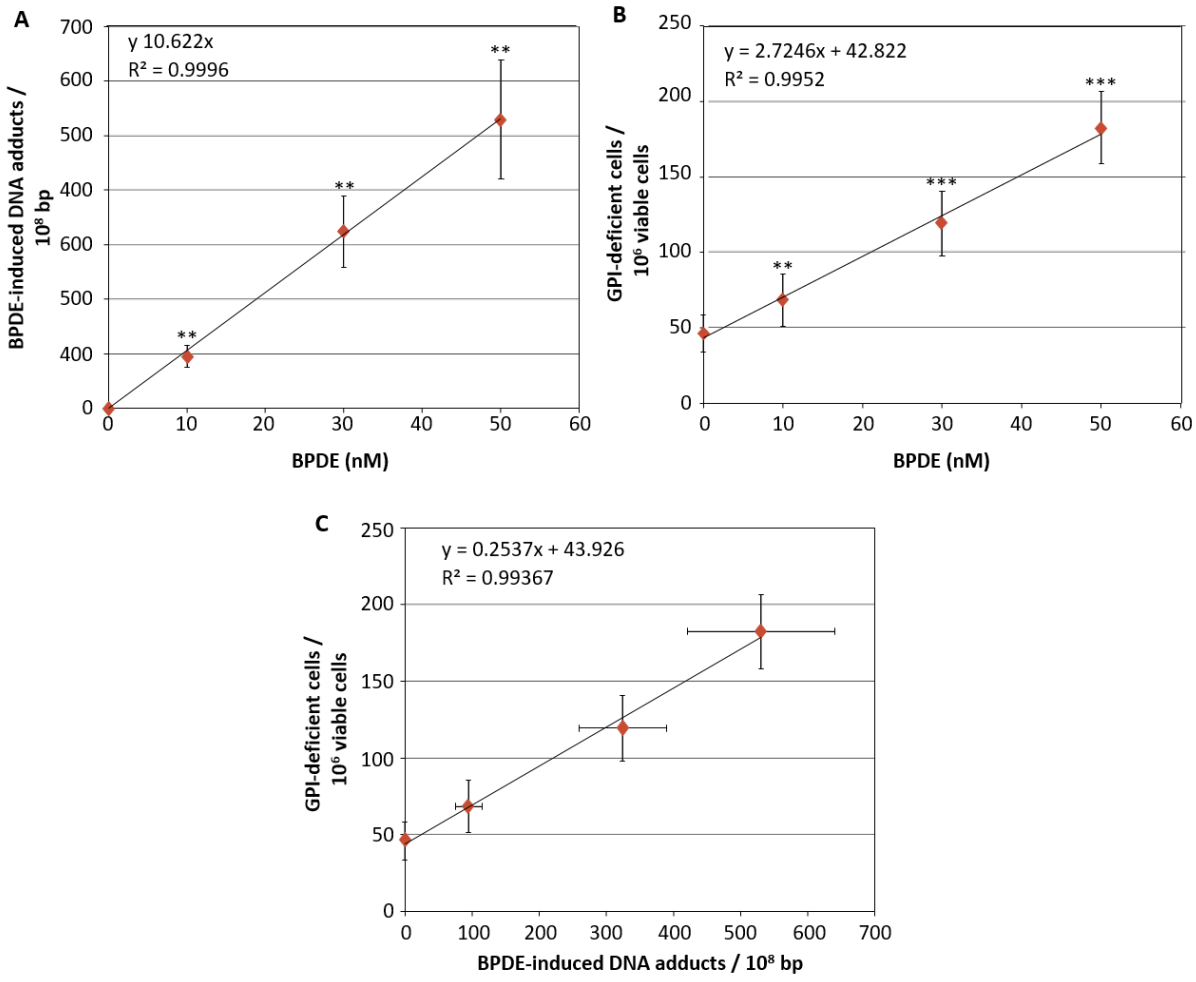


Figure 10-6: Dose-response relationship for BPDE-induced DNA adducts (A) and mutations (expressed as GPI-deficient cells) (B), and the correlation between the two parameters (C) (according to Piberger et al. 2018).

The repair kinetics of the DNA lesions can explain the induction of mutations also in the lower dose range; here, 40 % were still detected after 24 hours. In addition, the DNA adducts induced by the lowest BPDE concentration were also not fully repaired (Figure 10-7).

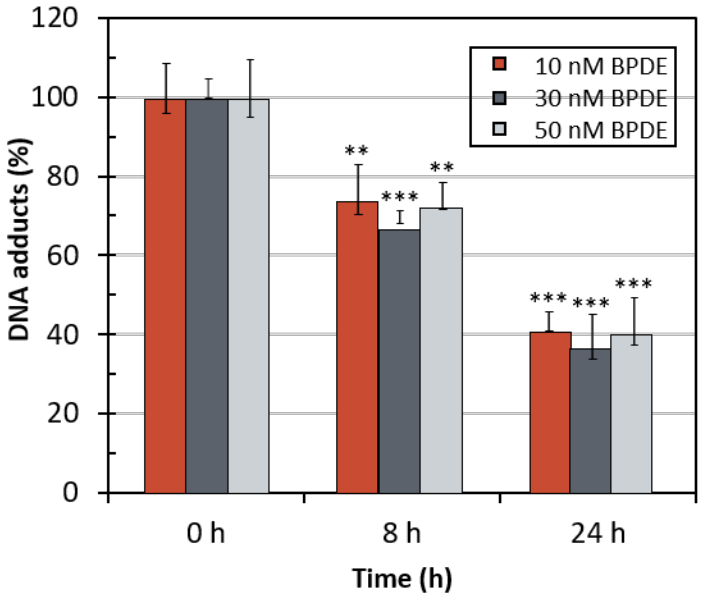


*Figure 10-7: Repair of BPDE-induced DNA adducts dependent on concentration and time (Piberger et al. 2018). Statistically significant different from the control: ** $p \leq< 0.01$; *** $p \leq 0.001$.*

The persistence of at least some PAH-induced DNA lesions was also confirmed in lung autopsy samples of non-smokers, ex-smokers and smokers. The lowest frequencies of lesions were found in the first group, intermediate frequencies in the second, while most DNA lesions occurred in the third group. Also the samples of the non-smoking group exerted small levels of PAH-induced DNA lesions, indicating that even low levels of environmental exposure lead to unrepaired DNA adducts (Lodovici et al. 1998).

The transcriptional response to DNA lesions was also investigated in TK6 cells under the same conditions after incubation with BPDE as outlined above. As expected, treatment with BPDE induced genes coding for DNA damage signalling, DNA repair factors and the tumour suppressor protein p53-dependent DNA damage response, as well as for genes involved in the oxidative stress response and the induction of programmed cell death (apoptosis). However, almost all significant changes in gene expression were restricted to the two highest concentrations applied, 100 BPDE and 200 nM BPDE, while highly significant increases in mutation frequencies were already observed at levels that were 10- and 20-fold lower. Therefore, neither the induction of DNA repair genes nor p53-dependent cell cycle control or apoptotic genes were able to protect against BPDE-induced mutations in the very low dose range (Piberger et al. 2018).

In summary, BPDE increased the frequency of mutations with no obvious deviation from linearity also at the lowest concentrations and correlated with the occurrence of DNA lesions. In contrast, a non-linear dose-response relationship for mutations was observed for some alkylating substances. This discrepancy is very likely due to the effectiveness of various DNA repair systems involved in the removal of different DNA lesions. Even though nucleotide excision repair is a largely error-free process that protects against mutagenicity, it has been shown to be slower and less complete than base excision repair (BER). Whether or not the results obtained with BPDE treatment also apply to other substrates of NER warrants further investigation. Generally it should be noted that the DNA repair capacities may differ in vivo in different tissues.

With regard to the risk assessment these results indicate that for the carcinogenicity of BaP, a linear dose response should be assumed. Accordingly, additional workplace cancer risks of

4:1,000 (tolerable risk) at an exposure of 700 ng m^{-3}, 4:10,000 at 70 ng m^{-3} and 4:100,000 at 7 ng m^{-3} were derived (BAuA 2011). According to calculations of the Indoor Air Hygiene Commission, there is an excess cancer risk of 10^{-6} for the general population at a BaP concentration of 0.033 ng m^{-3}. Current levels of indoor air pollution, calculated as the 95th percentile in indoor living spaces, of 0.79 ng m^{-3} point towards a significantly higher risk than 10^{-6}; for this reason, a preliminary guide value of 0.8 ng BaP m^{-3} was defined in 2021 (UBA 2021); this is known as a hazard guide value which, if exceeded, requires the supervisory authority to initiate measures to reduce exposure.

10.3.3 Example arsenic

Arsenic is a semimetal, existing in the oxidation states +5, +3, 0 and -3 in organic and inorganic compounds. Both natural and anthropogenic sources are relevant. Depending on the geological conditions, drinking water can be a significant source of exposure to arsenic. In drinking water, arsenic is present mostly in inorganic form as arsenate (+5), under reducing conditions also as arsenite (+3). The arsenic concentration in groundwater is normally less than 10 µg l^{-1}, but in some regions of the world, such as India or Bangladesh, concentrations may exceed 3,000 µg l^{-1}. Other significant sources of inorganic arsenic include, for example, rice and rice products. Even higher amounts may be ingested through the consumption of fish, seafood or algae, where arsenic is, however, mainly present in organic form as arsenobetaine or aresenosugar. Occupational exposure occurs, among others, during metal production and processing; here, arsenic and arsenic compounds are used in semiconductors as gallium arsenide, in wood preservatives and in alloys. In the past, arsenic-based pesticides further increased exposure in humans. Another anthropogenic source of arsenic release into the environment is the combustion of fossil fuels. From a toxicology point of view, inorganic arsenic, such as arsenate (+5) and arsenite (+3), is toxic and carcinogenic, while organic arsenic is considered less toxic. Inorganic arsenic compounds, particularly arsenic trioxide (As_2O_3), has been frequently used as poison in many murder cases. While 0.1 g arsenic trioxide ingested orally is already fatal, small doses of 2 mg – ingested daily by people known as the so-called “arsenic eaters” – have been claimed to have a performance-enhancing effect and to protect against poisoning; from today’s perspective, however, these intake amounts are unequivocally associated with chronic toxicity including carcinogenicity. The chronic toxicity of arsenic intake includes skin changes and circulatory disorders (“blackfoot disease”), cardiovascular disorders, neurotoxicity and developmental toxicity, and particularly carcinogenicity at very low concentrations (for reviews see (EFSA 2014a, Greim 2005, Hartwig 2016, IARC 2012)).

After inhalation or ingestion, inorganic arsenic is metabolised to organic compounds in humans and in many other mammals. After the reduction of arsenate, arsenite is metabolised to trivalent and pentavalent methylated species, namely monomethylarsonous acid (MMA(III)) and dimethylarsinous acid (DMA(III)), monomethylarsonic acid (MMA(V)) and dimethylarsinic acid (DMA(V)). The three trivalent methylated species in particular contribute to arsenic genotoxicity and presumably also to arsenic carcinogenicity. Epidemiological studies provide reliable evidence of an increased incidence of lung cancer after inhalation exposure and of lung, skin and bladder cancer after oral exposure to inorganic arsenic. For this reason, arsenic and its inorganic compounds were classified by the IARC (group 1) (IARC 2012) and by the MAK Commission (carcinogenic category 1) (Greim 2005) as carcinogenic in humans. The World Health Organization (WHO) and the United States Environmental Protection Agency (EPA) have specified a limit of 10 µg arsenic per litre of drinking water. For the daily oral intake of inorganic arsenic via food, the European Food Safety Authority (EFSA) established a lower confidence limit for a 1 % increased incidence of lung, skin and bladder cancer ($BMDL_{01}$) of 0.3 µg kg^{-1} (for lung cancer) to 8 µg kg^{-1} body weight; this is within the range of the estimated daily intake. These limit values are based on dose-response relationships derived from

epidemiological studies using benchmark estimations. As the estimated average dietary exposure to inorganic arsenic in the population is within this range even in Europe, a potential increased cancer risk for consumers in the order of 1 % cannot be ruled out, and a value for the tolerable daily intake (TDI) cannot be derived (EFSA 2014a). As a consequence, effective 1 January 2016, the European Union defined maximum levels of inorganic arsenic in rice and rice-based products (EU 2015) in order to reduce this source of exposure. The maximum levels range between 0.1 mg/kg for rice used for the production of food for infants and young children, 0.2 mg/kg for polished rice and 0.3 mg/kg for rice biscuits, rice waffles, rice crackers and rice cakes.

Regarding the mode of action of the carcinogenic effect of inorganic arsenic compounds, direct DNA interactions do not appear relevant in the low dose range, which is further supported by the absence of direct mutagenicity. Nevertheless, the frequency of mutations may be increased by indirect mechanisms, for example interference with virtually all important DNA repair systems. In this context, poly(ADP-ribose)-polymerase 1 (PARP-1) appears to be a particularly sensitive target, which is inhibited at low levels of arsenite, MMA(III) and DMA(III) in the nanomolar concentration range (Hartwig et al. 2003, Walter et al. 2007). This enzyme plays a central role in DNA damage recognition, cell cycle control and apoptosis. Since DNA damage is induced not only by exogenous mutagens, but also continuously by endogenous processes, this can lead to marked hypermutability of exposed cells. This has already been demonstrated in cell cultures in combination with BaP. Furthermore, other targets have been identified as being relevant for genomic instability, such as inhibition of the antioxidant defence systems, inactivation of the tumour suppressor functions and altered signal transduction processes. Epigenetic alterations also appear to be relevant. All of these characteristics alone could contribute to carcinogenicity; however, there combination is most likely to be of major importance. On the molecular level, the affinity of arsenite for thiol groups – particularly for dithiol or trithiol structures in proteins – seems to play a significant role; this could explain the inactivation of DNA repair systems at very low concentrations. PARP-1, for example, contains three zinc-binding domains that are involved in the recognition of DNA lesions and in interactions with other DNA repair proteins. Recent data suggests that zinc finger 1 in particular may not be saturated with zinc under normal cell conditions, which would explain the unusually high sensitivity towards arsenite. Similar zinc-binding structures are found in other DNA repair proteins, transcription factors and tumour suppressor proteins (Hartwig 2013a).

In principle, both the inhibition of DNA repair processes and alterations in signal transduction, as well as epigenetic effects are mediated by protein interactions, and in principle a threshold is likely. For inorganic arsenic, an increased cancer risk can, however, already be assumed for the population in Europe owing to the intake of inorganic arsenic via drinking water and food, as corresponding threshold doses are already exceeded.

10.4 Consequences for the risk assessment

The three examples above illustrate that a differentiated risk assessment, also of direct or indirect genotoxic carcinogens, is feasible and meaningful. For this reason, the joint working group of the MAK and SKLM Commission has proposed a concept that takes into account both the respective modes of action and the background exposure (Figure 10-8).

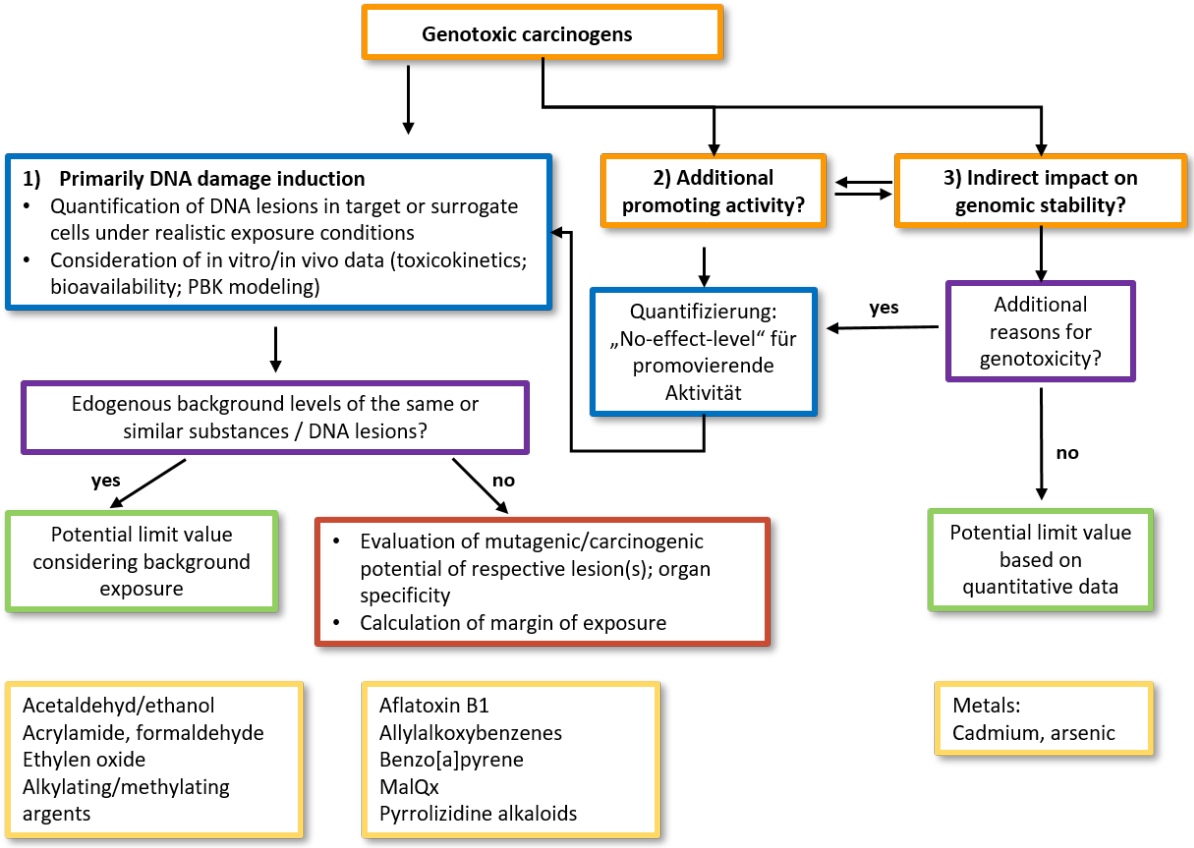


Figure 10-8: *Proposed strategy for assessing the carcinogenic risk of selected genotoxic compounds (according to Hartwig et al. 2020*)

The first step of the strategy illustrated in Figure 10-8 is an initial distinction of whether carcinogenic substances act primarily via the induction of DNA lesions (1), whether additional promotional effects are present (2) or whether they (possibly additionally) reduce the genomic stability through indirect modes of actions, e. g. by inhibiting DNA repair processes or exerting epigenetic effects. In the first case (1) a quantitative comparison with potentially identical DNA lesions caused by endogenous processes may prove helpful for a quantitative risk assessment. If this is not the case, a linear extrapolation of tumour incidences, also in the low dose range with a corresponding risk calculation, can be performed. If additional promotional effects play an important role in tumour development (2), such as tissue irritation or chronic inflammation, these must be prevented in any event; subsequently the risk assessment is carried out as outlined for (1). If indirect modes of actions, such as an inhibition of DNA repair processes, are dominant (3), then in principle practical threshold values exist below which these protein-mediated interactions are not relevant. This mode of action nevertheless warrants special attention as – in contrast to many other promotional effects – the relevant interactions can occur partly at particularly low concentrations, with a subsequent accumulation of endogenous and exogenous DNA lesions and resulting mutations. Known examples include inorganic arsenic compounds, but also other metal compounds. In this regard it is important to minimise exposure to a level where these indirect genotoxic effects do not occur. This can be rather difficult to implement in practice, as shown by the example of inorganic arsenic, where increased tumour incidences – as outlined above – can already be assumed under the exposure conditions that are relevant for the population. Generally speaking, just like in radiation protection, it must be considered that a background exposure already exists for many chemicals, which can comprise natural sources in the environment (like for arsenic) as well as contaminants in the air, in soils and in drinking water derived from anthropogenic sources and, as a consequence, is present also in food. To

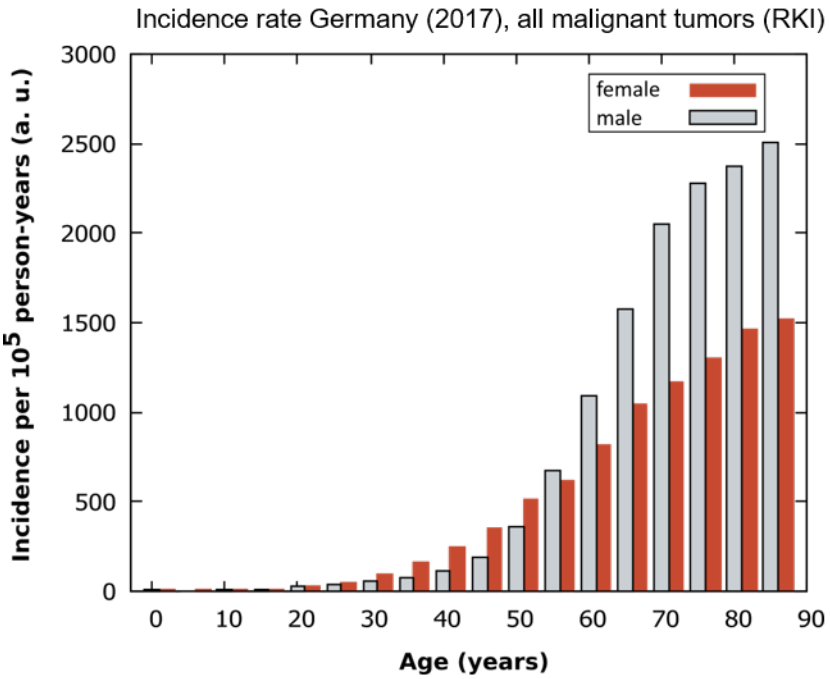
what extent this contamination already contributes to an increased cancer risk is dependent on the respective substance and cannot be answered generally for all – several tens of thousands – of chemicals.

Annex A: Data sources used

A-1 Cancer incidence rates in Germany

The incidence rates are based on data for Germany in the year 2017, in cases per 10^5 person-years. The age ranges 0 years to 90 years and 0 years to 30 years are shown. Data of the Robert-Koch-Institut (RKI).

A-1.1 Malignant tumours



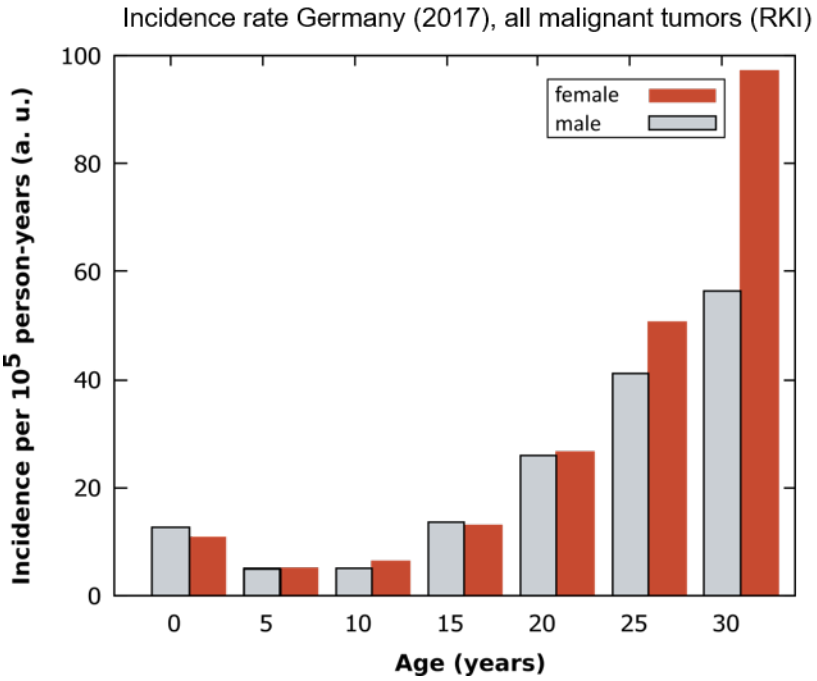


Figure A-1.1: All malignant tumours (ICD-10: C00-C80) without other malignant neoplasms of skin (ICD-10: C44)

A-1.2 Leukaemia

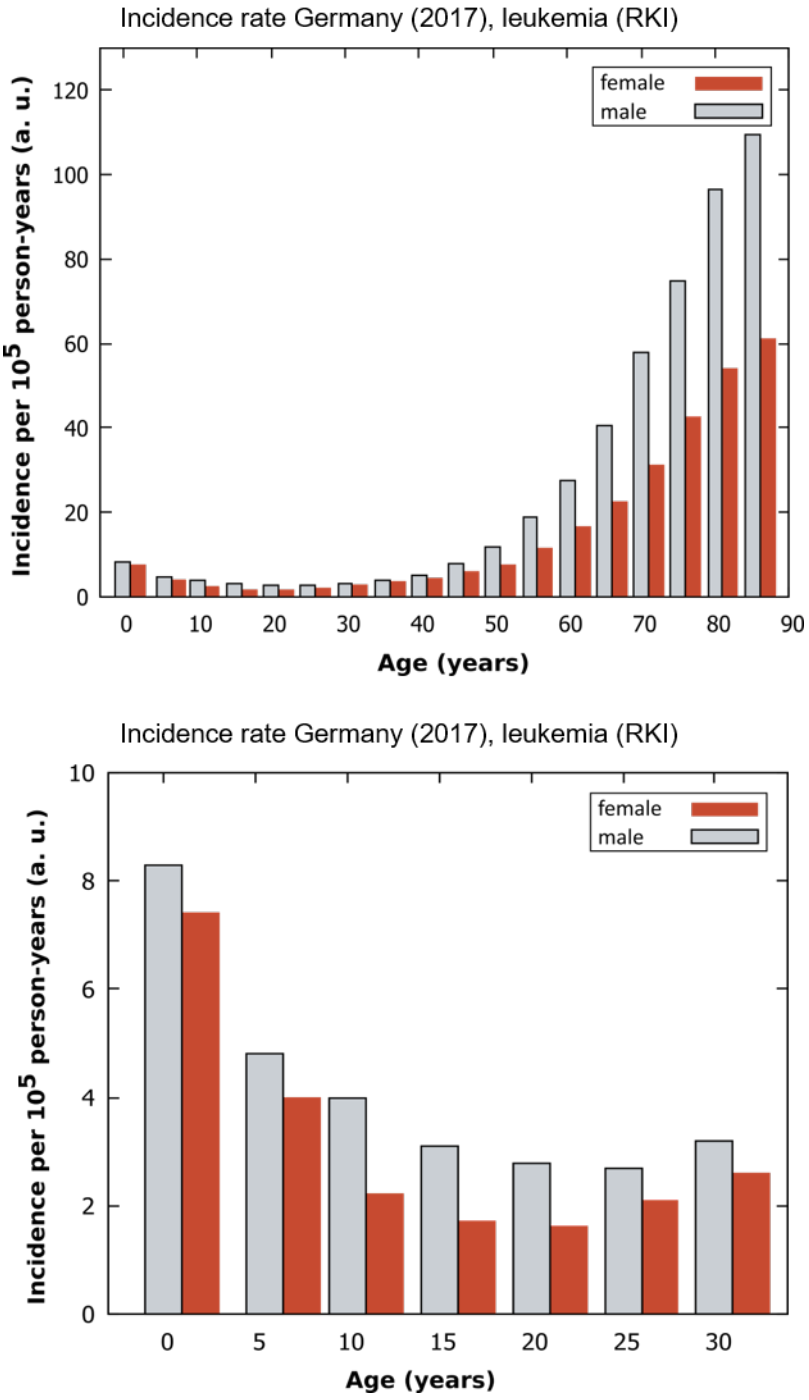


Figure A-1.2: Leukaemia (ICD-10: C91-C95)

A-1.3 Thyroid cancer

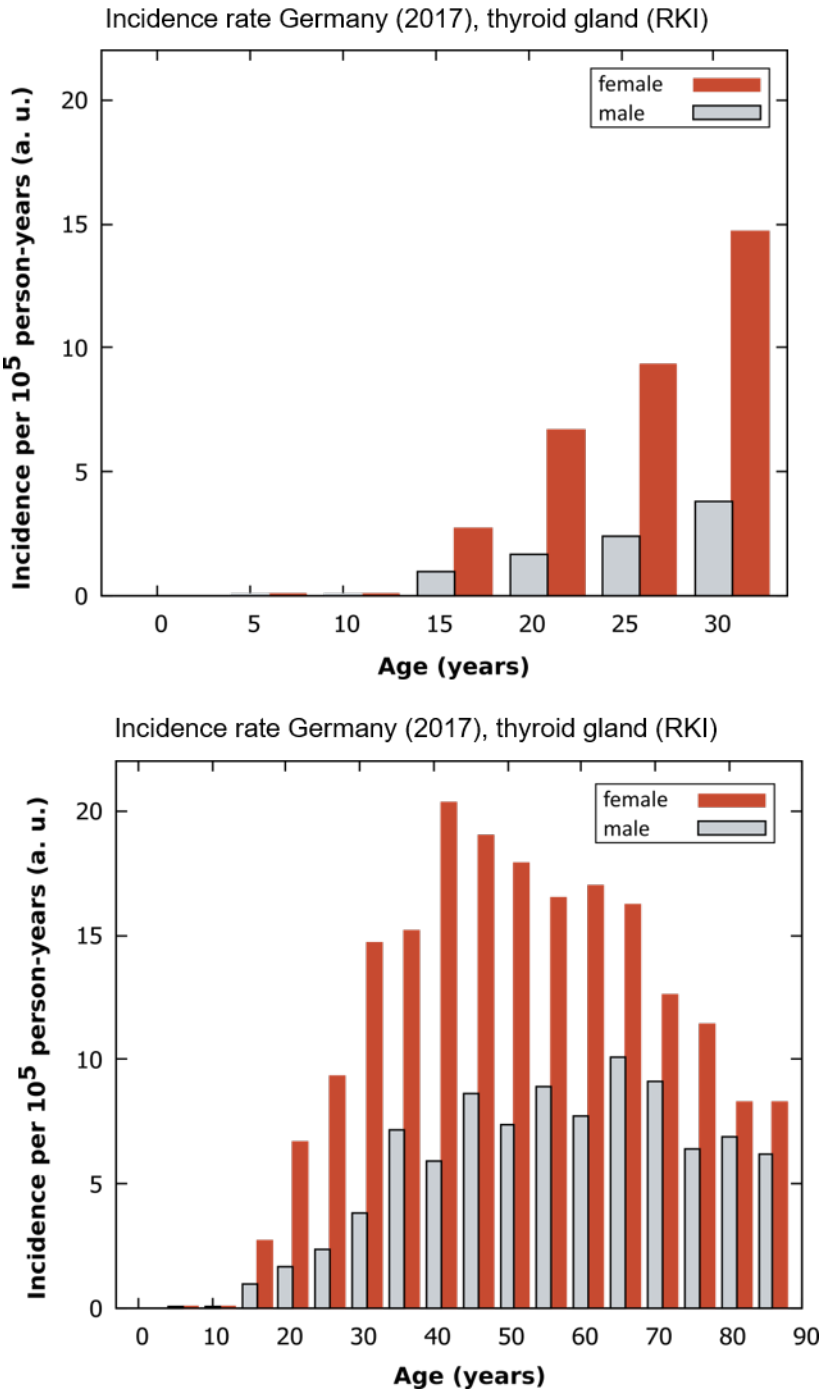


Figure A-1.3: Malignant neoplasm of thyroid gland (ICD-10: C73)

A-2 Population survival

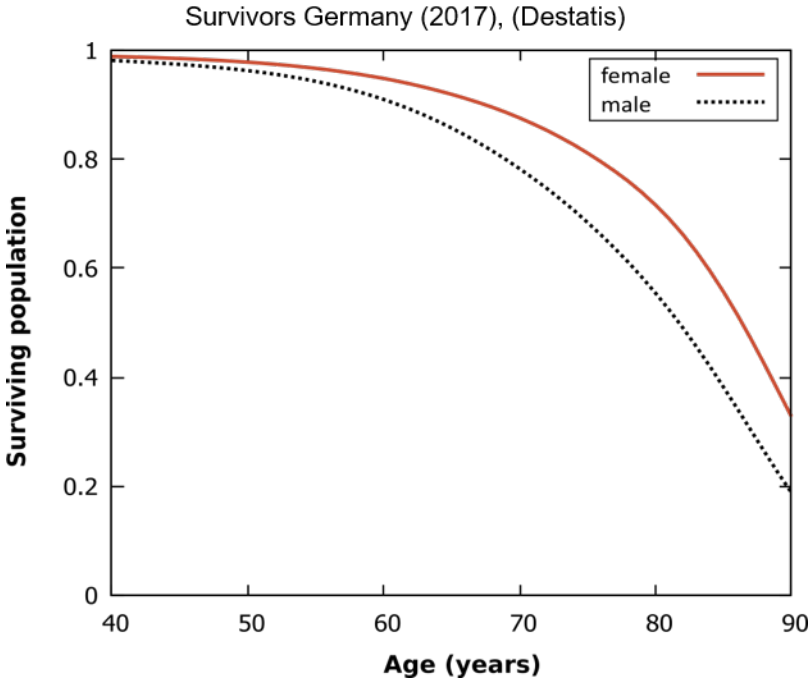


Figure A-2-1: Survival of the population in Germany in the year 2017. Data of the Federal Statistical Office of Germany (Destatis).

Annex B: Models for the excess relative risk per dose

B-1 Radiation exposure during childhood and adolescence and during adulthood

The described models for all malignant tumours, for leukaemia and for the thyroid are used both for exposure during childhood and adolescence and for exposure during adulthood.

B-1.1 Malignant tumours

The preferred model for the calculation of lifetime risks for all malignant tumours is the model MT_1, the model developed by (Grant et al. 2017) for the excess relative cancer rate, ERR, in the LSS with a linear dose-response relationship. The ERR is dependent on attained age and age at exposure. In addition, two comparison models of (Grant et al. 2017) for the excess relative cancer rate in the LSS are calculated. The model MT_2 is structurally similar to the model MT_1, but with a linear-quadratic dose-response relationship for men. The model MT_3 has a simple linear dose-response relationship and is not dependent on age. A latency period of five years is used.

Preferred model (MT_1):

The model MT_1 is dependent on the cumulative dose *d*, the age at exposure *e* and the attained age *a*, the index *s* characterises the sex (*m*: male, *f*: female):

$$\mathrm{ERR} = \beta_{1s} \cdot d \cdot \exp\left[\delta_{1s} \ln\left(\frac{a}{70}\right) + \delta_{2s} \frac{e-30}{10}\right].$$

$$\beta_{1f} = 0.60\ \mathrm{Gy}^{-1}$$
$$\beta_{1m} = 0.33\ \mathrm{Gy}^{-1}$$
$$\delta_{1f} = \delta_{1m} = -1.66$$
$$\delta_{2f} = \delta_{2m} = -0.236$$

Comparison model 1 (MT_2):

$$\mathrm{ERR} = (\beta_{1s} d + \beta_{2s} d^2) \cdot \exp\left[\delta_{1s} \ln\left(\frac{a}{70}\right) + \delta_{2s} \frac{e-30}{10}\right].$$

$$\beta_{1f} = 0.64\ \mathrm{Gy}^{-1}$$
$$\beta_{2f} = 0$$
$$\beta_{1m} = 0.094\ \mathrm{Gy}^{-1}$$
$$\beta_{2m} = 0.11\ \mathrm{Gy}^{-2}$$
$$\delta_{1f} = -1.36$$
$$\delta_{1m} = -2.70$$
$$\delta_{2f} = \delta_{2m} = -0.248$$

Comparison model 2 (MT_3):

$$\mathrm{ERR} = \begin{cases} 0.64 Gy^{-1} \cdot d(\mathrm{woman}) \\ 0.27 Gy^{-1} \cdot d(\mathrm{men}) \end{cases}$$

B-1.2 Leukaemia

The preferred model L_1 for the excess relative leukaemia risk is a model developed by (Hsu et al. 2013) for the excess relative leukaemia rate in the LSS with an explicit dependence on time

since exposure and attained age. The model has a linear-quadratic dose-response relationship. In addition, two comparison models of (Hsu et al. 2017) for the excess relative leukaemia rate in the LSS are calculated. The model L_2 is linear in the dose and dependent on age at exposure. The model L_3 has a simple linear dose-response relationship and is not dependent on age. For leukaemia, a latency period of two years is assumed.

Preferred model (L_1):

The preferred model L_1 is dependent on time since exposure *tse* and attained age *a*. Because the model very strongly depends on age below tse<5 years, but no epidemiological data exists in this range, the excess relative risk between 2<*tse*<5 years is kept constant at the ERR rate (*tse*=5). Below *tse*<2 years, the excess relative risk disappears due to the latency period.

$$\mathrm{ERR} = (\beta_1 \cdot d + \beta_2 \cdot d^2) \cdot \exp\left[\alpha \ln\left(\frac{a}{70}\right) + \gamma \ln\left(\frac{tse}{40}\right)\right]$$

$$\beta_1 = 0.79\ \mathrm{Gy}^{-1}$$

$$\beta_2 = 0.95\ \mathrm{Gy}^{-2}$$

$$\alpha = -1.09$$

$$\gamma = -0.81$$

Comparison model 1 (L_2):

$$\mathrm{ERR} = \beta \cdot d$$

Age at exposure (years)	β (Gy^{-1})
0–19	6.5
20–39	3.9
40+	4.0

Comparison model 2 (L_3):

$$\mathrm{ERR} = \beta \cdot d = 4.7 \cdot d$$

B-1.3 Thyroid cancer

The preferred model TH for the excess relative risk is the model developed by Furukawa et al. (2013) for the excess relative rate of thyroid cancer in the LSS with a linear dose-response relationship. The ERR is additionally dependent on attained age and age at exposure. A latency period of five years is assumed.

Preferred model (TH):

$$\mathrm{ERR} = \beta \cdot d \cdot (1 + \alpha \cdot m_s) \cdot \exp\left[\delta_1 \ln\left(\frac{a}{60}\right) + \delta_2 \frac{e - 10}{10}\right]$$

$$\beta = 1.28\ \mathrm{Gy}^{-1}$$

$$\alpha = 0.327$$

$$\delta_1 = -1.27$$

$$\delta_2 = -0.769$$

Here, $m_s = 1$ is for females and $m_s = -1$ for males[59].

[59] In (UNSCEAR 2019) the wrong plus/minus sign for sex dependency was used in the formula.

B-1 Radiation exposure in utero

For exposure in utero, two different models are used to estimate the risks in childhood and adolescence and the risks in adulthood. In both models, the risk coefficients apply both for malignant tumours and for leukaemia. A minimum latency period of five years for malignant tumours and of two years for leukaemia is assumed.

B-1.1 Risks during childhood and adolescence (0–17)

The preferred model for risks during childhood and adolescence following exposure in utero is the model U_1 with a linear dose-response relationship, which was considered by the SSK as being representative for the excess relative rate for cancer mortality, ERR (SSK 2008).

Preferred model (U_1):

$$\mathrm{ERR} = 40\ \mathrm{Gy}^{-1} \cdot d$$

B-1.2 Risks in adulthood (18–90)

The model U_2 for risks in adulthood is the model derived by (Sugiyama et al. 2021) for the excess relative mortality rate in the LSS. It is also linear in dose, but yields considerably lower risk coefficients. Seeing as the epidemiological data shows no evidence indicative of a risk, a zero risk was assumed for men.

Preferred model (U_2):

$$\mathrm{ERR} = \begin{cases} 1.84\ \mathrm{Gy}^{-1} \cdot d(\mathrm{women}) \\ 0(\mathrm{men}) \end{cases}$$

Annex C: Strategy of the literature search on cancer after exposure to ionising radiation during childhood

The starting point of the literature search was a search in the PubMed database using the criteria "childhood", "ionising radiation", "cancer" and "epidemiological study". The attempt to exclude studies in radiotherapy patients proved too restrictive. Furthermore, the UNSCEAR reports were included as they summarise – in varying degrees of detail – the current knowledge on diseases following radiation exposure during childhood.

Childhood	AND	**Cancer**	AND	**Ionising radiation**	AND	**Epidemiological study**
child [TI] OR childhood [TI] OR children [TI] OR paediatric [TI] OR pediatric [TI] OR young [TI] OR infancy [TI]		cancer OR tumour OR leukaemia OR Hodgkin OR myelodysplastic OR hemangioma		radiation [TI] OR irradiation [TI] OR CT [TI] OR tomography [TI] OR X-ray [TI] OR fluoroscopy [TI] OR radioiodine [TI]		odds ratio OR risk ratio OR relative risk OR hazard ratio OR ERR OR "case-control" OR cohort

Figure C-1: Literature search in PubMed

Table C-1: Review of the literature

	In-/exclusions
Literature search – initial hits	2,060
- excluded after reviewing the titles	-1,811
- excluded after reading abstracts	-138
- excluded after reading articles	-45
+ new citations in the reviewed literature	+18
Sum	**84**
of which pooled analyses	4
of which reviews	5
of which case control studies	11
of which cohort studies	64

The search on 3 September 2019 produced around 2,000 hits, with a review of the titles in the next step, followed by a review the respective abstracts, in an effort to identify studies containing information on the risk below several hundred milligrays, as well as review and meta-analyses. This was followed by a review of the literature citations of all retained studies for other possibly relevant literature. Pure modelling calculations on health risks as well as pure exposure determinations were not considered. Publications that did not contain any estimates per dose of ionising radiation for exposure during children are not suitable for an extrapolation of the lifetime risk. They were thus excluded from this review. Table C-2 contains a list of all publications that remained.

Table C-2: Case control studies

Lead author [Ref]	Country	Radiation exposure	Cases	Period of diagnosis	Health endpoint	# cases	# controls	Risk estimates
Cardis et al. 2005	Belarus and the Russian Federation	Iodine-131	< 15 at the time of the accident	01.01.1992 – 31.12.1998	Thyroid cancer	276	1300	
Zupunski et al. 2019	Belarus and the Russian Federation	Iodine-131	< 18 at the time of the accident	01.01.1992 – 31.12.1998	Thyroid cancer	298	1934	Update of Cardis 2005
Kopecky et al. 2006	Russia (Bryansk)	Iodine-131	0–19 years old at the time of the accident	26.04.1986 – 30.09.1998	Thyroid gland	66	132	
Noshchenko et al. 2010	Ukraine	external and internal radiation exposure	0–5 at the time of the accident	01.01.1987 – 31.12.1997	Leukaemia	246	492	
Kaletsch et al. 1999	Germany (Lower Saxony)	indoor radon	< 15 years	1988–1993	leukaemia and common solid tumours (nephroblastoma, neuroblastoma, rhabdomyosarcoma, central nervous system (CNS) tumours)	164	209	
Kendall et al. 2013	UK	background gamma radiation and radon		1980–2006	Leukaemia/other cancers (as a group)	27447	36793	
Nikkila et al. 2016	Finland	background gamma radiation	< 15 years	1990–2011	Leukaemia	1093	3279	
Nikkila et al. 2018	Finland	CT scans	< 15 years	1990–2011	Leukaemia	1093	3279	excess OR of 0.11 (95 % CI: 0.02–0.22) per mGy
Svahn-Tapper et al. 2006	Nordic countries	X-ray/gamma (radiotherapy)	Childhood cancer survivors	1960–1991	Malignant tumours	196	576	

Table C-2: Cohort studies

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
(Adams et al. 2010)	Adams et al. 2010	Radiat Res	USA	Radiotherapy: Thymus	Infants and children	1926–1957	X-ray	Thyroid cancer	Incidence	1953–2008		7490	857
(Berrington de González et al. 2016)	Berrington de Gonzàles et al. 2016	Br J Cancer	UK	Diagnostics: CT	< 22	1985–2002	CT scans	Leukaemia and CNS tumours	Incidence	1985–2008		176447	135
(Berrington de González et al. 2017)	Berrington de Gonzàles et al. 2017	Cancer Epidemiol Biomarkers Prev	UK	Diagnostics: CT	< 22	1985–2002	CT scans	Hodgkin's lymphoma	Incidence	1985–2008		178601	65
(Bhatti et al. 2010)	Bhatti et al. 2010	Radiat Res	USA	Radiotherapy: Childhood cancer (CCSS)	diagnosed < 21 years and had survived for at least 5 years	1970–1986	Radiotherapy	Thyroid cancer	Incidence	-2000		12547	119
(Boice, Jr. et al. 1991)	Boice Jr. et al. 1991	Radiat Res	USA	Diagnostics: TBC	TBC patients	1925–1954	X-ray	Breast cancer	Incidence	–01.01.1986		4940	234
(Davis et al. 1989)	Davis et al. 1989	Cancer Res	USA	Diagnostics: TBC	TBC patients	1925–1954	X-ray	Cancer (by type)	Mortality	–01.01.1986		20485	7735
(de Vathaire et al. 1993)	de Vathaire et al. 1993	Arch Intern Med	France + UK	Radiotherapy: Childhood cancer	Alive 3 years after solid cancer diagnosis before age 15 and before 1986	1947–1992	Radiotherapy	Thyroid cancer	Incidence	–01.01.1992 (France), –01.01.1991 (UK)		4400	57

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
(de Vathaire et al. 1999)	de Vathaire et al. 1999	Radiat Res	France (Institut Gustave Roussy)	Radiotherapy: Haemangioma			various	Thyroid nodules				396	
Del Risco Kollerud et al. 2014	Del Risco Kollerud et al. 2014	Br J Cancer	Norway, Oslo region	Resident population	0–15	1967–2009	Radon	Leukaemia and CNS tumours	Incidence	01.01.1967–31.12.2009		712674	864 CA / 437 leuk / 427 CNS
(Delongchamp et al. 1997)	Delongchamp et al. 1997	Radiat.Res.	Japan	Atomic bomb survivors	< 6	-	-	Cancer (by type)	Mortality	1950–1992			83
(Dondon et al. 2004)	Dondon et al. 2004	Radiother Oncol	France (Institut Gustave Roussy)	Radiotherapy: Haemangioma	< 15	1954–1973	Radiotherapy: Beta, gamma, X-ray	All cancers, other	Mortality	1969–1997		7037	16
(Doody et al. 2000)	Doody 2000	Spine (Phila Pa 1976)	USA	Diagnostics: Scoliosis	Female patients with scoliosis < 20	1912–1965	X-ray	Breast cancer	Mortality	-1997		5573	77
(Eidemüller et al. 2011)	Eidemüller et al. 2011	Radiat Prot Dosimetry	Sweden	Radiotherapy: Haemangioma	Women < 2	1920–1965	Radium-226	Breast cancer	Incidence	01.01.1958–31.12.2004		17158	678
(Evrard et al. 2006)	Evrard et al. 2006	Health Phys	France	Resident population	< 15	1990–2001	Indoor radon, terrestrial and cosmic gamma radiation	Leukaemia: ALL	Incidence				5330
(Furukawa et al. 2012)	Furukawa et al. 2012	Int J Cancer	Japan	Atomic bomb survivors	No cancer < 1958, with known	-	-	Thyroid cancer	Incidence	1958–2005		105401	

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
					vital status								
(Haddy et al. 2006)	Haddy et al. 2006	Eur.J.Cancer	France + UK	Radiotherapy: Childhood cancer	Survivors > 3 years after a malignant tumour	1947–1986	Radiotherapy	Leukaemia	Incidence	–1993 (France), –1991 (UK)		4204	11
(Haddy et al. 2009)	Haddy et al. 2009	Radiother Oncol	France (Institut Gustave Roussy)	Radiotherapy: Haemangioma	< 18 (63 % < 1)	1940–1973	Radiotherapy: Beta, gamma, X-ray	Thyroid cancer	Mortality	-2000		3795	9
(Hahn et al. 2001)	Hahn et al. 2001	Radiat Res	Germany	Diagnostics: Thyroid gland	< 18	1958–1978	Iodine-131/controls	Thyroid cancer	Incidence	-1986		2262+2711	
Hammer et al. 2009	Hammer et al. 2009	Radiat Res	Germany	Diagnostics: X-ray	Children < 15	1976–2003	X-ray	Cancer (by type)	Incidence	1980–2006		92957	
(Hauri et al. 2013)	Hauri et al. 2013	Environ Health Perspect	Switzerland	Resident population	< 16 on 5 December 2000	1985–2000	Radon	All cancers, leukaemia, ALL, CNS tumours	Incidence	2000–2008		-	997
(Hempelmann et al. 1967)	Hempelmann et al. 1967	J.Natl.Cancer Inst.	USA (New York)	Radiotherapy: Thymus	< 1	-1954	X-ray	Cancer (by type)	Incidence	-1965		7884	43
(Hempelmann et al. 1975)	Hempelmann et al. 1975	J.Natl.Cancer Inst.	USA (New York)	Radiotherapy: Thymus	< 1	-1954	X-ray	Cancer (by type)	Incidence	-1974		7883	66
(Hildreth et al. 1989)	Hildreth et al. 1989	N Engl J Med	USA (Monroe County, New York)	Radiotherapy: Thymus	Infancy, females	1926–1957	X-ray	Breast cancer	Incidence	1953–1985		3670	34
(Holmberg et al. 2002)	Holmberg al. 2002	Radiat Res	Sweden	Radiotherapy: Haemangioma	< 1.5 years	1920–1965	Radiation	Parathyroid adenoma	Incidence	1958–1997		27925	43
(Hsu et al. 2013)	Hsu et al. 2013	Radiat Res	Japan	Atomic bomb survivors	All ages	-	-	Leukaemia (by type)	Incidence	01.01.1950–31.12.2001		113011	

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
(Huang et al. 2014)	Huang et al. 2014	Br J Cancer	Taiwan	Diagnostics: CT	< 18	1998–2006	CT scans	All cancers, leukaemia, ALL, AML, CNS tumours	Incidence	1998–2008		24418	122
(Imaizumi et al. 2006)	Imaizumi et al. 2006	JAMA	Japan	Atomic bomb survivors	All ages	-	-	Thyroid nodules and autoimmune disorders	Incidence	2000–2003		4091	1833
(Ivanov et al. 2006)	Ivanov et al. 2006	Radiat Environ Biophys	Russia (Bryansk)	Accident: Chornobyl	0–17 years	-	Chornobyl	Thyroid cancer	Incidence	1991–2001		373827	199
(Iwanaga et al. 2011)	Iwanaga et al. 2011	J Clin Oncol	Japan	Atomic bomb survivors	All ages	-	-	Myelodysplastic syndromes	Incidence	1985 to 2004		86271	198
(Journy et al. 2016)	Journy et al. 2016	J Radiol Prot	France	Diagnostics: CT	Children	2000–2010	CT scans	Leukaemia and CNS tumours	Incidence	2000–2011		58620	39
(Kaiser and Walsh 2013)	Kaiser 2013	Radiat Environ Biophys	Japan	Atomic bomb survivors	All ages	-	-	Leukaemia	Mortality	1950–2003		86611	318
(Karlsson et al. 1998)	Karlsson et al. 1998	Radiat Res	Sweden (Gothenburg, Stockholm)	Radiotherapy: Haemangioma	< 1.5 years	1930–1965 and 1920–1959	Radium-226 (almost exclusively)	CNS tumours	Incidence	1958–1993		28008	86
(Kleinerman et al. 2005)	Kleinerman et al. 2005	J.Clin.Oncol.	USA	Radiotherapy: Retinoblastoma	< 8	1914–1984	X-ray (90 %)	Cancer (by type)	Incidence	-2000		1601	
(Krestinina et al. 2013)	Krestinina et al. 2013	Br J Cancer	Techa River Cohort	Techa River Cohort	Born < 1950 and resident 1950–1960		External gamma radiation, ingested radionuclides	Leukaemia other than CLL	Incidence	1953–2007		29730	72
(Lindberg et al. 1995)	Lindberg et al. 1995	Acta Oncol	Sweden (Gothenburg)	Radiotherapy: Haemangioma	< 1.5 years (95.5 %)	1930–1965	Radium-226	Cancer (by type)	Incidence	1958 to 1989		11807	248

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
(Little et al. 2014)	Little et al. 2014	PloS One	Ukraine	Accident: Chornobyl	< 18	-	Iodine-131	Thyroid cancer	Incidence	1996–2004		13127	45
(Little et al. 2015)	Little et al. 2015	PloS One	Belarus and the Russian Federation	Accident: Chornobyl	< 18	-	Iodine-131	Thyroid cancer	Incidence	1996–2004		11732	87
(Lubin et al. 2004)	Karlsson et al. 2004	Radiat Res	Israel	Radiotherapy: tinea capitis		Tinea capitis	X-ray	Thyroid cancer	Incidence				
(Lundell et al. 1994)	Lundell et al. 1994	Radiat Res	Sweden	Radiotherapy: Haemangioma	< 1	1920–1959	X-ray	Thyroid cancer	Incidence	1958–1986		14351	17
(Lundell and Holm 1996)	Lundell and Holm 1996	Radiat Res	Sweden (Radiumhemmet)	Radiotherapy: Haemangioma	< 18 months, haemangioma	1920–1959	Radium-226	Leukaemia	Incidence	1920–1986		14624	20
(Lundell et al. 1996)	Lundell et al. 1996	Radiat Res		Radiotherapy: Haemangioma	< 18 months, haemangioma	1920–1959	Radium-226	Breast cancer	Incidence	1920–1986		9675	75
(Mathews et al. 2013)	Mathews et al. 2013	BMJ	Australia	Diagnostics: CT	< 20	Born 1985–2005	CT scans	Cancer (by type)	Incidence	1985–2007		680221	3150
(Mattsson et al. 1993)	Mattsson et al. 1993	J Natl Cancer Inst	Sweden	Radiotherapy: benign breast disease	Women of all ages	1925–1954	X-ray	Breast cancer	Mortality	-1985		3090	198
(McLaughlin et al. 1993)	McLaughlin et al. 1993		Toronto, Canada	Diagnostics: Fluoroscopy	< 19	1950 and 1965	X-ray	Cancer (by type)	Incidence	-1986			13
(Meulepas et al. 2019)	Meulepas et al. 2019	J Natl Cancer Inst	Netherlands	Diagnostics: CT	< 18	1979–2019	CT scans	Cancer (by type)	Incidence	-2014		168394	84
(Mihailescu et al. 2002)	Mihailescu et al. 2002	J Clin Endocrinol Metab	USA	Radiotherapy: various benign conditions	< 16	1939–1962	X-ray	Head and neck tumours	Incidence	-2000		4296	615
(Modan et al. 2000)	Modan et al. 2000	Int J Epidemiol	Israel	Diagnostics: Fluoroscopy	< 18	1950–1970	X-ray	Cancer (by type)	Incidence	-1996		674	11

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
(Pearce et al. ss2012)	Pearce et al. 2012	Lancet	UK	Diagnostics: CT	< 22	1985–2002	CT scans	Leukaemia and CNS tumours	Incidence	1985–2008		178604	74+135
(Pottern et al. 1990)	Pottern et al. 1990	J Clin Epidemiol	USA	Radiotherapy: lymphoid hyperplasia	< 18	1938–1969	X-ray	Thyroid nodules	Incidence	-1969		2258	?
(Preston et al. 1994)	Preston et al. 1994	Radiat.Res.	Japan	Atomic bomb survivors	All ages	-	-	Leukaemia, lymphoma and myeloma	Incidence	-1987			501
(Preston et al. 2004)	Preston et al. 2004	Radiat.Res.	Japan	Atomic bomb survivors	LSS	-	-	Cancer (by type)	Mortality	-2000			
(Preston et al. 2007)	Preston et al. 2007	Radiat Res	Japan	Atomic bomb survivors	All ages	-	-	Malignant tumours	Incidence	1958–1998		111952	17448
(Preston et al. 2008)	Preston et al. 2008	J Natl Cancer Inst	Japan	Atomic bomb survivors	In utero or < 6	-	-	Malignant tumours	Incidence	– 31.12.1999		2452+15388	94+649
(Ron und Modan 1980)	Ron and Modan 1980	J.Natl.Cancer Inst.	Israel	Radiotherapy: tinea capitis	< 18	1948–1960	X-ray	Thyroid cancer	Incidence	1950–1974		10842	32
(Ron et al. 1989)	Ron et al. 1989	Radiat.Res.	Israel	Radiotherapy: tinea capitis	< 18	1948–1960	X-ray	Thyroid cancer	Incidence	1950–1986		10834	98
(Ronckers et al. 2001)	Ronckers et al. 2001	J.Natl.Cancer Inst.	Netherlands	Radiotherapy: eustachian tube dysfunction	18	1945–1965	Radium	Cancer (by type)	Mortality	– 15.09.1997		5392	96
(Ronckers et al. 2010)	Ronckers et al. 2010	Radiat Res	USA	Diagnostics: Scoliosis	Women < 20	1912–1965	X-ray	Cancer (by type)	Incidence	– 31.12.2004		5573	355
(Sadetzki et al. 2005)	Sadetzki et al. 2005	Radiat Res	Israel	Radiotherapy: tinea capitis	< 18	1950s	X-ray	Brain tumours (by type)	Incidence	– 31.12.2002		10834	21668
(Sadetzki et al. 2006)	Sadetzki et al. 2006	J Clin Endocrinol Metab	Israel	Radiotherapy: tinea capitis	< 18	1950s	X-ray	Thyroid cancer	Incidence	– 31.12.2002		10834	21668
(Schneider et al. 1993)	Schneider et al. 1993	J.Clin.Endocrinol.Metab	USA (Chicago)	Radiotherapy: Head and neck region (benign)	< 18	1939–1962	X-ray	Thyroid cancer	Incidence	1990		5300	309

RefMan_ ID	Lead author, year	Journal	Country	Category	Cohort	Period of exposure	Radiation exposure	Health endpoint	Inc./ mort.	Follow-up	Recording of exposure	# N	# cases
(Shore et al. 1985)	Shore et al. 1985	J.Natl.Cancer Inst.	USA (New York) / Hempelmann	Radiotherapy: Thymus	< 1		X-ray	Thyroid cancer and nodules	Incidence	?		7884	30
(Shore et al. 1993)	Shore et al. 1993	Am.J.Epidemiol.	USA (New York) / Hempelmann	Radiotherapy: Thymus	< 1		X-ray	Thyroid gland	Incidence	1986		7490	37
(Shore et al. 2003)	Shore et al. 2003	Health Phys.	USA (New York)	Radiotherapy: tinea capitis	< 16	1940–1959	X-ray	Cancer (by type)	Incidence	1993		3604	
(Smoll et al. 2016)	Smoll 2016	Cancer Epidemiol	Japan	Atomic bomb survivors	All ages	-	-	Brain tumours	Incidence	1958–1998		105427	281
(Spycher et al. 2015)	Spycher et al. 2015	Environ Health Perspect	Switzerland	Resident population	< 16	1990–2000	Background gamma	Cancer (by type)	Incidence	-2008		2093660	1782
(Thompson et al. 1994)	Thompson et al. 1994	Radiat Res	Japan	Atomic bomb survivors	All ages	-	-	Malignant tumours	Incidence	1958–1987		79972	8613
(Tucker et al. 1991)	Tucker et al. 1991	Cancer Res	USA	Radiotherapy: Childhood cancer	< 18 and survived 2 years	1955–1986	Radiotherapy	Thyroid cancer	Incidence			9170	23
(Walsh and Kaiser 2011)	Walsh 2011	Radiat Environ Biophys	Japan	Atomic bomb survivors	< 25 years	-	-	Leukaemia	Mortality	1950–2000		86611	296
(Zablotska et al. 2011)	Zablotska et al. 2011	Br J Cancer	Belarus	Accident: Chornobyl	< 18	-	Iodine-131	Thyroid cancer	Incidence	-2004		38543	87
(Zablotska et al. 2014)	Zablotska et al. 2014	Am J Epidemiol	Canada (Canadian Fluoroscopy Cohort Study)	Diagnostics: TBC	TBC patients	1930–1952	X-ray	Malignant tumours, ischaemic heart disease	Mortality	01.01.1950–31.12.1987		63707	9505

Abbreviations

ABDI Nagasaki University Atomic Bomb Disease Institute

ADR Accord européen relatif au transport international des marchandises dangereuses par route (*European Agreement concerning the International Carriage of Dangerous Goods by Road*)

AGS Committee on Hazardous Substances (German: *Ausschuss für Gefahrstoffe*)

ALARA As Low As Reasonably Achievable

ALL Acute Lymphocytic Leukaemia

AML Acute Myeloid Leukaemia

AOPs Adverse outcome pathways

AVV General Administrative Provision (German: *Allgemeine Verwaltungsvorschrift*)

BaP Benzo[*a*]pyrene

BAT Biological tolerance for working materials (German: *Biologischer Arbeitsstoff-Toleranz*)

BfS Federal Office for Radiation Protection (German: *Bundesamt für Strahlenschutz*)

BMD Benchmark dose

$BMDL_{10}$ Benchmark dose lower bound

BMU Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (German: *Bundesministerium für Umwelt, Naturschutz und nukleare Sicherheit*)

BPDE *syn*- and *anti*-Benzo[*a*]pyrene-7,8-dihydrodiol-9,10-epoxide

Bq Becquerel

CLL Chronic Lymphocytic Leukaemia

CML Chronic Myeloid Leukaemia

CNS tumour Central nervous system tumour

D Absorbed dose

DDR DNA damage response

DDREF Dose and dose-rate effectiveness factor

DFG German Research Foundation (German: *Deutsche Forschungsgemeinschaft*)

DMA Dimethylarsinic acid

DMAA 1,3-dimethylamylamine

DNA Deoxyribonucleic acid

DSB Double-strand breaks

E Effective dose

EAR Excess absolute rate, frequently termed “excess absolute risk” in the literature

EFSA European Food Safety Authority

EOR	Excess odds ratio
EPA	United States Environmental Protection Agency
ERB	Exposure-risk relationships (German: *Expositions-Risikobeziehungen*)
ERR	Excess relative rate
GefStoffV	Germany Hazardous Substances Ordinance (German: *Gefahrstoffverordnung*)
Gy	Gray
H	Equivalent dose
HL	Hodgkin's lymphoma
IAEA	International Atomic Energy Agency
IARC	International Agency for Research on Cancer
ICD	International Statistical Classification of Diseases and Related Health Problems (*Internationale statistische Klassifikation der Krankheiten und verwandter Gesundheitsprobleme*)
ICR	International Congress of Radiology
ICRP	International Commission on Radiological Protection
ICRU	International Commission on Radiation Units and Measurements
ILO	International Labour Organization
IMIS	Integrated Measuring and Information System for the Surveillance of Environmental Radioactivity
KE	Key events
KKI	Isar Nuclear Power Plant (German: *Kernkraftwerk Isar*)
LAR	Lifetime Attributable Risk
LET	Linear Energy Transfer
LNT model	Linear no-threshold model
LSA	Low specific activity
LSS	Life Span Study
MAK	Maximum workspace concentrations (German: *Maximale Arbeitsplatz-Konzentration*)
MDS	Myelodysplastic syndrome
MIE	Molecular initiating event
MM	Multiple myeloma
MMA	Monomethylarsonic acid
MMAA	Monomethylarsonous acid
MoA	Mode of action
MOE	Margin of Exposure
NCI	National Cancer Institute
NCRP	National Council on Radiation Protection and Measurements

NHL Non-Hodgkin's Lymphoma

NOAEL No observed adverse effect level

NORM Naturally occurring radioactive material

OSCC Oxford Survey of Childhood Cancer

PAH Polycyclic aromatic hydrocarbons

PARP-1 Poly(ADP-ribose) polymerase 1

RERF Radiation Effects Research Foundation

RNA Ribonucleic acid

RR Relative incidence rates

SCO Surface contaminated objects

SKLM Permanent Senate Commission of the DFG for the Investigation of Health Hazards of Chemical Compounds in the Work Area and on Food Safety (German: *Ständige Senatskommissionen der DFG zur Prüfung gesundheitsschädlicher Arbeitsstoffe (MAK) und zur Gesundheitlichen Bewertung von Lebensmitteln*)

SSK Commission on Radiological Protection (German: *Strahlenschutzkommission*)

StrlSchG Radiation Protection Act (German: *Strahlenschutzgesetz*)

StrlSchV Radiation Protection Ordinance (German: *Strahlenschutzverordnung*)

Sv Sievert

TDI Tolerable daily intake

TH Thyroid gland

TME Tumor microenvironment

TRGS Technical Rules for Hazardous Substances (German: *Technische Regeln für Gefahrstoffe*)

TRK Technical reference concentrations (German: *Technische Richtkonzentrationen*)

TSE Time since exposure

TTC Threshold of toxicological concern

UNSCEAR United Nations Scientific Committee on the Effects of Atomic Radiation

WHO World Health Organization

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