8 The chemical toxicity of uranium

8.1 Introduction

The chemical toxicity of a given elemental compound is related to the interaction of the compound with the biochemical processes of the human body. Some of these interactions may be beneficial or even essential, whereas others may be detrimental. For example, metal ions may interact in a positive or negative way with important functional sites of enzymes. Others may compete with essential metals for uptake or incorporation into proteins. Often the mechanisms of these effects are poorly understood particularly where different species of the same metal are likely to exist in different environments within the body across a wide variety of spatial and temporal scales. The chemical action of all isotopes and isotopic mixtures of uranium are identical, and independent of the specific activity, because chemical action depends only on chemical properties. Thus the chemical toxicity of natural, depleted, and enriched uranium are identical (ATSDR, 1999). The health effects from exposure to uranium have been recently reviewed (WHO, 1998a and b; ATSDR, 1999; Fulco et al., 2000, Durakovic`, 1999).

In the 1990s, the subjective symptoms and signs of disease among Gulf War veterans have been extensively studied, and the role of exposure to uranium as a possible underlying causative agent has been explored (Fulco et al., 2000; Harley et al., 1999b; CHPPM, 2000; Durakovic`, 1999).

The health risks caused by chemical effects of uranium exposure, that is effects not related to ionizing radiation, can be assessed using the IPCS guidelines for derivation of guidance values for health-based exposure limits (WHO, 1994), which are the basis of the risk estimates in the IPCS Environmental Health Criteria Document and Concise International Chemical Assessment Document series.

Tolerable intake (TI: usually expressed as mg/kg of body weight per day) in these guidelines is defined as ‘an estimate of the intake of a substance which can occur over a lifetime without appreciable health risk’. For chemicals like uranium, for which it is likely that a threshold below which no adverse health effect will occur, the approach used is based on a perceived No Observed Adverse Effect Level (NOAEL) or Lowest Observed no Adverse Effect Level (LOAEL) and uncertainty factors (UF).

The NOAEL is defined (WHO, 1994) ‘as the greatest concentration or amount of a substance, which causes no detectable adverse alteration of morphology, functional capacity, growth, development or life span of the target organism under defined conditions of exposure. Alterations of morphology, functional capacity, growth, development or life span of the target may be detected which are judged not to be adverse’.

In order to derive a tolerable intake from a NOAEL, the NOAEL is divided by an uncertainty factor, which is (WHO, 1994) ‘a product of several single factors by which the NOAEL or LOAEL of the critical effect is divided to derive a TI. These factors account for adequacy of the pivotal study, interspecies extrapolation, inter-individual variability in humans, adequacy of the overall database, and nature of toxicity’.

Components of the applied total uncertainty factor are based on ‘best judgement’ from available data; when no adequate data exist for a specific factor, a default value is used. For example, for the extrapolation between species, the default uncertainty factor is 10,

which is composed of factors of 4.0 for toxico-kinetic and 2.5 for toxico-dynamic uncertainties. Similarly in the assessment of uncertainties associated with extrapolation between various human sub-populations (comprising all age groups, and healthy as well as sick people) a default inter-individual human uncertainty factor of 10 has been recommended (WHO, 1994). Combination of these factors leads to a total default uncertainty factor of 100. Other uncertainty factors may be applied to account for inadequacies in the database and/or critical study (WHO, 1994).

The consideration of uncertainty factors described above relates primarily to exposure of a general population. While similar principals may be used to estimate tolerable daily intakes for occupational exposure this has not gained general acceptance (WHO, 1994). Two reasons for this are:

(i) that the more vulnerable members of the human population (children, the sick and the elderly) do not form part of the generally exposed occupational population.

(ii) that workplace exposures can be controlled and monitored.

Methodologies for deriving occupational exposure limits for uranium and DU are presented separately in Chapter 10 and in Annex 5.

8.2 Toxicity in experimental animals and humans

8.2.1 Experimental animals

Inhalation

The dose response behaviour of a specific inhaled substance is highly dependent on the particle size distribution and chemical nature of a given inhalation experiment. While some useful data in this respect is given in the early literature, in almost all cases a significant amount of such contextual data relating to the conditions of the exposure are lacking. Because of these factors it is difficult in the case of inhalation to interpret LOAEL and NOAEL data solely from the quantities and chemical form of inhaled material. Because of this, supplementary data giving concentrations for a specific target organ is especially useful when deriving a LOAEL or NOAEL for that particular organ. Such data is tabulated later in this Chapter for the kidney in animal experiments.

Pulmonary toxicity of uranium varies among species and is dependent on the chemical form of uranium (Tannenbaum et al., 1951). Mortality can be induced in rats and guinea pigs at high concentrations of uranium hexafluoride (about 26 to 35 mg U/m^3). The cause of acute death is apparently irritative damage to the respiratory tract and this is probably due not to uranium but to hydrofluoric acid, a hydrolysis product of uranium hexafluoride (Spiegel, 1949; Leach et al., 1984) although mortality may be due to kidney effects. Pulmonary edema, haemorrhages, inflammation and emphysema were also observed in rats, mice and guinea pigs after 30 days exposure to 13 mg U/m^3 as uranium hexafluoride (Spiegel, 1949).

Slight degenerative changes in lung histology were observed in rats and dogs exposed to uranium trioxide and dogs exposed to uranyl nitrate hexahydrate at exposure levels of approx. 10 mg U/m^3 for 4 to 5 weeks, but not after similar exposure to uranium dioxide or triuranium octaoxide (Roberts 1949; Rothstein 1949; Dygert 1949).

Rabbits are sensitive to uranium-induced pulmonary damage: pulmonary edema and haemorrhages were reported after exposure to ammonium diuranate, uranium peroxide, uranium trioxide, and carnotite, but not after exposure to uranium dioxide (Dygert, 1949; Rothstein, 1949; Pozzani, 1949).

In long-term studies, with exposure up to one year with several animal species (rats, rabbits, guinea pigs, hamsters and dogs) and various uranium compounds (soluble and insoluble), no signs of pulmonary changes were observed in a concentration range of 0.05 to 10 mg U/m^3 (Cross et al., 1981a, 1981b). Chronic exposure of rats, dogs and monkeys to 5 mg U/m^3 for 1 to 5 years, as uranium dioxide did not reveal histological changes in the lung nor damage to the kidneys. A post-exposure follow-up study showed slight interstitial and vascular fibrosis in dogs and some pulmonary fibrosis in monkeys (Leach et al., 1970, 1973). However, investigators stated that radiation rather than chemical toxicity was believed to have caused the injuries noted.

Renal effects can be produced in animals after acute-duration and intermediate-duration inhalation exposures to uranium. A 10-minute exposure to 675 mg U/m^3 as uranium hexafluoride produced severe degeneration of the cortical tubules 5 to 8 days later in rats (Spiegel, 1949). These same effects were observed in dogs 1 to 3 days after a 1-hour exposure to 250 mg U/m^3 as uranyl fluoride (Morrow et al., 1982). Proteinuria and glucosuria were also observed in rats after 2 to 10-minute exposures to uranium hexafluoride (Leach et al., 1984).

In intermediate-duration studies with guinea pigs, mice, rats, cats, rabbits, and dogs, inhalation exposures to a variety of uranium compounds were damaging to the kidneys. The effects were compound-dependent and concentration-dependent and ranged from minimal microscopic lesions in tubular epithelium (for low concentrations) to severe necrosis of the tubular epithelium (for high concentrations) in several species (Dygert, 1949; Pozzani, 1949; Roberts, 1949; Rothermel, 1949; Spiegel, 1949; Stokinger et al., 1953). In one of these studies, mice were exposed to uranium tetrachloride dust for 30-days. The exposure resulted in severe degeneration and necrosis of the renal-cortical tubular epithelium, and mortality, in the 11 mg U/m^3 group by the third day. At the end of the study, moderate tubular degeneration was observed in the 2.1 mg U/m^3 group and minimal degeneration in the 0.1 mg U/m^3 group.

The nephrotoxic effects of uranium in animals may include damage to the glomerulus as evidenced by histopathological signs in the kidneys of rats and rabbits exposed to 15.4 mg U/m^3 as uranium dioxide for 23 days (Dygert, 1949) and dogs exposed to 15 mg U/m^3 as uranyl fluoride for five weeks and to 16 mg U/m^3 as uranium trioxide for four weeks (Rothstein, 1949).
In long-term inhalation studies with rats and dogs, soluble and insoluble uranium exposures as low as 0.05 mg U/m^3 and as high as 10 mg U/m^3 for 1 to 5 years were damaging to the kidneys. Nephrotoxic effects found in these animals ranged from minimal microscopic lesion in tubular epithelium (for low concentrations) to acute tubular necrosis (for high concentrations) (Leach et al., 1970; Stokinger et al., 1953). For further comments on issues regarding inhalation toxicity, its incorporation into ICRP methodologies and occupational exposure standards see Annex 5.

Oral

The derivation of dose response data from ingestion is less dependent on experimental conditions and toxio-kinetics than that derived from inhalation. Making the commonly

used derivation of TDI values directly from concentrations of ingested material less subject to uncertainty.

The oral toxicity of uranium compounds has been evaluated in several animal species. Oral LD_{50} (dose producing 50% mortality rate) values of 114 and 136 mg U/kg have been estimated for rats and mice, respectively, following single gavage administrations of uranyl acetate dihydrate (Domingo et al., 1987).

Rats exposed to a single average dose of 5.6 mg U/kg suffered slight renal dysfunction and minimal microscopic lesions in the tubular epithelium (Domingo et al., 1987, 1989a). In intermediate-duration animal studies, exposure to uranium (uranyl fluoride, triuranium octaoxide, uranyl nitrate hexahydrate, uranium tetrachloride, uranium peroxide, ammonium diuranate) at oral doses as low as 0.05 mg U/kg/day and as high as 7858 mg U/kg/day for 30 days were damaging to the kidneys. Nephrotoxic effects found in these animals ranged from minimal microscopic lesions in the tubular epithelium (for low doses) to extensive necrosis in the tubular epithelium (for high doses of soluble compounds) (Maynard and Hodge, 1949).

Rats exposed to uranium as uranyl nitrate in drinking water for 91 days were found to have renal lesions of the tubules, glomeruli, and interstitium observed in the lowest exposure groups (males 0.06 mg U/kg/day; females 0.09 mg U/kg/day) (Gilman et al., 1998a). The studies by McDonald-Taylor et al. (1992, 1997) produced similar renal lesions (thickened glomelular basement membrane) in rabbits.

For various endpoints and animal species ATSDR reported minimal effect levels in the range of 1 to 10 mg/kg of body weight per day (ATSDR, 1999). For example Ortega, (1989) observed adverse effects with rats at exposure levels, via ingestion, of 1.1 mg/kg per day. For cattle and sheep Puls (1990) reported that minimal effects are associated with a daily uranium intake of 400 or 50 mg U, respectively (corresponding to 1mg U/kg of body weight for both species).

For rabbits exposed to uranium as uranyl nitrate in drinking water for 91 days, dose-dependent histopathological changes were primarily limited to the kidney. Dose-dependent differences consisted of histopathological changes limited primarily to kidney; changes were more pronounced in male rabbits (Gilman et al., 1998b). In another study, male New Zealand rabbits were exposed to uranium as uranyl nitrate in drinking water for 91 days, and were then allowed to recover for several weeks (Gilman et al., 1998c). The lowest-observed-adverse-effect-levels (LOAELs) in these studies were 0.05 mg U/kg/day for non-Pasteurella free rabbits and 0.49 mg U/kg/day for Pasteurella free rabbits. While not being essential for deriving a tolerable intake, data relating to the concentration of uranium in kidney and bone is useful for linking LOAELs to organ-specific data produced from biokinetic models, commonly used for assessing radiological and chemical effects in radiological protection (e.g. Spoor and Hursh, 1973; also see Chapters 10, 12 and Annex 5). This data is summarized from the recent studies by Gilman et al. (1998a, 1998b, 1998c) in Table 8.1.

Table 8.1 Kidney and bone concentrations observed in experiments performed by Gilman et al., during the 1990s.

Study	SEX/Type	LOAEL mg U/kg body wt / day	Kidney µg/g	Bone µg/g
1	M Rat	0.060	<0.2	<1.78
	F Rat	0.090	<0.2	<1.78
2	M Rabbit	0.050	0.04 ± 0.03	0.09 ± 0.05
	F Rabbit	0.490	0.019 ± 0.01	0.053 ± 0.004
3	M Rabbit	<1.360	0.18 ± 0.13	0.20 ± 0.05
	F Rabbit	<1.360	0.18 ± 0.13	0.20 ± 0.05

1 Gilman et al. (1998a) 91 day experiment Sprague-Dawley Rat
2 Gilman et al. (1998b) 91 day experiment New Zealand White Rabbits (Specific Pathogen Free (SPF) derived)
3 Gilman et al. (1998c) 91 day experiment New Zealand White Rabbits (SPF)

The pathogenesis of the kidney damage in animals indicates that regeneration of tubular epithelium occurs in survivors upon discontinuation of exposure to uranium (Bentley et al., 1985; Dygert, 1949; Maynard and Hodge, 1949; Pozzani, 1949; Rothemel, 1949; Rothstein, 1949; Spiegel, 1949; Stokinger et al., 1953).

Leggett (1989) cites that tolerance may develop following repeated exposure to uranium, but this tolerance does not prevent chronic damage to the kidney, as the regenerated cells are quite different. Persistent changes in the proximal tubules of rabbits have been reported to be associated with the kidney's ability to store uranium (McDonald-Taylor et al., 1997). In another study Gilman et al. (1998c) describes a recovery study performed on New Zealand White Rabbits exposed to uranium nitrate (24 or 600 mg/l corresponding to 1.4 mg U/kg body wt/day and 41 mg U/kg body wt/day respectively) for 91 days. Renal tubular injury with degenerative nuclear changes, cytoplasmic vacuolation, and tubular dilation were seen in the high dose group without consistent resolution even after 91 days. Kidney concentrations observed in the high exposure group decreased from 3.48 ± 1.54 to 0.02 ± 0.01 µg/g over the 91 day recovery period in an exponential manner.

Reproductive and developmental toxicity In several studies with mice given soluble uranium compounds (uranyl nitrate hexahydrate, uranyl acetate dihydrate), the teratogenic, embryotoxic and reproductive effects of uranium have been studied (Domingo, 1989a,1989b). Exposure-related fetotoxicity, reduced fetal body weights, external and internal malformations, increased incidence of developmental variations, and decreased fertility were observed. In rats, unspecified degenerative changes in the testes have been reported following chronic administration of uranyl nitrate hexahydrate and uranyl fluoride in the diet (Maynard and Hodge, 1949; Maynard et al., 1953; Malenchenko et al., 1978).

Carcinogenicity Although bone cancer has been induced in experimental animals by injection or inhalation of soluble compounds of high-specific-activity uranium isotopes or mixtures of uranium isotopes, no carcinogenic effects have been reported in animals ingesting soluble or insoluble uranium compounds (Wrenn et al., 1985). However, given the nature of ionizing radiation damage to DNA, retention of any radioactive material in the body will have associated an increase in the probability of cancer; albeit small and depending on the radiation dose.

8.2.2 Implanted depleted uranium fragments

The chronic long-term health consequences of exposure to depleted uranium (DU) fragments have been addressed by Benson and Schnieder (1998) and Pellmar et al. (1999a).

Pellmar et al. (1999a) undertook studies in rats surgically implanted with sterilized DU and/or Tantalum pellets (see Chapter 7). The results of these studies concluded that in a rat animal model, uranium could accumulate within the central nervous system and testicles. A follow-up study by the same group (Pellmar et al., 1999b) assessed the potential for electrophysiological changes in the hippocampus of rats implanted with DU fragments. At 12 months, the amplitudes of synaptic potentials were significantly greater in tissues derived from high-dose DU-implanted rats compared with controls. But, in the same animal model, uranium did not affect locomotive activity, discrimination learning, or the results of a battery of general functional measures (Pellmar et al., 1997), which makes it difficult to interpret the significance of uranium accumulation in the brain. No nephrotoxicity was observed in these animals or in studies of kidney function performed in female rats implanted with depleted uranium pellets for a period of 84 days (Benson and Schneider, 1998). These observations are markedly inconsistent with observations made on rats and other mammals in which exposure to uranium occurred through oral ingestion (e.g. those discussed in 8.2.1 above).

8.2.3 Dermal absorption

Soluble uranium compounds such as nitrate can be absorbed through the skin (Orcutt, 1949; DeRey et al., 1983, 1984). In studies with rabbits, death due to renal failure was observed to occur via this mode of exposure with a lowest LD_{50} value of 28 mg U/kg as uranyl nitrate in an ethereal solution (Orcutt, 1949). Rats and guinea pigs were observed to be significantly less sensitive. In the specific case of acute exposure of animals to uranyl nitrate, penetration into the intracellular space between the granular and horny layers of the skin was observed to occur within a period of 15 minutes; after 48 hours no residual uranium was observed in the skin (DeRey et al., 1983). These authors considered this to be due to absorption of uranium into the systemic circulation resulting in weight loss and, in severe cases, death. More recent studies of sub-acute dermal exposure to uranyl nitrate (typical applied concentrations 0.6 g/ml uranyl hexahydrate to skin areas of between 0.5 and 16 cm^2) by Lopez et al. (2000) confirm the observations of earlier studies of acute exposure. In these studies histological alterations of the kidney that increased in severity with the magnitude of exposure were noted along with a dose-dependent reduction in bone volume and bone alteration. Parameters describing dermal absorption coefficients for various compounds have not been reported although studies indicating changes in skin permeability with exposure to uranium (thereby favouring the entry of uranium into the body) have been reported. For example Ubios et al. (1997) have determined that application of acute levels of soluble uranium compounds (i.e. 0.012 g U/day) to the skin can significantly reduce the thickness of the epidermis (41 ± 14 to 21 ± 10 µm). Such thinning of the epidermis was also observed to be present 60 days after the cessation of a 31 day, daily application regime. Results of these tests were considered by the authors to be due to the chemical rather than radiological effects of U.

8.2.4 Humans

Inhalation

Inhalation of dusts of various uranium compounds will have different chemical toxicity depending mainly on the biological solubility and chemical reactiveness with body tissues.

Despite evidence indicating lethal effects of uranium to various animals (including rabbits, which appear to be particularly sensitive to the toxic effects of uranium), epidemiological studies indicate that routine exposure to airborne uranium is not associated with increased mortality (ASTDR, 1999). Brief accidental exposure to high concentrations of uranium hexafluoride has caused acute respiratory illness, which may be fatal. However, this is most likely to be due to the hydrogen fluoride liberated from uranium hexafluoride upon hydrolysis.

In studies on uranium miners and those mining other ores (e.g. tin and iron), an increased risk of lung cancer has been attributed mainly to exposure to radon decay products (see Chapter 9.4). Studies of these underground miners indicate that risks of a few other types of cancer and of chronic respiratory disease might be increased, although not due to radon (Darby et al., 1995; NRC, 1999; Fulco et al., 2000). However, it is unclear which out of the other toxicants in mines (including engine exhausts, silica, nickel oxide, cobalt oxide, vanadium pentaoxide, inhalable dust particles and uranium) might be relevant to the aetiology of these diseases

Studies of uranium workers other than miners while reducing the importance of these confounders may also be sensitive to other data inadequacies and/or confounders. For example the largest exposures are likely to have occurred in the 1940s and 1950s at a time when safety requirements were less stringent, record keeping by employers was poorer and testing was less commonplace. Similar deficiencies exist in the accuracy by which various health outcomes (i.e. nephritis) are codified and/or recorded, although generally this is less of a problem for cancer than for other diseases. In over 10 studies on such workers no excess of respiratory cancer or non-malignant respiratory disease has been established in relation to uranium exposure. (ATSDR, 1999 studies also cited and reviewed in Fulco et al., 2000). However, the statistical power of these studies was generally low. In particular, Fulco et al. (2000) concluded that there was limited/suggestive evidence of no association between exposure to uranium and lung cancer for cumulative internal doses below 200 mSv, but that there was inadequate/insufficient evidence to determine whether or not there is an association at higher doses. Fulco et al. (2000) also concluded that there was inadequate/insufficient evidence to determine whether or not there is an association between uranium and either lymphatic cancer or bone cancer.

Several epidemiological studies have found no increased mortality in uranium workers due to renal disease (Archer et al., 1973a, 1973b; Brown and Bloom, 1987; Checkoway et al., 1988; Polednak and Frome, 1981). Also, case studies showed that workers accidentally exposed to high levels of uranium did not suffer renal damage, even up to 38 years post-exposure (Eisenbud and Quigley, 1956; Kathren and Moore, 1986), although the tests for renal damage used in these studies were not very sensitive. A recent comparison of kidney tissue obtained at autopsy from seven uranium workers and six control subjects with no known exposure to uranium showed that the groups were indistinguishable by pathologists experienced in uranium-induced renal pathology

(Russell et al., 1996). One study on the kidney function of uranium mill workers chronically exposed to insoluble uranium (uranium dioxide) revealed renal tubular dysfunction as manifested by mild proteinuria, aminoaciduria, and a concentration-related clearance of β_2-microglobulin relative to that of creatinine when compared to a reference group of cement workers. The incidence and severity of these nephrotoxic signs correlated with the length of time that the uranium workers had spent in the area where insoluble uranium oxide yellowcake was dried and packaged (Saccomanno, 1982; Thun et al., 1985). The data from this study are indicative of reduced re-absorption in the proximal renal tubules.

Delayed renal effects were observed after a male worker at a uranium enrichment plant was accidentally exposed to a high concentration of uranium tetrafluoride powder for about five minutes in a closed room (Lu and Zhao, 1990). Renal effects were not observed in another accidental exposure (Fisher et al., 1990) in which 24 of 31 workers were followed for two years. However, an increased standardized mortality rate has been observed for chronic nephritis amongst a 2514-strong cohort of uranium processing workers, although this was based on just six deaths and was not statistically significant (Dupree-Ellis et al., 2000).

Oral

Few data are available that adequately describe the dose-response toxicity of uranium after an oral exposure in humans. Although the negative findings regarding renal injury among workers exposed over medium to long time periods to insoluble compounds (McDiarmid et al., 2000 and Eisenbud and Quigley, 1956) and shorter periods of exposure to relatively soluble uranium compounds (Kathren and Moore, 1986) are particularly significant in view of the high levels of exposure reported in these studies.

A recent review of human toxicity undertaken by Fulco et al. (2000) covering both epidemiological and experimental studies concludes that 'although uranium is a heavy metal that causes transient renal dysfunction, the preponderance of evidence indicates little or no clinically important renal effects of exposure to uranium'. However, at least two studies have shown changes in renal function (e.g. Lu and Zhao, 1990 and Zamora et al., 1998). Whilst, Dupree-Ellis et al. (2000) have recently reported an increased rate of chronic nephritis and a dose-response relationship between external radiation and kidney cancer amongst a cohort of 2514 uranium processing workers, these findings are based on small numbers of deaths and neither increase is statistically significant. As pointed out by Dupree-Ellis et al. (2000) potential inaccuracies in data, even amongst a relatively large cohort, can lead to a significant degree of uncertainty in the interpretation of epidemiological data.

In the study by Lu and Zhao (1990) delayed renal effects were observed after a male worker at a uranium enrichment plant was accidentally exposed to a high concentration of uranium tetrafluoride powder for about five minutes in a closed room. A trend towards increasing excretion of urinary β_2-microglobulin, as indicator for an early tubular defect, and increasing concentration of uranium in well-water was observed during clinical studies performed in Canada by Moss et al. (1983). Although it was suggested that the suspected tubular defect might well be rapidly reversible. Elevated levels of protein and β_2-microglobulin have also been observed in the urine of uranium mill workers (study of 39 exposed individuals to 36 unexposed controls) and presented data was considered to be consistent with uranium nephrotoxicity (Thun et al., 1985). In

a further study, a statistically significant association ($p = 0.03$) was observed between increasing but normal levels of urine albumin and the uranium cumulative index (Mao, 1995).

In the study of Zamora et al. (1998) two groups of biomarkers were used as indicators of kidney function and cellular toxicity between two communities. One community (the control) was supplied with well-mixed mains water containing typically less than 1 µg U/l, whereas the other community represented exposed individuals whose water supply contained between 2 and 780 µg U/l. The total number of individuals partaking from each community was 20 and 30, respectively. Estimated total intakes of uranium in each group (including uranium from drinking water) were 0.3 to 20 and 3 to 570 µg/day. Urinary glucose was found to be significantly different and correlates positively with uranium intake for males, females, and pooled data. Increases in alkaline phosphatase and $\$_2$-microglobulin were also observed to be correlated with uranium intake for pooled data. In contrast, the indicators for glomerular injury, creatinine and protein were not significantly different between the two groups nor was their urinary excretion correlated to uranium intake. Because of the uncertainty of the clinical significance and possible reversibility of the observed changes, their clinical significance has been questioned (e.g. Harley et al., 1999b; Fulco et al., 2000). In addition, a possible role of confounding factors such as other compounds in drinking water has not been clarified.

Embedded DU fragments

Dipino et al. (1998) compared five measurements of premorbid intellectual functioning amongst a group of patients injured by DU munitions during the Gulf War. Unfortunately only inter-group comparisons were made and it was considered impossible to compare scores with those suffering from injuries not associated with depleted uranium.

McDiarmid et al. (2000) studied a cohort of Gulf War veterans who had fragments of depleted uranium in their soft tissues. Results from a battery of computer-based neurocognitive tests suggest a statistical relationship between elevated urinary uranium levels and 'problematic performance on automated tests assessing performance efficiency and accuracy' (McDiarmid et al., 2000). Traditional tests of neurocognitive function (pen-and-pencil tests) did not show any statistical difference in performance between the veteran cohort and a control group. However, as discussed by the Committee on Health Effects Associated with Exposure During the Gulf War (Fulco et al., 2000), because of methodological problems, it is difficult to draw firm conclusions from this study. Kidney function was normal in Gulf War veterans with embedded DU fragments, years after exposure, despite urinary uranium concentration up to 30.7 µg U/g creatinine (McDiarmid et al., 2000).

8.3 In-vitro studies

In-vitro studies on human osteoblast cells have indicated that they may be transformed to the tumorigenic phenotype (i.e. exhibiting morphological changes, anchorage independent growth in soft agar, induction of tumours when implanted into nude mice, and differences in *ras* oncogene expression and pRb phosphorylation) by DU administered as uranyl chloride (Miller et al., 1998a). The authors considered this transformation to be primarily due to chemical rather than radiological effects; such as the interaction of uranium with phosphorus-containing groups in DNA, and consider the magnitude of activity to be similar to that observed for nickel sulphate and lead acetate (both known transforming metals).

Uranyl nitrate was cytotoxic and genotoxic in Chinese hamster ovary cells. There was a dose-related decrease in the viability of the cells, a decrease in cell cycle kinetics, and increased frequencies of micronuclei, sister chromatid exchanges and chromosomal aberrations (Lin et al., 1993). The genotoxic effects in this study were thought to have occurred through the binding of the uranyl nitrate to the phosphate groups of DNA. It was suggested that these results provide a possible mechanism for the observed teratogenic effects (WHO, 1998b). Miller et al. (1998b) also observed mutagenic activity (Ames *Salmonella* reversion assay) in the urine of rats implanted with DU pellets (in muscle tissue), although no significant mutagenicity was observed in serum.

In-vivo and *in-vitro* testing on the clam *Corbicula fluminea*, the worm *Eisenia fetida andrei* and the teleost fish *Brachydanio rerio* by (Labrot et al., 1996) was used to determine if changes in the activities of various biomarkers (lipid peroxidation, acetylcholinesterase, catalase and glutathione peroxidase) and other postmitochondrial fractions could be identified. Results of these studies indicated that exposure to uranium resulted in an increase in malondialdehyde (an indicator of oxidative stress) whereas no increase in lipid peroxidation was observed *in-vivo*. With some exceptions exposure to uranium was also observed to result in decreased activities of acetylcholinesterase, catalase and glutathione peroxidase in all three species. However acute toxicity was only observed in the case of *Eisenia fetida andrei* and *Brachydanio rerio.*

8.4 Derivation of a tolerable intake for uranium

The renal toxicity of various uranium species given in repeated oral doses is given in Table 8.2 and in repeated inhalation is given in Table 8.3 (from ATSDR, 1999).

8.4.1 Soluble uranium compounds (group F: $UO_2(NO_3)_2$, uranium carbonates)

Oral A LOAEL has been established as 50 µg/kg in male rabbits in 91-day studies (Table 8.2) with the end point being slight microscopical changes in the kidney. From this, a TI can be derived using a 100 fold total uncertainty factor (3 for LOAEL to NOAEL, 3 for toxico-dynamic and toxico-kinetic differences between species (comparative data from animals and humans indicate that the absorption in humans is no greater than in animals; therefore a full 10 interspecies uncertainty factor is not applied), and 10 for intraspecies variation. As uranium seems to have a biological half life (time for half the material to be eliminated from the body) of approximately 15-days, steady state already having been reached in the 91 day study, and no adjustment for subchronic to chronic studies is required (WHO, 1998a). Thus the TI is 0.5 µg/kg bw/d.

Inhalation A NOAEL can be approximated as 0.1 mg/m^3 from several medium- and long-term studies (Table 8.3). Adjusting this to the exposure difference in the experimental studies and general population exposure (24 hour exposure rather than 5 to 6; 7 day/week rather than 5.5 to 6 day/week), this gives an effective air concentration of 20 µg/m^3. As the inhalation volume of rat is 0.1 l/min, i.e., 150 l/d, this means an inhalation dose of 15 µg/d, which, using 250 g as an average weight of a rat, translates to 60 µg/kg/d. Using the default uncertainty factor of 100 (10 for interspecies and 10 for intraspecies variation) as no information is available for inhalation exposure that would allow use of a specific uncertainty factor, this means a TI of 0.6 µg/kg/d, which is in good agreement with the figure derived from the oral studies above.

Table 8.2. Renal toxicity (chemical) of uranium species in repeated doses –oral (ATSDR, 1999)

	Reference Chemical Form	Species	Exposure /duration /frequency	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)	Reference
F	UO2(NO3)2*6H2O	Rat	28d W	35.3 M	40.0 F	Gilman et al. 1998a
F	UO2(NO3)2*6H2O	Rat	30d F	3.3	16.6	Maynard & Hodge 1949
F	UO2(NO3)2*6H2O	Rat	91d W		0.06M, 0.09F	Gilman et al. 1998a
F	UO2(NO3)2*6H2O	Rat	2y F	16.6	33	Maynard & Hodge 1949, Maynard et al. 1953
F	UO2(NO3)2*6H2O	Rabbit	30d F		2.8	Maynard & Hodge 1949
F	UO2(NO3)2*6H2O	Rabbit	91d W		0.05M, 0.49F	Gilman et al. 1998b
F	UO2(NO3)2*6H2O	Rabbit	91d W		1.36 M	Gilman et al. 1998c
F	UO2(NO3)2*6H2O	Rabbit	91d W		0.93 M	McDonald-Taylor et al. 1992, 1997
F	UO2(NO3)2*6H2O	Dog	138d F	47	95	Maynard & Hodge 1949
F	UO2(NO3)2*6H2O	Dog	1y F	47	95	Maynard & Hodge 1949
F	UO2F2	Rat	30d F	5.4	27	Maynard & Hodge 1949
F	UO2F2	Mouse (C3F	48w ad lib F		452 M	Tannenbaum & Silverstone 1951
F	UO2F2	Mouse (DBA	48w ad lib F		452 M	Tannenbaum & Silverstone 1951
F	UO2F2	Dog	30d 6d/w F	7.7	15.4	Maynard & Hodge 1949
F	UO2F2	Dog	1y F	8		Maynard & Hodge 1949, Maynard et al. 1953
M	UCl4	Rat	30d F	88	438	Maynard & Hodge 1949
M	UCl4	Dog	30d 6d/w F	63	313	Maynard & Hodge 1949
M	UCl4	Dog	1y F	6.3	31	Maynard & Hodge 1949, Maynard et al. 1953
M	UF4	Dog	30d 6d/w F		3790	Maynard & Hodge 1949
M	UF4	Rat	2y F	1061	10611	Maynard & Hodge 1949, Maynard et al. 1953
M	UO3	Rat	30d F	11650M		Maynard & Hodge 1949
M	UO3	Dog	30d 6d/w F		83	Maynard & Hodge 1949
S	U3O8	Dog	30d 6d/w F		5653	Maynard & Hodge 1949
S	UO2	Rat	30d F	12342		Maynard & Hodge 1949
S	UO2	Dog	30d 6d/w F	17.6	441	Maynard & Hodge 1949
S	UO2	Rat	2y F	12341		Maynard & Hodge 1949, Maynard et al. 1953
	(NH4)2U2O7	Dog	30d 6d/w F		38	Maynard & Hodge 1949
	Na2U2O7	Dog	30d 6d/w F		37	Maynard & Hodge 1949
	UO2(C2H3O2)2*2H2O	Rat	30d F	786 M	7858 M	Maynard & Hodge 1949
	UO2(C2H3O2)2*2H2O	Rat	4w W		1.1 M	Ortega et al. 1989a
	UO4	Rat	30d F	55	138	Maynard & Hodge 1949
	UO4	Dog	30d 6d/w F		15.4	Maynard & Hodge 1949

Type: This reflects the absorption rate of uranium compounds in the lung. F (fast)=rapid, almost total, absorption into the blood usually within 10 minutes, M (moderate)=about 70% of deposited material reaches blood eventually, S (slow)=about 10% reaches blood eventually (ICRP 66, 1994)

Exposure/duration/frequency: y=year(s), w=week(s), d=day(s), h=hour(s), ad lib=ad libitum, F=food, W=water
NOAEL=no-observed-adverse-effect level, LOAEL=lowest-observed-adverse-effect level, M=male, F=fe,male

Table 8.3. Renal toxicity (chemical) of uranium species in repeated doses – inhalation (ATSDR, 1999)

Type	Reference Chemical Form	Species	Exposure/duration/ /frequency	NOAEL (mg U/m3)	LOAEL (mg U/m3)	Reference
F	UF6	Rat	30d 6h/d	0.2		Spiegel 1949
F	UF6	Rat	1y 5.5d/w 6h/d	0.05	0.2	Stokinger et al. 1953
F	UF6	Mouse	30d 6h/d	2	13	Spiegel 1949
F	UF6	Gn Pig	30d 6h/d	2	13	Spiegel 1949
F	UF6	Gn Pig	36w 5.5d/w 6h/d	0.2		Stokinger et al. 1953
F	UF6	Rabbit	36w 5.5d/w 6h/d		0.25	Stokinger et al. 1953
F	UF6	Dog	1y 5.5d/w 6h/d		0.05	Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Rat	30d Cont.		0.13	Roberts 1949
F	UO2(NO3)2*6H2O	Rat	1y 5.5d/w 6h/d	0.15	0.25	Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Rat	2y 5.5d/w 6h/d		2	Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Gn Pig	26w 5.5d/w 6h/d	2 M		Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Rabbit	30d Cont.		0.13	Roberts 1949
F	UO2(NO3)2*6H2O	Rabbit	26w 5.5d/w 6h/d		0.25	Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Dog	30d Cont.		0.13	Roberts 1949
F	UO2(NO3)2*6H2O	Dog	1y 5.5d/w 6h/d	0.15	0.25	Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Dog	1y 5.5d/w 6h/d	0.15	0.25	Stokinger et al. 1953
F	UO2(NO3)2*6H2O	Dog	2y 5.5d/w 6h/d		2	Stokinger et al. 1953
F	UO2F2	Rat	5w 6d/w 6h/d	0.5	2.2	Rothstein 1949a
F	UO2F2	Gn Pig	5w 6d/w 6h/d	2.2	9.2	Rothstein 1949a
F	UO2F2	Cat	5w 6d/w 6h/d	2.2	9.2	Rothstein 1949a
F	UO2F2	Dog	5w 6d/w 6h/d		0.15	Rothstein 1949a
M	UCl4	Rat	1y 5.5d/w 6h/d		0.2	Stokinger et al. 1953
M	UCl4	Gn Pig	30w 5.5d/w 6h/d		0.2	Stokinger et al. 1953
M	UCl4	Dog	1y 5.5d/w 6h/d	0.05	0.2	Stokinger et al. 1953
M	UF4	Rat	30d 6h/d	4	18	Dygert 1949a
M	UF4	Rat	1y 5.5d/w 6h/d		0.5	Stokinger et al. 1953
M	UF4	Gn Pig	30d 6h/d	4	18	Dygert 1949a
M	UF4	Gn Pig	34w 5.5d/w 6h/d		3	Stokinger et al. 1953
M	UF4	Dog	30d 6h/d	0.5	3	Dygert 1949a
M	UF4	Rabbit	30d 6h/d		0.4	Dygert 1949a
M	UF4	Rabbit	34w 5.5d/w 6h/d		2	Stokinger et al. 1953
M	UF4	Cat	30d 6h/d		18	Dygert 1949a
M	UO3	Rat	4w 6d/w 6h/d	16		Rothstein 1949c
M	UO3	Rabbit	4w 6d/w 6h/d		16	Rothstein 1949c
M	UO3	Cat	4w 6d/w 6h/d		16	Rothstein 1949c
M	UO3	Dog	4w 6d/w 6h/d		16	Rothstein 1949c
S	U3O8	Rat	26d 4-6h/d		4.8	Dygert 1949c
S	UO2	Rat	1y 5.5d/w 6h/d	1	10	Stokinger et al. 1953
S	UO2	Mouse	5w 6d/w	19.4		Rothstein 1949b
S	UO2	Gn Pig	28w 5.5d/w 6h/d	10		Stokinger et al. 1953
S	UO2	Rabbit	5w 6d/w	9.2	19	Rothstein 1949b
S	UO2	Rabbit	30w 5.5d/w 6h/d		1	Stokinger et al. 1953
S	UO2	Dog	5w 6d/w	1.1	8.2	Rothstein 1949b
S	UO2	Dog	1-5y 5d/w 5.4h/d	5.1		Leach et al. 1970
S	UO2	Dog	1-5y 5d/w 5.4h/d	5.1		Leach et al. 1973
S	UO2	Monkey	5y 5d/w 5.4h/d	5.1		Leach et al. 1970
S	UO2	Monkey	1-5y 5d/w 5.4h/d	5.1		Leach et al. 1973
	(NH4)2U2O7	Rat	30d 6h/d		6.8	Dygert 1949b
	(NH4)2U2O7	Rabbit	30d 6h/d		6.8	Dygert 1949b
	Carnotite U ore	Mouse	30d 4.4-6h/d		2.9	Pozzani 1949
	Carnotite U ore	Gn Pig	30d 4.4-6h/d	0.8	2.9	Pozzani 1949
	Carnotite U ore	Dog	30d 4.46h/d		0.8	Pozzani 1949
	Carnotite U ore	Rabbit	30d 4.4-6h/d	0.8	2.9	Pozzani 1949
	Na2U2O7	Rat	5w 5.5d/w 6h/d		15	Rothstein 1949d
	Na2U2O7	Rabbit	5w 5.5d/w 6h/d		15	Rothstein 1949d
	UO4	Rabbit	23d 5d/w 5h/d		15.4	Dygert 1949d
	UO4	Cat	23d 5d/w 5h/d		15.4	Dygert 1949d

Type: This reflects the absorption rate of uranium compounds in the lung. F (fast)=rapid, almost total, absorption into the blood usually within 10 minutes, M (moderate)=about 70% of deposited material reaches blood eventually, S (slow)=about 10% reaches blood eventually (ICRP 66, 1994)

Exposure/duration/frequency: y=year(s), w=week(s), d=day(s), h=hour(s), ad lib=ad libitum
F=food,W=water. M=male, F=female
NOAEL=no-observed-adverse-effect level, LOAEL=lowest-observed-adverse-effect level.

8.4.2 Uranium compounds with limited solubility (Type M: UO_3, UF_4, UCl_4)

The database is rather limited, and it is not apparent that there is a justification for the generation of this type: differences within the group are large, and not much different from those between this group and the other two types, notably when the exposure is by inhalation. This is, however, in part, due to the fact that there is a major difference in the toxic potency observed in the early studies, and more recent studies: the recent studies observe effects at levels that are generally lower than those where effects are reported in the old studies. For the Type M uranium species, no recent studies are available. It does not seem justified to derive a separate TI for the Type M; rather, the TI derived for Type F should be used.

8.4.3 Uranium types practically insoluble in water (Type S: UO_2, U_3O_8)

Again, the database is limited, and only old studies are available. However, it would seem that both in inhalation and oral studies, the doses that induce effects are higher than in the case of the Types F or M. This difference is especially marked for oral exposure. For oral exposure, however, only one study, using two species and two uranium compounds is available. For inhalation exposure, the database is somewhat more extensive, and it may be estimated that the toxicity of the group S uranium species is approximately one tenth that of the group F. This would lead to a TI of 5 µg/kg/d. Note U_3O_8 may also have Type M absorption behaviour (see Chapter 7).

8.4.4 Other uranium compounds

Limited information on the different chemicals in this group (e.g., UO_4, $UO_2(C_2H_3O_2)_2$, $(NH_4)_2U_2O_7$, $Na_2U_2O_7$, Carnotite ore) and apparent variation between the different chemicals of this group make it impossible to give a separate TI value for either this group, or any uranium species in this group. It would be prudent to use the TI of the group F, 0.5 µg/kg for all uranium species other than those in group S.

8.5 Uncertainties of chemical risk assessment

The studies in humans cannot be used in quantitative risk estimation, as the information of exposure, both qualitatively and quantitatively, is inadequate.

The database on the toxicity of uranium is limited; most of the studies are old, meaning that not all present methods available to assess renal toxicity were available at the time of these studies. Information, especially on long-term effects of different uranium species, is based on studies from a limited number of researchers. Information is very limited for many uranium species, especially those with limited water solubility. The different studies tend to give rather different results *vis a vis* the quantitative risk estimates. In many studies, dose-response and dose-effect relationships cannot be assessed because of limited dose levels studied. In inhalation studies, the physical–chemical characteristics of the aerosols are often not well characterized, and are likely to be different for different uranium species. There appear to be differences in the sensitivity of different species to uranium toxicity, but no general picture seems to emerge.

The tolerable intake derived is applicable to long-term exposure, intakes lower than the tolerable intake should not lead to adverse health effects. It is apparent that single or short-term exposures lower than the tolerable intake similarly do not adversely affect health. It is likely that in single exposures and short-term exposures, even higher

exposure levels will be well tolerated. However, quantitative information to assess, how much the long-term tolerable intake values may be temporarily exceeded without risk, is not available.

In the extrapolation from experimental animals to humans, comparative information on the toxico-dynamics is not available. Similarly, for inhalation exposure, reliable comparative information is not available on the toxico-kinetics. Thus for these parameters, default values for the extrapolation (10) have to be used. On the other hand, available information would tend to indicate that the oral absorption in humans is not greater than that in experimental animals and the default value for toxico-kinetics in this setting can be replaced by unity. Very limited information is available on the inter-individual variation in uranium toxicity within the human species, and thus the default uncertainty factor for the general population, 10, has to be applied.

8.6 Summary

The primary routes of exposure to uranium for humans are through ingestion or inhalation. The effects of embedded shell fragments containing depleted uranium (among other things) have also been studied (e.g. Fulco et al., 2000).

The target organ to be considered for uranium toxicity is the kidney (also considered to be the primary target organ for ingested uranium in WHO (1998b).

Uranium hexafluoride induces irritative effects at high doses; some uranium compounds may cause pulmonary effects at relatively high inhalation exposures. However, long-term exposure to lower concentrations (generally less than 10 mg/m^3) has usually not resulted in pulmonary toxicity. Carnotite mineral dust causes haemorrhages in dog lungs. Other factors such as diverse inorganic inhalable dust particles, radium, or radon progeny may contribute to these effects. No increase in malignant or nonmalignant respiratory disease mortality has been established in cohorts exposed to uranium in uranium processing. However, the available epidemiological data are generally limited by low statistical power, uncertainties in the assessment of uranium exposure, and/or the paucity of data on exposures to other agents.

In the kidney, proximal tubules are considered to be the main target (ATSDR, 1990, 1999). Currently, uranium is regarded as a less potent nephrotoxin than the classical nephrotoxic metals (cadmium, lead, mercury) (Goodman, 1985). No kidney toxicity related to urinary uranium concentrations was observed in people with embedded DU fragments.

Tolerable intakes for soluble (F and M type) and insoluble (S type) compounds can be derived for inhalation and ingestion. The TI for soluble uranium compounds is 0.5-µg/kg of bw/day and is 5.0 µg/kg of bw/day for insoluble compounds.

9 Health effects due to the presence of radioactivity

9.1 Mechanisms and background

Study of the toxicological and medical effects of radiation on human beings, and the control of exposure to radiation is generally undertaken under the broad disciplines known as radiobiology and health physics. In such studies, it is generally assumed that any resulting health detriment (e.g. cancer, cellular damage etc.) is brought about by exposure to a radioactive substance, and is primarily a function of the amount of energy (as ionizing radiation) absorbed per unit mass of tissue through which it passes. The detailed mechanisms by which radiation interacts with biological materials are the subject of continuing research. However, it is thought that one of the ways in which the energy deposited by radiation may damage cells is by causing changes to occur in deoxyribonucleic acid (DNA), a biologically important molecule that controls cell structure and function, and which is found mainly in cell nuclei. The type of change and the likelihood of error-proof repair depend upon the amount of energy (or dose) deposited. Thus biologically significant effects that lead to the development of cancers or inherited genetic defects may result.

Based on these fundamental principles the assessment of the effects of exposure to radioactive substances has developed in a somewhat different, although often parallel, manner to those commonly used in the assessment of chemical toxicity. The primary concept in radiation protection is that of radiation dose (energy absorbed from ionizing radiation per unit mass by a target organ or tissue). For further information on the usage of terms related to radioactivity and radiological protection the reader is directed to BSS, (1996), ICRP-67 (1993) and ICRP-60 (1991b) onwards or to the RASANET home page at www.iaea.org.

Ionizing radiation emitted by different radionuclides differ in their ability to penetrate matter depending both on the type of radiation emitted and its energy. Alpha particles are hardly able to penetrate the outer layer of skin and do not constitute a hazard when emitted outside the body. Beta particles are able to penetrate the outer layers of skin and can give rise to a localized dose to the skin when in contact. Gamma radiation is potentially more penetrating and can deposit energy to internal organs when outside the body, the magnitude of which depends on the energy of the gamma radiation emitted. Thus, exposures from radionuclides may be both external and internal to the body and the relative importance of these exposure pathways depends upon the type of radiation and the radionuclides involved.

The amount of energy deposited per unit mass of material, such as human tissue, is called the *absorbed dose* and is given the unit gray, symbol Gy (1 Gy is equivalent to 1 J/kg). However, since different types of ionizing radiation differ in the ways in which they interact with biological materials, equal amounts of energy may not result in the same level of biological effects. For example, when alpha-particles are emitted within the body, they deposit energy more densely than either beta particles or gamma radiation, with the result that 1 Gy of alpha radiation is more harmful than 1 Gy of gamma radiation. This potential for causing harm is taken into account in the quantity *equivalent dose*, called sievert and given the symbol Sv (by using a weighting factor of 20 for alpha particles, and 1 for beta and gamma radiation). Another quantity that is commonly referred to in radiological protection is *effective dose*, which is also given in sieverts (or often mSv which is one thousandth of a sievert). In calculating this quantity

the equivalent doses to organs are multiplied by tissue weighting factors that relate to the relative risk of cancer associated with each organ or tissue. This quantity has the advantage that it gives a general indication of the level of risk implied by a given dose, and allows internal and external exposures and uniform and non-uniform irradiation to be quantified on the same basis.

The effective dose, while useful in providing a measure of the health detriment implied by a radioactive substance, is not a directly measurable quantity. A detailed explanation of the dose quantities for measurement purposes is beyond the scope of this report. In this context it is sufficient to note that effective doses are often calculated on the basis of measured dose rates (e.g. in Gy/h) and activity concentrations (e.g. in Bq/kg). Activity is given the name becquerel (symbol Bq) and is equivalent to the number of disintegrations per second. To calculate external dose, it is possible to use dose rate information or calculated coefficients that relate activity to effective or equivalent dose to the skin (e.g. in $Sv/Bq/m^2$). Internal doses are generally calculated from standardized tables of coefficients that give the effective (or equivalent organ doses) arising from a unit intake of activity (Sv/Bq). These coefficients are included in the BSS (1996). Coefficients are given separately for inhalation and ingestion and for different age groups. They take account of the biokinetics and the forms of emission, of both the principal radionuclide and its decay products.

Explanation of the basis behind the calculation of radiation dose is out of the scope of this document and the reader is guided to various publications of the International Commission for Radiological Protection (ICRP) and the International Atomic Energy Agency (IAEA) (for example see ICRP-66 (1994a), ICRP-60 (1991b) and IAEA (1989a) and the principals laid out and described in the Basic Safety Standards for protection against Ionizing Radiation and for the Safety of Radiation Sources (commonly referred to as the BSS) which was jointly agreed by the FAO, IAEA, ILO, NEA, PAHO, and WHO (BSS, 1996). The BSS have been designed to be fully applicable to the occurrence of any isotopic combinations of radionuclides, including DU.

Two categories of health effect have been shown to result from exposure to ionizing radiation; deterministic and stochastic effects. Deterministic effects are those that occur at high doses and dose rates. These effects occur at dose levels far higher than those encountered from the use of, or exposure to, radioactive materials under normal environmental conditions and exposures to the general public. Erythema, or reddening of the skin, is a form of deterministic effect that may result from skin exposure (at instantaneous absorbed doses of 5 Gy or more). Above the dose threshold, the likely severity of such effects is affected by the dose received.

The primary stochastic effect associated with radiation exposure is cancer induction. Most of the information relating radiation doses to an increased risk of cancer is derived from situations in which people have been exposed at higher doses and dose rates than normally encountered (e.g. Nagasaki and Hiroshima bomb survivors). At lower levels of dose and dose rate, it is difficult to demonstrate an increased cancer incidence from radiation exposure because of the high natural incidence of cancer, which is a major confounding factor in epidemiological studies, particularly at low doses and dose rates. Information about the way in which radiation interacts with cells, however, supports what has become known as the linear no-threshold hypothesis. Thus, for radiation protection purposes, it is assumed that there is no level of dose below which there is no risk of a radiation-induced cancer and that the probability (and not the severity) of

cancer increases in proportion with an increase in radiation dose. This assumption has the implication that different sources of radiation can be considered separately, and that limits, or other action levels set for protection purposes, are not based on a borderline between what is safe and unsafe, but on a balance of risk and benefit. As a result, different dose limits or action levels are used for different protection situations.

Dose limits have been recommended by the ICRP-60 (1991b) for controlling the additional radiation doses that arise from normal operations. These limits are based on studies of the 'acceptability of risk' and represent the upper bound on the additional level of risk which may tolerated on a continuing basis from practices involving deliberate application of ionizing radiation. These limits have been incorporated into international and national standards, including the International Basic Safety Standards (BSS, 1996).

9.2 Dose Limits

The International Basic Safety Standards for Protection against Ionizing Radiation and for Safety of Radiation Sources (BSS,1996) require that:

- the occupational exposure of any adult worker shall be so controlled that the following limits are not exceeded
  a. an effective dose of 20 mSv per year averaged over five consecutive years
  b. an effective dose of 50 mSv in any single year.

- the estimated average doses to the relevant critical groups of members of the public that are attributable to practices shall not exceed the following limits
  a. an effective dose of 1 mSv in a year
  b. in special circumstances, an effective dose of up to 5 mSv in a single year provided that the average dose over five consecutive years does not exceed 1 mSv per year; the special circumstances are not defined.

These limits are based on the 1990 recommendations of the International Commission on Radiological Protection (ICRP-60, 1991b) and are also embodied in European Legislation (OJEC, 1996). For a detailed explanation of the models, the reader is referred to the original publications but brief synopses are given in Annex 4.

These limits apply to additional doses from normal planned operations, where the additional level of dose received can be controlled at source; they are not applicable to situations, for example when there is pre-existing contamination, when the decision about whether it is necessary to apply measures to reduce doses are based on the balance between the risk and benefit implied by the intervention measure (and not the source). The recently published ICRP-82 (1999b), includes dose levels above which intervention would be justified to reduce prolonged exposures to members of the public from, for example, radionuclides present in the environment. These recommendations imply that intervention measures are unlikely to be justified at annual doses below than 10 mSv and almost always likely to be justified at annual doses exceeding 100 mSv. An additional annual dose level of 1 mSv is recommended for derivation of intervention exemption levels for commodities (e.g. building materials).

9.3 External radiation exposure

In addition to exposure to anthropogenically introduced substances such as DU, all life on earth is exposed to the presence of external irradiation through a wide range of radiation sources outside the body. Recently processed DU or chemically pure unenriched uranium, consisting solely of naturally occurring uranium isotopes, principally decays through the emission of alpha particles. However, as discussed in Chapter 2 relatively rapid ingrowth of beta- and gamma- emitting progeny occurs in the months following chemical and isotopic separation. Any potential for external exposure is generally considered to be limited to a localized dose to the skin from direct physical contact with DU mainly due to beta emissions of ^{234m}Pa, a progeny of ^{238}U and gamma radiation (AEPI, 1995; Danesi, 1990). This may either occur to the hands when physically handling DU metal or through physical contact with dust derived from the oxidation of DU. AEPI, (1995) states that all DU weapons systems used by the USA army are shielded to control beta radiation emitted to DU when handled by military personnel prior to firing.

The most obvious target for external radiation exposure from DU deposited on the body is the skin. The outermost layer of skin is composed of a layer of dead cells described collectively as the epidermis, while the lower and basal layers are composed of living cells and are therefore susceptible to the effects of ionizing radiation. The average thickness of the epidermis, measured in males of between 26 and 30 years is considered to be around 50 µm with a thickness range between 20 and 100 µm ICRP-23 (1974) and ICRP-59 (1991a). This compares to a typical range in tissue for an alpha particle from ^{238}U of 28 µ, and, therefore, provided that redistribution or sorption of uranium into the epidermis does not occur, alpha particles cannot penetrate to the sensitive lower or basal layers. However, DU greater than 24 days old has quantities of ^{234m}Pa which emits a 2.29 MeV average energy beta that is capable of irradiating the basal layers of the skin. Effects of acute dermal exposure to DU are unlikely but could result in erythema (redness of the skin) or epilation (loss of hair) (Upton, 1992).

Case studies confirm this observation, generally indicating that exposure to basal cells even during prolonged, often aggressive, physical contact does not occur to a significant degree. For example, skin cancer was only rarely observed during the study of 11-cohorts of underground uranium mine workers (Sevcova, 1978). Where skin cancer was observed in these workers, it was considered more likely that this was caused by the presence of arsenic in ores mined from Czechoslovakia and China. In addition there have been no recorded incidents of skin cancers being observed in nuclear workers whose skin has been exposed to occasional hot spots of alpha-emitting radioactive materials (Harley et al., 1999a). During studies undertaken by the US Army it has been established that US occupational exposure standards (NRC–10 CFR 20.1201) covering radioactive exposure of skin (in this case due to exposure to a combination of alpha, beta and gamma radiation) would only be exceeded by holding an unshielded DU projectile in the hand for a period in excess of 250 hours (AEPI, 1995).

It has been estimated that the maximum radiation dose rate from DU armour and DU munitions received by a tank commander, gunner and/or loader working in a fully loaded Mark 1 Abrams battle tank is 0.1 to 0.2 µSv/h (AEPI, 1995). Because of the configuration of the tank and its armour, the driver of the tank may receive a slightly higher dose (1.3 to 0.3 µSv/h). The skin dose rate received when handling a bare penetrator is estimated to be 2 mSv/h (200 mrem/hr; AEPI, 1995).

Penetrator, bullet and armour are contained in a protective coating and adsorption through the skin can therefore be considered to be negligible in these cases. The potential external dose received in the vicinity of a target following attack by DU munitions has been theoretically estimated to be in the order of 4 μSv/year (UNEP/UNCHS, 1999) based on gamma ray exposure. Such doses are small when compared to recommended guidelines for human exposure to ionizing radiation (20 mSv/annum for a worker for penetrating whole body radiation or 500 mSv/year for skin (BSS, 1996).

The radiation doses received from handling other uranium products, which are not made of depleted or chemically pure uranium, may be higher than those described above, particularly where the material also contains progeny of uranium, such as radium. It is impossible to quantify the dose received unless the composition of the material is known and hence both chemical and radiochemical determinations are required in such circumstances, prior to calculation of any potential radiation dose.

9.4 Internal exposure

Internal exposure to ionizing radiation is a function of the route of a given nuclide through the body and its residence time amongst various organs. Doses are therefore calculated, based on the use of biokinetic models that describe the passage and kinetics of various given radionuclides throughout the body. A brief overview of biokinetic models currently employed to calculate dose coefficients in radiation protection is given in Annex 4, and output from these models that may be applied to exposure to DU and uranium in an occupational and public context are described in the following Chapters-10, 11 and 12.

Current epidemiological evidence concerning the carcinogenicity of uranium, both natural and enriched, comes from studies of uranium miners and studies of nuclear workers in fuel enrichment and production facilities.

Among uranium miners, epidemiological studies provide consistent and convincing evidence of excess lung cancer, but not of leukaemia. The information comes from numerous mortality studies of miner cohorts in Australia, Canada, China, Europe and the USA (IARC, 1988; NRC 1999). The lung cancer risk is associated with alpha particle exposure from ^{222}Rn and its decay products, which arise in uranium mines from the decay of ^{238}U. In these studies, the quality of the information on the level of exposure to radon varies across cohorts and over time, from a few air measurements of radon gas and radon decay products in the early years, or re-creation of early mining conditions, to real time individual exposure estimates (taking into account ventilation patterns, ore characteristics, mining methodology, weekly surveys of gamma radiation, radon and dust levels and location and duration of work of individual miners), and even to individual estimates from personal alpha dosimeters in more recent years in France (Tirmarche et al., 1993). The risk of lung cancer appears to be proportional to the radiation dose received. Critical reviews of these studies can be found in IARC (1988) and NRC (1999). There are also a number of epidemiological studies of other alpha emitting radionuclides (e.g. radium, thorium) that also show very clear increases of cancer risk in specific organs (IARC, 2001; NRC, 1999). On the basis of the 1988 review, IARC has classified radon and its decay products as carcinogenic to humans. IARC, in its most recent review of ionizing radiation, has also classified "Internally deposited radionuclides that emit α particles" as carcinogenic to humans (Group 1) (IARC, 2001).

Studies of cancer risk among nuclear workers in nuclear fuel enrichment and production facilities are fewer, although the body of literature is increasing rapidly (Fulco et al, 2000; Cardis and Richardson, 2000). At uranium fuel production facilities, inhalation of airborne uranium dust may represent an important potential source of radiation exposure. Workers in these facilities therefore have two main possible sources of radiological exposure to tissues of the whole body; external gamma-ray exposure which results in a fairly uniform distribution of dose and internal depositions that deliver radiation doses (mainly from alpha-particles) primarily to the lung and lymphatic system. If the uranium dust is solubilized, exposure may also result in other tissues such as the liver, the kidney and the bone. Tumours occurring in these organs are therefore, *a priori*, of particular interest in epidemiological studies of workers at uranium production facilities.

Comparison of findings between uranium processing facilities is, however, complicated by the fact that processes and historical periods of operation have differed between facilities, leading to differences in exposure conditions and follow-up between cohorts. Further, assessment of past internal uranium exposure of nuclear workers is complicated by methodological difficulties of internal dosimetry, as well as by inadequate historical information with which to accurately quantify internal radiation doses. These exposure measurement problems pose significant problems for epidemiology: the inability to accurately classify workers by level of internal radiation exposure may lead to confounding of the analyses of radiation-cancer associations, since workers with significant dose from internal contamination are often persons with substantial external exposure.

Lung cancer has been the primary outcome of interest in studies of workers in fuel enrichment and production facilities. Lung cancer mortality was found to be significantly elevated, compared to national rates, among workers in nuclear fuel processing facilities (Loomis and Wolf, 1997; Checkoway et al., 1988; Frome et al., 1990), but not in others (Dupree et al., 1995; Polednak and Frome, 1981; Hadjimichael et al., 1983; Waxweiler et al., 1983; Stayner et al., 1985; Brown and Bloom, 1987; Ritz, 1999; Dupree et al., 1987). An association between external radiation dose and lung cancer mortality was observed in two cohorts in the US (Ritz, 1999; Checkoway et al., 1988) and an association with lung cancer incidence and radiation dose (using a 20 year lag) in one study in the UK (McGeoghegan and Binks, 2000a). No association was found in other studies on US (Ritz et al., 2000; Hadjimichael et al., 1983;) and UK (McGeoghegan and Binks, 2000b) cohorts where this was studied. An association with estimated dose from internal contamination was observed by Checkoway et al.(1988) but not in another US cohort (Ritz et al., 2000). In contrast, a US multi-facility case control study of lung cancer among workers exposed to uranium dust found no such association, however, there was a suggestion of positive associations among workers hired at ages over 45 years (Dupree et al., 1995). Future research with these cohorts may help to understand the role of uranium dust exposure in cancer risk.

10 Biokinetics for uranium after internal exposure

10.1 Introduction

The aims of this Chapter are to:

- calculate intakes of natural uranium and DU that correspond to dose limits that apply to occupational and public exposure (20 mSv and 1 mSv, respectively) both in terms of radioactivity and mass.
- ascertain whether intakes should be restricted by radiation dose or mass.
- describe the biokinetics of uranium (DU will be identical) in man after inhalation using the generic models recommended by ICRP for soluble (Type F), moderately soluble (Type M) and relatively insoluble (Type S) compounds after deposition in the respiratory tract; emphasis is placed on chest retention, and urinary and faecal excretion rates which are the parameters normally used to assess intake and dose.
- describe the biokinetics of inhaled uranium octoxide (U_3O_8), uranium dioxide (UO_2), uranium trioxide (UO_3) and mixed uranium oxides in man using material-specific parameters derived experimentally; these oxides are the ones of immediate concern during the testing and use of DU munitions.
- comment on the limits on annual intake by ingestion for members of the public.

For ease and consistency of presentation, it is emphasized that the biokinetic data are presented in terms of either unit intake (acute exposure), or unit intake per day (chronic exposure). Hence, in principle, the data can be scaled to the intake of choice, or conversely chest retention or excretion rates can be scaled for the purpose of predicting the intake. However, both approaches should be treated with caution if the temporal pattern of intake is unknown, or the contribution to the excretion rates is influenced by extraneous and variable sources such as uranium present in the diet. Dose limits are expressed in terms of the annual intake limit by mass. However it should be emphasized that these should be reduced as far as is practicable (see Chapter 9).

Compliance, or otherwise, with the limits for internal contamination can be achieved by assessing intakes and doses using the following procedures:

- combining measurements of DU in the environment (airborne concentrations, aerosol size, bioavailability, concentrations in contaminated food and drink etc.) with the suite of biokinetic models recommended by ICRP, namely, the Human Respiratory Tract Model (ICRP-66, 1994a), the systemic model for uranium (ICRP-69 1995a), and the model for uptake via the gastrointestinal tract (ICRP-30, 1979).

- using these biokinetic models to interpret external measurements of uranium in the chest or in excreta.

10.2 Inhalation dose coefficients and annual intake limits

For the purpose of recommending dose coefficients, or dose per unit intake for radionuclides, ICRP considered three types of compounds (ICRP-66, 1994a) in which the absorption rates from the lungs to blood are deemed to be fast (Type F), moderate (Type M) or slow (Type S). The default absorption parameter values are given in Table 10.1.

Table 10.1 Default absorption parameters for Type F, M and S materials

ICRP -66 absorption type	F (fast)	M (mod.)	S (slow)
Model parameters:			
Fraction dissolved rapidly, f_r	1	0.1	0.001
Dissolution rate:			
Rapid (per d), s_r	100	100	100
Slow (per d), s_s	-	0.005	0.0001

Notes

F (fast) materials that are readily absorbed into blood (corresponding to 'Class D'). There is significant absorption from ET_2 and BB_1 (see Annex 4), but some material in these regions will remain in solution in mucus and be swallowed, rather than be absorbed through the epithelium. Hence the default for such materials is s_r=100 per d ($t_{½}$ ~ 10 min).

M (moderate) materials with intermediate rates of absorption (corresponding to 'Class W'). For such materials the percentage absorbed rapidly is on the order of 10%, and the slow-phase retention time of the order of 100 d. This is represented by f_r = 0.1%; s_r = 100 per d; and s_s = 0.005 per d.

S (slow) relatively insoluble materials (corresponding to 'Class Y'). It is assumed that for most of the material the rate of absorption to blood is 0.0001 per d. This equals the particle transport rate from the most slowly cleared AI compartment. However, it is characteristic of even very insoluble materials that some rapid uptake to blood occurs immediately after inhalation. As a default it is assumed that 0.1% of the deposited material is rapidly absorbed. While the effect of this on doses is likely to be negligible, it may significantly affect the interpretation of measurement of activity in urine. This is represented by f_r = 0.001; s_r = 100 per d; and s_s = 0.0001 per d.

Based on a considerable amount of published biokinetic data (ICRP-71 1995b, ASTDR, 1999, Scripsick et al. 1985a, 1985b) obtained primarily from animal studies, uranium compounds were assigned to one of these types. The biokinetics of UO_3 are mostly consistent with assignment to Type M compounds and UO_2 to Type S compounds. For U_3O_8, some studies indicate Type M behaviour and others Type S (ICRP-71, 1995b).

Based on the human respiratory tract, systemic and gastrointestinal tract models referred to above, ICRP–68 (1994b), ICRP-72 (1996) and BSS (1996) have recommended dose coefficients, or dose per unit intake, expressed as Sv/Bq for all the important isotopes of uranium. These dose coefficients take account of several age groups within the population, but only those for adults and isotopes appropriate for natural and DU are listed here (Table 10.2).

The values for individual isotopes can be used to derive the dose coefficients for any isotopic composition of uranium. The Annual Intake Limits (AIL) for uranium and DU for adults, which correspond to dose limits of 20 mSv and 1 mSv, expressed as Bq, and calculated by dividing the dose limit (Sv) by the dose coefficient (Sv/Bq) are given in Table 10.3. Also included in the table are the equivalent masses of uranium and DU based on the isotopic composition and specific activities given with Table 10.3. These comparisons are important since they can be used for assessing whether exposure criteria for radiotoxicity or chemical toxicity will be more important for different chemical forms of uranium and DU.

Table 10.2 Dose coefficients, Sv/Bq, for uranium isotopes: public and occupational exposure (OJEC, 1996; BSS, 1996; ICRP-68, 1994b)

Type/Isotope[a]	**AMAD** 1μm (Public)	**AMAD** 5μm (Occupational.)
Type F	10^{-7}	10^{-7}
Uranium-234	5.6	6.4
Uranium-235[b]	5.2	6.0
Uranium-238[b]	5.0	5.8
Type M	10^{-6}	10^{-6}
Uranium-234	3.5	2.1
Uranium-235[b]	3.1	1.8
Uranium-238[b]	2.9	1.6
Type S	10^{-6}	10^{-6}
Uranium-234	9.4	6.8
Uranium-235[b]	8.5	6.1
Uranium-238[b]	8.0	5.7

Notes
a Uranium-236 is not considered, as it contributes less than 0.0003% of total activity. Other transuranics excluded as contributing less than 1% of dose (CHPPM, 2000; Annex 2)
b Includes contribution from short-lived progeny

Table 10.3 Dose coefficients[a] and AIL for natural uranium and DU: occupational and public exposure (rounded values).

Isotopic composition	**Worker** (5 μm, dose limit 20 mSv)		**Public** (1 μm, dose limit 1 mSv)	
	U-nat	DU	U-nat	DU
ICRP Type F compound				
Dose coefficient (Sv/Bq) 10^{-7}	6.15	5.92	5.26	5.06
Intake limit (Bq) 10^{3}	32.5	33.8	1.90	1.98
Intake limit (mg U)	1290	2270	75	133
ICRP Type M compound				
Dose coefficient (Sv/Bq) 10^{-7}	18.5	16.8	31.6	29.6
Intake limit (Bq) 10^{3}	10.8	11.9	0.32	0.34
Intake limit (mg U)	430	800	13	23
ICRP Type S compound				
Dose coefficient (Sv/Bq) 10^{-7}	62.9	59.2	87.1	82.6
Intake limit (Bq) 10^{3}	3.18	3.38	0.12	0.12
Intake limit (mg U)	130	230	4.5	8.1

Note
a Includes contribution from short lived progeny

Composition	by mass (%)			By activity (%)			Specific activity of mixture
	^{234}U	^{235}U	^{238}U	^{234}U	^{235}U	^{238}U	Bq /mg
a: U-nat	0.5×10^{-3}	0.72	99.3	48.9	2.2	48.9	25.2
b: DU	1.0×10^{-3}	2.0×10^{-1}	99.8	15.5	1.1	83.4	14.8

Chemical toxicity is discussed further in Chapter 8 and Annex 5. However it is important to recognize at this juncture that based on an occupational exposure limit of 0.2 mg/m^3 for soluble and insoluble forms of uranium (ACGIH, 2000; NIOSH, 2000; FRA, 1988; HSE, 2000), equivalent to 2 mg/d. It can be deduced from Table 10.3 (see also Stradling et al., 1997, Stradling et al., 1998, ICRP-78, 1997) that:

- daily intakes of Type F and Type M compounds will always be limited by chemical toxicity; daily intakes of Type M compounds will always be limited by chemical toxicity; annual intakes of Type M compounds will be limited by consideration of radiation dose
- daily intakes of Type S compounds will be limited by chemical toxicity while annual intakes will be limited by radiation dose

On the basis of the OSHA (1989) limit for soluble uranium of 0.05 mg/m^3, annual intakes of Type M compounds would also be restricted by chemical toxicity. Similar considerations should apply to exposure of the public using the appropriate recommendations for airborne dust and dose limit.

10.3 Biokinetics of Type F, M and S compounds of uranium after inhalation.

Because uranium and DU are identical chemically, their biokinetic behaviour will be the same. For workers, the predicted time-dependent retention in the chest and systemic tissues, and excretion, can be modeled using the default absorption parameters (Table-10.1) with other default parameter values for particle size, density, aerosol deposition in the respiratory tract and exercise levels (ICRP-66 1994a). These are given in Table 10.4.

The default absorption parameters, and density, are also used for members of the public. The other default parameter values, also given in Table 10.4 are different.

Table 10.4 Deposition of inhaled aerosols in the human respiratory tract: occupational and public exposure.

Region[c]	**Worker**[a] (%)	**Adult male**[b] (%)
ET_1	33.9	14.2
ET_2	39.9	17.9
BB	1.8 (33% in BB_2)	1.1 (47% in BB_2)
Bb	1.1 (33% in bb_2)	2.1 (49% in bb_2)
AI	5.3	11.9
Total deposit	82.0	47.3

a **Occupational exposure** 5 μm AMAD (σ_g = 2.5), 3.5 μm AMTD, density 3.0 g/cm^3, shape factor 1.5 (see Chapter 5); fraction breathed through nose is 1.31% sitting and 69% light exercise; mean ventilation rate is 1.2 m^3/h. (ICRP-66, 1994a).

b **Environmental exposure** 1 μm AMAD (σ_g = 2.47), 0.69 μm AMTD, density 3.0 g/cm^3, shape factor 1.5; fraction breathed through nose is 1.55% ventilation rate is 0.78 m^3/h. 33.3% sleeping, 25% sitting, 40.6% light exercise and 1.0% heavy exercise.

c The extrathoracic airways consist of the anterior nasal passages (ET_1) and posterior nasal and oral passages, pharynx and larynx (ET_2).

The thoracic regions are bronchial (BB and bb) and alveolar-interstitial (AI). For the purposes of external monitoring, the retention in the chest would be the activity retained in the thoracic regions.

10.3.1 Acute exposure

As illustrative examples, the chest retention for workers and members of the public after unit intake (radioactivity or mass) are shown in Figure 10.1. The figure emphasizes the difference in retention in the chest due to different particle size, breathing pattern and exercise level. The chest retention of Type F compounds within a few hours of exposure is negligible, and hence is not included in the figure.

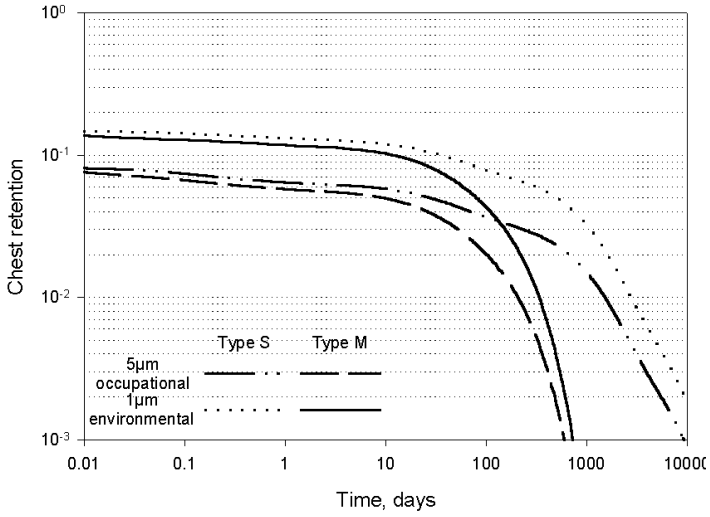

Figure 10.1 Fractional retention of inhaled uranium in the chest after acute inhalation of Type M and S compounds: occupational and public exposure.

The predicted urinary excretion rates for occupational exposure is given in Figure 10.2 and for public exposure in Figure 10.3.

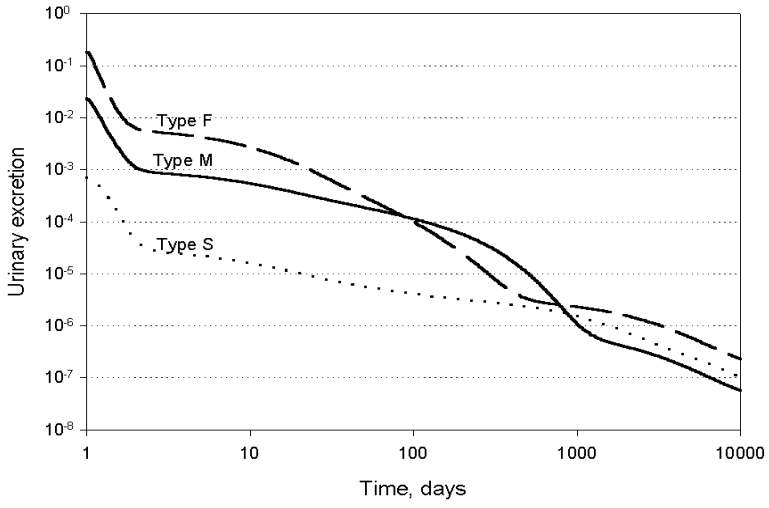

Figure 10.2 Fractional urinary excretion rate of inhaled uranium after acute inhalation of Type F, M and S compounds: occupational exposure.

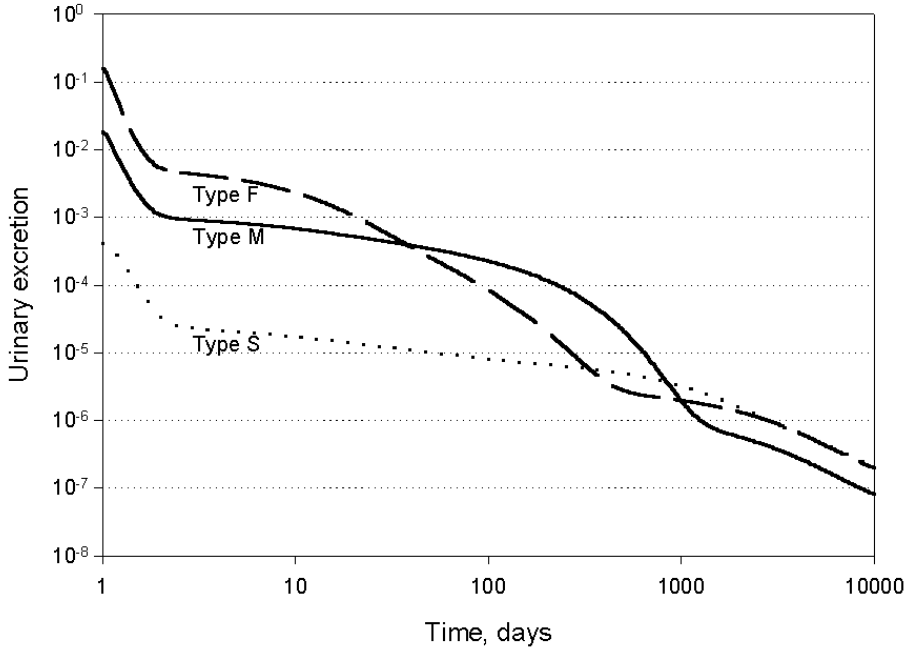

Figure 10.3 Fractional urinary excretion rate of inhaled uranium after acute inhalation of Type F, M and S compounds: public exposure.

The predicted faecal excretion rates for occupational exposure is given in Figure 10.4 and for public exposure in Figure 10.5.

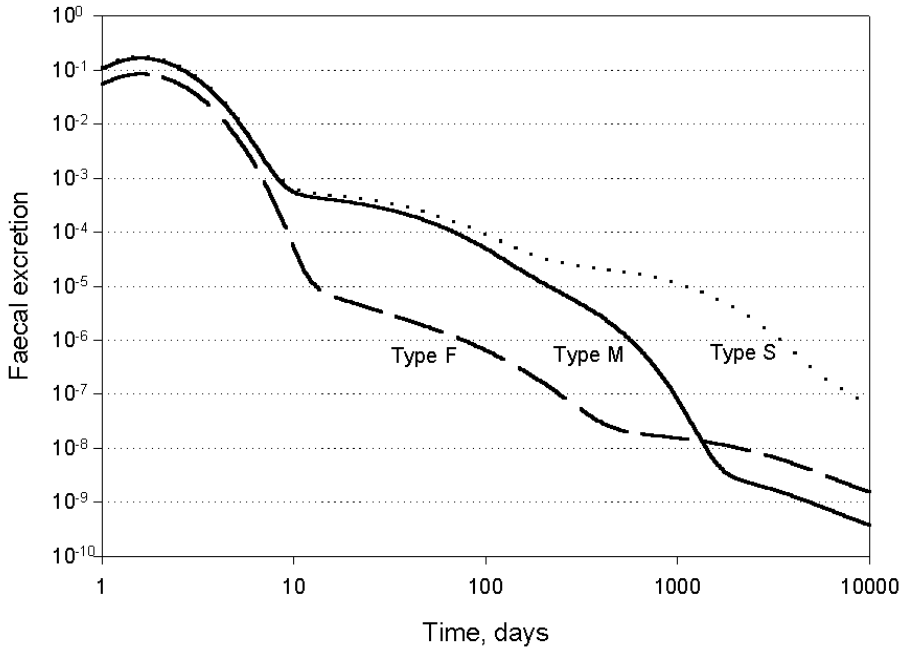

Figure 10.4 Fractional faecal excretion rate of inhaled uranium after acute inhalation of Type F, M and S compounds: occupational exposure.

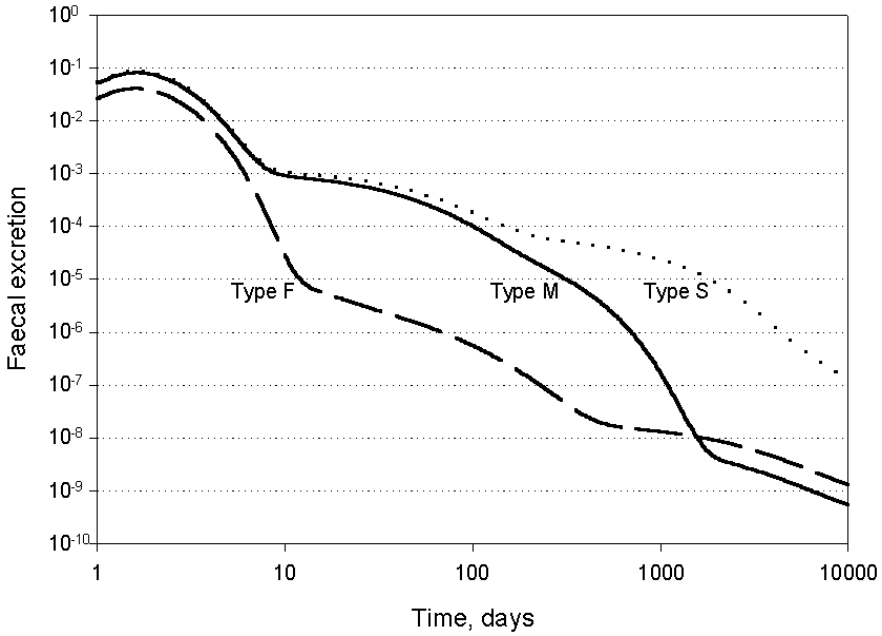

Figure 10.5 Fractional faecal excretion rate of inhaled uranium after acute inhalation of Type F, M and S compounds: public exposure.

Figure 10.2 shows that while there are large differences in the fractional excretion rates at early times after exposure, the rates beyond about 700 d are closely similar for the three absorption types. A comparison of Figures 10.2 and 10.3 shows that the fractional rate for occupational exposure is always higher than for public exposure. However, the curves in Figure 10.3, like those in Figure 10.2, converge at about 700 d. It is noteworthy that the faecal excretion curves for Type M and Type S compounds in Figure 10.4 are almost coincident up to about 100 d after exposure. Figures 10.4 and 10.5 demonstrate that the faecal rates after occupational and public exposure exhibit the same trends. However, in the latter case, the rates for Type M and S compounds are slightly higher beyond about one week after exposure. The rates for Type F compounds after public exposure are slightly lower than after occupational exposure during the first week; thereafter the curves are coincident.

In principle, assessments of intake and dose can be extrapolated from measurable amounts of uranium and DU in the chest or in urine or faeces a long time after intake. This approach should be treated with caution since the actual pattern of intake and airborne concentrations are unlikely to be known with certainty, and normal dietary intakes of natural uranium, could substantially distort the assessment. For example, a urinary excretion rate of say 1 μg/d of uranium observed several years after an assumed occupational intake of DU, a value which could be accounted for by a small and recent intake of a soluble form of uranium from the normal diet, would suggest that the original intake may have been about 1 g.

On the other hand, the urinary excretion curve could be used with advantage if very low levels of DU can be detected. For example, if the excretion of DU in urine several years after an assumed occupational exposure was 10 ng/day, then the maximum predicted intake would be only about 10 mg. This amount equates to a committed effective dose of only about 1 mSv for a Type S compound. (see Table 10.3).

10.3.2 Chronic intake

In this chapter, consideration is given only to members of the public. The biokinetics of uranium after chronic intake have been based on unit intake per day, say 1Bq or 1 μg. The data may be interpolated for any other intake rate if warranted. For example, in some cases it may be appropriate to consider chronic intake rate corresponding to the annual intake limit (see Table 10.3) i.e. at a rate of (annual intake limit) / 365 per day. While it is impossible to consider all the alternative exposure scenarios for continued exposure, this model is perfectly acceptable for illustrative purposes, and is consistent with one of the approaches used by ICRP-78 (1997)

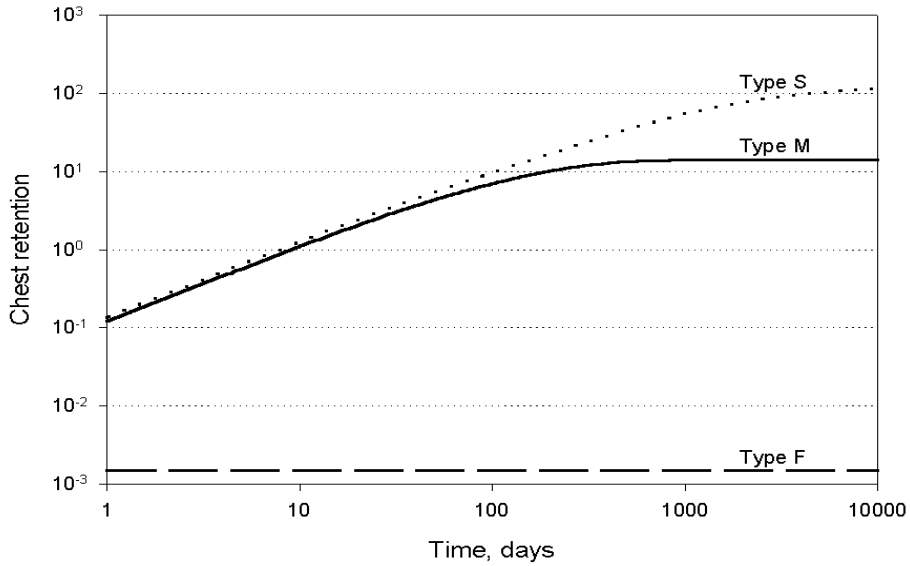

Figure 10.6 Chest retention of inhaled uranium after chronic inhalation of Type F, M and S compounds: public exposure.

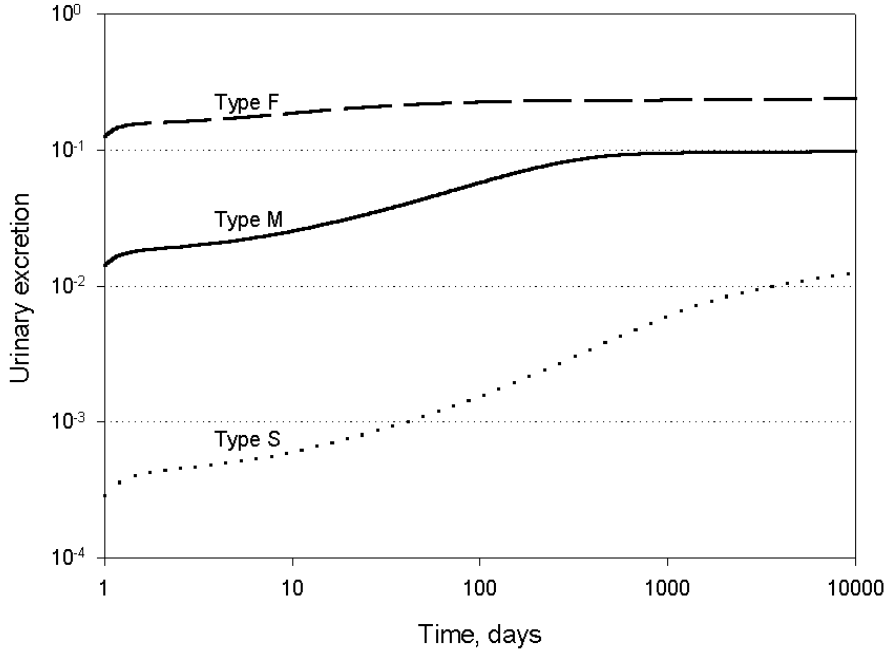

Figure 10.7 Fractional excretion rate of inhaled uranium in urine after chronic inhalation of Type F, M and S compounds: public exposure.

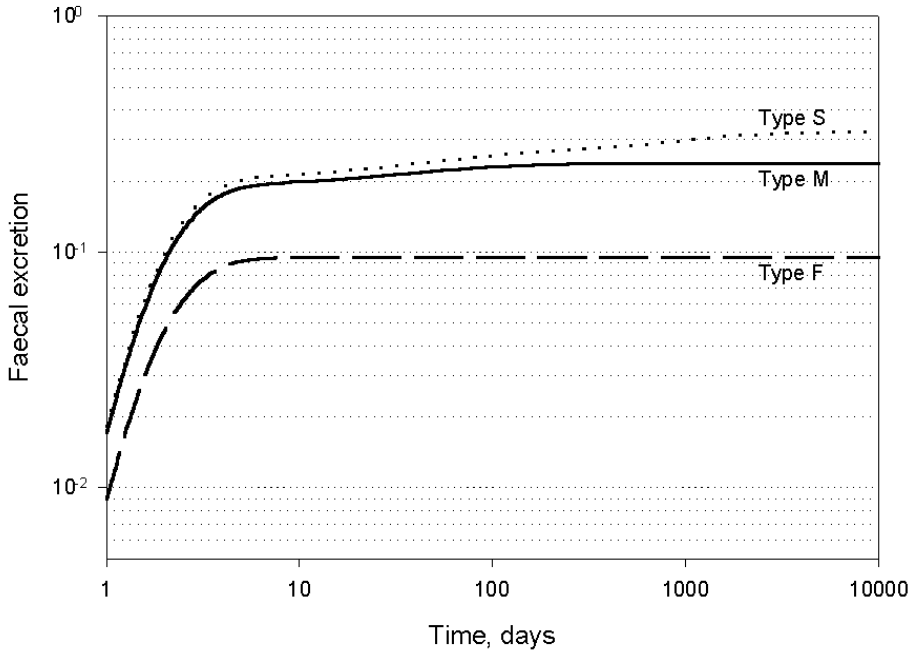

Figure 10.8 Fractional excretion rate of uranium in faeces after chronic inhalation of Type F, M and S compounds: public exposure.

Figure 10.6 shows that the amounts present in the chest after the inhalation of Type M and S compounds are closely similar up to about 100 d after the commencement of exposure. The data in Figure 10.7 show that the urinary excretion rates differ by about an order of magnitude over the first 100 or so after the commencement of exposure before slowly converging. Figure 10.8 shows that the faecal excretion rates are much closer than those for urinary excretion; indeed they only differ overall by about three-fold after 10 000 d. However it should be borne in mind that the curves represent idealized intake and excretion rates.

10.4 Material specific biokinetic behaviour of inhaled uranium oxides

Biokinetic studies have been conducted on all natural uranium compounds present in the nuclear fuel cycle (e.g. Hodgson et al., 2000, Ansoborlo et al., 2001; ICRP-71, 1995b). In comparison, very few studies have been conducted with DU. However since uranium and DU are identical chemically, the database on the former is relevant for the biokinetics of DU. However the discussion here is limited to the oxides which are reported to be present in the air in the aftermath of the use of DU munitions, or after a uranium fire. For DU used in warfare, U_3O_8 and to a lesser extent UO_2 and UO_3 are the compounds of most immediate interest. In addition, consideration is also given to the biokinetics of mixed uranium-iron (U/Fe) oxides, which may also be present.

Whilst many studies on the biokinetics of uranium oxides have been reported, very few of them have been designed to assess the absorption parameters of uranium as defined in the human respiratory tract model (ICRP-66, 1994a). For the purpose of this monograph, the values used have been obtained for materials formed during the fabrication of nuclear fuels in the UK (Hodgson et al., 2000), although similar data have been derived for similar compounds in the French nuclear industry (Ansoborlo et al., 2001). This latter publication also provides extensive dissolution data. The absorption parameters for reprocessed UO_3 (Moody et al., 1997) are similar to those obtained for

the compound formed in nuclear fuel fabrication (Hodgson et al., 2000). Information on mixed uranium-iron oxides has been obtained from an industrial source (Ansoborlo et al., 1998).

The values obtained from these studies are used here for illustrative purposes. For more detailed information on the application of the ICRP respiratory tract model, the reader is referred to a forthcoming technical document (ICRP, 2001)

It should be noted that the material specific absorption parameters are quite different from the default values (Table 10.1), which is not unexpected. Indeed, ICRP have continually acknowledged the importance of such data, and these results support this recommendation. In calculating these data it has been assumed that the absorption parameters in animals are the same as those in man. The evidence available at present suggests that this assumption is justifiable, since in other studies the observed biokinetic behaviour of U_3O_8 and UO_2 in workers is closely similar to that predicted by extrapolation from animal studies (Stradling et al., 1989, Bertelli et al., 1998).

The material specific absorption parameter values (Table 10.5) have been used with the other default parameter values for members of the public (Table 10.4) to calculate exposure limits (Table 10.6).

Table 10.5 Absorption parameter values for uranium oxides and DU default material.

Material	f_r	s_r, per d	s_s, per d	f_1	
				Inhaled	Ingested
U_3O_8	0.044	0.49	3.5×10^{-4}	0.002	0.002
UO_2	0.011	0.95	6.1×10^{-4}	0.002	0.002
UO_3	0.92	1.4	3.6×10^{-3}	0.02	0.02
U/Fe oxide[a]	0.12	1.45	2.6×10^{-3}	0.02	0.02
DU default[b]	0.2	1	1.0×10^{-3}	0.02	0.002

Notes

a mixture of UO_2, U_3O_8, UO_3, FeO, Fe_2U

b best judgement values. The value for f_r is based on DU with a large soluble fraction as determined from *in-vitro* studies (Scripsick, 1985a, 1985b); the value for s_r is based on the results of several experimental studies with uranium oxides and other compounds (Hodgson et al., 2000, Ansoborlo et al., 2001); s_s is representative of values obtained from several experimental studies with U_3O_8 (Hodgson et al., 2000, Ansoborlo et al., 2001). A material density of 9 is assumed since this is considered more appropriate than the ICRP default value of 3. The high value for f_r may be due to the presence of ultrafine metal or oxide particles; this has been demonstrated for other aerosols (Ansoborlo et al 1998)

Table 10.6 Dose coefficients[a] and annual intake limits for industrial uranium compounds and DU with default parameter values[b]: occupational and public exposure (rounded values).

Isotopic composition	**Worker** (5 µm, dose limit 20 mSv)		**Public** (1 µm, dose limit 1 mSv)	
	U-nat	DU	U-nat	DU
UO_3				
Dose coefficient (Sv/Bq) 10^{-7}	3.88	3.63	6.60	6.25
Intake limit (Bq) 10^3	51.6	55.0	1.51	1.60
Intake limit (mg U)	2040	3700	60	110
UO_2				
Dose coefficient (Sv/Bq) 10^{-7}	43.9	41.0	59.0	55.6
Intake limit (Bq) 10^3	4.56	4.88	0.17	0.18
Intake limit (mg U)	180	330	6.7	12.1
U_3O_8				
Dose coefficient (Sv/Bq) 10^{-7}	48.5	45.5	65.3	61.6
Intake limit (Bq) 10^3	4.12	4.40	0.15	0.16
Intake limit (mg U)	160	300	6.1	10.9
U/Fe Oxide				
Dose coefficient (Sv/Bq) 10^{-7}	25.7	23.8	36.6	34.3
Intake limit (Bq) 10^3	7.77	8.40	0.27	0.29
Intake limit (mg U)	310	560	10.8	19.6
DU default [b]				
Dose coefficient (Sv/Bq) 10^{-7}	35.7	33.2	55.6	52.3
Intake limit (Bq) 10^3	5.60	6.03	0.18	0.19
Intake limit (mg U)	220	410	7.1	12.8

Notes
a includes contribution from short lived progeny
b see Table 10.5 for absorption parameters

It is noteworthy that the exposure limits for uranium and DU in Table 10.6 for U_3O_8 and UO_2 lie between those of Type M and S compounds, and those for UO_3 between Type F and M compounds. The retention kinetics of uranium in the chest and excretion rates in urine have also been predicted using the material-specific absorption parameters in Table 10.5.

10.4.1 Acute exposure

The retention kinetics of uranium in the chest after unit intake for workers is shown in Figure 10.9 and for members of the public in Figure 10.10.

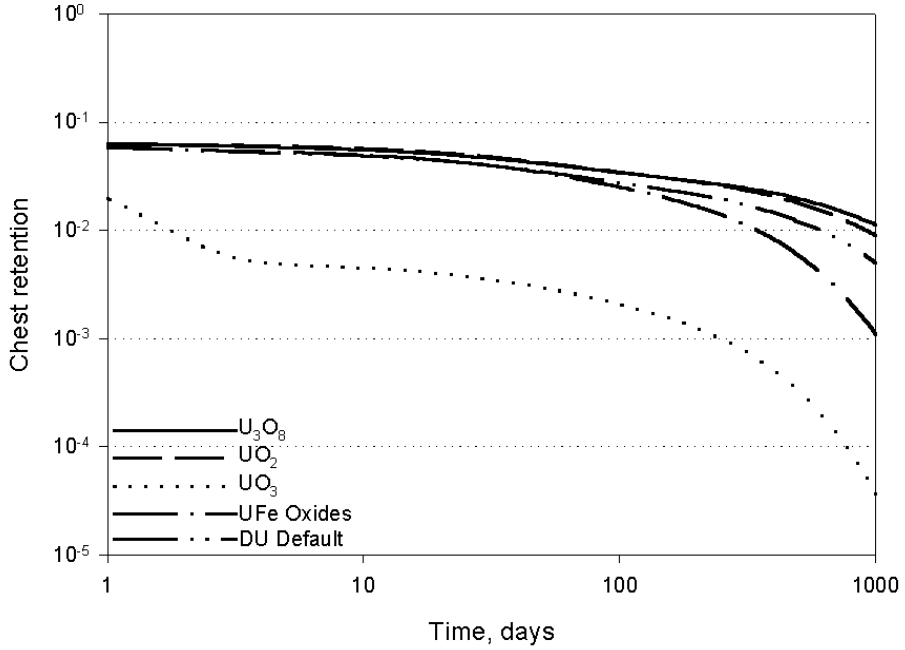

Figure 10.9 Fractional retention of inhaled uranium in the chest after acute inhalation of uranium oxides and the DU default: occupational exposure.

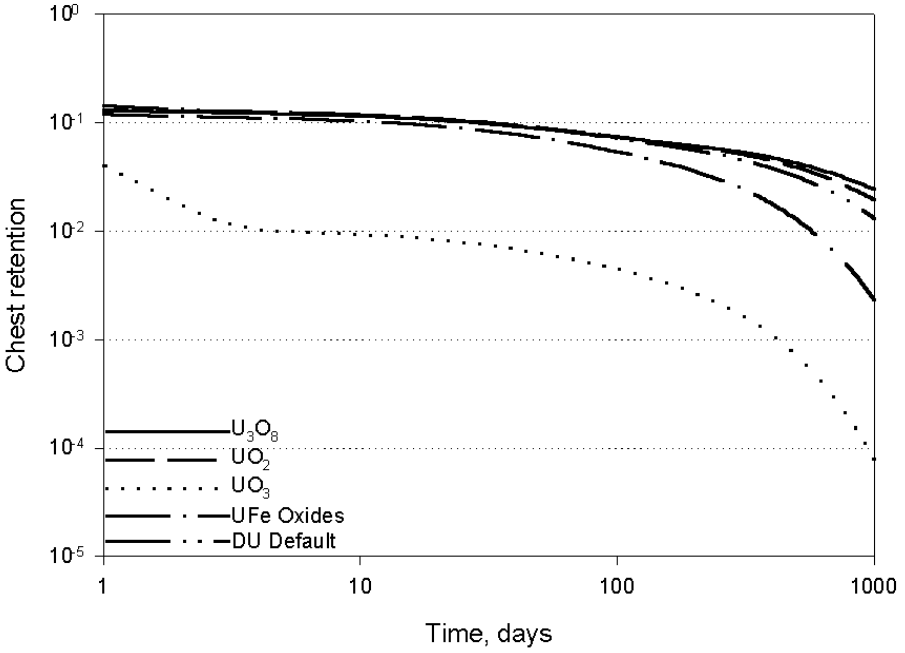

Figure 10.10 Fractional retention of inhaled uranium in the chest after acute inhalation of uranium oxides and the DU default: public exposure.

Figure 10.9 shows that apart from UO_3, the retention in the chest is similar for all the materials up to about 100 d after exposure. For the oxides, the chest retention kinetics lie between those for Type M and Type S compounds (Figure 10.1). The chest retention kinetics for each material after public exposure, shown in Figure 10.10, are closely similar to those after occupational exposure, reflecting the fact that most of the clearance from the respiratory tract occurs by particle transport to the gastrointestinal tract.

The fractional urinary excretion rates for uranium oxides after acute occupational and public exposure to uranium oxides and default DU are shown in Figures 10.11 and 10.12 respectively.

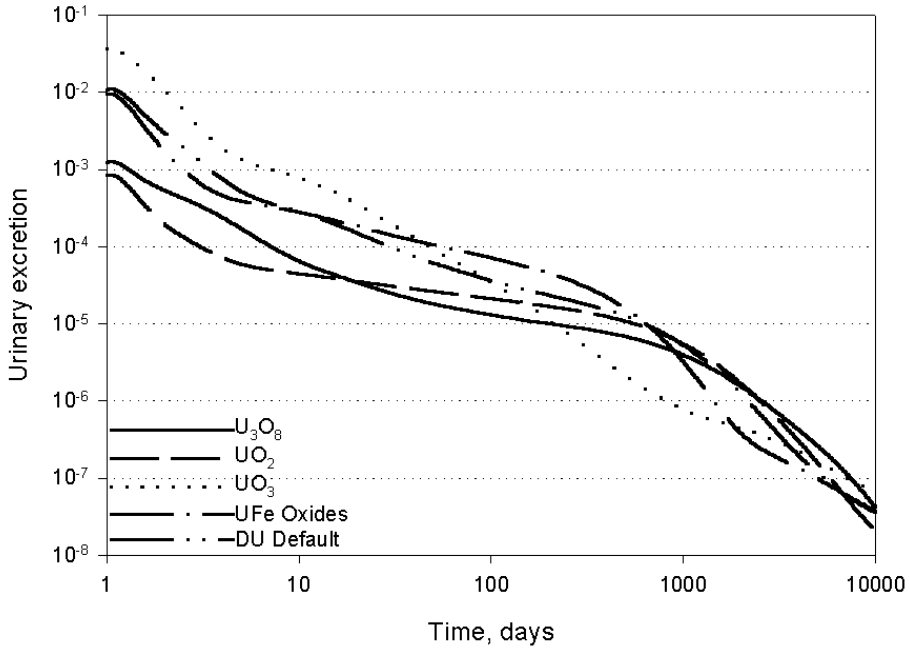

Figure 10.11 Fractional urinary excretion rate of inhaled uranium after acute inhalation of uranium oxides and the DU default: occupational exposure.

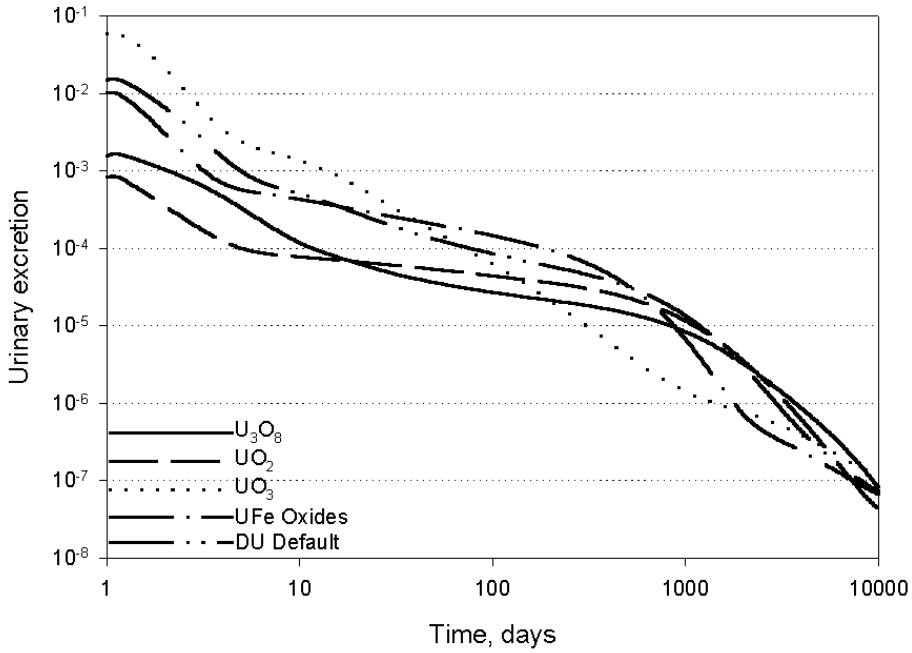

Figure 10.12 Fractional urinary excretion rate of inhaled uranium after acute inhalation of uranium oxides and the DU default: public exposure.

Figure 10.11 shows that up to 100 d after exposure, the urinary excretion rates for the various oxides can differ by an order of magnitude or more. It is noteworthy that, as for Type F, M and S compounds (Figure 10.2), the rates at about 1000 d are closely similar. However, it should be noted that for the oxides, the excretion rates are higher than for their assigned absorption type, due probably to a higher value of f_r (see 10.4). This

should facilitate interpolations from excretion data in so far that lower values on the assessment of intake should be possible.

Figure 10.12 shows that the urinary excretion rates are similar to those predicted after occupational exposure. From two days onwards, the rate for public exposure is always between 1.5 to 2.5 faster than for occupational exposure when the same material is inhaled.

The fractional faecal excretion rates for uranium oxides after acute occupational and public exposure to uranium oxides and default DU are shown in Figures 10.13 and 10.14 respectively.

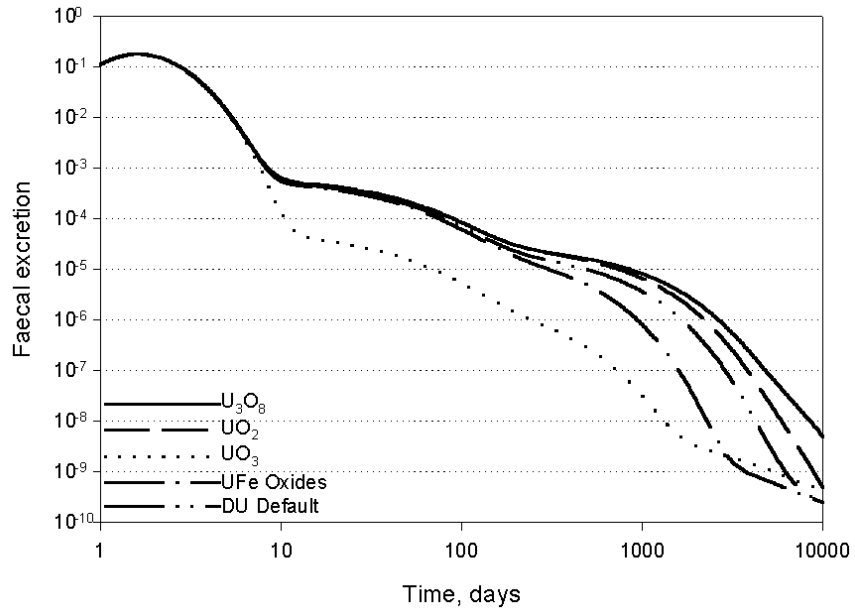

Figure 10.13 Fractional faecal excretion rate of inhaled uranium after acute inhalation of uranium oxides and the DU default: occupational exposure.

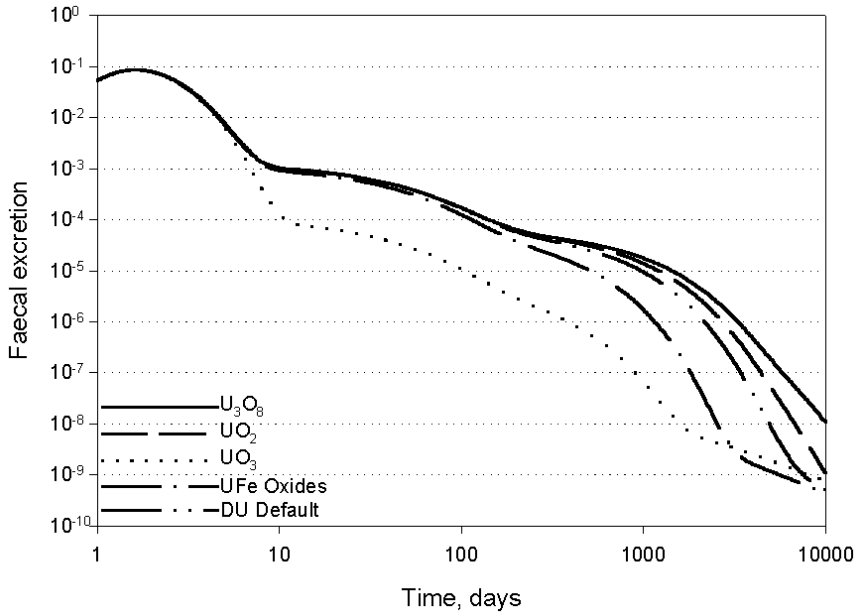

Figure 10.14 Fractional faecal excretion rate of inhaled uranium after acute inhalation of uranium oxides and the DU default: public exposure.

Figure 10.13 shows that, other than for UO_3, the faecal excretion rates are the same for the first week after exposure and then closely similar up to several hundred days. The faecal excretion rates after public exposure, shown in Figure 10.14 are closely similar to those obtained after occupational exposure.

This Chapter has shown that the differences in biokinetic behaviour when using default or material specific values may be important for optimising the assessment of intake from chest monitoring or the assay of excreta. This subject is discussed in later in Chapter 11.

10.4.2 Chronic exposure

The fractional retention of the uranium oxides and default DU after continuous chronic intake by adult members of the public is shown in Figure 10.15.

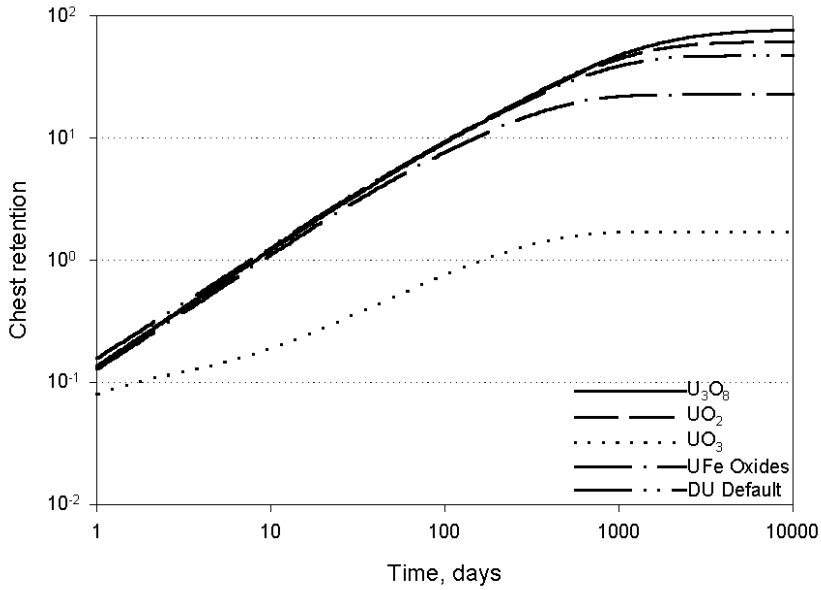

Figure 10.15 Fractional retention of inhaled uranium in the chest after chronic inhalation of uranium oxides and the DU default: public exposure.

Figure 10.15 shows that, apart from UO_3, the retention of uranium in the chest is closely similar for all materials up to about 600 d after the commencement of exposure. The fractional urinary and faecal excretion rates after chronic exposure are shown in Figures 10.16 and 10.17.

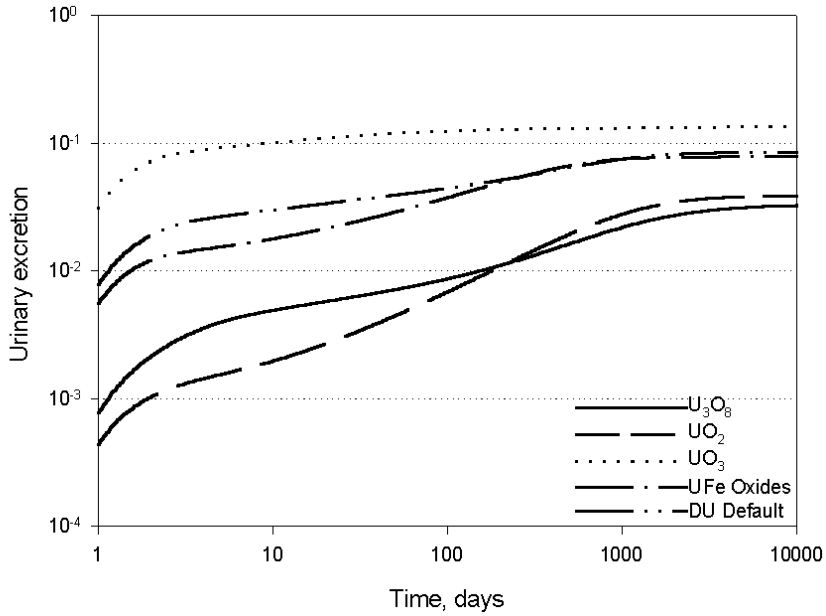

Figure 10.16 Fractional urinary excretion rate of inhaled uranium after chronic inhalation of uranium oxides and the DU default: public exposure.

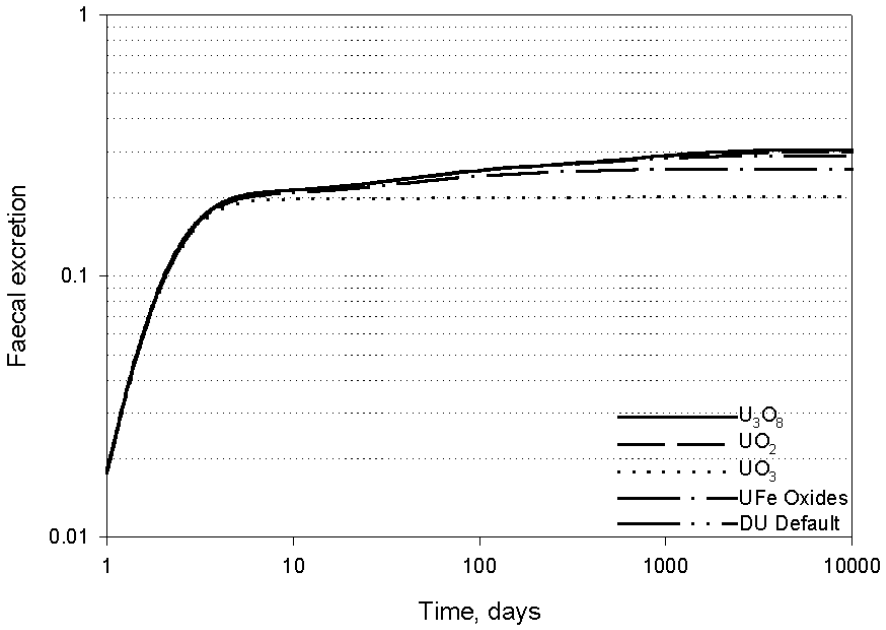

Figure 10.17 Fractional faecal excretion rate of inhaled uranium after chronic inhalation of uranium oxides and the DU default: public exposure.

Figure 10.16 shows that differences in the urinary excretion rate of an order of magnitude or more occur up to 100 d after the commencement of exposure, the curves slowly converging thereafter. The data for the faecal excretion rate in Figure 10.17 show that they are closely similar up to 10 000 d after exposure.

It should be emphasized that usually, there is less certainty about the chemical form of the uranium and DU inhaled by the public than during occupational exposure. In such circumstances, and until further information becomes available, it may be prudent to assume that for the purpose of radiological dose assessment the dust is assigned to inhalation Type S. It is also emphasized that from a toxicological standpoint, the dust should be assigned to inhalation Type F if a conservative assessment is required.

10.5 Ingestion coefficients and annual intake limits for adult members of the public

This Chapter concerns uptake from the gastrointestinal tract by adult members of the public from food and drink. As for inhalation, ICRP-72 (1996) and IAEA 1996) have recommended dose coefficients, or dose per unit intake, expressed as Sv/Bq for all the isotopes of uranium. For this purpose, the model of the gastrointestinal tract, summarized in Annex 4, is coupled to the systemic model for uranium (ICRP–69, 1995a). The generic values for natural uranium and DU are given in Table 10.7. In general, there is less certainty about the chemical form of the uranium and DU after ingestion rather than after inhalation. In such circumstances it may be prudent to assume that the dust is of inhalation Type F.

Table 10.7 Dose coefficients and annual intake limits for Type F compounds of natural uranium and DU after ingestion (f_1=0.02)

Isotopic composition	**U-nat**	**DU**
Type F		
Dose coefficient (Sv/Bq) 10^{-8}	4.82	4.77
Intake limit (Bq) 10^{3}	20.7	21.0
Intake limit (mg U)	820	1400

10.6 Wound contamination.

At present, there is no appropriate biokinetic model, which describes the behaviour of radionuclides after entry into the body from superficial or deep-seated wounds, or from embedded DU fragments. However in such cases estimates of the systemic tissue content can be made by extrapolating from the urinary excretion rate using the ICRP systemic model for uranium (ICRP-69, 1995a).

10.7 Summary

In order to make the amount of data manageable for the reader, this chapter has been limited to intakes and doses for only two generic potentially exposed groups of people, namely workers and adult members of the public as defined by ICRP. It is concluded that:

- chemical toxicity and radiotoxicity should be considered carefully in assessing the risk to the individual since either could dominate under different exposure scenarios.
- the likely exposure pattern should be identified as far as possible since this will substantially affect body retention and excretion parameters, and hence assessment of intake and dose.
- the chemical forms of uranium or DU, and their proportions, in the aerosol should be identified as far as possible since this will considerably improve assessments of intake and dose.
- material-specific data should be used whenever possible for predicting the biokinetics of uranium and DU; while much of this information has yet to emerge, the known behaviour of the likely constituents of the aerosol will make a substantial contribution towards realistic assessments of intake and dose.
- until more information on the chemical form of uranium and DU in the environment is obtained, it would be prudent to assume that it is in a soluble form (ICRP Type F).

- the lack of an appropriate wound model should not prejudice estimates of the uranium content of systemic tissues, notably the kidneys (See Chapter 12).

Currently there are gaps in knowledge in the following areas:

- Biokinetic data on DU aerosols with emphasis on the effect of variable physical-chemical composition resulting from the use of munitions.
- Bioavailability of uranium after dispersion and re-suspension of DU dusts and aerosols.

11 Monitoring for internal exposure to depleted uranium

In principle, the deposition of DU in the respiratory tract after inhalation and its subsequent uptake to organs in the body can be assessed from:

- external radiation measurements of DU in the chest
- the assay of DU excreted in urine
- the assay of DU excreted in faeces

The introduction of DU into the body via ingestion can be assessed using similar techniques for urine and faecal assessment. The specific case of DU ingestion is described in more detail in Chapter 12.

For wounds, DU can be measured directly at wound sites, and uptake can be assessed by excretion measurements.

The choice and efficacy of each procedure is dictated by the route of intake, the pattern of exposure, the physical and chemical form of the uranium, the time between intake and measurement, and the limit of detection of the analytical procedure used. The use of bio-indicators for assessing nephrotoxicogical effects in the kidneys is discussed in Chapter 8.

11.1 External monitoring of the chest

Measurements can be made of DU in the respiratory tract by external radiation counting. Such monitoring is sometimes referred to as 'Whole Body Monitoring'. To make a positive identification of DU (rather than natural uranium), it is necessary to measure both the ^{235}U and ^{238}U lung contents. The main gamma-emissions for these two radionuclides are at 186 keV (^{235}U), 63 keV and 93 keV (^{238}U). The last two are actually from the ^{234}Th daughter of ^{238}U, which will, in practice, always be present. All are low intensity emissions: the gamma-emission for ^{235}U is relatively high yield, but the activity fraction of ^{235}U in DU is low (~ 1.1%), while the gamma-emissions for ^{238}U are both low yield. The low intensities, taken together with the relatively low gamma energies, mean that specialized counting systems (for example using germanium (Ge) semiconductor detectors) are required.

Under optimum conditions, the minimum detectable amount of natural uranium in the chest may be as low as 2 to 3 mg (Lane et al., 1985, Palmer and Rieksts, 1985, Pomroy and Malm, 1985; Toohey et al., 1991). For DU, the value is in practice likely to be rather higher, at about 8 mg for a 45 minute measurement (see Table 11.3). Chest monitoring using Ge detectors is feasible if measurements can be made soon after the exposure took place. However, for exposures taking place years previously, only a small fraction of the amount initially deposited remains in the lung. Significant intakes may then result in lung activities that are below the limit of detection for chest monitoring, and so in these circumstances chest monitoring may not be useful.

Amounts remaining in the respiratory tract at various times following inhalation have been calculated under two separate conditions, broadly characterized as occupational exposure (Table 11.1) and public exposure (Table 11.2). The occupational exposure case is appropriate for military personnel who may have been exposed to DU as a result of a single incident on the battlefield (i.e. 'acute' exposure) or remediation. The public

exposure case is appropriate for the general population who may have been exposed over a protracted period, up to the time of measurement, to DU in the form of general environmental contamination (i.e. 'chronic' exposure). Calculations were performed using the ICRP-recommended default model parameters for occupational or public exposure, and default absorption parameters for moderately soluble (Type M) and insoluble (Type S) materials; and also using estimates of the most appropriate model parameters for DU (Tables 10.1, 10.4, 10.5). The time-dependent retention for Type M and Type S materials in the lungs after acute or chronic exposure are shown in Figures 10.1 and 10.6.

A measure of the sensitivity of the measurement technique is the minimum detectable intake of DU. This depends not only on the minimum detectable amount (MDA) in the respiratory tract, but also on the time between intake and measurement. Tables 11.3 and 11.4 give the minimum detectable intakes for lung measurements made at the times given in Table 11.1, for an acute occupational exposure and for chronic public exposure.

Table 11.1 Uranium lung retention after an acute intake by inhalation: occupational exposure.

Time after intake (d)	**Lung retention [c] (% of intake)**		
	Type M [a]	**Type S [a]**	**DU [b]**
1	5.76	6.43	5.98
7	5.18	5.95	5.03
30	3.84	4.94	4.02
365	0.40	2.65	1.56
3650	~ 0	0.33	0.01

a For Type M and Type S, ICRP-recommended default model parameter values for occupational exposure were used (see Tables 10.1 and 10.4 for values)
b For DU, estimates for the most appropriate model parameter values for occupational exposure were used (see Table 10.4 and 10.5 for values)
c Retention in the tracheo-bronchial airways and thoracic lymph nodes is included

Table 11.2 Uranium lung retention after a chronic intake by inhalation: public exposure.

Time after start of intake (d)	**Lung retention [c] (% of daily intake)**		
	Type M [a]	**Type S [a]**	**DU [b]**
1	12.2	13.6	15.8
7	79.2	89.4	92.3
30	292	348	346
365	1260	2710	2340
3650	1410	9430	4670

a For Type M and Type S, ICRP-recommended default model parameter values for public exposure were used (see Tables 10.1 and 10.4 for values)
b For DU, estimates for the most appropriate model parameter values for public exposure were used (see Table 10.4 and 10.5 for values)
c Retention in the tracheo-bronchial airways and thoracic lymph nodes is included

Table 11.3 Minimum detectable acute intakes for DU by lung counting: occupational exposure.

Time after intake (d)	Minimum detectable intake (mg)					
	Based on detection of ^{238}U [a]			Based on detection of ^{235}U [b]		
	Type M	Type S	DU	Type M	Type S	DU
1	140	130	130	380	340	370
7	160	140	160	420	370	440
30	210	160	200	570	440	550
365	2000	300	520	5500	830	1400
3650	2×10^{11}	2400	79 000	4×10^{11}	6600	210 000

a MDA for ^{238}U in lung is estimated to be 100 Bq (~ 8.0 mg DU), based on counting statistics
b MDA for ^{235}U in lung is estimated to be 3.5 Bq (~ 22 mg DU), based on counting statistics

Table 11.4 Minimum detectable chronic intakes for DU by lung counting: public exposure.

Time after start of intake (d)	Minimum detectable intake (mg) [a]					
	Based on detection of ^{238}U [b]			Based on detection of ^{235}U [c]		
	Type M	Type S	DU	Type M	Type S	DU
1	66	59	51	180	160	140
7	71	63	61	190	170	170
30	82	69	70	230	190	190
365	230	110	130	640	300	340
3650	2100	310	630	5700	850	1700

a Sum of daily intakes
b MDA for ^{238}U in lung estimated to be 100Bq (~ 8.0 mg DU), based on counting statistics
c MDA for ^{235}U in lung estimated to be 3.5 Bq (~ 22 mg DU) , based on counting statistics

As indicated in Table 10.6, for the acute occupational exposure case, an intake of 410 mg DU would result in a committed effective dose equal to the annual dose limit of 20 mSv. Thus, if a positive identification of ^{235}U is required, it can be seen that the sensitivity of chest monitoring is barely adequate even if monitoring takes place within the first few days. However, if the assessment of intake can be based on the measurement of ^{238}U only, chest monitoring could be usefully employed for a few months after the exposure. This would be the case where the exposure to DU could have been the only inadvertent exposure to uranium; note that exposure to natural sources of uranium would be extremely unlikely to result in amounts in the chest approaching the MDA.

It should be noted, however, that even under optimum conditions, the minimum detectable intake corresponds to a dose that is a significant fraction of the annual dose limit for occupational exposure. Furthermore, it should be noted that chest monitoring would have inadequate sensitivity whatever the time of measurement if the material were to be more soluble than has been assumed here. This would be the case if a large fraction of the DU was in the form of UO_3, rather than UO_2 and U_3O_8.

For the chronic public exposure case, chest monitoring does not have sufficient sensitivity to detect intakes that would result in a committed effective dose of 1 mSv.

11.2 Urine and faecal monitoring

In principle, the assay of uranium in urine can be used for dose assessment after the uptake of any chemical form of uranium after inhalation and ingestion, or from wounds. However, the use of faecal assay is confined to intakes by inhalation of relatively insoluble forms such as UO_2 and U_3O_8.

Measurement of uranium excreted in urine at known times after the exposure is potentially a more sensitive method than chest monitoring for determining the amount of DU inhaled. However, uncertainties in the assessed intake can be quite large, because many assumptions concerning the aerosol size, solubility, and rates of movement around the body must be made. Another problem is that natural uranium is present in urine because of the ingestion of natural uranium in food and drink. Typically, an individual may excrete between 10 and 400 ng of natural uranium in urine each day, but levels can be much higher (ICRP–23, 1975, Roth et al., 2001). Differentiating between uranium that is excreted as a result of dietary intake of natural uranium, and uranium, that is excreted as a result of exposure to DU is a significant problem for any measurement technique.

The amounts of DU present in urine following a DU exposure may well be similar to, or even less than, the naturally occurring amount. For instance, an intake of 100 mg of DU by inhalation would give rise to about 25 ng DU in a 24-hour urine sample taken ten years after the exposure (based on default model parameters for occupational exposure to DU, Table 10.5). It is therefore necessary to measure the ^{235}U : ^{238}U isotopic ratio to determine the fraction of the measured uranium in urine that arises from a DU intake. Tables 11.5 and 11.6 give the excretion rates of uranium at various times following inhalation, as a percentage of the intake, for an acute occupational exposure and for chronic public exposure. The time-dependent excretion of DU after acute occupational exposure is shown in Figures 10.2 and 10.11, and after chronic exposure of the public in Figures 10.7 and 10.16.

Table 11.5 Urinary and faecal excretion rates of uranium after an acute intake by inhalation: occupational exposure.

Time after intake (d)	Urine (% / day)			Faeces (% / day)		
	Type M [a]	Type S [a]	DU [b]	Type M [a]	Type S [a]	DU [b]
1	2.32×10^{-0}	7.04×10^{-2}	1.09×10^{-0}	10.7	11.4	11.2
7	6.50×10^{-2}	1.93×10^{-3}	3.67×10^{-2}	2.26×10^{-1}	2.47×10^{-1}	2.35×10^{-1}
30	2.65×10^{-2}	7.70×10^{-4}	9.87×10^{-3}	2.72×10^{-2}	3.50×10^{-2}	3.04×10^{-2}
365	2.81×10^{-3}	2.64×10^{-4}	1.61×10^{-3}	3.45×10^{-4}	2.21×10^{-3}	1.29×10^{-3}
3650	2.21×10^{-5}	3.56×10^{-5}	2.46×10^{-5}	1.46×10^{-7}	8.16×10^{-5}	2.62×10^{-6}

a For Type M and Type S, ICRP-recommended default model parameter values for occupational exposure were used (see Tables 10.1 and 10.4 for values)

b For DU, estimates for the most appropriate model parameter values for occupational exposure were used (see Table 10.4 and 10.5 for values)

Table 11.6 Urinary and faecal excretion rates of uranium after a chronic intake by inhalation: public exposure.

Time after start of intake (d)	Urine (% of daily intake / day)			Faeces (% of daily intake / day)		
	Type M [a]	Type S [a]	DU [b]	Type M [a]	Type S [a]	DU [b]
1	1.42	2.84×10^{-2}	7.80×10^{-1}	1.71	1.82	1.81
7	2.32	5.45×10^{-2}	2.82	19.5	21.0	20.9
30	3.61	8.78×10^{-2}	3.60	21.2	23.1	23.0
365	8.70	3.29×10^{-1}	5.93	23.7	27.6	27.0
3650	9.67	1.00	8.40	23.8	32.0	28.7

a For Type M and Type S, ICRP-recommended default model parameter values for public exposure were used (see Tables 10.1 and 10.4 for values)
b For DU, estimates for the most appropriate model parameter values for public exposure were used (see Table 10.4 and 10.5 for values)

The main techniques available for measurement of uranium in urine are fluorimetry, alpha spectrometry and mass spectrometry. The capabilities of these techniques for DU monitoring are discussed below.

11.2.1 Fluorimetry

The minimum detectable amount for fluorimetry, based on empirical formulae, is in the range 1.5 to 7 ng of total uranium in a 24-hour urine sample, using the Kinetic Phosphorescence Analysis method. However fluorimetry cannot provide isotopic analysis, and so cannot differentiate between DU and natural uranium in urine. One possible use would be to screen samples for unusually high levels of uranium; the isotopic composition of samples above a screening level could then be measured using another technique. However, caution would need to be exercised, because the potentially large range of natural uranium urine levels could mean that screening levels would have to be set so high that significant levels of DU in urine could be missed.

11.2.2 Alpha spectrometry

The minimum detectable amount for alpha spectrometry, based on counting statistics, is approximately 0.1 mBq of ^{234}U, ^{235}U or ^{238}U in a 24-hour urine sample. Count times of approximately one week are required to achieve this sensitivity. For natural uranium, a measurement of 0.1 mBq of either ^{234}U or ^{238}U would correspond to about 8 ng of total uranium. Thus, naturally occurring levels of uranium in urine could be detected, although not with high precision. A sample containing natural uranium would need to contain about 200 ng of uranium before ^{235}U could be detected, because of this isotope's low activity fraction.

For DU, measurement of the ^{238}U activity would again allow the detection of about 8 ng total uranium. However, to make a positive identification of DU, either the ^{234}U or ^{235}U activities would have to be measured. The minimum masses of DU necessary to detect ^{234}U or ^{235}U are about 40 ng and 600 ng, respectively. If the uranium present was predominantly DU rather than natural, it should be possible to make a positive identification of DU at these levels. However, if a significant fraction of the uranium were natural, higher levels would be needed in order to determine the amount of DU present. The amount of DU that could be detected depends on the content of natural uranium and the accuracy of the determination of the ^{235}U (or ^{234}U) and ^{238}U levels.

Because of the relatively poor sensitivity of alpha spectrometry to ^{235}U in either natural uranium or DU, the determination of the fraction of the uranium in urine that is DU would normally be done on the basis of the measured ^{234}U : ^{238}U ratio. However, a problem arises because this ratio measured in urine can vary from 1:1 up to 3:1 (Hurtgen, 2001). The increase in this ratio above its expected value of 1:1 arises because of the influence of geochemical processes on uranium in groundwater. In order to use the technique, it would be necessary to establish the isotopic ratio of natural uranium in urine for each potentially contaminated individual measured, perhaps by the use of control measurements on uncontaminated individuals living at the same location. It is necessary to take a sufficiently large number of baseline measurements so that the background distribution can be reasonably established. For an occupational monitoring program, the measured distribution (typically log-normal) can be used to establish a confidence interval above which exposures are considered to be occupationally derived. The frequency of sample collection can then be adjusted accordingly.

11.2.3 Mass spectrometry

Specialized mass spectrometric techniques (such as Multi Collector Inductively Coupled Plasma MS, MC-ICP-MS; High Resolution Inductively Coupled Plasma MS, HR-ICP-MS; or Thermal Ionization MS, TIMS) can provide isotopic analysis at levels lower than can be achieved by alpha spectrometry. Depending on the technique, amounts of total uranium in a 24-hour urine sample in the range 1 fg to 5 pg can be detected. However, larger amounts are required to detect the change in isotopic ratio that would indicate the presence of DU. Again, the amount of DU that could be detected depends on the content of natural uranium and the accuracy of the determination of the ^{235}U and ^{238}U levels. On current information, it appears that the minimum detectable reduction in $^{235}U/^{238}U$ ratio from its natural value is approximately 10% (Harwell, 2001). For typical levels of natural uranium, amounts of DU in a 24-hour urine sample as low as about 10 ng (perhaps lower than this in some cases) could therefore be detected. Caution is needed since further development of their methods is needed to allow a satisfactory determination of the $^{235}U/^{238}U$ ratio in urine samples that contain natural uranium levels typical of healthy subjects (Roth et al., 2001).

On the assumption that 10 ng of DU in a 24-hour sample can be detected, Tables 11.7 and 11.8 give the corresponding minimum detectable intakes for measurements of 24-hour urine and faecal excretion made at the times given in Table 11.5, for an acute occupational exposure and for chronic public exposure.

Table 11.7 Minimum detectable acute intake for DU by bioassay/mass spectrometry: occupational exposure.

Time after intake (d)	Minimum detectable intake (mg)					
	Urine excretion			Faecal excretion		
	Type M	Type S	DU	Type M	Type S	DU
1	0.00043	0.014	0.00092	0.000093	0.000088	0.000089
7	0.015	0.52	0.027	0.0044	0.0040	0.0043
30	0.038	1.3	0.10	0.037	0.029	0.033
365	0.36	3.8	0.62	2.9	0.45	0.78
3650	45	28	41	6800	12	380

Minimum detectable amount of DU assumed to be 10 ng in a 24-hour sample

Table 11.8 Minimum detectable chronic intake for DU by bioassay/mass spectrometry: public exposure.

Time after start of intake (d)	Minimum detectable intake (mg) [a]					
	Urine excretion			Faecal excretion		
	Type M	Type S	DU	Type M	Type S	DU
1	0.00070	0.035	0.0013	0.00058	0.00055	0.00055
7	0.0030	0.13	0.0025	0.00036	0.00033	0.00033
30	0.0083	0.34	0.0083	0.0014	0.0013	0.0013
365	0.042	1.1	0.062	0.015	0.013	0.014
3650	0.38	3.7	0.43	0.15	0.11	0.13

a Sum of daily intakes
Minimum detectable amount of DU assumed to be 10 ng in a 24-hour sample

For the acute occupational exposure case, it can be seen that mass spectrometric measurements of DU in urine can detect intakes as low as about 40 mg DU, ten years after the exposure. Such an intake would give rise to a committed effective dose of about one tenth of the annual dose limit for occupational exposure.

For the chronic public exposure case in which the intake is spread uniformly over a period of exposure of up to ten years and continues up to the time of measurement, mass spectrometric measurements of DU in urine can detect intakes as low as 0.43 mg. In practice, the exposure pattern is unlikely to be so well characterized, but sensitivity should be adequate to determine an intake resulting in a committed effective dose of 1 mSv.

The data given in Table 11.7 and 11.8 for DU indicate that faecal monitoring has comparable sensitivity to urine monitoring, and furthermore that if the material were more insoluble than expected, would actually have significantly greater sensitivity. However, faecal monitoring has some significant disadvantages. Firstly, the natural variability in the amount of uranium ingested results in a large day-to-day variability in faecal excretion, which would present additional problems for the determination of the amount of DU. Secondly, the difficulty in obtaining samples in most cases would probably mean that its potential advantages could not be exploited, except where a special investigation was being carried out.

11.3 Wound monitoring

DU fragments present in the body as a consequence of wounds have been identified by clinical examination using X-rays (Hooper et al., 1999; McDiarmid et al., 1999). The results suggest that small fragments can penetrate deep into soft tissue without clear evidence of a superficial wound. Some fragments about 20 mm in diameter could be identified by this procedure, but most were less than 1mm. In some cases, elevated urinary excretion of uranium was observed, although DU fragments could not be identified by this procedure. Hence, X-ray techniques should not be regarded as definitive, and at best can provide only a semi-quantitative indication of internal contamination.

Following the Gulf War, probes have been developed for the specific purpose of assessing wound contamination with DU (Chandler, 2000). Tissue equivalent wound

phantoms containing various amounts of DU metal embedded at various depths (0.97 cm, 3.91 cm, 7.73 cm) were used to compare the efficiencies of bismuth germinate (BGO) and sodium iodide (NaI(Tl)) detectors. The results showed that the lowest minimum detectable activities for the shallow, medium and largest depth phantoms were 5.8 kBq, 3.5 kBq and 10 kBq respectively.

11.4 Monitoring for individuals potentially exposed to DU aerosols

The data presented in Tables 11.1 to 11.8 demonstrate the importance of carrying out monitoring as soon as possible after a potential acute exposure. In the case of chest monitoring, useful results are obtainable for a few months after an intake, although sensitivity greater than that which is presently achievable would be desirable. For urine monitoring with isotopic analysis by mass spectrometry, adequate sensitivity is probably achievable for samples taken ten years or more after a potential acute exposure, but uncertainties in assessed intakes are likely to be quite large. With the present state of knowledge of long-term uranium excretion, it is difficult to quantify uncertainties, but errors of up to a factor of 10 are possible. Uncertainties would be significantly reduced if monitoring were to take place soon after a potential exposure.

For retrospective assessment of potential exposures taking place more than one year previously, measurements of DU in urine using high sensitivity mass spectrometry (e.g. High Resolution Inductively Coupled Plasma Mass Spectrometry, HR-ICP-MS; Multi-Collector Inductively Coupled Plasma Mass Spectrometry, MC-ICP-MS; or Thermal Ionization Mass Spectrometry, TIMS are recommended. However, there remains considerable uncertainty about the capabilities of these techniques for this particular application, and it will be important for methods to be validated and performance-tested before they are used as part of a screening programme.

Initial screening using lower cost, lower sensitivity methods (e.g. Quadrupole ICP-MS) could be considered, but it would be necessary to confirm that such methods have the capability to detect the presence of (if not to quantify) significant levels of DU in urine. If DU is detected in urine in significant amounts, chest monitoring could provide additional useful information for intakes that could have taken place up to a few months previously. However, for potential exposures occurring approximately ten years before a measurement, chest measurements are unlikely to provide useful information.

11.5 Monitoring for those with health effects attributed to exposure to depleted uranium

All of the monitoring techniques available for retrospective assessment of intake have large inherent uncertainties. For the small number of people for whom it has been suggested that observed health effects are a result of exposure to DU, all possible monitoring methods should be considered.

For *in vivo* (body) monitoring, chest monitoring should be performed; consideration should also be given to the measurement of skeletal activity, although there appears to be no publications on this matter at present. Assessment of activity in tracheo-bronchial and broncho-pulmonary lymph nodes should also be considered (although it is recognized these would be difficult measurements to perform and interpret).

For bioassay monitoring, assessments of DU urine and faecal excretion rates using high sensitivity mass spectrometry techniques should be performed.

11.6 Summary

Monitoring for internal exposure to DU, particularly where single intakes may have occurred more than about one year previously, presents significant difficulties. High sensitivity mass spectrometric measurement of uranium isotopes excreted in urine is recommended as the main monitoring method. However, the capabilities of these techniques for the measurement of DU in urine should be confirmed before they are used as part of a screening programme. Body monitoring, to determine the amount of any uranium contamination in the lungs, may also be of some use for the assessment of occupational exposure during the first few months following an intake.

12 Biokinetics of uranium species from the standpoint of nephrotoxicty

The behaviour of uranium in the body predicted using ICRP biokinetic models, in association with default absorption parameter values for Type F, M and S compounds, and material-specific absorption parameter values for the oxides have been described in Chapter 10. In this Chapter, the focus is on the potential nephrotoxicity of uranium after inhalation of these materials, or after ingestion of soluble forms of the element.

12.1 Inhalation of uranium

Using the same default parameter values for uranium Type F, M and S compounds as given in Table 10.1, the time-dependent retention of uranium in the kidneys after an acute unit intake (Bq or µg) by occupationally exposed workers and chronic intake (Bq/d or µg/d) by members of the public are given in Figures 12.1 and 12.2. For comparison, the predicted kidney retention kinetics after the inhalation of U_3O_8, UO_2, U_3O_8, mixed U/Fe oxide and DU default using the same absorption parameters as given in Table 10.5 are shown in Figures 12.3 and 12.4.

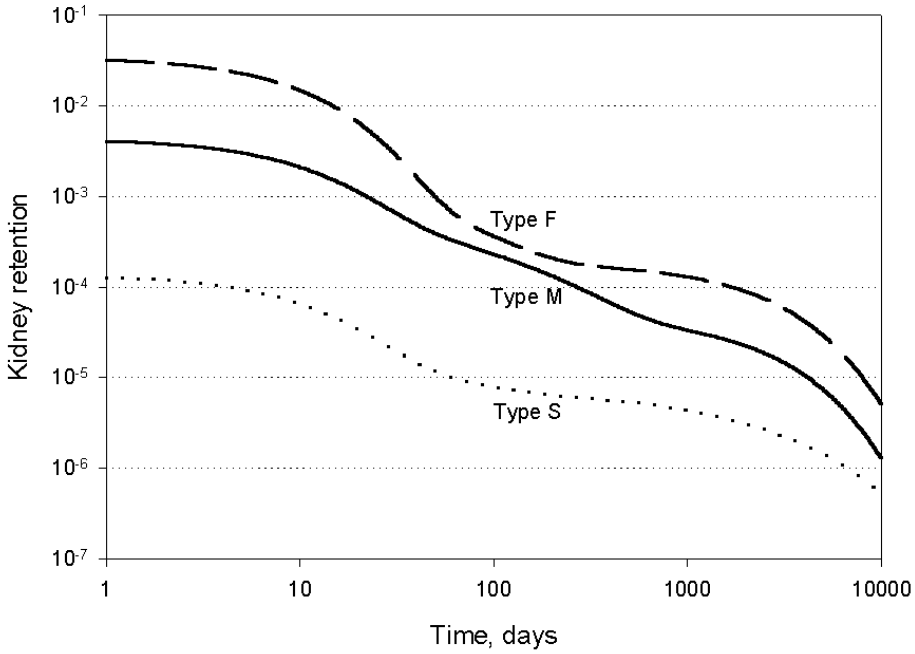

Figure 12.1 Fractional retention of inhaled uranium in the kidneys after acute inhalation of Type F, M and S compounds: occupational exposure.

After acute intake by workers, the maximum concentration of uranium in the kidneys occurs about one day after exposure. The intake that will result in a specified amount, or concentration in the kidneys (assuming that the mass of the organ is 310 g), can be deduced from Figures 12.1 and 12.3. The intake values given in Table 12.1 refer to the usually accepted kidney limit of 3 µg/g; the intake for any other specified concentration e.g. 0.3 µg/g of kidney will of course be proportional. Table 12.1 shows that for workers, the permissible concentration of uranium in the kidneys for U_3O_8 and UO_2 in particular are most unlikely to be exceeded in any exposure scenario. Similar conclusions may apply for members of the public, even if the acceptable concentrations in the kidneys were reduced by an order of magnitude to 0.3 µg/g.

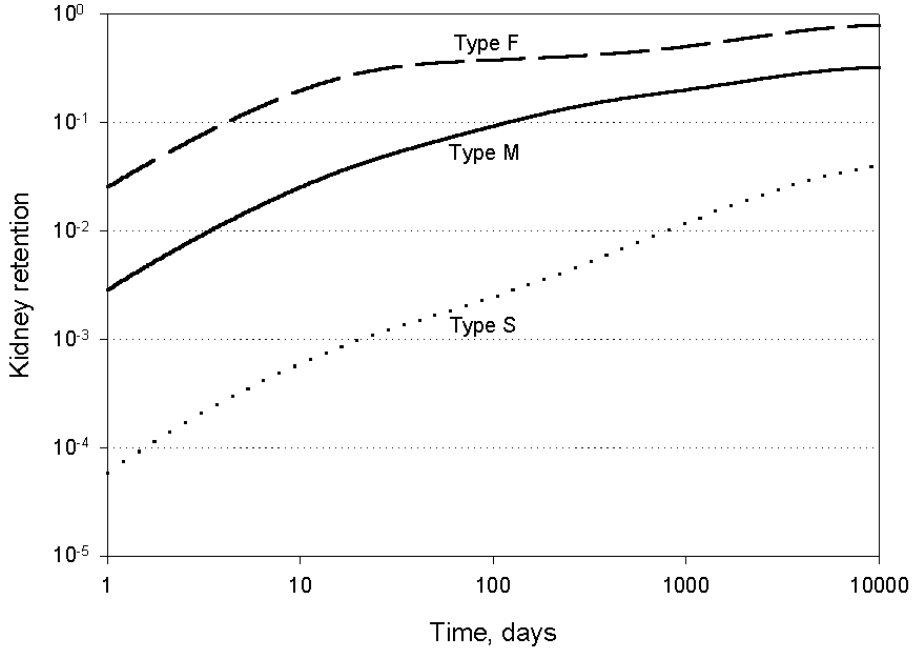

Figure 12.2 Fractional retention of inhaled uranium in the kidneys after chronic inhalation of Type F, M and S compounds: public exposure.

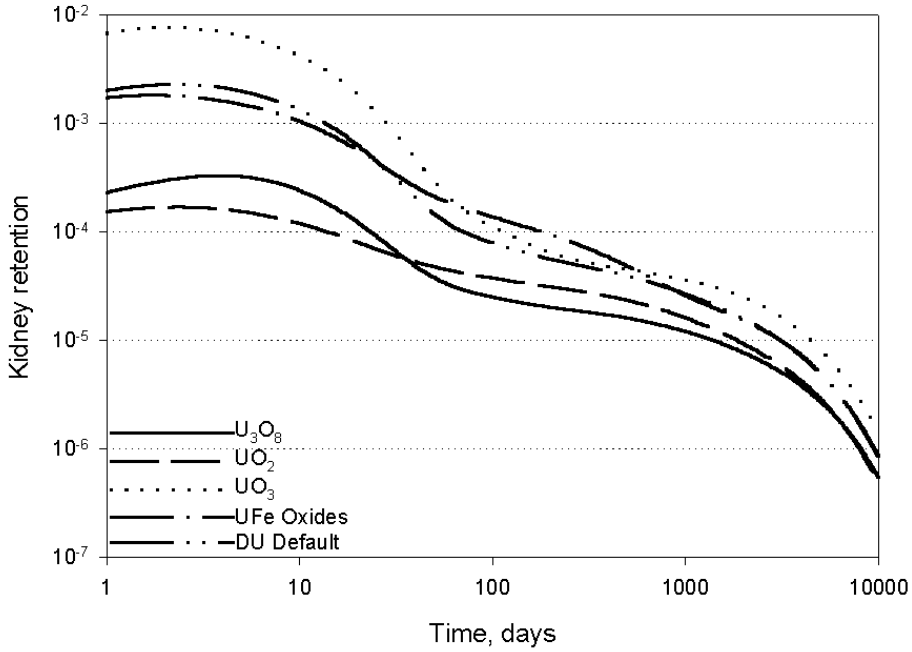

Figure 12.3 Fractional retention of inhaled uranium in the kidneys after acute inhalation of uranium oxides and the DU default: occupational exposure.

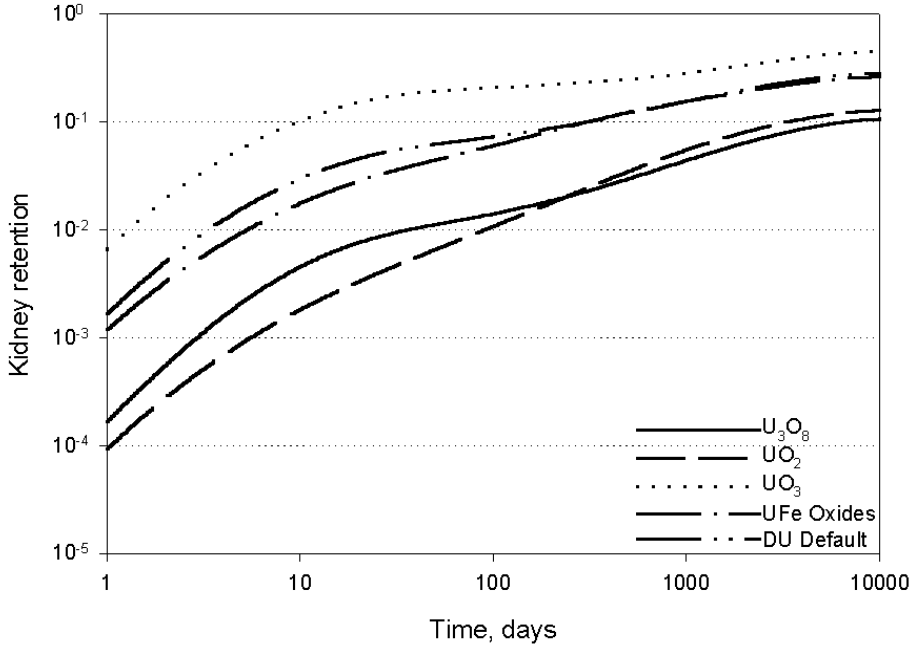

Figure 12.4 Fractional retention of inhaled uranium in the kidneys after chronic inhalation of uranium oxides and the DU default: public exposure.

Table 12.1 Inhalation intakes of uranium which result in a maximum concentration of 3 μg/g in the kidneys: occupational and public exposure.

Compound	**Intake (mg)**	
	Occupational (5μm)	Public (1μm)
Type S	7400	12510
Type M	230	290
Type F	30	35
U_3O_8	4010	3050
UO_2	6060	5920
UO_3	140	85
UFe oxide	540	490
DU default	460	325

Interestingly, workers whose intakes have exceeded the daily intake limit for moderately soluble (Type M) compounds of uranium (2 mg) by about five-fold have shown no evidence of nephrotoxicity or kidney malfunction (Boback, 1975). This would appear to support the choice of 3 μg/g as a 'safe' limit for the uranium concentration in the kidneys. However, the information given in Table 12.1 indicates that, using the current ICRP models, the amounts deposited in the kidneys as a consequence of intakes in excess of 10 mg or so would have been considerably less than those estimated using the historical model on which the occupational exposure standard was based (see Annex 5).

After chronic intake by members of the public, the concentration in the kidneys will increase progressively with time (Figures 12.2, 12.4). For an assumed intake of 1 mg/d of uranium it can be deduced from Figure 12.2, that the concentration in the kidneys will exceed 0.3 μg/g (93 μg total) after about four days for a Type F compound and about 100 days for a Type M compound. In both cases a concentration of 3 μg/g

(930-μg total) would not be exceeded until after 10 000 days. Values for the oxides can be calculated from Figure 12.4. Clearly material-specific information is vital for assessing the potential nephrotoxicity of uranium.

12.2 Ingestion of uranium in drinking water and foods

The information given in Figure 12.5 shows the amount of uranium present in the kidneys after a continuous chronic intake of a unit amount, say 1 μg/day. For comparison, the amounts present in the skeleton and excreted daily in urine are included. The calculations are based on the ICRP systemic model for uranium, assuming that the fractional uptake from the gastrointestinal tract is 0.02 (ICRP-69, 1995a). Figure 12.5 shows that at equilibrium the fractional amount present in the kidneys is 0.067. In other words, a continuous daily intake of 4 μg/d (the current WHO recommended guideline, Chapter 14) would result in a kidney content of 0.27 μg, and a kidney concentration of 0.0009 μg/g. This value is substantially below what is generally regarded as a safe value.

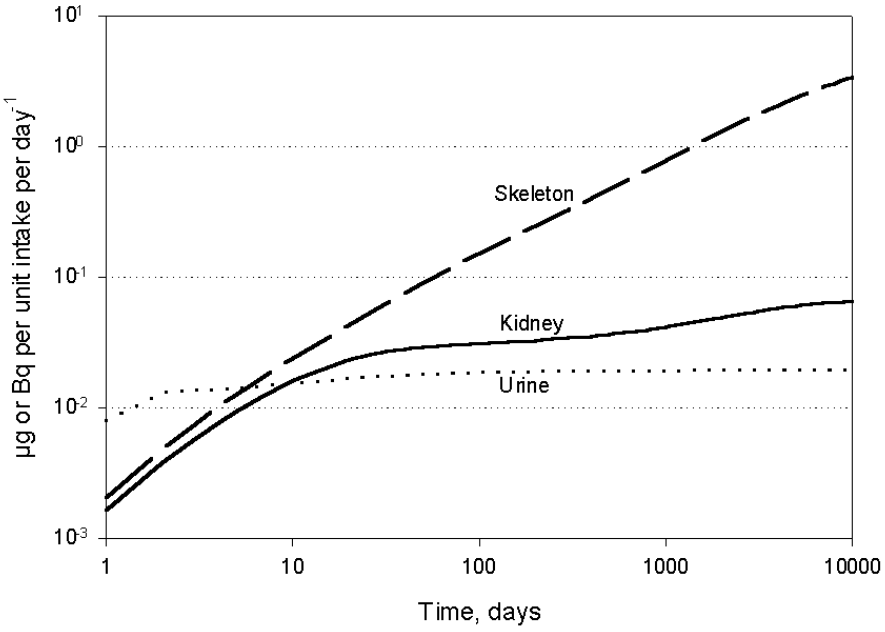

Figure 12.5 Fractional retention of ingested uranium in the kidneys and skeleton, and urine excretion rate after chronic ingestion of a Type F compound.

Whilst the discussion here has been concerned with drinking water, similar considerations would apply to the total dietary intake of uranium.

12.3 Relationship between kidney content and urinary excretion

The relationship between contemporary kidney content and urinary excretion after the acute and chronic inhalation of Type F and M compounds, using the HRTM (ICRP-66, 1994a) and systemic model for uranium (ICRP-69, 1995a) is shown in Figures 12.6 and 12.7.

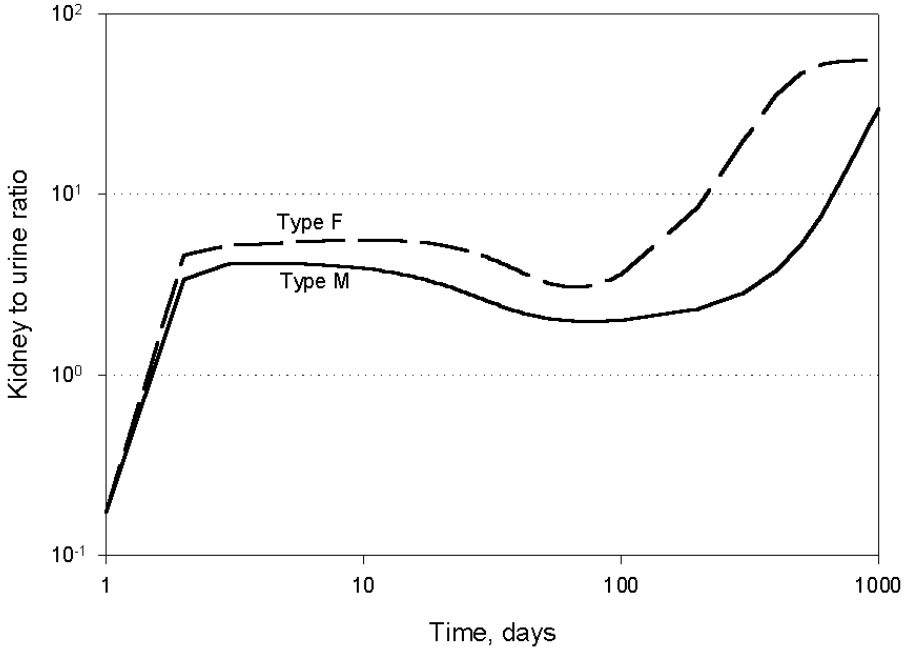

Figure 12.6 Kidney to urine ratio of uranium in the kidneys after acute inhalation of Type F and M compounds: occupational exposure.

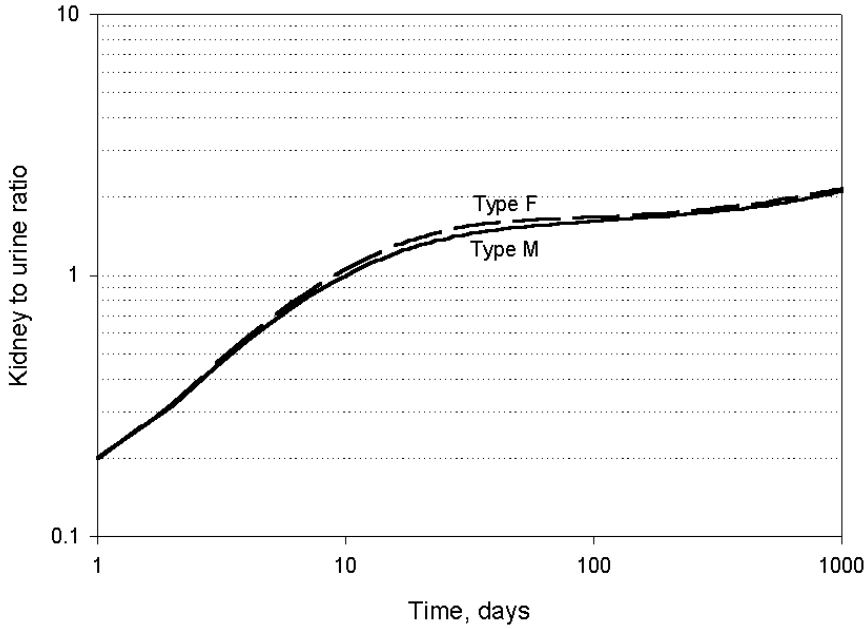

Figure 12.7 Kidney to urine ratio of uranium in the kidneys after chronic inhalation of Type F and M compounds: public exposure.

It is noteworthy that the ratios for Type F and M compounds up to 100 days after acute intake and up to 10 000 days after chronic exposure are closely similar.

It can be deduced from Figures 12.6 and 12.7 that between 7 days and 100 days the kidney to urine ratio is reasonably independent of the chemical form of intake, particle size of the aerosol or pattern of exposure. The variation in ratio during this interval is from about 1:1 to about 5:1. An assumed average value of 2.5:1 would appear to be a useful compromise. Thus, judgements on the health status of the individual could be

readily made by comparing the calculated kidney content with that obtained using the threshold value of 3 μg/g or an acceptable fraction of it, say 0.3 μg/g (see Annex 5) .

Similar calculations have been made after direct intravenous injection of uranium into the blood, simulating absorption from a contaminated wound. The values for the kidney:urine ratios are similar to those obtained after inhalation (information from A Phipps, UK-NRPB 2001).

It is concluded therefore that the kidney:urine ratio could be used with advantage in some circumstances for assessing the likelihood of potential nephrotoxic effects. However, it should be recognized that excessive concentrations in the kidneys may suppress the kidney:urine ratios. Studies with rats have indicated that this is less than two fold even when the kidney concentration is 3 μg/g (Hodgson et al., 2000).

12.4 Modelled kidney concentrations resulting from WHO standards

Uranium concentrations in the human kidney ranges from 0.000 33 to 0.0055 μg/kg with a median of 0.0022 μg U/kg kidney (converted from Bq/kg as ^{238}U from UNSCEAR, 2000). The results of the modelling of derived WHO tolerable intakes are (see Chapter 8 and WHO, 1998b) described in the following sections.

12.4.1 Oral consumption at the TI (soluble compounds*)*

In Chapter 8 WHO derives a tolerable daily intake of 0.5 to 0.6 μg/kg/d. For a 60 kg adult this corresponds to a daily intake of 36 μg/day (13.14 mg/annum). Based on a fractional intake at biokinetic equilibrium for the kidney of 0.067 (Figure 12.5) this would result in a kidney content of 2.41 μg and a resulting kidney concentration (assuming a kidney weight of 310 g) of 0.008 μg/g.

Estimated radiological dose (to kidney or whole body) resulting from the ingestion of 13.14 mg/y of DU to an adult member of the public and based on ICRP biokinetic models is 9.4×10^{-3} mSv/year.

12.4.2 Ingestion at the WHO drinking water guideline value

The current WHO recommended drinking water guideline (for natural uranium, Chapter 14) is 2 μg/l which is considered to be protective, and is based on the assumption that allows 10% of the TI intake of uranium to come from uranium derived from drinking water (at a drinking water consumption of 2 l/day, 60 kg adult). Consumption at the guideline level gives a daily uranium intake of 4 μg (1.46 mg/y). Based on a fractional intake at equilibrium for the kidney of 0.067 (Figure 12.5) this would result in a kidney content of 0.268 μg and a resulting kidney concentration (assuming a kidney weight of 310 g) of 0.0009 μg/g. This value is substantially below what is generally regarded as a safe value within the occupational context. However, it is recognized that this standard is not applied universally and is significantly lower than that suggested in other countries (see Chapter 14).

Estimated radiological dose (to kidney or total body) resulting from the ingestion of 1.46 mg/y of DU by an adult member of the public is 1×10^{-3} mSv/year.

Consumption of drinking water containing natural uranium at levels significantly above this is possible in a number of countries (See Annex 3 and Chapter 3). This could result in significantly greater kidney concentrations (at which changes in kidney function, that

might be considered to be detrimental, may be observed e.g. Zamora et al., 1998). For example exposure to uranium in drinking water at non atypical vales (20 μg/l) and maximum concentrations (1600 μg/l) of U observed in studies cited in Annex 3 would result in kidney concentrations of 0.009 μg/g and 0.72 μg/g respectively.

Estimated radiological dose to an adult member of the public resulting from the ingestion of drinking water containing 20 μg/l and 1600 μg/l of DU is 1×10^{-2} and 0.8 mSv/year respectively.

12.4.3 Inhalation at the TI for Type F (soluble)

The recommended TI for inhalation for Type F compounds in Chapter 8.4 (0.6 μg/kg/day) is equivalent to an intake of 36 μg/day (13.14 mg/y, DU Type F, Table-10.3). Using the information from Figure 12.2, for chronic exposure, it can be deduced that the kidney content at equilibrium will be 36 μg, and the concentration 0.12 μg/g of U. This is reasonably consistent with the suggested value of about 0.3 μg/g (Annex 5).

Estimated radiological dose resulting from the inhalation of 13.14 mg/y of DU by a member of the public is 9.9×10^{-2} mSv/year.

12.4.4 Inhalation at the TI for Type M (moderately soluble) compounds

The recommended TI for inhalation of Type M compounds in Chapter 8.4 (0.6 μg/kg/day) is equivalent to an intake of 36 μg/day (13.14 mg/y), DU Type M, Table 10.3). Using the information from Figure 12.2, for chronic exposure, it can be deduced that the kidney content at equilibrium will be 30 μg, and the concentration 0.10 μg/g.

Estimated radiological dose resulting from the inhalation of 13.14 mg/y DU (Type M) by an adult member of the public is 0.58 mSv/year.

12.4.5 Inhalation at the TI for Type S (insoluble) compounds

The TI for inhalation of Type S compounds in Chapter 8.4 (5 μg/kg/day) is equivalent to an intake of 300 μg/day (110 mg/y, DU Type S, Table 10.3). Using the information from Figure 12.2, for chronic exposure, it can be deduced that the kidney content at equilibrium will be 21 μg, and the concentration 0.12 μg/g. This is reasonably consistent with the suggested value of 0.07 μg/g (Annex 5).

Estimated radiological dose resulting from the inhalation of 110 mg/y of DU by an adult member of the public = 13.4 mSv/year. (Note whilst unacceptable for a member of the public this dose may be acceptable for a worker (see Chapter 9 and Annex 5).

12.5 Summary

The time-related retention of uranium in the kidneys has been discussed after acute and chronic inhalation of compounds with widely different solubility characteristics by workers and adult members of the public. The chronic ingestion of soluble uranium in drinking water has also been addressed. It is concluded that:

- the likely exposure pattern should be identified since this will substantially affect the time-related amounts retained in the kidneys, and hence judgements on nephrotoxicity.
- nephrotoxicity after intakes of Type S compounds, and uranium octoxide and dioxide is considered most unlikely in view of the considerable amounts that would need to be inhaled; even the inhalation of other materials such as mixed U/Fe, and a DU mixed oxide with a highly soluble component (20%) would need to be appreciable.
- in certain circumstances effective judgements on the likely nephrotoxicity of uranium can be deduced from kidney content extrapolated from the urinary excretion rate; the kidney to urine ratio is reasonably independent of the chemical form and exposure pattern from a few days to several months
- upper values for the kidney content of uranium can be deduced from consideration of its concentration in drinking water and daily intake.

Our current knowledge gaps include:

- Chemical composition and solubility of the aerosol inhaled.
- Chemical forms and solubility of uranium in drinking water.

13 Protective measures, health monitoring, and medical management

This chapter is intended for medical officers and health physicists who are not familiar with the detailed health and radiological protection issues associated with DU, but who need guidance on these matters. Hence, it is anticipated that it may be consulted in isolation. Inevitably there will be some repetition of material contained in other chapters, and the reader is referred to them when more information is required.

This chapter addresses practical questions concerning:

- background information useful for considering the nature and extent of contamination and response actions
- protective measures needed to prevent possible health effects from DU exposure
- health monitoring or medical surveillance of people living or working in areas where DU has been or is being used
- medical management of persons contaminated internally with DU

Protective measures, health assessment, and medical monitoring and management of public and occupational exposures are considered.

13.1 Background information

13.1.1 Public exposure

Area of contamination The area and levels of DU contamination in the environment should be determined. DU munitions produce fragments and dust of uranium metal and oxides, the extent of which depends on the magnitude of the impact, heat generated and explosive force. Heavier fragments and dust settle close to the site of impact while finer dust is carried further afield. Consequently, contamination levels decrease rapidly with distance. Finer dust produced on impact may be carried tens to hundreds of metres from the impact site. However, with increasing distance from the impact site, the DU dust concentrations will decrease rapidly. DU can also be released into the air from production and processing facilities. DU released to water through factory effluent, direct fallout, or erosion may settle onto silt or dissolve and be transported into groundwater. (For further information see Chapter 6).

Routes of exposure and magnitude of intake Assessment of the levels of intake of uranium and DU provide a basis for determining the potential for adverse health effects since every person exposed to DU is also exposed to uranium in air, food, and water. When civilians inhabit areas that contain DU, exposure could occur by inhalation of airborne contamination or resuspended dust, or ingestion of drinking water, contaminated food or soil, or by dermal contact. The human body contains about 90 μg of uranium from the normal intake of food, air and water. About 66% is present in the skeleton, 16% in the liver, 8% in the kidneys and 10% in other tissues. For further information on routes of exposure see Chapters 3, 5 and 6, and for the assessment of levels of intake see Chapters 10, 11 and 12.

13.1.2 Occupational exposure

In occupational situations the primary principle is to identify potential hazards and then control them with engineering and administrative measures supported by environmental monitoring and, if necessary, biological monitoring.

Hazard identification A hazard identification and control program should be established for workplaces when DU exposures are likely to occur. Occupational exposure to DU can occur during the production and handling of DU containing materials (shells, armour, ballast, shielding), and in the remediation and reclamation of contaminated areas. Additionally, people working in previously contaminated sites in occupations such as construction, farming, and other dust-producing activities may also be at increased risk of exposure to DU. Military personnel in combat situations are clearly at potential risk of DU exposure

Any operation or activity that handles or processes un-encapsulated DU should consider measures to protect workers from the potential chemical and radiological hazards. The level of protection to be used and the extent of the required monitoring program will depend on:

- the quantities of material being handled or processed.
- the physical and chemical properties of the material (e.g. chemical form and particle size).
- the nature of the operations being conducted.

Under normal circumstances, appropriate occupational health standards (see Chapter 14 and Annex 5) will apply to workers in both production facilities and environmental remediation activities.

Inhalation The most likely route of exposure at the workplace is the inhalation of uranium or DU. As indicated in Table 14.4, exposure limits exist for the control of uranium inhalation (HSE, 2000; ACGIH, 1993; NIOSH, 1994; ICRP, 1994a; NRC 1991). To verify that contamination control measures are effective, and to confirm that worker exposure is maintained within the appropriate limits, routine measurements of the levels of airborne DU should be conducted. Depending on the nature of the exposure, these measurements may need to be supplemented with urine sampling, faecal sampling and/or *in vivo* monitoring of the lungs for uranium.

The following sections highlight some of the major elements of an adequate monitoring program. Since a number of guidance documents exist for implementing such monitoring programs (ANSI, 1995; ICRP-54, 1988; ICRP-78, 1997; Rich, 1988; Stather, 1994), the reader is referred to these documents for further discussion, and other relevant chapters in this monograph.

13.2 Protective measures

Identifying appropriate protective measures for exposed individuals first involves establishing a framework for decision making by defining the range of protection measures and then identifying relevant protective actions.

Measures to protect the public from DU exposure are divided into the broad categories of locality-based, environment-based and medical-based actions, as described below, in response to a perceived, potential, or actual health threat. The initial response may be generic in nature, with actions becoming more focused and appropriate as data are collected and assessed as to level, chemical and physical form, and solubility relative to prescribed standards.

13.2.1 Locality-based protective measures

Locality-based protective measures are taken when data on which to base decisions are insufficient to determine if individuals are being exposed to DU, and that the situation indicates a reasonable probability of exposure. This could occur following the military or civilian use of DU, when a DU processing facility is suspected of releasing quantities of DU above allowable limits, when environmental monitoring results indicate new or elevated levels in any medium e.g. drinking water, or when medical symptoms may suggest an over exposure.

Precautionary actions include general advice published or reported by national or international organisations to reach as wide a cross-section of the population as possible. These should be coordinated with environmental and medical monitoring activities and be subject to constant assessment and revision following any specific environmental or medical investigations of the situation.

13.2.2 Environment-based protective measures

Environment-based protective measures are taken when sampling and survey results demonstrate the presence of excessive levels in a specified environmental medium to which the public is or may be exposed, or when a direct exposure pathway has been established. This occurs when levels measured in air, food, or water exceed regulatory limits or guideline levels (see Chapter 14 for more detail) or are likely to do so based on the anticipated spread of known contamination. Environmental response actions include limiting human and animal exposure to the contamination, or providing access to alternative clean or less contaminated supplies. These actions will need to be revised as further information becomes available.

13.2.3 Medical-based protective measures

Medical-based protective measures are taken when medical results confirm that an individual's health is being, or likely to be, compromised by exposure to DU. This could include measurements of uranium in the chest, biological samples (generally urine) along with assessment of renal proximal tubule damage (see Chapters 11, 12). Since no biomarker is specific to DU, and it is often impossible to quantify the measured value and potentially toxic effect, a combination of laboratory tests may be useful (Chapter 8). Care should be taken not to overlook other potential causes of adverse health effects, such as other toxicants or stressful conditions.

Screening for DU-associated disease in asymptomatic individuals or populations is generally not recommended. In individuals with high levels of uranium in urine, medical assessment should be undertaken.

13.2.4 Occupational measures

Control of DU exposure in an occupational environment also requires management directives on organizational and individual worker practices, such as restricting eating, drinking, or smoking in areas where DU exposures could occur, restriction of admittance to various work areas, training, record keeping, and hazard communication. The choice of appropriate monitoring programmes will be essential for adequate protection of the worker. These include:

Air monitoring Workplace air monitoring is the primary means available to demonstrate that the airborne levels of DU in a facility or project are within the desired exposure limits. When it is believed that air concentrations have the potential to exceed a pre-established fraction of the applicable exposure limits, a general area air-sampling program should be in place. The fraction of the regulatory limit at which monitoring is required will vary depending on local regulatory requirements. In the absence of local regulatory guidance, a value of 10% is commonly used.

For work practices that are difficult to cover using a fixed sampling location, such as remediation/clean-up activities, consideration should be given to the use of a personal air sampling device. These portable units have sampling heads that can be attached directly to a worker's collar, thereby providing a more accurate estimate of exposure than is possible with a fixed head unit. However sampling rates are low, typically 2l per minute, and results can be biased unless a centripeter device is used to remove non-respirable particles.

Internal exposure monitoring (biological monitoring) The worker protection program should include measurements that are capable of evaluating the extent to which workers are internally exposed to uranium. These measurements, which include urine sampling, faecal sampling and other *in vivo* examinations such as external monitoring of the chest, are referred to as bioassay measurements. When used in conjunction with appropriate metabolic models (ICRP-54 1988, ICRP-78 1997), and ideally, material-specific data on particle size and absorption parameter values for absorption to blood, these bioassay samples can be used to evaluate the extent of a worker's internal exposure to DU (see Chapters 10,11). It is important that measurements are undertaken, and assessments of exposure are undertaken by organisations validated to do so. As part of the bioassay program, action levels should be clearly defined. The intent of these action levels is to ensure that acute effects due to chemical toxicity do not occur and that a worker's radiological exposure is minimized. A number of guidance documents on establishing a bioassay program (with associated recommendations for chemical and radiological action levels) have been published (Rich, 1988; Stather, 1994 (see comments above); ANSI, 1995; ICRP-54, 1988; ICRP-78, 1997).

The choice of bioassay sample type and monitoring frequency is dependent on the solubility of the material being evaluated (see Chapter 11). For highly soluble uranium compounds, such as UF_6, urine samples will need to be collected as soon as possible after known or potential acute exposures. For routine monitoring purposes, and when exposures are likely to be significant, sampling intervals of about one week may be necessary. On the other hand, assessment of intake of poorly soluble forms such as UO_2, might be better evaluated using faecal sampling. In either situation, it may be desirable to supplement urine and/or faecal monitoring with external measurements of the chest. Being a direct measurement of the lungs, it ensures that any large intakes of uranium are not missed. Chest monitoring can be used to assess the contemporary lung content (limit

of detection about 8 mg) but if measurements are made soon after exposure, doses of a few tens of mSv can be identified (see Chapter 11).

Because uranium is naturally present in both urine and faecal samples, care should be exercised in the interpretation of positive results. All positive bioassay results should be interpreted in the light of the natural distribution of uranium present in the worker population. Prior to the initiation of work in a contaminated area, all workers should be required to submit a baseline bioassay sample. All bioassay results should be provided to workers with an explanation and counselling about their meaning and implications.

In some cases, it may be determined that bioassay monitoring is insufficient to evaluate a worker's exposure. This can be the case for facilities that handle highly insoluble forms of DU. In this situation, the use of supplemental breathing zone air samplers (BZAs or personal air samplers) should be considered. Many commercially available BZAs are capable of sustained flow-rates of up to five litres per minute. If one assumes a worker's breathing rate of 20 litres per minute, the BZA can be considered as a surrogate bioassay sample, which measures 25% of a worker's intake.

External exposure monitoring While the primary hazard from working with un-encapsulated DU is from internal exposure, as discussed in Chapter 9, large quantities of DU may present an external radiation hazard. In particular, exposures to the whole body (by gamma radiation from uranium and the progeny) and to the skin (from ^{234m}Pa, a beta-emitting member of the uranium decay series) can be significant. When large quantities of uranium are stored, there is also a potential for penetrating whole body exposure from DU which can reach a surface dose rate of 0.1 mSv/hr

If an environmental characterization indicates that there is a potential for workers to receive external doses or dose rates that exceed those identified in relevant regulations, then workers should be provided with personal dosimeters. These limits may vary with the regulatory agency. Dosimeters should be selected so that their energy response characteristics are appropriate for the radiation field being evaluated. Guidance documents for the implementation of an external dosimetry monitoring program are available (e.g. NCRP, 1999; Rich, 1988).

13.3 Preventative actions

This section covers a range of preventative actions available to communities and individuals for protection against DU over exposure, which may be achieved through changes to habits and activities.

13.3.1 Air

When the public have been advised that DU levels in air exceed regulatory or guidance values (such as may occur during military activities in which DU is used or released from a DU facility) some level of protection may be offered by closing windows and doors, securing ventilation, wearing a filtered respirator or mask or breathing through a damp cloth. Resuspension of DU dusts through wind erosion and both foot and vehicle traffic may be a source of continued low-level exposure. Exposure in these situations may be reduced through minimizing activities likely to resuspend dusts (e.g. removal of surface materials, fixation of the contamination, or watering and tilling to dilute the surface material available for resuspension or limiting access)

13.3.2 Children

Children should not play in areas where DU has been used or transported until the soil is acceptably clean. Two reasons for concern are that children exhibit hand-to-mouth activities leading to soil ingestion (especially geophagic children who can eat large amounts) and military activities may contaminate surface soil and dust accessible to children.

13.3.3 Concerned individuals

Individuals concerned about potential over exposure to uranium should consult a physician.

13.3.4 Contaminated items

Outer clothing and shoes that have possibly become contaminated should be removed outdoors. Before washing, segregate gently to minimize airborne levels, then wash groups of these clothes in succession, double-washing the most soiled, and including a clothes-free cycle to prepare the washer for uncontaminated clothing. Contaminated tools and vehicles, including the underside of vehicles and tires, should be washed in designated areas, where particulate contamination is removed in a suitable trap and disposed of appropriately.

13.3.5 Drinking water

Consumption of contaminated drinking water should be limited or avoided when total uranium (natural and DU) exceeds established limits or guidelines (see Chapter 14). This may be resolved by using appropriate filters, changing to bottled water that is known to contain acceptably low levels of uranium, or collectively on a community basis through mixing and blending with other uncontaminated water sources.

13.3.6 Exposed skin

If work or play occurs on contaminated soil, carefully wash hands, face and other exposed skin areas (e.g. the soles of the feet) thoroughly and again before eating or drinking.

13.3.7 Food

Food grown in DU contaminated areas may contain DU primarily attached to the surface of roots or leaves. Much of the DU should be removable by thoroughly washing or peeling all edible surfaces and removing any rough outer membrane. The drying of foods on potentially contaminated soils should be avoided. Governmental advice should be sought on levels of contamination that may restrict food consumption (Chapter 14).

13.3.8 Impacted areas

Where practicable, areas where significant DU contamination actually or potentially exists should be cordoned off until a survey has determined that it is safe for habitation. If levels warrant a clean-up of the area, the cordons should be retained and appropriately adjusted for actual conditions until results of a final status survey show the area is safe for unrestricted access.

13.3.9 Metal fragments, depleted uranium munitions, scrap metal and souvenirs

In all locations where DU has been used militarily, it is recommended that the public do not handle remnants of armaments (not least because of other more immediate hazards associated with unexploded ordinance). While the radioactivity of DU is low, large pieces of DU are capable of delivering significant doses to the skin (see Chapter 9).

Thus collecting of intact or fragmented DU penetrators, unexploded munitions/armour or other equipment containing DU for souvenirs or fabrication into other products should be actively discouraged (see Chapter 4).

13.4 Environmental monitoring

Environmental monitoring includes conducting radiation-level surveys and chemical-contamination surveys with portable equipment, and virtually always will include the collection of samples of environmental media (see Chapter 6 and Annex 6).

13.4.1 Radiation surveys

Surveys for DU may typically involve the use of hand-held monitors (such as an NaI(T1) type scintillation detector) with determinations being performed on a regular grid or being undertaken based on a local knowledge of areas of particular concern or vulnerability. Samples may also be taken from the field for more accurate chemical and radiochemical analysis in the laboratory (see below). Alternatively more complex surveys may be undertaken from the air or in specially equipped vehicles. In general, radiation surveys must only be undertaken by qualified professional bodies or persons who can demonstrate both professional competence in the detection of DU and have appropriate quality assurance and quality control in place.

13.4.2 Chemical contamination surveys

Contamination surveys for DU typically involve the removal of representative samples of material (water, soil, food, vegetation, dust, airborne dust etc.) from various locations of interest and transferring the samples in sealed containers back to a laboratory for detailed characterisation. The 3-dimensional location (ideally a recognized spatial grid coordinate and sample depth) being accurately recorded and selected based on the likelihood of including contamination or the vulnerability of a particular media to contamination (e.g. water sources used by many people). Sampling for DU could include air samples up- and down-wind of the impact or discharge point, surface soil samples for recent fallout or thicker samples for aged fallout, occasional core soil samples (for uranium and DU depth profiles and uranium reference levels for that area), river sediment and water up- and down-stream of any air plume or water discharge point (for accessibility to potable water for humans, food animals, and food crops), surface drinking water supplies, and locally produced food. Groundwater can also be collected, but its contamination from any source of DU is less likely; however, it is more likely than surface water to contain high levels of natural uranium and its decay products (see Chapter 3). Surveys of chemical contamination may be complex and if inappropriately conducted may lead to misleading positive and/or negative results. For this reason such studies are best undertaken by qualified professional bodies or persons which can demonstrate both professional competence in environmental sampling techniques and the chemical analysis of DU, and have appropriate quality assurance and quality controls in place. Some methods appropriate for the determination of DU and uranium in environmental media are described in Annex 6.

13.5 Health assessment

To determine if a health assessment program might be beneficial, an investigation should assess whether realistic circumstances exist for DU exposure. For example could a person, during the course of their activities, have ingested, inhaled or come into contact with significant amounts of DU? In such an appraisal it may be appropriate to reference international standards and guidelines (Chapter 14), provided that information relating to levels of actual exposure are available.

The conclusions presented in this report indicate that consideration should be given to both the radiological toxicity and chemical toxicity of DU. Dose limits for limiting effects due to ionizing radiation are given in Chapter 9 and their implications to various levels of DU exposure are described in Chapters 10 and 11. While the question of chemical toxicity is discussed in Chapters 8, 12 and Annex 5.

Health assessments may be conducted on overexposed individuals immediately following releases of DU through military operations or from processing plants or storage areas etc. It is also implemented in a phased manner on other individuals based on their potential for overexposure to DU from any source. This potential can be assessed, based on environmental monitoring results and medical monitoring of patients who present with symptoms that relate to DU over exposure, which can be further assessed through biological sampling. In essence, environmental and biological samples are analysed, the results used to assess exposure, which provides feedback to the sampling programs, ultimately ending in a risk assessment for individuals or population groups as a function of estimated exposure and potential health endpoint.

The sections below address the diagnosis, monitoring and treatment of medical conditions associated with exposure to DU or U.

13.5.1 Medical diagnosis

Pathophysiology

The pathophysiology of uranium and DU are discussed briefly below and in more detail in Chapters 7, 10 and 12.

Inhalation

Under various circumstances DU and uranium may become liberated in the form of dust and aerosols. Particles typically less than 10 μm AMAD will enter the deep lung, while the larger ones will be trapped by the upper respiratory tract and then either expectorated or swallowed. The amount of uranium or DU entering the blood and the rate of absoprtion will depend upon the particle size and chemical form (the smaller, more biologically soluble, particles tending to enter more efficiently and quickly). Elimination from the blood occurs primarily through the kidneys. During the first 24 hours after incorporation, up to 60% will be excreted and about 90% in the following few days. Most of the remainder will be deposited in the skeleton (see Chapters7, 9, 10, 11 and 12)

Ingestion

Absorption from the intestinal tract may vary from a few per cent to less than 0.2% depending on its chemical form. The remainder is excreted in faecal material. About 90% of the absorbed part will be eliminated by the kidneys, while the remaining part will mainly accumulate in the skeleton, with a biological half-life of about 300 days (see Chapter 7, 10, 11 and 12)

In the kidneys, uranium accumulates mainly in the proximal tubules. At elevated levels uranium is considered as nephrotoxic and can cause glucosuria and an albuminuria (see Chapters 8 and 12).

Dermal contact and uranium in wounds
Prolonged and direct contact with uranium may cause skin erythema, but at DU exposure levels it is not considered likely to reach a significant level of toxicity (see Chapter 8).

Embedded fragments
Soldiers with retained DU fragments typically demonstrate an enhanced level of urinary excretion of uranium than control groups. This finding may still be present seven years after exposure, suggesting a slow controlled release from the disintegrating fragments (see Chapter 12).

Long term pathophysiology
Below a certain concentration, kidney damage may be transitory (see Chapter 8). The only known human pathology due to the chemotoxicity of uranium is the destruction of renal tubules, without clinical manifestation, but causing a diminution of the kidney reserve function.

Theoretically, exposure to DU or uranium may lead to effects associated with ionizing radiation. Considering the amount of radioactivity involved, deterministic acute effects are excluded. Long term effects are represented by the increased probability of developing a cancer, although this risk remains extremely low (see Chapter 8). Modelling of exposure in extreme conditions (inhalation of dust shortly after the impact of projectiles) suggests that a calculated radiation dose of 10 mSv would occur, representing half of the maximum yearly dose limit for workers.

Diagnosis
Persons exposed to uranium normally show no specific clinical sign, apart from those non-specific symptoms associated with exposure to many other heavy metals.

If it is strongly suspected or known that a person has either inhaled or ingested large amounts of uranium dust, a presumption of uranium exposure can be gained by a thorough anamnesis. Details such as the time of the exposure, the exact location of the person, the distance from the impact etc, need to be determined to properly assess the extent of exposure. If the exposure extends over a long period of time and occurred mainly through ingestion, alimentary habits must be checked.

If the physician is convinced that there has been an exposure to uranium, the following routine laboratory tests should be performed:

- routine urine analysis (especially checking for albumin and glucose).
- blood urea and creatinine for kidney function.
- a complete blood count for anaemia.
- chest X-ray in case of a possible inhalation exposure to exclude lung damage.

In cases of severe exposure, the kidney may be the critical organ. Signs indicating a tubulopathy should be looked for. If the tubules are damaged, there will be many low molecular weight proteins that appear in the urine, among which the β_2-microglobulin is the most commonly assessed. Therefore the diagnostic procedure should be:

- determine the dosage of β_2-microglobulin in a 24-hours urine collection. Most major hospitals and medical laboratories are able to perform this analysis. The patients should be informed how to correctly collect the 24 hours urine sample. It should be

remembered that this protein is unstable in acid urine, so that it is important that the collection of the urine is performed according to the instructions of the laboratory

- if the result of this determination is pathologic, the amount of uranium excreted in urine in 24 hours should be determined. However, as only few laboratories are equipped for the determination of uranium in the urine, it is absolutely necessary to contact such a laboratory before collecting the urine and to follow their instructions. A spot urine analysis is of considerably less value, even when coupled with a creatinine determination. These factors are discussed in detail in Chapter 11, Annex 6 and the following sections.

Prognosis

So far only very few cases of acute uranium overdose have been reported in the literature. They are characterized by an acute renal failure, which may lead to a complete anuria and need temporary dialysis. An incomplete Fanconi syndrome, in the form of a renal tubular acidosis, may persist more than six months after exposure, requiring a daily supplement of sodium bicarbonate (Pavlakis et al., 1996).

For chronic exposure at low uranium levels no permanent damage has been reported. Occupational exposure of uranium mine workers is not known to have been detrimental to their health; only a few have developed transitory anaemia. Soldiers who have incorporated uranium fragments have not shown any renal problems. The radiological hazard is likely to be very small. No increase in leukaemia or other cancers has been established following exposure to uranium or DU (see Chapter 8).

13.5.2 Medical monitoring

Medical monitoring may include examination by a physician and the collection and analysis of biological samples for DU and indicators of potential health problems. At low levels of exposure to DU, no links to disease have been identified from pathology but there are data that subclinical indicators of renal function may be altered. There is a low risk of cancer from any radioactive material but no clear link has been established between exposure to DU and any specific type of cancer (See Chapter 8).

As discussed in Chapter 11 medical monitoring for exposure to DU via inhalation or via ingestion can be achieved by determining the presence of DU in the chest, urine or faecal material. Sampling and analysis methods should be appropriate to the task, and these may be different for assessing total uranium content relative to threshold levels and actual DU present in any medium. Kinetic phosphorescence analysis (KPA) is the standard, low-cost method to determine total uranium, and is preferred if total uranium content relative to a limiting concentration is sufficient. DU analysis, however, requires more sophisticated equipment and techniques that are capable of determining isotope composition and proportions. Accurate measurement of these proportions enables the calculation of the DU portion of total uranium present in each environmental and biological sample.

Results should be high quality, demonstrating adequate quality assurance and quality control and provide suitably low detection limits along with total analytical uncertainty. Appropriate reference background samples (free of DU but with typical levels of natural uranium) should be analysed so that the excess due to DU is determinable for each sample analysed. The selection of appropriate techniques is discussed in more detail in Chapter 11 and Annex 6.

13.5.3 Treatment of human contamination

Once uranium or DU has entered the body there is little that can be done to remove it or increase the excretion rate. The patient can only be treated symptomatically.

Acute exposure When acute intake of DU or uranium has occurred various methodologies have been tried to remove the contaminant from the human body. Sodium bicarbonate has been recommended, and other substances such as Ca-ETDA and Zn-DTPA have been suggested, for enhancing the elimination of uranium from the body (Bhattacharyya et al., 1992). While temporary increases in urinary excretion are likely to occur after their administration, there appears to be no evidence that they cause a marked reduction in the content of the kidney or skeleton.

Animal experiments have shown that some phosphonates are able to reduce the uranium content in the kidneys to about 10% of those in controls when treatment commences within a few minutes of uranium administration; however under realistic conditions, when treatment is delayed for several hours, or longer, these substances are ineffective (Henge-Napoli et al., 2000)

Inhalation Lung lavage is a recognized procedure for the treatment of obstructive lung diseases. However, for reducing the radiation risk from inhaled insoluble compounds of uranium, it is unlikely to have much impact. In these circumstances, lung lavage is not normally advised unless the lung dose is likely to exceed 5 Sv over a few weeks (Henge-Napoli et al., 2000) or the intake is in excess of 100 times the annual limit (Battaacharyya et al., 1992). The information given in Chapter 10 (Table 10.3) for Type S compounds of DU shows that the mass inhaled would need to exceed 23 g, a most improbable scenario. On the other hand, the use of lung lavage may be justifiable if lower intakes of DU are likely to seriously impair lung function.

Long-term follow up If significant incorporation of uranium has been diagnosed, clinical follow up over subsequent years for early detection of any cancer may be recommended. Patients however should be told that the probability that they would develop a cancer due to irradiation through uranium is extremely low, based on current knowledge.

Of greatest value is the psychological therapeutic approach. Patients should be told that the only established consequence of uranium exposure is damage to the kidneys, and that at anticipated levels of exposure this would most likely be transitory and not even clinically detectable. To relate the patient’s problems to uranium contamination, especially the presence of any malignancy, is highly improbable and would be contradictory to current medical knowledge.

14 Health standards, guidelines and recommendations

This chapter summarizes available information on public health standards, guidelines and recommendations relating to exposure to uranium and DU. Analytical methods that may be used to determine the concentration of uranium in environmental materials, prior to applying these standards, are summarized in Annex 6.

From available biological and health effects data, some countries and organisations, such as WHO, have adopted a tolerable intake (TI) approach to derive a guideline value for the chemical toxicity of uranium. Others have proposed minimal risk levels or suggested acceptable intakes based on chemical toxicological and radiological studies. It should be noted that, in all of the cases described below, the health-related exposure standards, guidelines and recommendations have incorporated uncertainty factors into the TI to allow for unknowns.

14.1 Generic

The generic standards, guidelines and recommendations given in Table 14.1 apply to the total intake from all sources and are commonly used together with a knowledge of the relative importance of various exposure routes as a basis for defining specific guidelines for the individual exposure routes.

In constructing many of the generic standards, guidelines and recommendations given below, it was assumed that chemical toxicity effects outweigh potential radiological effects. It should also be noted that exposure to soluble uranium via lung uptake should be included as a component of ingested uranium when applying these standards, guidelines and recommendations.

Table 14.1 Generic standards, guidelines and recommendations for total intake from all sources.

WHO—Chemical*	For oral exposure, a Tolerable Intake (TI) for uranium of 0.0006 mg per kg of body weight per d was established by the WHO (1998a, b) based on the adverse effects observed by Gilman, (1998a). In this report this has been slightly modified to 0.0005 mg per kg of body weight per day. The uncertainty factors used in this calculation were: three for LOAEL to NOAEL, three for extrapolation from animals to humans and ten for human variability. Giving a total uncertainty factor of ninety.
US NRC **	Occupational annual intake limit of 14.8 g natural uranium (CFR 20, 1991)
US—Agency for Toxic Substances and Disease Registry (ATSDR, 1999)	A minimal risk level for intermediate-duration ingestion has been proposed by ATSDR of 0.002 mg per kg of body weight per day based on the study of rats by Gilman et al. (1998a). This minimum risk level is also considered to be protective for chronic exposures. The uncertainty factors used in this calculation were: three for use of a minimum LOAEL, one for extrapolation from animals to humans and ten for human variability. Giving a total uncertainty factor of thirty.
United States Environmental Protection Agency	US EPA have defined a reference dose (RfD) For uranium (soluble salts) of 0.003 mg per kg of body weight per day based on a 'critical effect' of losses in initial body weight and moderate nephrotoxicity. The EPA considers that intake of this amount or less over a lifetime is unlikely to result in the occurrence of chronic non-cancer effects. EPA considers that there is insufficient knowledge to suggest guidelines based on reproductive or developmental effects, while also acknowledging that animal studies have reported foetal toxicity and degenerative changes in the testes from oral exposure to uranium.
Germany	Jacob et al. (1997) proposed a TDI of 0.0007 mg per kg of body weight per day based on effects observed by McDonald-Taylor et al. (1997)

* Based on derivation of water guideline value by WHO (1998a; 1998b) and this work.

** Occupational limit

14.2 Drinking water

For drinking water guidelines WHO (1998a, b) using an earlier study on rats as the basis, in which the NOAEL was 60 µg/kg bw/d, derived a provisional TI value of 0.6 µg/kg.

Standards, guidelines and recommendations for water quality (Table 14.2) are generally derived from generic standards based on total ingestion by apportioning a specific fraction of the total exposure that may be allowed to originate from the ingestion of drinking water. Radiologically based guidelines for the level of uranium in drinking water may be derived in a similar manner or alternatively through the application of separate regulations based on the gross alpha and beta activity in water.

Table 14.2 Standards, guidelines and recommendations for water.

WHO Radiological (Member of the Public, excess dose 0.1 mSv/year)*	Pure natural uranium = 0.16 mg per l DU = 0.28 mg per l
WHO—Chemical	The WHO has derived a provisional** guideline for drinking-water quality of 0.002 mg/l. This value is considered to be protective for subclinical renal effects reported in epidemiological studies (WHO, 1998a).
US EPA—Chemical	Based on the Clean Water Act, US EPA has proposed a drinking water standard for naturally occurring uranium of 0.020 mg/l (US EPA, 1990). This standard is currently under review (56 FR 33050) and may be set at a practicable level of 0.030 mg/l. See also US EPA (1995a).
Canada—Chemical	Canadian limit 0.020 mg/l.
US EPA Groundwater standards for remedial actions at inactive uranium processing sites	Maximum combined limit for ^{234}U and ^{238}U of 1.11 Bq/l (US EPA, 1995b). This is equivalent to 0.044 mg/l assuming secular equilibrium between ^{238}U and ^{234}U.
Australia	National Health and Medical Research Council (NHRMC) guideline value = 0.020 mg/l (1996).
Russia	Maximum allowable concentration in bottled mineral water = 1.7 mg/l (Misund et al., 1999).

* Calculated for an adult using ICRP-72 (1996) and WHO guidelines, which states that excess radiological dose due to radioactivity in drinking water should be limited to 0.1 mSv (WHO, 1993).

** This term is used for constituents for which there is some evidence of a potential hazard, but where the available information on health effects is limited; or where an uncertainty factor of greater than 1000 has been used in the derivation of the tolerable daily intake (TDI). Other guideline values for inorganic water quality parameters listed as being provisional by (WHO, 1998a) include, boron, copper, nickel and chronic exposure to nitrite.

14.3 Food

Health standards for the quality of food may be derived in a similar way to that suggested for drinking water (i.e. derived from generic standards based on total ingestion by apportioning a specific fraction of the total exposure that may be allowed to originate from the ingestion of the given food). Radiological quality may be derived in a similar manner or alternatively through the application of separate regulations based on the gross alpha and beta activity of foods.

Because of the diversity of foods and their importance to human nutrition it is assumed that levels of uranium derived from all food should not exceed the total generic intakes described in 14.1 above.

The WHO has recently derived intervention levels for radionuclides in food to be used following nuclear accidents (WHO, 1998d). The calculated values (Table 14.3) are, of necessity, based on an effective dose of 5 mSv for each nuclide in isolation in a single food category, since it is not possible to generalize regarding which nuclides will be most important in each food category after an accident. Similar generic guidance following emergency situations is given in BSS (1996)

Table 14.3 **G**uideline values for radioactivity in food following a nuclear emergency in Bq/kg (WHO, 1998d). Note uranium isotopes present in DU fall between high and low dose unit intake factors, in the classifications (see Table 5.2). For comparison 1 ppm depleted uranium (1 mg/kg) is approximately equivalent to 14.8 Bq/kg.

Class of radionuclide	**Cereals**	**Roots and tubers**	**Vegetables**	**Fruit**
High dose per unit intake factor (10^{-6} Sv/Bq)	35	50	80	70
Low dose per unit intake factor (10^{-8} Sv/Bq)	3500	5000	8000	7000
Class of Radionuclide	**Meat**	**Milk**	**Fish**	**Drinking Water**
High dose per unit intake factor (10^{-6} Sv/Bq)	100	45	350	7
Low dose per unit intake factor (10^{-8} Sv/Bq)	10 000	4500	35 000	700

14.4 Soil

Soil and dust derived from soil may either be readily ingested or inhaled and as such may be required to meet both a chemically and radiologically defined quality.

In the case of ingestion the presence of soluble compounds of uranium maximize both the radiological and chemical hazards. The opposite is true when dust containing

uranium is inhaled, as soluble uranium is more readily excreted and not stored in the lungs.

There are currently no generally accepted guideline concentration values relating to the quality of soils or dusts in respect of contamination from DU.

14.5 Air

Table 14.4 Standards, guidelines and recommendations for air.

United Kingdom Occupational exposure standards, EHE/40, HSE, (2000)	United Kingdom Occupational exposure standards for soluble natural uranium compounds (HSE, 2000); Long term—0.2 mg/m^3 Short term—0.6 mg/m^3
Agency for Toxic Substances and Disease Registry	ATSDR derived a Minimal Risk Level (MRL*) for chronic inhalation exposure of 0.008 mg/m^3 and 0.0004 mg/m^3 for intermediate duration inhalation of insoluble and soluble uranium respectively (ATSDR, 1999). For chronic inhalation of soluble uranium the MRL is 0.0003 mg/m^3. The uncertainty factors used in this calculation were: three for extrapolation from animals to humans and ten for human variability. Giving a total uncertainty factor of thirty.
Germany	Jacob et al. (1997) proposed a tolerable air concentration of 0.000 07 mg/m^3 of uranium, based on studies of exposure of rats to uranium. Currently in Germany 0.25 mg/m^3 for insoluble uranium compounds (Roth et al., 2000)
American Conference of Governmental Industrial Hygienists **	ACGIH adopted the maximum permissible concentration of 0.2 mg/m^3 for medium term exposure to soluble and insoluble natural uranium in air, and a short-term exposure limit of 0.6 mg/m^3 (ACGIH, 1993)
US Occupational Safety and Health Administration (OSHA)	OSHA recommends a limit of 0.25 mg/m^3 for insoluble uranium and 0.05 mg/m^3 for soluble uranium based on an 8-hour working day.
National Institute for Occupational Safety and Health **	NIOSH recommends a limit of 0.2 mg/m^3 for insoluble uranium (time-weighted average) for chronic occupational exposure, and a short-term exposure limit of 0.6 mg/m^3 in air. For soluble uranium the corresponding levels are 0.5 mg/m^3 and 10 mg/m^3 respectively, (NIOSH, 1994).

* MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health

assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites.

** Note, based on occupational exposure corresponding levels for population exposure after correction for a 24 hour, 7 day per week are 0.069 and 0.21 mg/m^3 for short-term exposure and long-term exposure (based on insoluble compounds as might be encountered immediately following combustion of uranium). This correction from occupational exposure is based on that suggested by the US EPA where:

$$Level_{pub} = Level_{occ}\ (mg/m^3) \times VEho/VEh \times L_{occ}/\ L_{pub}$$

Where: $Level_{pub}$ = public exposure level; $Level_{occ}$ = occupational exposure level; VEho = human occupational default respiration rate (9.6 m^3 per day); VEh = human ambient default respiration rate (20 m^3 per day); L_{occ} = length of a standard working week (5 days) and L_{pub} = length of standard week (7-days)

Chemical health risks are considered to be negligible when exposure levels in air are below these exposure limits (Table 14.4). It is difficult to assess the potential health risk for humans at higher levels of exposure because information describing dose response relationships for potential deleterious effects in humans is lacking. However, animal studies point to concentrations showing no or minimal effects (particularly kidney damage) following short to chronic inhalation exposure in the range of 0.15 mg/m^3. Assuming that humans are equally sensitive, this indicates that levels above 0.15 mg/m^3 would be required to induce clinically significant toxic effects in humans.

15 Summary, Conclusions and Research Needs

15.1 Summary

Objectives

The principal objective of this monograph is to assess any health impacts of exposure to DU using existing knowledge about uranium and DU, and to provide a framework for identifying the likely consequences of public and occupational exposure to DU.

To achieve this objective, information is given on situations where exposures might arise, the likely routes of intake, the potential risks from radiological and chemical toxicity, and future research needs. Background data and scenarios are also provided from which numerical estimates may be constructed from knowledge of local exposure.

Uranium and depleted uranium

- Uranium is a naturally occurring heavy metal found in various chemical forms in all soils and rocks, seas and oceans, and in drinking water and food.
- Natural uranium consists of a mixture of three radioactive isotopes ^{238}U (99.27% by mass), ^{235}U (0.72%) and ^{234}U (0.0054%). All these isotopes were present when the Earth's crust was formed.
- Uranium is used primarily in nuclear power plants. However, most reactors require uranium in which the ^{235}U content is enriched from 0.72% to about 3%.
- The uranium remaining after removal of the enriched fraction contains about 0.25% of ^{235}U, 99.8% ^{238}U and 0.001% ^{234}U by mass; this is referred to as depleted uranium or DU.
- The behaviour of uranium and DU in the body is identical. However for the same mass, the radiation dose from DU is about 60% of that from uranium (without daughters).
- Spent uranium fuel and other forms of uranium from nuclear reactors are reprocessed by placing them in the same enrichment plants as is used for natural uranium enrichment. This can cause some reactor-created radioisotopes to contaminate the reprocessing equipment. These reactor-created radioisotopes can then contaminate the DU from natural uranium enrichment. Under these conditions another uranium isotope, ^{236}U, may be present together with very small amounts of the transuranic elements plutonium, americium and neptunium, and the fission product technetium-99. However, the increase in radiation dose following uptake into the human body of these additional radioisotopes in DU will be less than 1%.
- As a radioactive element, freshly produced DU emits mainly alpha (α) radiation. DU produces progeny or daughter radio-isotopes that emit beta (β) and only a small amount of gamma (γ) radiations. Because α and β radiations are not very penetrating, external radiation exposure resulting from DU is mainly limited to the skin. However, α radiation is most important for internal exposures.
- As a consequence of using DU munitions, the predominant chemical forms of uranium present in the atmosphere are likely to be uranium trioxide (UO_3), uranium octoxide (U_3O_8) and uranium dioxide (UO_2), although the presence of aerosols containing mixtures of metals with uranium has been established. In the general environment, uranium trioxide (UO_3), and soluble forms such as carbonates, are most likely to predominate in due course.

Applications of depleted uranium

- The main civilian uses of DU include counter weights in aircraft, radiation shields in medical radiation therapy machines and containers for the transport of radioactive materials.
- Due to its high density, which is about twice that of lead, and other properties, DU is used in munitions designed to penetrate armour plate and in other forms of armour plate for protection of military vehicles such as tanks.

DU exposure and exposure pathways

Exposure to DU

On average, approximately 90 μg of uranium exists in the human body from normal intakes of food, water; and air; approximately 66% is found in the skeleton, 16% in the liver, 8% in the kidneys and 10% in other tissues. The average annual intake of uranium by adults has been estimated to be 460 μg from ingestion and 0.59 μg from inhalation.

Smoking two packets of cigarettes per day may allow inhalation of up to 50 ng of uranium per day. Coal fired power stations have been reported to produce $3ng/m^3$ of uranium downwind from their discharges.

Until recently, the public was not exposed to DU. With the use of DU counterweights in aircraft, there is a possibility that people near an aircraft crash may be exposed to DU dusts if the counterweights were to combust on impact. Significant exposure to people in this situation is unlikely. Exposure of clean-up and emergency workers following aircraft accidents is possible but normal occupational protection measures should prevent any significant exposure occurring.

Since 1991, when DU weapons were first used in conflict, exposure may occur to people working or living in areas where DU munitions were used and where they hit targets and formed various uranium compounds, predominantly oxides A recent UNEP report giving field measurements taken around selected impact sites in Kosovo found that contamination by DU in the environment was localised to a few tens of metres around impact sites. Contamination by DU dusts to local vegetation and water supplies was found to be extremely low. Thus the possibility of significant exposure to the local populations was found, at least where measurements were made, to be very low.

DU exposure pathways

Individuals can be exposed to DU in the same way they are exposed to natural uranium i.e. by inhalation, ingestion, dermal contact or injury (e.g. embedded fragments). The relative contribution from each of these pathways to the total DU uptake into the body depends on the physical and chemical nature of the DU as well as the level and duration of exposure. Each of these exposure situations needs to be assessed to determine any potential health consequence.

Most (>95%) uranium entering the body entering the body via inhalation or ingestion is not absorbed, but is eliminated via the faeces. Of the uranium that is absorbed into the blood, approximately 67% will be filtered by the kidney and excreted in the urine within 24 hours and about 90% in a few days. Typical gastrointestinal (GI) tract absorption rates for uranium in food and water are about 2% for soluble uranium compounds and down to 0.2% for insoluble uranium compounds.

- **Intake by ingestion** is important for populations having their drinking water or food contaminated by DU. In addition, the ingestion of soil by children via geophagia or hand-to-mouth activities is also potentially important.
- **Intake by inhalation** can be important following the use of DU munitions during or immediately following conflict or when DU deposits in the environment are re-suspended in the atmosphere by wind or other forms of disturbance. Accidental inhalation may also occur as a consequence of a fire in a DU store, an aircraft crash, or the decontamination of vehicles from within or close to conflict areas.
- **Intake** through intact skin is very low and considered to be relatively unimportant.
- **Intake from wound contamination** or embedded fragments in skin tissues allows DU to enter the systemic circulation.

Behaviour of DU in the body

In this monograph, consideration is given to occupational and public exposure, short- and long-term intakes and uptake by inhalation and ingestion of compounds with widely different solubility characteristics. The behaviour of uranium in the body has been described using both reference and material specific absorption parameters for the uranium compounds likely to be present in DU aerosols; calculations have also been performed for a reference DU aerosol. Emphasis has been placed on lung retention, and urinary and faecal excretion rates, since assessments of intake are usually based on such measurements.

The amounts and concentrations of uranium in the kidneys after exposure have also been derived from information on the known nephrotoxicity of uranium. In certain circumstances effective judgements on the likely nephrotoxicity of uranium can be deduced from kidney content extrapolated from the urinary excretion rate; the kidney to urine ratio is reasonably independent of the chemical form and exposure pattern from a few days to several months.

ICRP Models

The models recommended by the International Commission on Radiological Protection (ICRP) are embodied in the internationally recommended Basic Safety Standards for radiation protection and in the legislation of many countries, including those in the European Union. In the context of this report, the appropriate generic models are those for the human respiratory tract (not specific for uranium), the systemic behaviour of uranium and uptake from the GI tract.

- These ICRP models can be combined to calculate the radiation dose from intakes of uranium and DU, and for a given intake to predict the retention of DU in the important organs of the body e.g. lungs, bone, kidneys, and urinary and faecal excretion rates.
- The models consider materials assigned to one of three types that describe absorption from the lungs to the blood, or uptake from the GI tract to blood. These materials are referred to as Type F (fast absorption), Type M (moderate absorption) and Type S (slow or poor absorption). In broad terms UO_2 is considered a Type S compound, UO_3 a Type M compound and uranyl carbonate a Type F compound. The absorption characteristics of U_3O_8 can vary between those for Type M and S compounds.
- The human respiratory tract model has reference values assigned for deposition and particle transport to the GI tract. Reference values for uptake of uranium from the GI tract are given for Type F, M, or S compounds.

- The ICRP has recommended that material specific values for aerosol parameters such as size and density, absorption parameter values from the lungs to blood, together with appropriate exercise levels and breathing patterns should be used whenever possible. Most of these factors are considered in the monograph.

Health effects

DU has both chemical and radiological toxicity with the two important target organs being the kidneys and the lungs.

Kidney

Retention of uranium in the kidney has been attributed to the creation of complexes with proteins and phospholipids in the proximal tubules; considered to be the main site of kidney damage. Animal studies have shown that long-term exposure to uranium causes nephrotoxic effects that ranged from minimal microscopic lesion in the tubular epithelium (low concentrations) to tubular necrosis (high concentrations).

Long-term studies of workers chronically exposed to uranium have reported impairment of the kidneys (proximal tubular epithelium) that depended on the level of exposure. Studies of members of the public chronically exposed to uranium in drinking water have also shown similar signs of impairment of kidney function. There is some evidence that kidney function returns to normal once the source of excessive uranium exposure has been removed.

Lung

Pulmonary toxicity of uranium varies depending on the animal species studied and the chemical form of the uranium. Some early studies on animals reported pulmonary oedema and haemorrhage following exposure to some uranium compounds (e.g. uranium peroxide, uranium trioxide) but not others (uranium dioxide). However, more recent long-term studies using a range of animals inhaling various uranium compounds, both soluble and insoluble, did not reveal any histological damage to the lungs.

In a number of studies on uranium miners, an increased risk of lung cancer has been demonstrated but this has been attributed to exposure from radon decay products. There is a possibility of lung tissue damage leading to a risk of lung cancer if a high enough radiation dose results from insoluble DU compounds remaining in the lungs over a prolonged period (many years).

Skin

Erythema or other effects on the skin should not occur even if DU is held against the skin for prolonged periods (weeks). There are no established data to suggest that skin cancer occurs from skin contact with uranium dusts.

Liver and skeleton

Autopsies of individuals chronically exposed to uranium have found that the average ratios of the amount of uranium in the skeleton, liver and kidney was 63:2.8:1. The uranium content in the skeleton may reflect its affinity for phosphate which is abundant in the bone. No consistent or confirmed adverse effects have been reported for the skeleton or liver. However, few studies have been conducted.

Reproductive and developmental effects

Reproductive and developmental effects have been reported in rodent studies ingesting or being exposed via dermal contact to extremely high levels of soluble uranium compounds. No such effects have been reported in humans; however very few studies are available. Further studies are needed to clarify if these effects occur in other animals and whether they are likely to occur in humans.

Central nervous system

Although uranium released from embedded fragments may accumulate in CNS tissue, and some animal and human studies are suggestive of effects on CNS function, it is difficult to draw firm conclusions from the results available. Better designed and focussed studies are needed to clarify if any effects on CNS occur from exposure to uranium.

International limits for radiological exposure

This monograph uses the radiation dose[1] limits published in the International Basic Safety Standards (BSS) for Protection against Ionizing Radiation and for the Safety of Radiation Sources. The following doses are in addition to those from normal background exposures. They should not be exceeded:

Public exposure

- an effective dose of 1 mSv in a year
- in special circumstances, an effective dose of up to 5 mSv in a single year provided that the average dose over five consecutive years does not exceed 1 mSv per year
- an equivalent dose to the skin of 50 mSv in a year

Occupational exposure

- an effective dose of 20 mSv per year averaged over five consecutive years
- an effective dose of 50 mSv in any single year
- an equivalent dose to the extremities (hands and feet) or the skin of 500 mSv in a year

Guidance on exposure based on chemical and radiological toxicity

Chemical toxicity of a given material is related to its detrimental interaction with biochemical processes in the human body. WHO has guidelines for determining the values of health-based exposure limits or tolerable intakes for chemical substances. Tolerable intake (TI) is an estimate of the intake of a substance that can occur over a lifetime without appreciable health risk. The TI is usually expressed as mg per kg of body weight per day.

[1] The amount of energy deposited per unit mass is called the *absorbed dose* and is measured in gray where 1 Gy is equivalent to one joule per kilogram. Since alpha particles can deposit more energy in tissue than gamma or beta radiation, they have a greater ability to do more damage. Thus, a weighting factor is given to all radiations (20 for alpha and 1 for beta and gamma radiations) and is multiplied by the *absorbed dose* to give the *equivalent dose*. The unit of *equivalent dose* is the sievert (Sv). Another quantity used in radiation protection is the *effective dose*. It is calculated by multiplying the *equivalent dose* by tissue weighting factors that relate to the relative risk of cancer associated with each organ or tissue. Thus the *effective dose*, also in Sv, gives a general indication of the level of risk implied by the dose; a measure of health detriment. The *collective dose* is an expression for the total radiation dose incurred by a population and is expressed in man-sieverts (man.Sv).

The effect observed at the lowest exposure level is used to determine the TI value. This is usually due to chemical toxicity when intake is by ingestion or inhalation of Type F or M uranium compounds and due to radiological toxicity for Type S uranium compounds after exposure by inhalation. These are discussed below for both public and occupational exposure. The TIs derived are applicable to long-term exposure. In single and short-term exposures, higher exposure levels can be tolerated without adverse effects. However, quantitative information is not available to assess how much the TI values may be temporarily exceeded without risk. Limits derived for uranium compounds are equally applicable to DU.

Public exposure by ingestion

- Based on medium-term and long term toxicity studies in experimental animals, a TI of 0.5 µg per kg of body weight per day (i.e. about 11 mg/y for an average adult) was derived for Type F uranium compounds.
- The same TI should be used for Type M uranium compounds as the data available do not consistently demonstrate lower nephrotoxicity for these compounds.
- The value of the TI would, on the basis of the ICRP biokinetic models, result in an effective dose of about 10 µSv.
- Uranium compounds with low absorption (Type S) are markedly less nephrotoxic, and a tolerable intake of 5 µg per kg of body weight per day is applicable.
- When the solubility characteristics of the uranium species are not known, which is often the case in exposure to DU, it would be prudent to apply the more stringent tolerable intakes, i.e., 0.5 µg per kg of body weight per day for oral exposure.

Public exposure by inhalation

- The data on the nephrotoxicity of Type F and M uranium compounds are consistent with a TI for oral exposure of 0.5µg per kg of body weight per day; this translates to an airborne concentration of uranium of about 1.5 µg/m^3, or approximately 1-µg/m^3 (in the respirable fraction).
- For Type S compounds, exposure corresponding to a daily intake of 5 µg per kg of body weight (as derived for the exposure by ingestion above) would lead to a total radiation dose of about 13 mSv per year. As the accepted upper limit for radiation exposure to the general public is 1 mSv/year, it would be appropriate to reduce the TI to 0.5 µg per kg of body weight per day, equivalent to a tolerable concentration in ambient air of 1 µg/m^3 (respirable fraction).

Occupational exposure by inhalation

- The ICRP model indicates that an effective radiation dose limit for workers of 20-mSv per year, averaged over five consecutive years, leads to an 8-hour time-weighted average (TWA) inhalation limit of 0.05 mg/m^3 for Type S uranium compounds.
- As consideration of chemical toxicity led to an inhalation exposure limit for the more soluble uranium compounds that is identical to that derived for Type S compounds based on radiological toxicity for the general population (see above), it seems appropriate to apply an 8-hour TWA inhalation exposure limit of 0.05 mg/m^3 for exposures from Type F and M uranium compounds.

Monitoring and treatment of exposed individuals

For the general population, neither civilian or military use of DU is likely to produce exposures to DU much above normal background levels produced by uranium. Thus an exposure assessment for DU will not normally be required.

When an individual is suspected of being exposed to DU at a level significantly above the normal background, an assessment may be required. In principle this assessment may be undertaken by extrapolation from the amounts of DU excreted in urine and faeces and by external radiation monitoring of the chest.

- **Urine measurement:** Provided that the dietary concentrations of uranium are low, assessment of DU exposure is best achieved by analysis of daily urine excretion. The amount of DU in the urine is determined from the ^{235}U:^{238}U ratio, obtained using sensitive mass spectrometric techniques. Assessment of DU intake is then determined by back extrapolation using appropriate graphs and information in this monograph. In such circumstances it should be possible to assess doses from DU intake at the mg per day or mSv level.
- **Faecal measurement** can give useful information on intake if samples are collected soon after exposure (a few days).
- **External radiation measurements** over the chest, using a whole-body radiation monitor for determining the amount of DU in the lungs, has limited application since it requires specialist facilities and can only assess relatively large amounts of DU in the lungs.

Treatment of overexposure

There are no specific means to decrease the absorption of uranium from the gastrointestinal tract or lungs, or increase its excretion. Thus general methods appropriate to heavy metal poisoning could be applied. Similarly there is no specific treatment for uranium poisoning and the patient should be treated based on the symptoms observed. Dialysis may be helpful in extreme cases of kidney damage.

15.2 Conclusions

This review concludes that:

- Limitation on public intake of soluble DU compounds (Type F and M) should be based on a TI value of 0.5 µg per kg of body weight per day and for insoluble (Type-S) DU compounds on 5 µg per kg of body weight per day.
- The TI value of 0.5 µg per kg of body weight per day leads to a limitation on public inhalation of soluble DU compounds to 1 µg/m^3 DU in air; the same guideline air concentration for insoluble DU compounds comes from the radiation limit dose of 1-mSv/year.
- The 8-hour time-weighted average (TWA) limitation on worker inhalation of soluble and insoluble DU compounds is 50 µg/m^3 DU in air.
- Under most circumstances, use of DU will make a negligible contribution to the overall natural background levels of uranium in the environment. However, levels of DU may be significantly raised over background levels in close proximity to DU contaminating events. Over the days and years following such an event the contamination will become dispersed into the wider natural environment.
- The greatest potential for DU exposure will follow conflict where DU munitions are used and people living or working in these areas inhale dusts and consume contaminated food and drinking water. Measurements of DU in conflict areas indicate only localised (within a few tens of metres from impact sites) contamination at the ground surface. However, levels of contamination in food and drinking water could rise after some years and should be monitored where it is considered that there

is a reasonable possibility of significant quantities of DU entering the ground water or food chain.

- Where possible, clean up operations in impact zones should be undertaken where there are substantial numbers of radioactive projectiles remaining and DU contamination levels are deemed unacceptable by qualified experts. If very high concentrations of DU dust or metal fragments are present, then areas may need to be cordoned off until removal can be accomplished.
- Guidance on the necessity for clean up of radioactive materials has been provided by the ICRP (1999b). Similar methodologies employed during the cleanup of land contaminated with heavy metals resulting from industrial activity are also appropriate, particularly as radiation dose levels of DU in conflict areas would not normally exceed those recommended for clean up by the ICRP.
- Young children could receive greater exposure to DU when playing in or near DU impact sites. Typical hand-to-mouth activity could lead to high DU ingestion from contaminated soil. Necessary preventative measures should be undertaken.
- General screening or monitoring for possible DU related health effects in populations living in conflict areas where DU was used is not recommended. Rather individuals who believe they have had excessive intakes of DU should consult their medical practitioner for an examination and treatment of any symptoms.
- Since DU is a radioactive metal, restrictions are needed on the disposal of DU. There is the possibility that DU scrap metal could be added to other scrap metals for use in refabricated products. DU is a pyrophoric metal that can produce oxides that can be inhaled when heated (welded). Disposal of DU should normally come under appropriate national or international (IAEA) recommendations for use of radioactive materials.

15.3 Research needs

Priorities for research that would significantly enhance knowledge and lead to better assessments of health risks from exposure to DU are given below.

- Studies are needed to clarify our understanding of the extent, reversibility and possible existence of thresholds for kidney damage in people exposed to DU. Important information could come from studies of populations exposed to naturally elevated concentrations of uranium in drinking water.
- WHO, through its International Agency for Research on Cancer (IARC), continues to study the effects of low-level exposure to ionizing radiation in order to improve the scientific base for health risk assessment and radiation protection. The utility and feasibility of studies to assess whether there has been an increased rate of cancer amongst military personnel who served in the Gulf or Balkans conflicts, and to evaluate the possible role of DU if an increase is found, should be investigated.
- Studies are needed that will allow better exposure assessments of children. This is particularly important given their unique exposure scenarios such as geophagia and hand-to-mouth activities.
- Studies are required to validate transfer coefficients for DU compounds entering the human food chain. For example, this is important given the amount of soil ingested by many livestock during browsing.
- There is a lack of information about the possible biological action of uranium or DU in the following areas:
  - Neurotoxicity: Other heavy metals, e.g. lead and mercury are known neurotoxins, but only a few inconsistent studies have been conducted on uranium. Focused studies are needed to determine if DU is neurotoxic.

- Reproductive and developmental effects have been reported in single animal studies but no studies have been conducted to determine if they can be confirmed or that they occur in humans.
- Haematological effects: Studies are needed to determine if uptake of DU into the bone has consequences for the bone marrow or blood forming cells.
- Genotoxicity: Some *in vitro* studies suggest genotoxic effects occur via the binding of uranium compounds to DNA. This and other mechanisms causing possible genotoxicity should be further investigated.

- Investigations are needed on the chemical and physical form, physiological behaviour, leaching and subsequent environmental cycling of specific forms of uranium from various industrial and military sources (e.g. depleted uranium alloys, phosphate by-products). Particular attention should be paid to where the bulk of DU finally goes.