

Annex 4 ICRP biokinetic models

A4.1 The Human Respiratory Tract Model (HRTM)

The ICRP Publication 66 Human Respiratory Tract Model for Radiological Protection (HRTM) (ICRP-66, 1994a) has been applied with the new generation of systemic models (ICRP-67, 1993; ICRP-69, 1995a) to calculate general-purpose dose coefficients. The effective dose coefficients for workers and the public given in ICRP-68, (1994) and ICRP-72 (1996) were adopted in the International Basic Safety Standards (BSS, 1996) and in the Euratom Directive (EC, 1996).

The HRTM is described in detail in ICRP-66 (1994a). Summaries are given in the ICRP Publications in which it is applied (ICRP-68b, 1994; ICRP-71, 1995b; ICRP-72, 1996; ICRP-78, 1997), and elsewhere (Bailey, 1993, 1994). Only an outline is given here. The main functions of the HRTM are to provide:

- a qualitative and quantitative description of the respiratory tract as a route for radionuclides to enter the body
- a method to calculate radiation doses to the respiratory tract for any exposure
- a method to calculate the transfer of radionuclides to other tissues

The HRTM is comprehensive. It applies to:

- assessing doses from exposures, and assessing intakes from bioassay measurements
- radionuclides associated with particles (aerosols) of all sizes of practical interest (0.0006–100 μm) and to gases and vapours
- all members of the population, giving reference values for children aged 3 months, 1, 5, 10 and 15 years, and adults. Guidance is provided for taking into account the effects of factors such as smoking, diseases and pollutants

A4.1.1 Morphometry

In the HRTM the respiratory tract is represented by five regions, based on differences in radio-sensitivity, deposition and clearance. The extrathoracic (head and neck) airways (ET) are divided into ET₁, the anterior nasal passage, and ET₂, which consists of the posterior nasal and oral passages, the pharynx and larynx. The thoracic regions (the lungs) are Bronchial (BB, airway generations 1–8), Bronchiolar (bb), and Alveolar-Interstitial (AI, the gas exchange region). Lymph nodes are associated with the extrathoracic and thoracic airways (LN_{ET} and LN_{TH} respectively). Target cells are identified in each region: for example the basal cells of the epithelium in both ET regions; basal and secretory cells in the bronchial epithelium. Reference values of dimensions are given which define the mass of tissue containing target cells in each region for dose calculations. They are assumed to be independent of age and sex.

A4.1.2 Physiology

The breathing rate (frequency and volume) is the main factor in the model that depends on age and physical activity. This is also one aspect for which there are comprehensive data relating to women and children. Reference values of important parameters are

recommended for the population groups noted above, for four levels of exercise: sleep, sitting, light and heavy exercise, and taking account of both nose- and mouth-breathing. These have been combined with habit survey data to give the reference volumes inhaled per working shift or per day. Thus light work is a combination of light exercise and sitting. These parameters determine intakes per unit exposure (time-integrated air concentration) but are also used with the deposition model to determine regional deposition.

A4.1.3 Deposition of particles

The deposition model evaluates the fraction of activity in the inhaled air that is deposited in each region. Deposition in the ET regions was determined mainly from experimental data. For the lungs, a theoretical model was used to calculate particle deposition in each region, and to quantify the effects of the subject's lung size and breathing rate. For particles larger than 1 μm , the 'aerodynamic' mechanisms of gravitational settling (sedimentation) and inertial impaction, which increase with particle size and density, dominate. For particles smaller than 0.1 μm , the 'thermodynamic' mechanism of diffusion, which increases with decreasing particle size, dominates. In the range 0.1–1 μm all are important. The aerodynamic equivalent diameter of a particle (d_{ae}) is the diameter of a unit density sphere with the same sedimentation velocity as the particle. The thermodynamic equivalent diameter of a particle (d_{th}) is the diameter of a sphere with the same diffusion coefficient as the particle.

Regional deposition for each age group and exercise level was calculated for aerosols with lognormal particle size distributions, and tabulated as a function of the median size. This may be the activity median aerodynamic or thermodynamic diameter, AMAD or AMTD. (50% of the activity in an aerosol is associated with particles with d_{ae} greater than the AMAD, or with particles with d_{th} greater than the AMTD). AMAD is used when deposition depends on sedimentation and inertial impaction, typically when AMAD less than 0.5 μm . AMTD is used when deposition depends on diffusion, typically when AMAD greater than 0.5 μm . In general, values of regional deposition are lower than corresponding values using the ICRP-30 model (ICRP-30, 1979), and do not vary markedly with age.

The ICRP default values for deposition in the respiratory tract after occupational and public exposure are shown in Table A4.1.

A4.1.4 Gases and vapours

Unlike deposition of particles, respiratory tract retention of gases and vapours is material specific. Virtually all inhaled gas molecules contact airway surfaces, but are usually re-essuspended in the air unless they dissolve in, or react with, the surface lining. The fraction of an inhaled gas or vapour that is retained in, or absorbed from, each respiratory tract region thus depends on its solubility and reactivity and, except in simple cases, has to be treated on an individual basis. The model assigns gases and vapours to three classes:

- i) SR-0. Insoluble and non-reactive. No deposition, or uptake to blood. In most cases external radiation from the surrounding cloud dominates exposure.

- ii) SR-1. Soluble or reactive, some exposure to all airways, and absorption into blood. They require individual evaluation, but the most important parameter is often the fraction absorbed into blood.
- iii) SR-2. Highly soluble and reactive. Complete and instantaneous uptake assumed.

Table A4.1 Deposition of inhaled aerosols after occupational and public exposure

Region ^c	Occupational ^a (%)	Public ^b (%)
ET ₁	33.9	14.2
ET ₂	39.9	17.9
BB (bronchial)	1.8 (33% in BB ₂)	1.1 (47% in BB ₂)
bb (bronchiolar)	1.1 (33% in bb ₂)	2.1 (49% in bb ₂)
AI	5.3	11.9
Total deposit	82.0	47.3

Notes

a Occupational exposure. Worker, 5- μm AMAD ($\sigma_g = 2.5$), 3.5- μm AMTD, density 3.0 g/cm³, shape factor 1.5 (see Chapter 5); fraction breathed through nose is 1. 31% sitting and 69% light exercise; mean ventilation rate is 1.2m³/h. (See Table 6.)

b Environmental Exposure (indoors at home). Adult male, 1- μm AMAD ($\sigma_g = 2.47$), 0.69- μm AMTD. density 3.0 g/cm³, shape factor 1.5; fraction breathed through nose is 1. 55% ventilation rate is 0.78 m³/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 (ET₁) and posterior nasal and oral passages, pharynx and larynx (ET₂). The thoracic regions are bronchial and bronchiolar (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 region.

A4.1.5 Clearance

The model describes three clearance pathways (Figure A4.1). Material deposited in ET₁ is removed by nose blowing. In other regions clearance results from a combination of movement of particles to the gastrointestinal (GI) tract and lymph nodes (*particle transport*), and movement of radionuclides into the blood (*absorption*). It is assumed that:

- all clearance rates are independent of age and sex.
- particle transport rates are the same for all materials.
- absorption into blood, which is material specific, occurs at the same rate in all regions except ET₁, where none occurs.
- fractional clearance rates vary with time, but to simplify calculations are represented by combinations of compartments that clear at constant rates. Since particle transport rates are the same for all materials, a single compartment model applies to all, and it was based, so far as possible on human experimental data.

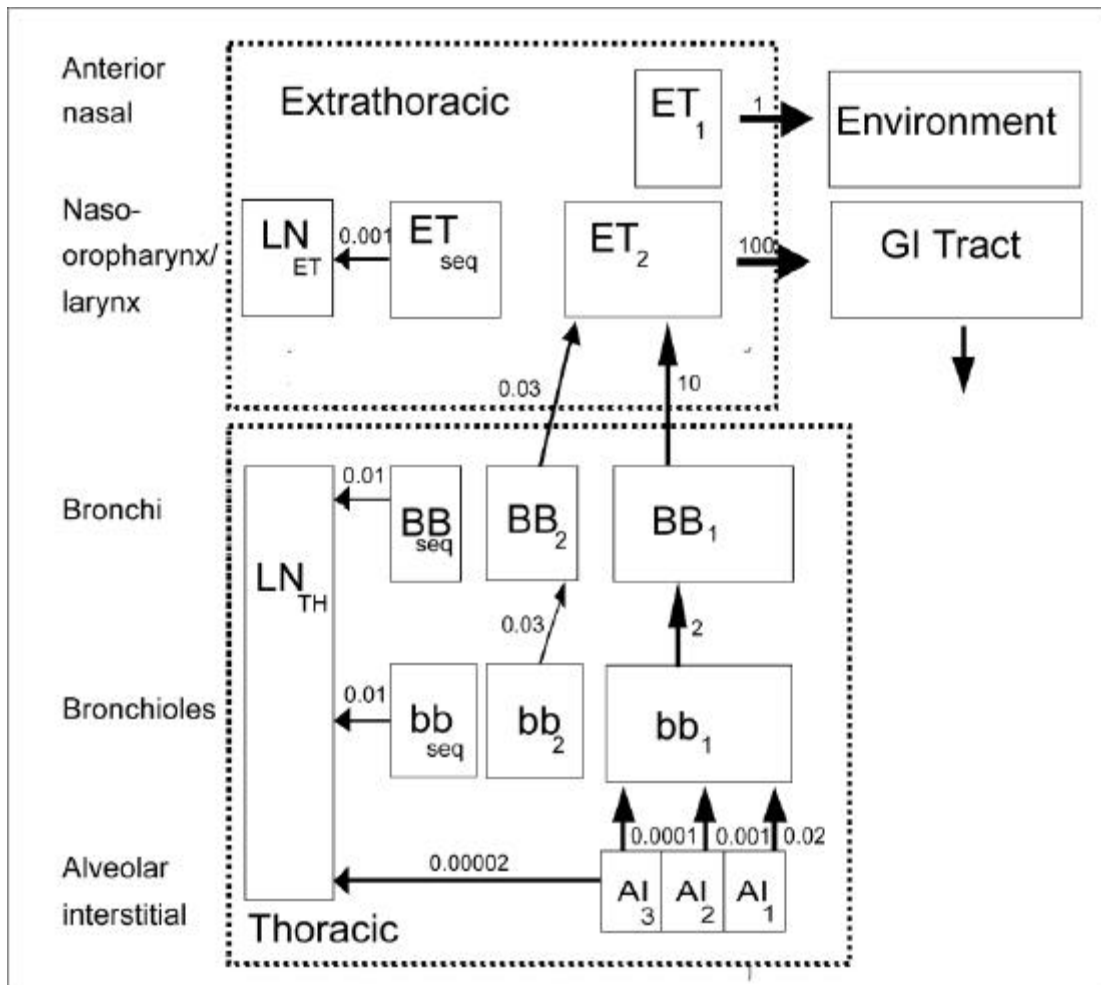


Figure A4.1 Compartment model to represent time dependent particle transport from each region of the respiratory tract. The rate constants down beside the arrows are reference values expressed as d^{-1} .

Absorption to blood is a two-stage process (Figure A4.2): dissociation of the particles into material that can be absorbed into blood (*dissolution*); and absorption into blood of soluble material and of material dissociated from particles (*uptake*). Both stages can be time-dependent. The simplest representation of time-dependent *dissolution* is to assume that a fraction (f_r) dissolves relatively rapidly, at a rate s_r , and the remaining fraction ($1-f_r$) dissolves more slowly, at a rate s_s . Provision is made in the HRTM for two fractions, to avoid undue complexity. *Uptake* to body fluids of dissolved material can usually be treated as instantaneous. In some situations, however, a significant fraction of the dissolved material is absorbed slowly. To enable this to be taken into account, the HRTM includes compartments in which activity is retained in each region in a ‘bound’ state. However, it is assumed by default that uptake is instantaneous, and the ‘bound’ state is not used and hence is not included in Figure A4.2.

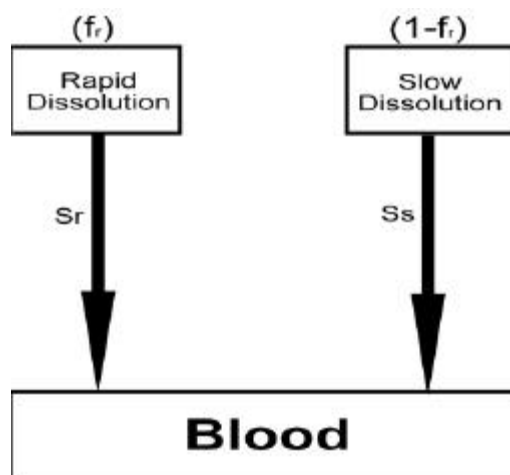


Figure A4.2 Model for time dependent absorption into blood.

It is recommended that material-specific rates of absorption should be used for compounds for which reliable experimental data exist. For other compounds, default values of parameters are recommended (Table A4.2), according to whether the absorption is considered to be fast (Type F), moderate (M) or slow (S) (corresponding broadly to inhalation Classes D, W and Y in the ICRP-30 model).

Table A4.2 Default absorption parameter values for Type F, M and S materials

ICRP Publication 66 absorption type	F (fast) ^a	M (moderate) ^b	S (slow) ^c
Model parameters:			
Fraction dissolved rapidly, f_r	1	0.1	0.001
Dissolution rate:			
Rapid (per day), s_r	100	100	100
Slow (per day), 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 ET₂ and BB₁, 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 day ($t_{1/2}$ approximately 10 minutes).
- 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 per d. This is represented by $f_r = 0.1$; $s_r = 100$ per day; and $s_s = 0.005$ per day
- 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 day. 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 day; and $s_s = 0.0001$ per day.

A4.1.6 Dose calculation

In accordance with the general approach taken by ICRP, the dose to each region is given by the average dose to the target tissue in that region. To take account of differences in sensitivity between tissues, the dose to each region i is multiplied by a factor A_i representing the region's sensitivity relative to that of the whole organ. The weighted sum gives the equivalent dose to the extrathoracic or thoracic airways.

A4.2 The systemic model for uranium

The fate of uranium that enters the bloodstream and systemic tissues cannot be observed or easily measured. Therefore, models are used to represent the movement of material around the body. These models can be used to calculate radiation doses to tissues and to predict the retention and excretion of the element.

The model used for uranium (Figure A4.3) is that recommended by ICRP-69 (1995a). This model describes the deposition of material from the blood into various organs or regions, the transfer from region to region, the return of material to blood, and the eventual excretion of the material. In keeping with ICRP's move towards physiological realism in its models, the uranium model includes recycling, i.e. the possibility for material to pass from region to region via the blood stream (Leggett, 1994). Previous models were simple catenary, or 'straight chain' models; the current uranium model is thus a marked improvement on earlier models.

The model is based on a number of sources which include data from both animal experiments (using baboons, dogs and rats) and studies on humans. Clearly human data is to be preferred, and for uranium, ICRP can draw on a large database, which is not the case for many other elements. In particular, there are data from the so-called Boston Subjects, a group of terminally ill patients who were injected with uranium in the 1950s. A brief overview of the human data that support the ICRP model is given in ICRP-69 (1995a). Other reviews are provided by Leggett and Harrison (1995) and Leggett (1989, 1992).

The principal sites of uranium deposition in the body are the kidneys, the liver and bones. In addition, some material is deposited in various other tissues generally at lower concentrations than the main sites of deposition; these are usually referred to as 'soft tissues'. Of the amount absorbed into the blood stream, the model assigns 30% to soft tissues (rapid turnover, ST0), this represents a pool of activity distributed throughout the body which exchanges rapidly with the blood stream. The remaining activity is apportioned as follows, kidneys 12%, liver 2%, bone 15%, red blood cells 1%, soft tissue (intermediate turnover, ST1) 6.7%, soft tissue (slow turnover, ST2) 0.3%, with 63% being promptly excreted in urine via the bladder.

Some of the material initially deposited in these regions can be returned to the blood stream while some is transferred to other regions of tissues (Figure A4.3). For example, material in the soft tissue compartments is returned only to blood while material in liver can be exchanged with blood or transferred to other regions of the liver (Liver 2 in Figure A4.3). The bone warrants additional comment. Material is initially deposited on the bone surface (either trabecular or cortical), from where it can be transferred to bone volume (exchangeable) or returned to the blood stream. Material which does reach the exchangeable bone volume can be buried deeper in the bone volume (non-exchangeable) or returned to the surface. Material in non-exchangeable volume is transferred slowly to blood. All the pathways used in the model are illustrated in Figure

A4.3. In time, most of the systemic uranium is excreted in urine via the bladder, a small fraction is also excreted in faeces.

The length of time that material remains in these regions is partly governed by a removal half-time, i.e. the time that it takes to remove half of the material present. This time varies from organ to organ, for example the removal half-time for ST0 is as little as two hours, while for ST2 it is one hundred years. The net or apparent time that it takes to halve the amount of material in an organ, however, can be very different from the removal half-time, since material is continually being re-deposited by the recycling nature of the model. The net half-time thus results from a combination of removal of existing material and deposition of new material from the blood stream. It is difficult to simply state values for net half-times. Table A4.3 complements Figure A4.3. It gives retention in liver, kidneys, bone (comprising the six skeleton compartments of Figure A4.1) and the whole body at a number of times after an acute intake directly into the blood stream. It also gives the amount of activity excreted in urine and faeces per day.

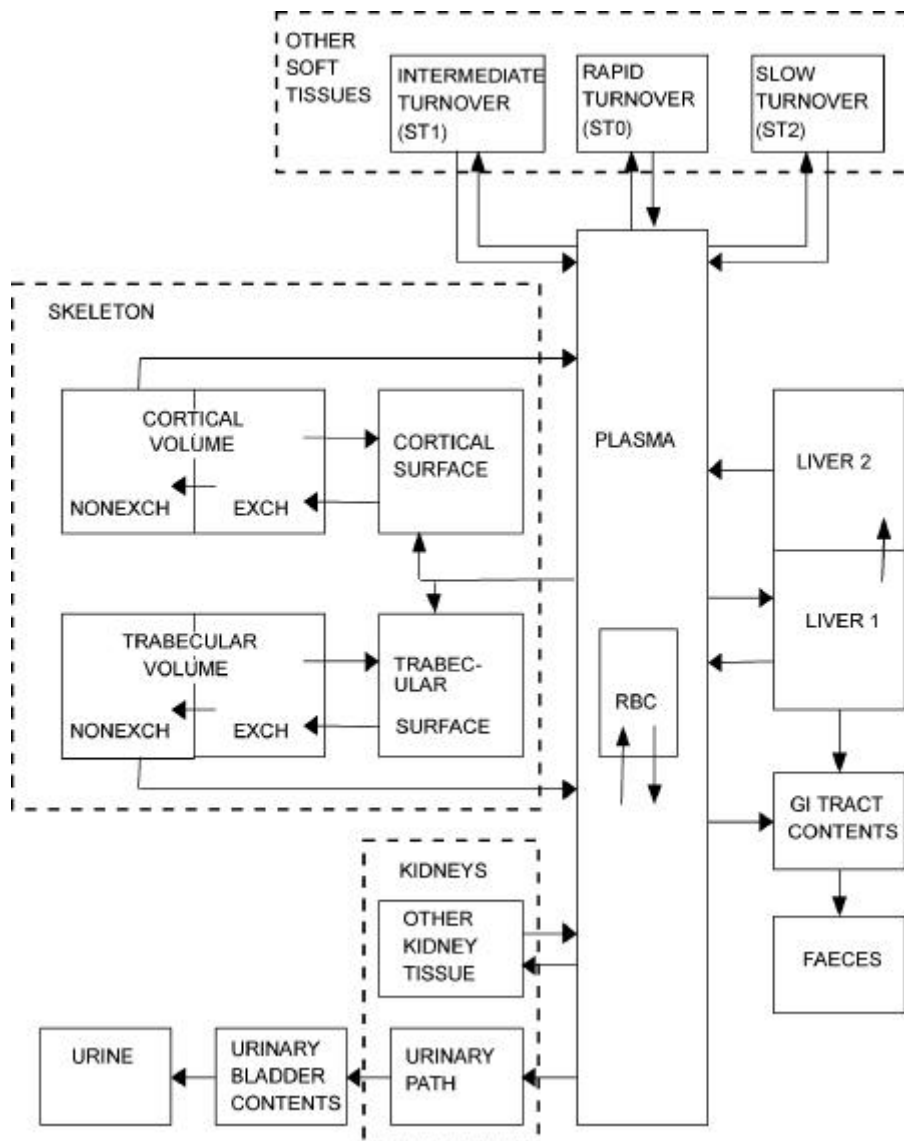


Figure A4.3 The biokinetic model for uranium.

A4.3 The model for the gastrointestinal tract.

ICRP recommended in Publication 30 (ICRP-30, 1979) the use of compartmental models to calculate the distribution of radioactive transformations in the body. Each organ is modelled as one or more compartments. For purposes of dose calculation, material is usually taken to be uniformly distributed throughout the organ. Transfers between compartments are assumed to obey first order kinetics. For the gastrointestinal (GI) tract the model has four compartments (see Figure A4.4).

Table A4.3 Retention and daily excretion following an acute unit intake (1 Bq or 1 µg) of DU directly into blood.

Time (days)	Faeces (Bq per day)	Urine (Bq per day)	Liver	Kidneys	Bone	Soft tissues	Whole Body
1	1.68×10^{-3}	6.45×10^{-1}	1.40×10^{-2}	1.12×10^{-1}	1.43×10^{-1}	7.06×10^{-2}	3.53×10^{-1}
3	9.47×10^{-4}	1.80×10^{-2}	1.20×10^{-2}	9.48×10^{-2}	1.31×10^{-1}	6.65×10^{-2}	3.10×10^{-1}
10	3.73×10^{-5}	9.43×10^{-3}	7.21×10^{-3}	5.27×10^{-2}	1.04×10^{-1}	5.63×10^{-2}	2.22×10^{-1}
30	1.11×10^{-5}	2.39×10^{-3}	2.41×10^{-3}	1.08×10^{-2}	8.08×10^{-2}	3.30×10^{-2}	1.27×10^{-1}
100	2.30×10^{-6}	3.51×10^{-4}	1.36×10^{-3}	1.26×10^{-3}	5.61×10^{-2}	7.60×10^{-3}	6.63×10^{-2}
1000	5.37×10^{-8}	8.09×10^{-6}	1.12×10^{-3}	4.51×10^{-4}	2.95×10^{-2}	3.79×10^{-3}	3.49×10^{-2}
10000	5.41×10^{-9}	8.15×10^{-7}	2.13×10^{-4}	1.80×10^{-5}	8.03×10^{-3}	3.26×10^{-3}	1.15×10^{-2}

A4.3.1 Stomach

It is assumed that no absorption takes place from the stomach and that material passes on to the next compartment with a mean residence time of one hour.

A4.3.2 Small intestine

The mean residence time is taken to be four hours. This is the compartment from which absorption takes place. It is normal to quantify absorption by using the f_1 value. f_1 is the fraction of material reaching body fluids following ingestion.

$$f_1 = \frac{I_B}{I_B + I_{SI}}$$

λ_B = rate constant for transfer to body fluids

λ_{SI} = rate constant for transfer from small intestine to upper large intestine.

It is worth noting that the small intestine is alkaline. This means that elements which hydrolyse, notably the actinides (but not uranium), are usually in an insoluble form and are not readily absorbed (i.e. have a low f_1 value).

A4.3.3 Upper large intestine

The mean residence time is taken to be 13 hours. In practice water is absorbed from the gut content in the upper large intestine. However, it is not necessary to model this since tritiated water is taken to be homogeneously distributed across all soft tissue.

A4.3.4 Lower large intestine

The mean residence time is taken to be 24 hours. It is important to realize that the lower large intestine may be the most heavily irradiated organ if the gut uptake factor is low. This will particularly be the case for materials emitting relatively non-penetrating radiation with a short physical half-life.

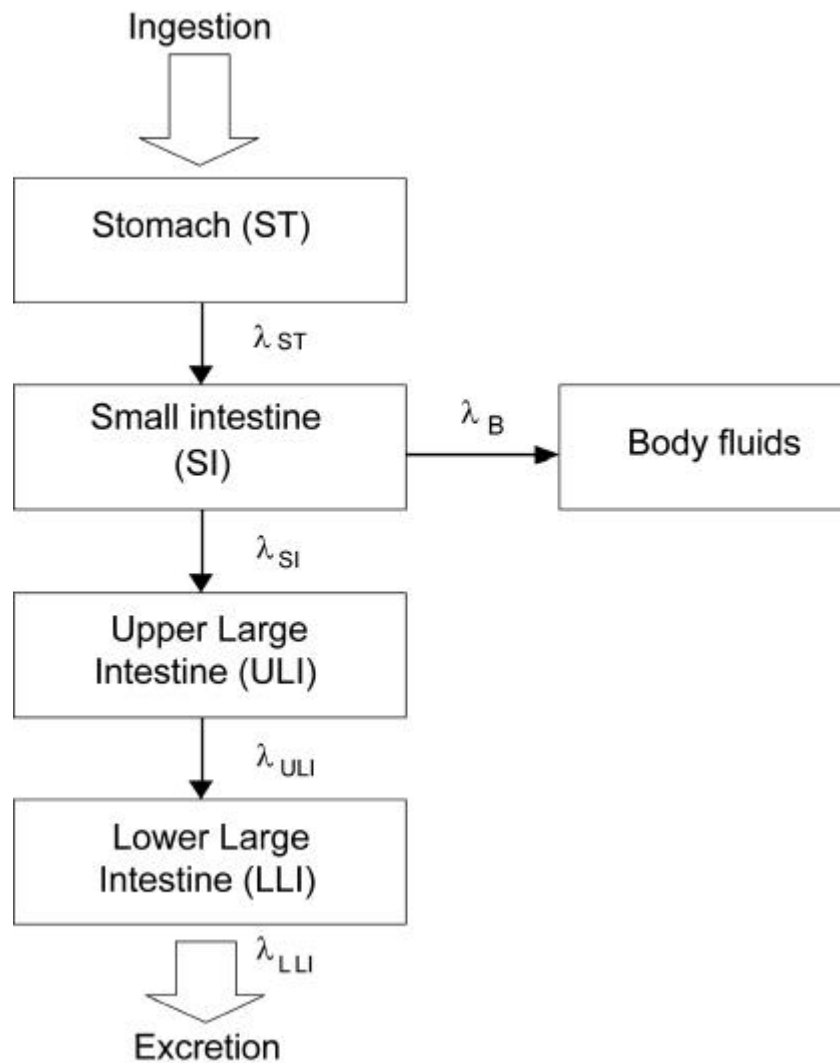


Figure A4.4 Mathematical model used to describe the kinetics of radionuclides in the gastrointestinal tract.

Annex 5 Chemical toxicity of uranium: Occupational exposure standards after inhalation and the impact of ICRP biokinetic models.

A5.1 Soluble uranium compounds

In order to appreciate the rationale behind the currently recommended exposure limits for uranium based on chemical toxicity, it is necessary to examine the developments and changes that have occurred during the past 40 years. (These are summarized in Table A5.1)

Table A5.1 Changes and developments in recommended occupational exposure limits for uranium based on chemical toxicity.

Year	Source	(MPC) _a /TLV mg/m ³	Daily limit mg
1940s/50s	Various	0.02–0.05	
1957	ACGIH	0.05	
1959	ICRP–2/ NCRP 2	0.2 ^a	1.5
1964	ICRP–6	0.2 ^b	2.5 ^c
1968	ICRP–10	0.2 ^b	2.5 ^c
1968	ACGIH	0.2	1.5 ^d
1969	Dept. Employment, UK	0.2	1.5 ^d
1979	ICRP–30	N/A	N/A ^e
1980	HSE, UK	0.2	2.0 ^f
1980	OJEC		2.5 ^c
1988	ICRP–54	0.2	2.0 ^f
1989	OSHA	0.05	0.5 ^f
1994	ICRP–68	N/A ^e	N/A ^e
1995	ICRP–71	N/A ^e	N/A ^e
1996	OJEC	N/A ^e	N/A ^e
1996	ACGIH	0.2	2.0 ^f
1997	HSE, UK	0.2	2.0 ^f
1997	ICRP–78	N/A ^e	N/A ^e
2000	NIOSH	0.2	2.0 ^f

a Value derived from the daily intake assuming a breathing rate of 6.9 m³ per 8 h working day; value correlates with (MPC)_a of 7×10⁻¹¹ μCi/cm³ (see Table A5.2)

b Value correlates with (MPC)_a of 7×10⁻¹¹ μCi/cm³ (see Table A5.2)

c Value based on short- term exposure rule

d Not listed but based on an average breathing rate of 6.9 m³ per 8 h working day

e Chemical toxicity not addressed

f Value not listed but based on a breathing rate of 9.6 m³ per 8 h working day

A5.1.1 Initial recommendations

During the late 1940s and 1950s, various recommendations on exposure limits were made as a consequence of discussions at international conferences (Spoor and Hursh 1973). The values for maximum airborne concentrations, based on toxicity data from animal studies conducted at the time, ranged from 25 μg/m³ to 50 μg/m³ (Spoor and Hursh, 1973). The latter value referred to as the Threshold Limit Value (TLV), was subsequently endorsed by the American Conference of Governmental Industrial Hygienists (ACGIH) in 1957 and the recommendations published in 1960 (Spoor and Hursh, 1973; NCRP, 1959; ACGIH, 1960). The current limits on exposure stem mainly from discussions between Committees II of ICRP and NCRP (National Committee on Radiological Protection) in 1959 (Spoor and Hursh, 1973; NCRP, 1959; ICRP, 1959). In formulating these limits, it was considered that the renal concentration of uranium

that could be safely tolerated by man was $3 \mu\text{g/g}$ (Spoor and Hursh 1973). This concentration was not listed as such by ICRP-2 (1959), but could be derived from three other listed values. These were, for a dose of 50 mSv/y which was the recommended limit at the time, the maximum permissible content of uranium in the total body with the kidney considered the critical organ (so called q value), namely $5 \cdot 10^{-3} \mu\text{Ci}$ (185 Bq); the fraction of the uranium in the kidneys relative to that in the total body (so called f_k value); and a kidney mass of 300 g (Spoor and Hursh 1973, ICRP 1959). At that time, the specific activity of natural uranium was considered to be $0.33 \mu\text{Ci/g}$ (12.2 kBq/g) (Spoor and Hursh, 1973; ICRP-2, 1959). Hence the permissible concentration in the kidney was calculated to be (Spoor and Hursh, 1973)

$$\frac{5 \times 10^{-3}}{0.33} \times \frac{0.065}{300} = 3.3 \times 10^{-6} \text{ g/g} = 3.3 \mu\text{g/g}$$

However, the evidence available from animal studies showed that mild to moderate kidney damage occurred in a variety of animal species at concentrations up to an order of magnitude lower than this. It has been suggested, therefore, that the Committees of ICRP and NCRP were less influenced in the choice of a safe kidney concentration by the animal data than by the concern that the calculation reflected the experience of many years of occupational exposure (Spoor and Hursh, 1973). This experience had shown no evidence of kidney malfunction in workers even at exposure levels in excess of those derived using the kidney concentration above. The procedure adopted by NCRP Committee II for deriving the exposure limit is summarized in Table A5.2.

Table A5.2 Derivation of the permissible daily intake and $(\text{MPC})_a$ for soluble natural uranium by NCRP Committee II (Spoor and Hursh, 1973).

Assumption	Source
A maximum permissible concentration of $3 \mu\text{g}$ uranium per gram kidney	Animal experiment results; Committee judgement decision.
An average kidney mass of 300 g	Standard Man (ICRP-2, 1959)
An effective half-life of 15 days for uranium in the kidney, i.e. $0.0462 \times$ the kidney content is excreted per day	Animal experiments: Human data
That 2.8% of the uranium inhaled was deposited in the kidney (f_a as denoted by ICRP-NCRP)	The lung model (ICRP Publication 2, 1959) specifies that the 25% deposited in the pulmonary lung is absorbed into the body for soluble compounds). The 50% deposited in the upper respiratory tract is transferred to the gut and because of the negligible absorption of uranium can be neglected. Of the systemic uranium, 78% is rapidly excreted and the remaining 22% is divided equally between bone and kidney. $f_a = 0.25 \times 0.11 = 0.028$
That a worker breathes in an average of $6.9 \times 10^6 \text{ cm}^3$ air per working day	Standard Man (ICRP-2, 1959)

The calculation of the maximum permissible concentration in air $(\text{MPC})_a$ for soluble uranium is as follows:

- The maximum permissible daily kidney input equals the daily rate of loss from the kidney when the burden is the maximum permissible = $0.0462 \times 900 = 41.5 \mu\text{g}$.
- The corresponding lung daily input = $41.5 / 0.028 = 1480 \mu\text{g}$.

Therefore, the $(\text{MPC})_a = 1480 / 6.9 \times 10^6 = 2.1 \times 10^{-4} \text{ g/cm}^3$.

This limit has been expressed (ICRP-2, 1959; ICRP-6, 1962) in terms of μCi per cm^3 air using the special curie unit used for natural uranium, $0.33 \mu\text{Ci/g}$. Accordingly, $210 \mu\text{g}$ natural uranium per m^3 air converts to $7 \times 10^{-11} \mu\text{Ci/cm}^3$, which is the value, cited in the above references.

This corresponded to a daily intake limit of 1.48 mg based on a breathing rate of 6.9 m^3 per working day and a maximum permissible concentration in air (MPC_a) of 0.21-mg/m^3 .

A5.1.2 Subsequent developments.

In 1964, ICRP recommended in Publication 6 that the inhalation of soluble uranium of any isotopic composition should not exceed 2.5 mg in any one day (ICRP-6 1964). This recommendation was re-affirmed in ICRP-10, (1968). In the same year, the ACGIH increased the TLV from 0.05 mg/m^3 to 0.2 mg/m^3 , presumably to be consistent with the earlier recommendation of NCRP and ICRP (ACGIH, 1968). It is noteworthy that in the UK, the revised value of the TLV was adopted by the Department of Employment in 1969 (DEP, 1969), and has remained in force ever since (HSE, 2000).

The chemical toxicity of uranium was not considered by ICRP-30 (1979), but the previous recommendation in Publication 10 in 1968 (ICRP-10, 1968) was incorporated into European legislation in 1980 (OJEC, 1980) with the statement 'In view of the chemical toxicity of water soluble compounds of uranium inhalation and ingestion should not exceed 2.5 mg and 150 mg respectively in any one day regardless of isotopic composition'. In hindsight, the choice of the phrase 'water soluble' was unfortunate since some uranium compounds such as the trioxide, tetrafluoride and tributylphosphate which have low aqueous solubility are rapidly absorbed into the blood after deposition in the lungs (Stradling et al., 1989; Stradling and Moody, 1995; Pellow et al., 1997; Ansoborlo et al., 2001).

The chemical solubility of uranium was considered again by ICRP in Publication 54 published in 1988 (ICRP-54, 1988). The advice is unequivocal, and states that 'For soluble forms of depleted, natural and low enriched uranium, the limit on intake is determined by consideration of chemical toxicity. Annual Limits on Intake are entirely inappropriate for such materials'. The proposed daily limit of 2 mg is based on an airborne concentration of 0.2 mg/m^3 and a breathing rate of $1.2 \text{ m}^3/\text{h}$ or 9.6 m^3 for a 8 h working day. These values are mutually incompatible when compared with the original procedure used for deriving exposure limits (see Table A5.2). In other words, an increase in the default value for the breathing rate from $6.9 \text{ m}^3/\text{d}$ to $9.6 \text{ m}^3/\text{d}$ should decrease the airborne concentration to 0.15 mg/m^3 whilst the daily limit should remain unchanged at 1.48 mg . Interestingly, in 1989 (OSHA, 1989), the Occupational Safety and Health Administration (OSHA) in the United States recommended a Permissible Exposure Limit (PEL) of 0.05 mg/m^3 for soluble compounds. This is equivalent to 0.5 mg/d on the basis of a breathing rate of $9.6 \text{ m}^3/\text{d}$.

Despite the pronouncement on chemical toxicity in ICRP Publication 54 (ICRP 1988), the subject was not addressed in Publication 60 in 1991 (ICRP-60, 1991b), nor Publication 68 in 1994 (ICRP-68, 1994b) which were intended to give advice on radiation dose only. As a consequence, advice on exposure limits based on chemical toxicity has not been included in the latest EURATOM directive (OJEC, 1996) and the International Basic Standards for Protection Against Ionizing Radiation (BSS, 1996). Nevertheless the dose coefficients (doses per unit intake, Sv/Bq) for different isotopes included in these documents are invaluable, since workers, particularly in the nuclear

industries, are potentially exposed to a mixture of radionuclides which require the committed effective dose to be assessed. However, it remains a matter of concern that the nephrotoxicity of uranium could be overlooked if the above publications alone were used to assess the health consequences of exposure to uranium compounds. Fortunately, this potential difficulty has been discussed more recently in ICRP Publication 78 (ICRP-78, 1997).

At present there is still widespread acceptance that the occupational exposure limit for soluble uranium compounds is 0.2 mg/m^3 (ACGIH 2000, NIOSH 2000, HSE 2000).

A5.1.3 The nephrotoxicity of uranium.

It is not the purpose of this section to review the nephrotoxicity of uranium. This is dealt with in Chapter 8. However there are issues relating to the basis of the normally accepted threshold concentration of uranium in the kidneys that need to be addressed.

If the current definition for the specific activity of uranium ($0.68 \text{ } \mu\text{Ci/g}$) and dose limit of 20 mSv/y were used in the original calculations, the permissible kidney concentration would be $0.6 \text{ } \mu\text{g/g}$, and the daily limit on intake 0.3 mg (see section A4.1). The kidney concentration would be reduced still further if the amount specified for the initial deposition in ICRP Publication 69 (ICRP-69, 1995a), 12%, was used instead of the original value of 6.5%. Together, all these factors suggest that the permissible concentration in the kidneys should be about $0.3 \text{ } \mu\text{g/g}$ rather than $3 \text{ } \mu\text{g/g}$. It is noteworthy that a review of the uranium concentrations in the kidneys of animals after exposure to soluble uranium compounds for up to one year indicated that mild to moderate damage occurred in the range $0.3\text{-}3 \text{ } \mu\text{g/g}$.

The threshold concentration of $3 \text{ } \mu\text{g/g}$ has also been challenged in two comprehensive review articles in which it is also claimed that this value has neither been supported by unequivocal human data, nor by studies with laboratory animals (Leggett 1989, Diamond 1998). The authors concluded that it would be prudent to lower this long-standing guidance level by at least three-fold until more is known about the physiological effects of low concentrations of uranium in the kidneys, particularly after chronic exposure. More recent animal studies would appear to support such a reduction. Recent studies by Gilman et al (1998a, b, c) with rabbits also support a reduction in kidney concentration. Moreover, it has been noted that the urinary excretion of uranium is impaired at kidney concentrations below $1 \text{ } \mu\text{g/g}$ (Hodgson et al 2000), presumably as a consequence of nephro-toxicological effects. In contrast, a recent American National Standard (ANS, 1996) has re-affirmed the $3 \text{ } \mu\text{g/g}$ kidney concentration limit as a basis for designing and interpreting bioassay programs. However, since the biokinetic model used for assessing this historical value is now obsolete, and the $3 \text{ } \mu\text{g/g}$ concentration value has been rigorously challenged, this approach has to be considered doubtful.

In conclusion, it should be stressed that a reduction in the acceptable kidney concentration does not imply a similar reduction in the value of the airborne concentration permitted in the workplace. The current ICRP physiological models show that substantially greater amounts of uranium need to be inhaled to result in the same kidney concentration as predicted by the original models (Stradling et al., 1998). The net effect is that the permitted airborne concentration of 0.2 mg/m^3 will in fact be conservative. This issue is also discussed in Chapter 9.

Table A5.3 Uranium concentration in the kidney after exposure of one year to inhalation of soluble uranium compounds^a
(from Spoor and Hursh 1973).

Uranium dust concentration $\mu\text{g}/\text{m}^3$	Compound	Dogs		Rats		Rabbits ^b		N
		No.	$\mu\text{g}/\text{g}$	No.	$\mu\text{g}/\text{g}$	No.	$\mu\text{g}/\text{g}$	
2000	$\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$	5	1.7 (1.2-2.3) ^c	24	5.6 (1.9-11.3)	3	1.4 (0.8-2.2)	1
250	$\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$	15	1.0 (0.1-1.9)	23	1.6 (0.1-4.4)	5	0.9 (0.4-1.9)	1
200	UF_6	10	0.4 (0.0-0.7)	23	2.7 (0.0-5.8)	7	0.3 (0.0-0.8)	-
200	UCl_4	13	0.2 (0.0-0.5)	12	0.4 (0.1-1.9)	10	0.4 (0.2-0.6)	1
150	$\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$	11	0.5 (0.2-1.0)	23	1.4 (0.6-3.3)	-	-	-
50	UF_6	12	0.3 (0.0-0.5)	26	0.9 (0.1-2.0)	-	-	1
50	UCl_4	15	0.2 (0.0-0.5)	7	0.4 (0.1-0.9)	-	-	-
40	$\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$	17	0.4 (0.1-1.0)	25	0.4 (0.1-2.0)	-	-	-

^a Data compiled from Hodge et al. (1953)

^b Exposure period was 7-9 months

^c Range of values in parentheses

A5.2 Insoluble uranium compounds.

The methodology for deriving the so-called maximum permissible concentration in air, MPC_a , for insoluble natural uranium is described in more detail elsewhere (Spoor and Hursh, 1973). This methodology is similar to that described for soluble uranium in that it is derived from the maximum permissible lung burden ($8.9 \times 10^{-3} \mu\text{Ci}$) recommended in ICRP-2 (1959) for an annual dose limit to this tissue of 15 rem, and converts radioactivity to mass at equilibrium conditions in the lung using a simplistic metabolic model and the specific activity of the 'special curie' for uranium.

Essentially the calculation proceeded as follows (Spoor and Hursh, 1973),:

Maximum permissible lung burden for annual dose of 15 rem = $8.9 \times 10^{-3} \mu\text{Ci}$.

At equilibrium, the rate of loss from the lungs using a clearance half-time of 120 d (ICRP-2, 1959) will be

$$0.693/120 \text{ d} \times 8.9 \times 10^{-3} \mu\text{Ci} = 5.1 \times 10^{-5} \mu\text{Ci/d}$$

On the assumption that the fraction of the inhaled material which is deposited in the lungs is 0.125 and the average breathing rate is $6.9 \times 10^6 \text{ cm}^3/\text{d}$ (ICRP-2, 1959), the

$$(MPC_a) = 5.1 \times 10^{-5} \mu\text{Ci per d} / [6.9 \times 10^6 \text{ cm}^3 \text{ per d} \times 0.125] = 6 \times 10^{-11} \mu\text{Ci/cm}^3$$

This is the value listed in ICRP-2 (1959) for a 40-hour week, 50 week year.

Based on the definition of the special curie (specific activity of natural uranium $0.33 \mu\text{Ci/g}$), this concentration converts to 0.18 mg/m^3 , rounded to 0.2 mg/m^3 . If the currently accepted breathing rate of $1.2 \text{ m}^3/\text{h}$ were used, then the annual intake based on a 40 hour week, 50 week year would be 480 mg.

Based on current dose limits and biokinetic models, discussed in Chapter 10, and the annual limits on intake for insoluble uranium listed for natural and depleted uranium in Table 10.3 of that chapter, it would seem prudent to reduce this value by four-fold and two-fold respectively.

However, the value of 0.2 mg/m^3 is still used in current recommendations of the American Conference of Governmental and Industrial Hygienists (ACGIH, 2000), and the US National Institute for Occupational Health (NIOSH, 2000). The value is also legally binding in France (FRA, 1988). In the UK, the Health and Safety Executive recommend values for soluble uranium compounds only (HSE, 2000).

Annex 6 Methods for chemical and isotopic analysis in support of public health standards and environmental investigations.

Methods for the determination of uranium in environmental materials such as soils and drinking water are diverse and over the past 20 years improvements in analytical techniques have considerably improved our knowledge of environmental levels (e.g. Toole et al., 1997). Techniques for the analysis of uranium can be divided into three distinctive groups.

A6.1 Non-nuclear instrumental techniques

This group of analytical techniques include inductively coupled plasma–mass spectrometry (ICP-MS), x-ray fluorescence analysis (XRF), thermal ionization mass spectrometry (TIMS) and electron microprobe analysis (EPMA) (Gill, 1997; Van Loon and Barefoot, 1989). Of these techniques the most robust and sensitive technique for the analysis of uranium in a wide variety of environmental matrices is ICP-MS. Typical detection limits for this technique in ideal matrices for uranium are in the order of 1 ng to 5 ng per litre (sample less than 10 cm³ in volume) (Taylor et al., 1998). The speed and versatility of this technique has led the nuclear industry to use it for the analysis of uranium and plutonium in urine during routine monitoring (Ejnik et al., 2000).

XRF is a useful robust technique particularly in solid matrices such as soils and foodstuffs where detection limits in the range of 1 mg/kg are commonly achievable. Although XRF cannot be used to differentiate various isotopes of uranium, its portable derivatives enable the analysis of uranium in the field to a detection limit of 50 mg/kg. Such methods greatly facilitate the identification and prioritisation of sampling strategies in the field.

Until recently TIMS was the preferred method for the determination of uranium isotopic ratios in environmental samples because of its unrivalled sensitivity, accuracy and precision. However, it is a particularly slow technique limiting its application to large-scale environmental surveys. Recently, the advent of magnetic sector and multi-collector ICP-MS offers similar accuracy and precision to TIMS but considerable advantages over this technique in terms of sample throughput and ease of use (Halliday et al., 1998).

For spatial analysis of uranium within samples, EPMA may be used with a resolution of 5 µm or better. However, the detection limit of this technique is rather poor (1000 mg/kg) and it is not possible to determine isotopic ratios using this technique. If high sensitivity spatial analysis of uranium-series isotopes is to be undertaken coupled techniques such as laser ablation ICP-MS or laser ablation multi-collector - ICP-MS offer the ability to determine mg/kg levels of uranium at a spatial resolution of 20 µm to 100 µm.

A6.2 Nuclear instrumental techniques

Prior to the advent of ICP-MS, nuclear based analytical techniques such as alpha spectrometry, gamma spectrometry, neutron activation analysis and fission track analysis (Gill, 1997; Ivanovich and Harmon, 1982; IAEA, 1989b) were routinely used

for the determination of uranium in a wide range of materials. However, each of these techniques either requires extensive sample preparation or pre-concentration to determine uranium at environmental levels, mainly because of the long half-life of ^{238}U . For this reason, the use of these techniques for the quantitative determination of uranium at environmental concentrations has generally dwindled over the past decade in favour of other methods. The use of these techniques in the field is practically limited to gamma ray spectroscopy, although some workers have used various forms of hand held proportional counters, ionization counters and GM tubes to detect surface contamination via the emission of beta particles of ^{234}Th , ^{234}Pa and ^{231}Th which 'in-grow' rapidly from pure uranium. The use of alpha and beta detectors in the field is generally inhibited by the relatively rapid absorption of alpha and beta particles by environmental media (i.e. soil). Because of this such detectors are best used for identifying surface contamination or metallic fragments of DU.

With respect to the use of gamma spectroscopy, the lack of a sufficiently high-energy, high-yield gamma emission by ^{238}U , the main constituent of DU, significantly reduces the effectiveness of this technique for the field identification, and survey, of areas impacted by DU. Gamma ray line intensities for typical samples of DU are reported in Moss (1985). The most abundant line being associated with the 1.001 MeV gamma ray from $^{234\text{m}}\text{Pa}$ with an absolute abundance of 103.7 photons/second /gram of ^{238}U .

A relatively portable (truck mounted) non-destructive field technique for the measurement of $^{238}\text{U}/^{235}\text{U}$ in depleted to moderately enriched uranium has been reported by Balagna and Cowan (1977) by comparing the ratio of the number of fission fragments produced during thermal and epithermal/fast fission of samples of uranium ore. Whilst accurate results were obtained, the technique requires a ^{252}Cf source (requiring associated radiological protection measures) and relatively high concentrations of total uranium (Ca. 20% U_3O_8).

Although time-consuming, fission track analysis does have the advantage of high spatial resolution (much less than 1 mm) with some degree of sensitivity (a few mg/kg) for natural uranium. Although the use of this technique for DU may require modification of irradiation conditions due to the relatively low abundance of ^{235}U .

Previous regulations concerning exposure to radioactivity in food and water have centred upon use of total alpha and total beta activity as a preliminary screening tool. However, the use of total alpha activity as a screening tool for DU, at levels close to those present in the natural environment, is severely hindered by the long half-life (and hence low specific activity) of ^{238}U , coupled to the often high levels of matrix elements in many, even ashed, foodstuffs and waters, particularly from arid and semi-arid environments.

A recent report by Haslip et al., (2000) describes a study undertaken to examine the capabilities of commercial radiation detection equipment for the detection of DU on the battlefield. The work involved some spectroscopic studies of DU munitions, and detection trials with a variety of DU sources, from large spheres to low-activity area sources. It was shown that while commercial equipment can detect alpha, beta, and gamma emission by uranium sources, beta detection is by far the preferred method to be used for contamination surveys. For example the sensitivity of the Eberlines ABP-100 alpha-beta probe (in beta mode) for DU is approximately 0.5 Bq/cm^2 where the contamination is over a large area. However, because the attenuation of beta radiation

by tissue is so great, the efficacy of this detector for detecting shards of DU embedded in wounds is much poorer. The report concluded that whilst such devices may be sufficient for detecting DU contamination on vehicles, it is probably insufficient for DU screening of wounds.



Figure A6.1 Typical hand held alpha-beta detector assembly.

A6.3 Other chemical techniques

Analytical techniques based on the complexation and subsequent spectrometric determination of uranium, such as fluorescence spectrometry have been employed (Van Loon and Barefoot, 1989). In particular, these have been used for the determination of uranium in waters and ores, and for the identification of uranium ore deposits in mineral exploration programmes. Unfortunately these techniques do not differentiate between the various isotopes of uranium and therefore cannot be used to infer the presence or absence of DU. Additionally these techniques are often subject to serious interference from the presence of other forms of contamination such as copper, molybdenum and naturally occurring dissolved organic compounds. However, they have been used to some effect to look at complexation mechanisms of uranium and can be used to provide information on chemical speciation.

