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## ASSESSMENT OF PHYSICO-CHEMICAL AND BIOKINETIC PROPERTIES OF URANIUM PEROXIDE HYDRATE $\text{UO}_4$

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**Abstract**—Comprehensive studies on the radiotoxicological risk of an intermediate compound  $\text{UO}_4$ , which is not specified in ICRP Recommendations, were motivated by its increased use in the nuclear fuel cycle and the lack of information such as physico-chemical and biokinetic properties. The aim of this work was to give an experimental basis for assessing the appropriate limits on intake for workers exposed to  $\text{UO}_4$  and to provide guidance for the interpretation of personal monitoring data. Particle size measurement of the  $\text{UO}_4$  dust indicated a geometric diameter  $D$  of  $0.5 \mu\text{m}$ , which corresponds to an activity median aerodynamic diameter (AMAD) of  $1.1 \mu\text{m}$ . *In vitro* experiments conducted in culture medium showed that  $\text{UO}_4$  is a soluble compound with 66.2% dissolved in 1.9 d and 33.8% in 78 d. Results of dissolution obtained with macrophages showed a significant decrease of 50% at 1 d in terms of solubility. Biokinetic data in the rat obtained from two *in vivo* studies involving intratracheal instillation in rats indicated half-times in the lung of 0.5 d (96.6%) and 27 d (3.4%) for an initial lung deposit (ILD) of  $195 \mu\text{g}$ , and 1.2 d (90.3%) and 38 d (9.7%) for an ILD of  $7.6 \mu\text{g}$ . Absorption parameters to blood as defined in the ICRP Publication 66 human respiratory tract model were calculated with the specific software GIGAFIT and led to the rapid fraction  $f_r$  (0.800 to 0.873), the rapid rate  $s_r$  ( $0.525$  to  $0.928 \text{ d}^{-1}$ ), and the slow rate  $s_s$  ( $1.57 \times 10^{-2}$  to  $2.42 \times 10^{-3} \text{ d}^{-1}$ ). Effective dose coefficients by inhalation for this  $\text{UO}_4$  compound using the *in vivo* experimental results were calculated to be between 0.52 and  $0.70 \times 10^{-6} \text{ Sv Bq}^{-1}$ . Comparison of these values with effective dose coefficients defined in ICRP Publication 68 for workers showed that  $\text{UO}_4$  could be considered as a fast soluble compound of Type F. *Health Phys.* 75(4):389–397; 1998

**Key words:** uranium; biokinetics; nuclear fuel cycle; occupational safety

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### INTRODUCTION

URANIUM PEROXIDE hydrate  $\text{UO}_4 \cdot n\text{H}_2\text{O}$  is a compound present at one step of the enriched uranium fuel cycle, which starts from enriched  $\text{UF}_6$  and finishes with  $\text{UO}_2$  pellet. It is formed during the treatment and recycling of production waste and represents a potential inhalation hazard to workers.

The production of  $\text{UO}_4$  involves oxidation and acidification of  $\text{UO}_2$  and  $\text{U}_3\text{O}_8$  rejects leading to uranyl nitrate  $\text{UO}_2(\text{NO}_3)_2$  and its subsequent precipitation by hydrogen peroxide,  $\text{H}_2\text{O}_2$ . Dehydration of  $\text{UO}_4$  results in the formation of  $\text{UO}_3$ , which is then reduced to  $\text{UO}_2$  by hydrogen for re-use in pellet fabrication.

$\text{UO}_4$  does not exist under anhydrous form but only under hydrate form, which is described by Katz and Rabinovitch (1951) either as peruranic acid or uranium peroxide hydrate  $\text{UO}_3 \cdot \text{H}_2\text{O}_2 \cdot \text{H}_2\text{O}$ .

Neither ICRP Publication 30 (1979), 54 (1988) (class D, W, Y) nor 68 (1994b) with introduction of Type F, M, and S, and more recently through the Journal Officiel des Communautés Européennes (1996), considers the *in vivo* solubility of  $\text{UO}_4$ . Numerous data have been published on compounds like  $\text{UO}_3$  or ammonium diuranate ADU (Eidson 1994), but very few data exist on  $\text{UO}_4$ . A recent *in vitro* dissolution study performed with lung fluid simulant (Metzger et al. 1997) showed that 97% was dissolved with a 0.3 d half-time and 3% with a half-time of 15.6 d. Despite of the lack of information on the specific surface area, Metzger et al. considered  $\text{UO}_4$  to be a class D compound.

The aim of the present study was to supply experimental data on  $\text{UO}_4$ , including physico-chemical and biokinetic properties, to assess effective dose coefficients, and provide guidance on interpretation of bioassay data in terms of the new ICRP recommendations. The lack of references on this industrial intermediate compound led us to carry out comprehensive characterization such as:

1. measurement of relevant physico-chemical parameters, such as geometric diameter, specific surface area, and density;
2. determination of *in vitro* dissolution either in serum simulant fluids such as Gamble's solution (Gamble 1967) or in cellular culture medium with or without macrophages;

3. determination *in vivo* of the lung retention, tissue distribution, and excretion after instillation in rats. Interpretation of *in vivo* data was based on absorption to blood and lung retention curves and achieved using a fitting software GIGAFIT (Birchall et al. 1995). This led to the assessment of rapid fraction  $f_r$  expressed in % and rapid and slow transfer rate to blood,  $s_r$  and  $s_s$  expressed in  $d^{-1}$ , defined in ICRP Publication 66 (1994a) for blood absorption; and
4. dose calculation using LUDEP computer program (Birchall et al. 1991) which is designed to implement the respiratory tract model, and which includes the systemic model of uranium defined in ICRP Publication 69 (1995), and summarized by Chevalier et al. (1997).

## MATERIALS AND METHODS

### Physico-chemical properties of industrial $UO_4$

Industrial  $UO_4$  dust was sampled during the precipitation process and analyzed in the laboratory. The density of the dust was measured with a pycnometer<sup>‡</sup> and the specific surface area was determined by the BET (Brunauer, Emmet, and Teller) absorption method using nitrogen gas.<sup>§</sup> The identification of the oxide was established by x-ray diffraction,<sup>||</sup> infra-red spectroscopy,<sup>¶</sup> and using a transmission electron microscope (TEM)<sup>#</sup> in conjunction with energy dispersive spectrometry (EDS).

### *In vitro* dissolution studies

The *in vitro* dissolution method developed in previous studies (Ansoborlo et al. 1989, 1992; Hengé-Napoli et al. 1994) was based on a static test with culture medium\*\* containing 10% of calf serum.<sup>††</sup>

Two different protocols were used to determine solubility: a short-term experiment (3 d) with or without alveolar macrophages harvested from bronchoalveolar lavage from Sprague-Dawley rats and a long-term study (30 d) without macrophages. A similar experiment (without macrophages) has been conducted with Gamble's solution (pH = 7.3 and under 5%  $CO_2$ ), which is a simulated lung fluid used in previous studies (Ansoborlo et al. 1989, 1994), whereas two short tests (1 d) were carried out with HCl 0.1 N and water fixed at pH 4.8 with diluted HCl (this pH mimics the pH in the lysosomes when uranium is present within the macrophages).

Results for long-term experiment were expressed either in terms of dissolution half-time and percent dissolved or as fraction and rate of dissolution, corresponding to the ICRP Publication 66 lung dissolution model (1994a) parameters  $f_r$ ,  $s_r$ , and  $s_s$ .

## *In vivo* experiments

**Sample preparation.** For use in animal experiments a small size particle fraction was obtained using a micronizing mill. After sedimentation in ethanol to eliminate clusters of particles, the geometric diameter  $D$  was determined by TEM. For administration of uranium to rats the ethanolic suspension was evaporated to incipient dryness and the dust resuspended in saline solution (0.9% NaCl).

**Administration of dust.** The rats used were males of the Sprague-Dawley strain,<sup>‡‡</sup> weighing  $300 \pm 20$  g. Food<sup>§§</sup> and water were freely available throughout the study. All procedures were performed by scientists certified by the French Ministry of Agriculture.

Before administration of the dust, the rats were anaesthetized with sodic pentobarbital.<sup>|||</sup>  $UO_4$  in 200  $\mu$ L of saline solution was administered to two groups of 34 rats and 12 rats by intratracheal instillation.

One rat was separately instilled and was killed two days after the instillation in order to conduct TEM observations on lung sections.

**Tissue analysis.** To assess the lung retention and transportability characteristics of uranium, groups of three rats (except at 4 h and 8 h, one rat) were sacrificed at 4 h, 8 h, 1, 2, 3, 5, 8, 16, 30, 50, 60 and 90 d after exposure. The lungs, liver, kidneys, carcass, and urine were digested in a microwave oven,<sup>¶¶</sup> ashed at 600°C. The residue was acidified and the uranium content determined by various techniques. Lungs were analyzed both with  $\alpha$  counting<sup>###</sup> and kinetic phosphorescence analysis.<sup>\*\*\*</sup> Other organs and tissue were analyzed either with fluorimetry<sup>†††</sup> or KPA.

The lung sections prepared from one rat killed after 1 d were fixed and then observed under ultrathin sections after a specific preparation described by Hengé-Napoli et al. (1996, 1998). Observations were made with TEM.

### Interpretation of data

The procedures used for recommending effective dose coefficients for inhalation expressed as Sv  $Bq^{-1}$ , and predicting the biokinetics of uranium in human beings, were based on the ICRP's new human respiratory tract model of ICRP Publication 66 (1994a) and the systemic biokinetic model for uranium of ICRP Publication 69 (1995). Thus, resulting effective dose coefficients were expressed in terms of ICRP Publication 68 (1994b).

In the respiratory model, it is assumed that for a given material particle transport rates are dependent on the mammalian species, for example being much faster in the rat than in the larger species and in the human beings.

<sup>‡</sup> Micromeritics Accupyc 1330, Creil, France.

<sup>§</sup> Micromeritics Gemini Vacprep 061, Creil, France.

<sup>||</sup> Philips PW 1730, Eindhoven, The Netherlands.

<sup>¶</sup> Unicam IRTF Genesis, Cambridge, United Kingdom.

<sup>#</sup> Philips CM 120 Bio TWIN, Eindhoven, The Netherlands.

<sup>\*\*</sup> Gibco 199, Sigma, Isle d'Abeau, France.

<sup>††</sup> Sigma, Isle d'Abeau, France.

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<sup>\*\*\*</sup> KPA, Chemcheck, Richland, VA, USA.

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On the other hand, on the limited amount of evidence available, absorption rates ( $s_r$  and  $s_s$ ) are reasonably independent of the species but in practice are assumed to be the same.

Thus the absorption parameters were obtained from animal experimental data using a graphically-interactive parameter-fitting personal computer program GIGAFIT described by Birchall et al. (1995) and critically analyzed by Bailey et al. (1997). In this automatic program the user has to supply initial model parameters values (guesses) that GIGAFIT uses to calculate lung and blood functions. GIGAFIT then compares these calculated values with the supplied data sets (measurements) and alters the parameter values iteratively until the best fit is obtained. Resulting absorption parameters to blood are then combined with human data on particle clearance and excretion, using the computer program LUDEP (Birchall et al. 1991), which was designed to implement the new respiratory tract model, together with the new systemic model for uranium (ICRP 1995). The predicted lung retention kinetics and excretion of uranium in humans, and also the dose coefficients of this specific  $\text{UO}_4$ , were then obtained.

## RESULTS

### Physico-chemical properties of industrial $\text{UO}_4$

A sample of  $\text{UO}_4$  dust was collected at the workstation and the isotopic composition by activity was determined as 81.0%  $^{234}\text{U}$ , 3.3%  $^{235}\text{U}$ , and 15.7%  $^{238}\text{U}$ , corresponding to an activity of  $76.1 \text{ Bq mg}^{-1}$ . Measurements of the physico-chemical characteristics of  $\text{UO}_4$  using x-ray analysis have confirmed its composition as a mixture of  $\text{UO}_4 \cdot 2\text{H}_2\text{O}$  (orthorhombic crystal system) and  $\text{UO}_4 \cdot 4\text{H}_2\text{O}$  (monoclinic crystal system). The IR spectrum (Fig. 1) revealed the presence of two major peaks related to  $\text{UO}_4$  at  $1,035$  and  $940 \text{ cm}^{-1}$  and two minor peaks at  $720$  and  $667 \text{ cm}^{-1}$ .

The density of the dust was 4.5 and the surface area, measured by the BET, was  $4.8 \text{ m}^2 \text{ g}^{-1}$ .

The geometric diameter corresponding to unit particle size was estimated to be  $0.5 \mu\text{m}$  from TEM

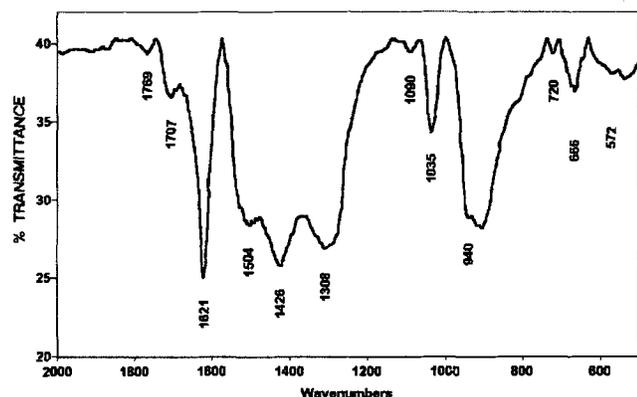


Fig. 1. Infra-red spectrum of  $\text{UO}_4$ .



Fig. 2. Micrograph of  $\text{UO}_4$  particles observed with TEM. Geometric diameter is ranging between  $0.2$  and  $0.7 \mu\text{m}$  (Magn.  $\times 11,000$ ).

micrograph (Fig. 2). A simplified formula  $D_{ae} = D\rho^{1/2}$  (Ansoborlo et al. 1997) allowed to estimate the aerodynamic diameter  $D_{ae}$ , using the geometric diameter  $D$  and the measured density  $\rho=4.5$ , leading to an equivalent activity median aerodynamic diameter (AMAD) of  $1.1 \mu\text{m}$ .

### In vitro dissolution

The *in vitro* dissolution data were given in Table 1. These data were fitted by a GIGAFIT multiexponential function. The fit revealed a rapid fraction of 66.2% with a half-time of 1.9 d and 33.8% with a half-time of 78 d in culture medium, and 5% with a half-time of 0.3 d and 95% with a half-time of 2,140 d in Gamble's solution.

Short tests at 1 d have shown that 98.3% was dissolved in 0.1N HCl and 0.6% dissolved in acidic water at  $\text{pH} = 4.8$ .

### In vivo intratracheal deposit and biokinetics of uranium in rats

Initial lung deposits (ILD) were, respectively,  $195 \pm 26 \mu\text{g}$  and  $7.6 \pm 0.9 \mu\text{g}$ . The tissue distribution and excretion data obtained from the rat study, expressed as a percentage of the initial lung deposit (ILD), were given in Tables 2 and 3. These results showed that the uranium was highly transportable; 34.7 to 43.5% and 73.7 to 77.8% of the ILD were absorbed into the blood by 1 d and 30 d, respectively, after exposure. A multi-exponential regression fit available in GIGAFIT was used to express retention data from the lungs in terms of

**Table 1.** Kinetic of *in vitro* dissolution for  $UO_4$  in Gamble solution and with or without alveolar macrophages (AM) in culture medium, and expressed as % ( $\pm$  SEM) of cumulated dissolved uranium.

Time (d)	$t = 1$ d	$t = 2$ d	$t = 3$ d	$t = 7$ d	$t = 15$ d	$t = 30$ d
% U dissolved in culture medium	$21.5 \pm 10.6^a$	$33.9 \pm 13.9$	$43.8 \pm 16.4$	$63.3 \pm 22.8$	$71.0 \pm 25.5$	$73.7 \pm 26.2$
% U dissolved in Gamble's solution	$4.6 \pm 1.1^a$	$4.9 \pm 1.1$	$5.1 \pm 1.1$	$5.2 \pm 0.8$	$5.7 \pm 1.1$	$5.8 \pm 1.2$
% U dissolved with AM in culture medium	$10.5 \pm 1.6^b$	$18.4 \pm 2.6$	$22.9 \pm 3.8$			

<sup>a</sup>  $n = 6$ .<sup>b</sup>  $n = 3$ .**Table 2.** Results of *in vivo* intratracheal deposit on  $UO_4$ , expressed for each organ as fraction of initial lung deposit (ILD = 195  $\mu$ g).

(days)	% Initial lung deposit <sup>a</sup> ( $x \pm$ SEM, $n = 3$ )					
	Lungs	Liver	Kidneys	Carcass	Urine	Absorption to blood <sup>b</sup>
0.17	81.1	0.11	2.3	6.8	3.7	13.0
0.33	66.7	0.21	6.7	10.3	11.9	29.1
1	$30.1 \pm 5.9$	$0.17 \pm 0.05$	$11.7 \pm 2.2$	$11.2 \pm 1.2$	$20.0 \pm 0.24$	$43.5 \pm 4.1$
2	$10.5 \pm 2.4$	$0.16 \pm 0.01$	$11.6 \pm 0.9$	$9.2 \pm 3.0$	$25.9 \pm 0.15$	$46.9 \pm 9.8$
3	$5.0 \pm 0.4$	$0.17 \pm 0.03$	$13.9 \pm 2.3$	$10.2 \pm 3.1$	$33.1 \pm 0.53$	$57.3 \pm 15.0$
5	$2.9 \pm 0.9$	$0.12 \pm 0.03$	$10.7 \pm 2.1$	$12.4 \pm 4.7$	$41.9 \pm 0.44$	$65.8 \pm 12.4$
8	$2.6 \pm 1.3$	$0.14 \pm 0.03$	$3.3 \pm 0.9$	$10.6 \pm 2.1$	$50.9 \pm 0.05$	$66.1 \pm 6.1$
16	$2.2 \pm 0.3$	$0.04 \pm 0.01$	$1.4 \pm 0.5$	$12.6 \pm 2.8$	$57.4 \pm 0.05$	$72.0 \pm 6.9$
30	$1.6 \pm 0.5$	$0.05 \pm 0.01$	$1.1 \pm 0.1$	$10.2 \pm 1.8$	$60.4 \pm 0.05$	$73.7^c \pm 2.2$
50	$1.0 \pm 0.4$	$0.22 \pm 0.15$	$0.4 \pm 0.2$	$8.2 \pm 3.3$	n.d. <sup>d</sup>	$75.4^c \pm 14.9$
60	$0.8 \pm 0.4$	$0.30 \pm 0.13$	$0.3 \pm 0.2$	$5.8 \pm 1.8$	n.d.	$76.0^c \pm 6.3$
90	$0.4 \pm 0.2$	$0.29 \pm 0.19$	$0.3 \pm 0.2$	$8.2 \pm 3.1$	n.d.	$77.2^c \pm 17.5$

<sup>a</sup> Initial lung deposit of uranium  $195 \pm 26$   $\mu$ g U (enrichment: 3.13% in  $^{235}U$ ).<sup>b</sup> Systemic content + cumulative urinary excretion.<sup>c</sup> Estimated values assuming that the rate of translocation from the lungs to blood is the same as in interval from day 2 to 16; namely  $0.077$   $d^{-1}$ .<sup>d</sup> n.d.: not determined.**Table 3.** Results of *in vivo* intratracheal deposit on  $UO_4$ , expressed for each organ as fraction of initial lung deposit (ILD = 7.6  $\mu$ g).

(days)	% Initial lung deposit <sup>a</sup> ( $x \pm$ SEM, $n = 2$ )					
	Lungs	Liver	Kidneys	Carcass	Urine	Absorption to blood <sup>b</sup>
0.25	88.0 <sup>d</sup>	0.30	2.1	5.0	n.d.	9.5 <sup>c</sup>
1	$60.6 \pm 19.3$	$0.25 \pm 0.03$	$9.4 \pm 2.7$	$8.4 \pm 1.0$	$16.7 \pm 5.4$	$34.7 \pm 9.2$
3	25.6 <sup>d</sup>	0.22	9.8	12.5	30.9	53.4
7	$10.2 \pm 0.8$	$0.28 \pm 0.23$	$10.1 \pm 6.1$	$13.1 \pm 0.6$	$41.3 \pm 3.4$	$64.8 \pm 10.3$
15	7.3 <sup>d</sup>	0.44	1.6	7.7	68.6	71.8 <sup>c</sup>
30	$5.6 \pm 0.1$	$0.28 \pm 0.03$	$3.5 \pm 3.6$	$7.9 \pm 4.3$	$63.1 \pm 8.9$	$77.8^c \pm 8.2$

<sup>a</sup> Initial lung deposit of uranium  $7.6 \pm 0.9$   $\mu$ g U (enrichment: 3.3% in  $^{235}U$ ).<sup>b</sup> Systemic content + cumulative urinary excretion.<sup>c</sup> Estimated from the fitting of the absorption to blood values.<sup>d</sup>  $n = 1$ .

two-component exponential functions with half-times of 0.5 d (96.6%) and 30 d (3.4%) for an ILD of 195  $\mu$ g and 1.2 d (90.3%) and 38 d (9.7%) for an ILD of 7.6  $\mu$ g.

Calculations of the specific absorption parameters  $f_r$ ,  $s_r$ , and  $s_s$  as defined in the human respiratory tract model of ICRP Publication 66 (1994a) were given in Table 4

and compared to default values for Type F and M compounds.

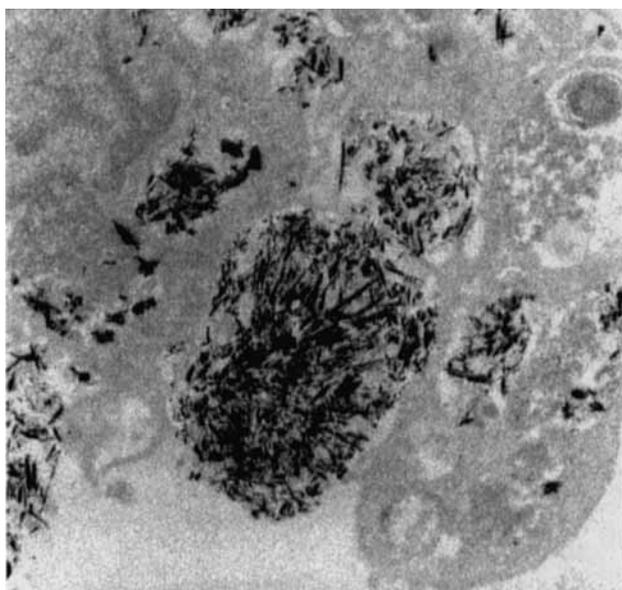
One day after phagocytosis, clusters of particles were concentrated in the phagosomes of some macrophages (Fig. 3). The fragments of  $UO_4$  particles were measured between 0.2 and 0.7  $\mu$ m size.

**Table 4.** Material specific absorption parameters for use with ICRP 66 respiratory tract model calculated for  $\text{UO}_4$  and default values.

Parameters	Rapid and slow dissolution fractions and transfer rates				
	Type F	Type M	<i>In vitro</i> <sup>a</sup>	$\text{UO}_4^a$ (ILD = 7.6 $\mu\text{g}$ )	$\text{UO}_4^a$ (ILD = 195 $\mu\text{g}$ )
$f_r^b$	1	0.1	0.662	0.800	0.873
$s_r$ ( $\text{d}^{-1}$ )	100100	—	0.361	0.525	0.928
$s_s$ ( $\text{d}^{-1}$ )	—	$5.0 \cdot 10^{-3}$	$8.8 \cdot 10^{-3}$	$1.57 \cdot 10^{-2}$	$2.42 \cdot 10^{-2}$

<sup>a</sup> Calculation were made with GIGAFIT software.

<sup>b</sup>  $f_r$  is the rapid fraction absorbed to blood;  $s_r$  and  $s_s$  are the rapid and slow transfer rate.

**Fig. 3.** *In vivo* phagocytosis of  $\text{UO}_4$  particles by rat alveolar macrophages after 1 d (Magn.  $\times 8,400$ ).

Different ratios such as C/B (C is carcass content, B is amount to blood), K/B (K is kidney content), U/B (U is urine content) and U/U+K previously described by Pasquier and Bourguignon (1977) were calculated at 1 d. These different ratios were given in Table 6.

### Dose calculation

The dose coefficients (Table 5) were calculated with the LUDEP program (Birchall et al. 1991) using either default absorption parameters for Type F, M or S materials, or specific experimental absorption parameters derived from the *in vitro* and the two *in vivo* experiments. This calculation was made with the given isotopic composition, a geometric diameter of 0.5  $\mu\text{m}$ , a geometric standard deviation  $\sigma_g$  of 1.2, a density of 4.5  $\text{g cm}^{-3}$ , a mean breathing rate of 1.2  $\text{m}^3 \text{h}^{-1}$ , and the ICRP Publication 69 (1995) biokinetic model for uranium.

For predicting the lung retention and urinary excretion of uranium in workers (Figs. 4 and 5), the characteristics calculated from the animal experiments have been combined in LUDEP with particle clearance data

**Table 5.** Dose coefficients calculated with LUDEP for  $\text{UO}_4$  (Sv  $\text{Bq}^{-1}$ ): Comparison of the doses calculated with experimental values (*in vitro* and *in vivo*) and with default values calculated with the geometric diameter of 0.5  $\mu\text{m}$ .

Dose coefficients (Sv $\text{Bq}^{-1}$ ) for $\text{UO}_4$ compound <sup>a</sup>				
Type F	Type M	<i>In vitro</i>	<i>In vivo</i> (ILD <sup>b</sup> = 7.6 $\mu\text{g}$ )	<i>In vivo</i> (ILD <sup>b</sup> = 195 $\mu\text{g}$ )
$0.47 \cdot 10^{-6}$	$2.49 \cdot 10^{-6}$	$1.04 \cdot 10^{-6}$	$0.70 \cdot 10^{-6}$	$0.52 \cdot 10^{-6}$

<sup>a</sup> Calculation were made using the isotopic composition expressed as a percent in activity:  $^{234}\text{U}$  (81%),  $^{235}\text{U}$  (3.3%) and  $^{238}\text{U}$  (15.7%). The following specific parameters were used: geometric diameter  $D = 0.5 \mu\text{m}$ ,  $\sigma_g = 1.2$ , density = 4.5 and a ventilatory rate of 1.2  $\text{m}^3 \text{h}^{-1}$ .

<sup>b</sup> ILD: initial lung deposit.

obtained from human exposure to other materials (ICRP 1994a).

## DISCUSSION

To assess radiotoxicological risks of  $\text{UO}_4$ , which is an intermediate compound encountered in uranium fuel fabrication, a detailed physico-chemical study of this compound, combined with *in vitro* and *in vivo* experiments, was undertaken. This investigation was designed to provide specific parameters needed for dose calculation. Among these absorption parameters to blood, the most sensitive were, respectively, the AMAD, the fraction  $f_r$ , and the rates  $s_r$  and  $s_s$ .

Hence the ICRP systemic model, in conjunction with the new respiratory tract model, was used as an appropriate methodology for assessing tissue dose and urinary excretion characteristics for the purpose of interpreting bioassay data.

### Physico-chemical properties of industrial $\text{UO}_4$

Physico-chemical characteristics of the  $\text{UO}_4$  compound have underlined the presence of 2 or 4 molecules of  $\text{H}_2\text{O}$  and the similarity with  $\text{UO}_3$  through the IR analysis (Fig. 1): the main large peak at 940  $\text{cm}^{-1}$  was identical to hydrated  $\text{UO}_3$  peak observed in a previous study (Ansoborlo et al. 1992), but the 1,035  $\text{cm}^{-1}$  peak was really specific of  $\text{UO}_4$ .

Measured specific surface area was 4.8  $\text{m}^2 \text{g}^{-1}$ , which is lower than values of some industrial  $\text{UO}_4$  preparations that can reach 10  $\text{m}^2 \text{g}^{-1}$ : this could explain significant variations in terms of dissolution between different studies and, consequently, the need of supplying such an information.

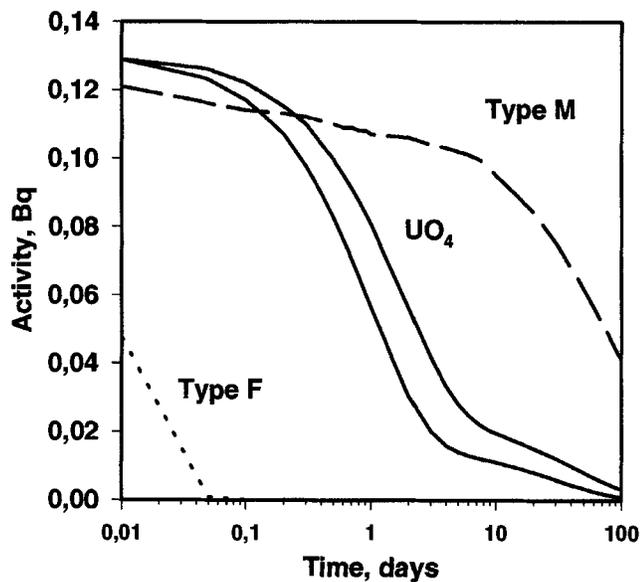
Observation on the TEM (Fig. 2) revealed that particles were agglomerated but the unit particle size corresponding to a geometric diameter  $D$  was about 0.5  $\mu\text{m}$ . This was confirmed in the TEM observations of alveolar macrophages of rats at 1 d after *in vivo* intratracheal deposit, showing the presence of  $\text{UO}_4$  fragments of 0.5  $\mu\text{m}$  unit size geometric diameter (Fig. 3). It is interesting to note that this AMAD and the particular shape of the particles (under fragment form), due to the industrial process, make the  $\text{UO}_4$  compound different

**Table 6.** Assessment of different ratios at 1 d after exposure and representative of the systemic model for uranium. Comparison of  $\text{UO}_4$  values with data from the literature.

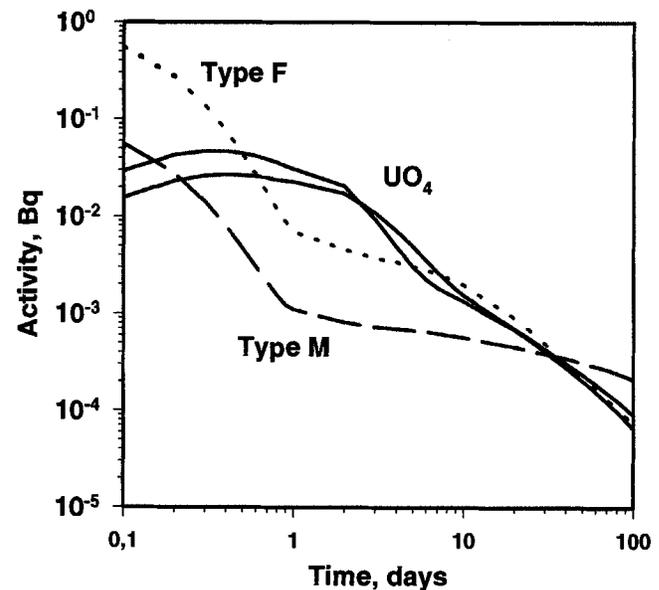
Uranium compound	Administration (Amount)	Authors	Ratios at 1 day after exposure of $\text{UO}_4$ in rats: C = Carcass content, K = Kidney content, B = Blood (absorbed amount), U = Urine (cumulative)			
			C/B	K/B	U/B	K/K + U
$\text{UO}_4$	Int.(195 $\mu\text{g}$ ) <sup>a</sup>	Ansoborlo et al. (this study)	0.26	0.27	0.46	0.37
	Int.(7,6 $\mu\text{g}$ ) <sup>a</sup>		0.24	0.27	0.48	0.36
$\text{UF}_4$	Inh.(130 $\mu\text{g}$ ) <sup>b</sup>	Stradling et al. (1985a)	0.23	0.32	0.45	0.41
$\text{UO}_3$	Int.(10 $\mu\text{g}$ ) <sup>a</sup>	Stradling et al. (1985b)	0.19	0.27	0.52	0.34
ADU	Inh.(16 $\mu\text{g}$ ) <sup>b</sup>	Stradling et al. (1987)	0.23	0.32	0.46	0.40
$\text{UO}_2(\text{NO}_3)_2$	Int.(52 $\mu\text{g}$ ) <sup>a</sup>	Ellender (1987)	0.36	0.17	0.46	0.27
	Int.(1 $\mu\text{g}$ ) <sup>a</sup>	Cooper et al. (1982)	0.14	0.22	0.64	0.25
$\text{UO}_2(\text{HCO}_3)_2$	Int.(1 $\mu\text{g}$ ) <sup>a</sup>	Cooper et al. (1982)	0.16	0.26	0.58	0.31
$\text{U}_3\text{O}_8$	Inh.(120 $\mu\text{g}$ ) <sup>b</sup>	Stradling et al. (1989)	0.24	0.17	0.59	0.23
$\text{UO}_2$	Int.(365 $\mu\text{g}$ ) <sup>a</sup>	Stradling et al. (1988)	0.31	0.19	0.51	0.27
Average values (SEM)			0.24 (0.07)	0.24 (0.06)	0.52 (0.07)	0.32 (0.06)

<sup>a</sup> Int: intratracheal instillation.

<sup>b</sup> Inh: inhalation.



**Fig. 4.** LUDEP predicted lung retention of uranium ( $^{234}\text{U}$ ) in humans after acute intake of 1 Bq, 0.5  $\mu\text{m}$  geometric diameter of  $\text{UO}_4$ . The two curves for  $\text{UO}_4$  correspond to two different *in vivo* initial lung deposits. Type F and Type M retention curves are given as references.



**Fig. 5.** LUDEP predicted instantaneous urinary excretion of uranium ( $^{234}\text{U}$ ) in humans after acute intake of 1 Bq, 0.5  $\mu\text{m}$  geometric diameter of  $\text{UO}_4$ . The two curves for  $\text{UO}_4$  correspond to two different *in vivo* initial lung deposits. Type F and Type M excretion curves are given as references.

from the other industrial uranium compounds. Thus the estimated AMAD of 1.1  $\mu\text{m}$  differs significantly from the average values of 5.5  $\mu\text{m}$  and 6.9  $\mu\text{m}$ , respectively, given by Ansoborlo et al. (1997) and Dorrian and Bailey (1995) for the uranium fuel cycle.

#### ***In vitro* dissolution**

Long-term dissolution measured *in vitro* showed a significant difference between percent dissolved in culture medium (21.5% at 1 d and 73.7% at 30 d) and in Gamble's solution (4.6% at 1 d and 5.8% at 30 d). Previous studies carried out on different uranium compounds such as  $\text{UF}_4$  (André et al. 1989; Ansoborlo et al.

1989),  $\text{UO}_3$  (Ansoborlo et al. 1992), or industrial  $\text{U}_3\text{O}_8$  (Ansoborlo et al. 1994) in Gamble's medium, have already shown such a lower solubility compared to other media, mainly due to the action of phosphate. The percent dissolved in culture medium after 1 d (21.5%) was very close to  $\text{UO}_3$  results obtained previously by Ansoborlo et al. (1992) in the same medium and giving a solubility between 18.3% and 38.3% at 1 d depending on the hydration state.

The half-times calculated from dissolution in culture medium corresponding to 1.9 d (66.2%) and 78 d (33.8%) were different from recent results obtained with  $\text{UO}_4$  by Metzger et al. (1997) in serum lung ultrafiltrate,

indicating half-times of 0.3 d (97%) and 15.6 d (3%). In this study (Metzger et al. 1997), dissolution was really faster and probably due to a higher specific surface area which was not given.

The results obtained at pH = 4, which showed a low solubility at 1 d (0.6%), could explain the difference at 3 d between the tests with and without macrophages, in terms of percent dissolved. The observed reduction in solubility within the macrophages corresponding to a decrease of 50% between 1 d and 3 d compared to culture medium without macrophages has been already demonstrated in previous studies (Hengé-Napoli et al. 1994; Ansoborlo et al. 1992; Galle et al. 1992) and related to interactions between the dust and constituents of cells such as lysosomes. Thus, two phenomena were pointed out: on one hand a direct effect of acidic pH within the lysosome on the low dissolution of  $\text{UO}_4$ , which was supported by the 0.6% dissolved *in vitro* at 1 d, and on the other hand the intracellular precipitation of uranium in the form of uranyl phosphate flakes, as reported by Hengé-Napoli et al. (1998).

This action of macrophages, which tends to reduce the dissolution, does not play a major role in the total mechanism of absorption, since 30.9 to 43.5% and 73.7 to 77.8%, respectively, have been transferred to blood between 1 d and 30 d.

However, culture medium gave a good representation of *in vivo* experiment and calculations were made from *in vitro* results to estimate absorption parameters. The values were  $f_r = 0.662$ ,  $s_r = 0.361 \text{ d}^{-1}$ , and  $s_s = 0.0088 \text{ d}^{-1}$ , respectively, and the two absorption rates  $s_r$  and  $s_s$  were derived from the two periods 1.9 d and 78 d using the formula  $s = 0.693/T$ . If we compare these values to default values F, M or S, from ICRP Publication 66 (1994a), it can be seen that the rapid fraction,  $f_r = 0.662$ , is intermediate between 1 for Type F and 0.1 for Type M, and  $s_s = 0.0088 \text{ d}^{-1}$  is close to 0.005 for Type M.

### **In vivo experiments**

The biokinetic data reported here (Tables 2 and 3) were very similar to those obtained after inhalation of  $\text{UO}_3$ , ADU, and  $\text{UO}_2(\text{NO}_3)_2$  by rats. Rat lung retention after instillation of  $\text{UO}_4$  led to half-times of 0.5 to 1.2 d (96.6 to 90.3%) and 27 to 38 d (3.4 to 9.7%), which was in the range of the <1 d (86%), 10 d (10%), and 170 d (4%) for ADU by Stradling et al. (1989), the 0.9 d (96%) and 60 d (4%) for  $\text{UO}_3$  by Stradling et al. (1985b) and the 2 d (44%) and 69 d (56%) for an  $\text{UO}_2(\text{NO}_3)_2$  compound with an AMAD of 0.5  $\mu\text{m}$  by Ballou et al. (1986).

The rapid clearance of uranium from the lungs resulted mainly from its translocation to the blood, most of which was subsequently excreted in the urine, e.g., 46 to 48%, 64 to 77%, and 82 to 85% by 1 d, 7 d, and 30 d, respectively. The principal sites of deposition were the carcass (8.4 to 11.2% at 1 d) and the kidneys (9.4 to 11.7% at 1 d).

The different ratios C/B, K/B, U/B and U/U+K given in Table 6 and calculated at 1 d were compared

with published results from other uranium compounds such as  $\text{UO}_3$ , ADU,  $\text{UF}_4$ , uranyl nitrate, uranyl carbonate,  $\text{U}_3\text{O}_8$ , or  $\text{UO}_2$ . Consequently, there was a good consistency between  $\text{UO}_4$  data derived from two different ILDs, and the results obtained on different compounds, including two routes of contamination (inhalation and instillation). The  $\text{UO}_4$  value for the ratio U/B (0.47) was in accordance with the average value of 0.52. These results were lower than those given by Wrenn and Bertelli (1994) and Durbin (1975), which ranged between 0.54 and 0.62 for humans.  $\text{UO}_4$  values for the ratio U/U+K (0.37) were also very consistent with the average value of 0.32 for the different compounds and very similar to the average value 0.37 given by Pasquier and Bourguignon (1977) at 2 d. This ratio U/U+K seemed to be a good indicator of the validity of an experiment and is independent of the amount absorbed to blood (respectively, 195  $\mu\text{g}$  and 7.6  $\mu\text{g}$ ) for the two  $\text{UO}_4$  experiments. This comparison with systemic data from other compounds showed that  $\text{UO}_4$  behaves as a soluble compound.

In the two *in vivo* experiments, the maximum contents in the kidneys were, respectively, 9.4% and 11.7%, corresponding to 0.4  $\mu\text{g g}^{-1}$  (ILD = 7.6  $\mu\text{g}$ ) and 8.8  $\mu\text{g g}^{-1}$  (ILD = 195  $\mu\text{g}$ ). The latter value is greater than the limit of 3  $\mu\text{g g}^{-1}$  adopted for humans and recently reaffirmed as a maximal permissible concentration in the kidney by the American National Standard (ANS 1996). In their comprehensive reviews, Diamond (1989) and Leggett (1989) highlighted the uncertainties associated with this level and suggested that there was good reason to lower this limit. However, Diamond (1989) noted that nephrotoxicity in rats associated with levels at or below 5  $\mu\text{g}$  uranium per g kidney is reversible. This experiment showed that both the K/K+U ratio and the biokinetic behavior were independent of the ILD and the kidney concentration.

The rapid fraction (34.7 to 43.5%) transferred to blood at 1 d is similar to the 39% measured for ADU (Stradling et al. 1987), and 46% (Bailey et al. 1998) for  $\text{UO}_3$ . On the basis of these data, and in agreement with ICRP Publication 30 (1979) classification,  $\text{UO}_4$  should be assigned to inhalation class D, since only a small proportion of the uranium, about 4%, has lung retention kinetics consistent with class W.

Calculation of transfer parameters with GIGAFIT (Table 4) led to a rapid fraction  $f_r$  0.800–0.873 and rapid and slow rate  $s_r$  of 0.525–0.928  $\text{d}^{-1}$  and  $s_s$  of  $1.57 \times 10^{-2}$  to  $2.42 \times 10^{-2} \text{ d}^{-1}$ , respectively. Comparing these values to default values F, M or S, from ICRP Publication 66 (1994a), the average rapid fraction  $f_r$  was very close to 1, which was the value for Type F, and  $s_s$  was much higher than  $5 \times 10^{-3} \text{ d}^{-1}$  for Type M, closer to Type F.

These calculations confirmed that in the absence of specific information  $\text{UO}_4$  can be considered as a fast soluble compound of Type F, according to ICRP Publication 66 (1994a).

### ***In vitro* solubility vs. *in vivo* experiments**

Comparison of *in vitro* solubility with *in vivo* results, and more precisely with percent transferred to blood, showed in this case that there was a good correlation with data resulting from culture medium dissolution after 3 d. The estimated percentage absorption to blood at 1 d was higher *in vivo* (34.7 to 43.5% *in vivo* and 21.5% *in vitro*); at 3 d this difference decreased (53.4 to 57.3% *in vivo* and 43.8% *in vitro*); and finally between 7 d and 30 d the results were very similar (64.8% to 77.8% *in vivo* and 63.3% to 73.7% *in vitro*).

The lower solubility observed *in vitro* at 1 d when compared to that *in vivo* was not very well explained: it was probably due to a rapid chemical transformation of small particles (the geometric diameter is 0.5  $\mu\text{m}$ ) related to an *in vivo* oxidation process which rapidly releases uranium as uranyl form. Similar results, showing an unexpected high transfer to blood ranging between 67.7% and 87.8% at 1 d, have been observed by Cooper et al. (1982) on ultrafine particles (<4  $\eta\text{m}$ ) of  $^{233}\text{UO}_2$ . The explanation for this transfer was assumed to be the rapid oxidation of  $\text{UO}_2$  into  $\text{UO}_3$ , which is a more soluble compound. This effect of rapid oxidation appeared to be less important for  $\text{UO}_4$  with 34.7 to 43.5% transferred to blood at 1 d.

### **Dose calculations**

The dose coefficients for the  $\text{UO}_4$  compound were calculated both from *in vitro* results and *in vivo* results (Table 5). *In vivo* results using both experiments were very similar and led to an effective dose coefficient ranging between  $0.52 \times 10^{-6}$  and  $0.70 \times 10^{-6}$  Sv Bq $^{-1}$ . These values were smaller than the *in vitro* dose coefficient ( $1.04 \times 10^{-6}$  Sv Bq $^{-1}$ ), which was consistent with the difference in dissolution observed between the two tests. Comparison with default values for Type F ( $0.47 \times 10^{-6}$  Sv Bq $^{-1}$ ) and Type M ( $2.49 \times 10^{-6}$  Sv Bq $^{-1}$ ) compounds of the same aerosol size and isotopic composition indicated that  $\text{UO}_4$  was close to a Type F compound.

These *in vivo* dose coefficients would correspond to an average ALI of 30 kBq or 400 mg of uranium with the isotopic composition specified in Table 5. However, in view of the rapid absorption of uranium into the blood and hence the potential damage to the kidneys, the daily intake should be limited to 2.5 mg (Journal Officiel 1988).

It is inferred from Figs. 4 and 5 that chest monitoring will be of little value for assessing intakes based on chemical toxicity and that urine analysis is the method of choice. The fraction of uranium excreted per day in urine after an acute intake diminished about threefold between the first and the third day after exposure, and about twentyfold between the first and the seventh day.

### **CONCLUSION**

The data presented in this paper, which includes physico-chemical properties and biokinetics of  $\text{UO}_4$ ,

have shown that the compound produced in the enriched nuclear fuel cycle differed appreciably from other uranium oxides such as  $\text{U}_3\text{O}_8$  and  $\text{UO}_2$ . One main characteristic identified in this study was the particle size of the dust which was 0.5  $\mu\text{m}$ , corresponding to an equivalent AMAD of 1.1  $\mu\text{m}$ . This is considerably smaller than the average value, ranging between 5.5  $\mu\text{m}$  (Ansoborlo et al. 1997) and 6.9  $\mu\text{m}$  (Dorrian and Bailey 1995), for uranium compounds in the uranium industry.

Biokinetic data obtained either *in vitro* or *in vivo* have shown that  $\text{UO}_4$  behaved like a soluble Type F compound and was similar to  $\text{UO}_3$ . This important solubility (64.8 to 77.8% transferred to blood between 7 d and 30 d) was due both to the small size of the particles (0.5  $\mu\text{m}$ ) and to the chemical dissolution which was related to a relatively high specific surface area of 4.8  $\text{m}^2 \text{g}^{-1}$ , compared to other uranium oxides.

Assessment of different ratios and particularly the ratio K/K+U (with K the percent in the kidney, and U the percent in the urine) have shown that the value obtained of 0.37 was within the range observed for other soluble uranium compounds (0.23 and 0.41). This ratio should be applied as a good indicator of kidney dysfunction in animal experiments and was the same for the two installations conducted with two different ILD.

Considering the retention curve in the lung and the urinary excretion function, it was recommended that intakes of  $\text{UO}_4$  should be limited by the chemical toxicity of the uranium and assessments of such intakes based on urine analysis.

### **REFERENCES**

- André, S.; Métivier, H.; Auget, D.; Lantenois, G.; Boyer, M.; Masse, R. Lung dissolution of uranium tetrafluoride in rats and baboons. Comparison with dissolution by alveolar macrophages in culture and chemical dissolution. *Human Toxicol.* 8:111-119; 1989.
- Ansoborlo, E.; Chalabreysse, J.; Hengé-Napoli, M. H.; Pujol, E. *In vitro* chemical and cellular tests applied to uranium trioxide with different hydration states. *Environ. Health Perspect.* 97:139-143; 1992.
- Ansoborlo, E.; Chalabreysse, J.; Escallon, S.; Hengé-Napoli, M. H. *In vitro* solubility of uranium tetrafluoride with oxidizing medium compared with *in vivo* solubility in rats. *Int. J. Radiat. Biol.* 58:681-689; 1989.
- Ansoborlo, E.; Hengé-Napoli, M. H.; Donnadiou-Claraz, M.; Roy, M.; Pihet, P. Industrial exposure to uranium aerosols at laser enrichment processing facilities. *Radiat. Prot. Dosim.* 53:163-167; 1994.
- Ansoborlo, E.; Boulaud, D.; Leguen, B. Distribution granulométrique d'aérosols d'uranium dans l'industrie française de fabrication du combustible. *Radioprotection* 32:319-330; 1997.
- Bailey, M. R.; Guilmette, R. A.; Jarvis, N. S.; Roy, M. Practical application of the new ICRP human respiratory tract model. *Radiat. Protect. Dosim.* 1998 (in press).
- Ballou, J. E.; Gies, R. A.; Case, A. C.; Haggard, D. L.; Bushbom, R. L.; Ryan, J. L. Deposition and early disposition of inhaled  $^{233}\text{UO}_2(\text{NO}_3)_2$  and  $^{232}\text{UO}_2(\text{NO}_3)_2$  in the rat. *Health Phys.* 51:755-771; 1986.

- Birchall A.; Bailey M. R.; James A. C. LUDEP: a lung dose evaluation program. *Radiat. Prot. Dosim.* 38:167–174; 1991.
- Birchall A.; Bailey M. R.; Jarvis, N. S. Application of the new ICRP respiratory tract model to inhaled plutonium nitrate using experimental biokinetic data. Proceedings of BNES conference on radiation dose management, Windermere. London: BNES; 1995: 216–223.
- Chevalier, C.; Roy, M.; Malarbet, J. L. Modèles dosimétriques pour les radionucléides incorporés par les travailleurs. *Radioprotection* 32:15–48; 1997.
- Cooper, J. R.; Stradling, G. N.; Smith, H.; Ham, S. E. The behaviour of uranium-233 oxide and uranyl-233 nitrate in rats. *Int. J. Radiat. Biol.* 41:421–433; 1982.
- Diamond, G. L. Biological consequences of exposure to soluble forms of natural uranium. *Radiat. Prot. Dosim.* 26:23–33; 1989.
- Durbin, P. W. Metabolism and effects of uranium in animals. In: Occupational health experience with uranium, proceedings of a U.S. Energy Research and Development Administration Conference. Washington, DC: U.S. Government Printing Office; ERDA 93, UC-41:68–129; 1975.
- Dorrian, M. D.; Bailey, M. R. Particle size distributions of radioactive aerosols measured in workplaces. *Radiat. Prot. Dosim.* 60:119–133; 1995.
- Eidson, A. F. The effect of solubility on inhaled uranium compound clearance: a review. *Health Phys.* 67:1–14; 1994.
- Ellender, M. The clearance of uranium after deposition of the nitrate and bicarbonate in different regions of the rat lung. *Human Toxicol.* 6:479–482; 1987.
- Galle, P.; Berry, J. P.; Galle, C. Role of alveolar macrophages in precipitation of mineral elements inhaled as soluble aerosols. *Environ. Health Perspect.* 97:145–147; 1992.
- Gamble, J. L. Chemical anatomy, physiology and pathology of extracellular fluids. 8th edition. Boston: Harvard University Press; 1967.
- Hengé-Napoli, M. H.; Ansoborlo, E.; Donnadiou-Claraz M.; Berry, J. P.; Gibert, R.; Pradal P. Solubility and transferability of several industrial forms of uranium oxides. *Radiat. Prot. Dosim.* 53:157–161; 1994.
- Hengé-Napoli, M. H.; Zhang, L.; Gibert, R.; Ansoborlo, E.; Pradal, B.; Galle, P.; Jeanguillaume, C.; Berry, J. P. Study of *in vivo* chemical behavior of specific uranium tetroxide particles in lung and alveolar macrophages of rats after intratracheal deposit. *J. Trace Microprobe* 16:195–208; 1998.
- Hengé-Napoli, M. H.; Ansoborlo, E.; Donnadiou-Claraz, M.; Berry, J. P.; Cheynet, M. C. Role of alveolar macrophages in the dissolution of two different industrial uranium oxides. *Cell. Mol. Biol.* 42:413–420; 1996.
- International Commission on Radiological Protection. Limits for intakes of radionuclides by workers. Oxford: Elsevier; Publication 30; Ann. ICRP 2; 1979.
- International Commission on Radiological Protection. Individual monitoring for intakes of radionuclides by workers: Design and interpretation. Oxford: Elsevier; Publication 54; Ann. ICRP 19; 1988.
- International Commission on Radiological Protection. Human respiratory tract model for radiological protection. Oxford: Elsevier; Ann. ICRP 24; Publication 66; 1994a.
- International Commission on Radiological Protection. Dose coefficients for intakes of radionuclides by workers. Oxford: Elsevier; Publication 68; Ann. ICRP 24; 1994b.
- International Commission on Radiological Protection. Age-dependent doses to members of the public from intakes of radionuclides, Part 3, ingestion dose coefficients. Oxford: Elsevier; Publication 69; Ann. ICRP 25; 1995.
- J. Officiel des Communautés Européennes. Normes de base relatives la protection sanitaire de la population et des travailleurs contre les dangers résultants des rayonnements ionisants. ISSN 0378-7060, L159; 1996 (In French).
- J. Officiel de la République Française. Protection des travailleurs contre les dangers des rayonnements ionisants dans les installations. Décret n° 88-662 du 8 mai 1988 (In French).
- Katz, J. J.; Rabinovitch, E. The chemistry of uranium. The element, its binary and related compounds. New York: Dover Publications, Inc.; 1951.
- Leggett, R. W. The behavior and chemical toxicity of U in the kidney: a reassessment. *Health Phys.* 57:365–383; 1989.
- Metzger, R.; Wichers, D.; Vasein, J.; Velasquez, P. Solubility characterization of airborne uranium from an *in situ* uranium processing plant. *Health Phys.* 72:418–422; 1997.
- Pasquier, C.; Bourguignon, M. Contamination aigüe par oxydes d'uranium. Fixation rénale et essais thérapeutiques. *Radiotoxicologie B* 40:1977.
- Stradling, G. N.; Stather, J. W.; Strong, J. C.; Sumner, S. A.; Towndrow, C. G.; Moody, J. C.; Lennox, A.; Sedgwick, D.; Cooke, N. Metabolism of some industrial uranium tetrafluorides after deposition in the rat lung. *Human Toxicol.* 4:159–168; 1985a.
- Stradling, G. N.; Stather, J. W.; Ellender, M.; Sumner, S. A.; Moody, J. C.; Towndrow, C. G.; Hodgson, A.; Sedgwick, D.; Cooke, N. Metabolism of an industrial uranium trioxide dust after deposition in the rat lung. *Human Toxicol.* 4:563–572; 1985b.
- Stradling, G. N.; Stather, J. W.; Gray, S. A.; Moody, J. C.; Hodgson, A. The metabolic behaviour of uranium octoxide bearing residues after their deposition in the rat lung: the implications for occupational exposure. *Exp. Pathol.* 37:76–82; 1989.
- Stradling, G. N.; Stather, J. W.; Gray, S. A.; Moody, J. C.; Ellender, M.; Hodgson, A.; Sedgwick, D.; Cooke, N. Metabolism of uranium in the rat after inhalation of two industrial forms of ore concentrate: the implications for occupational exposure. *Human Toxicol.* 6:385–393; 1987.
- Stradling, G. N.; Stather, J. W.; Gray, S. A.; Moody, J. C.; Hodgson, A.; Sedgwick, D.; Cooke, N. Metabolism of ceramic and non-ceramic forms of uranium dioxide after deposition in the rat lung. *Human Toxicol.* 7:133–139; 1988.
- Wrenn, M. E.; Bertelli, L.; Durbin, P. W.; Singh, N. P.; Lipsztein, J. L.; Eckerman, K. F. A comprehensive metabolic model for uranium metabolism and dosimetry based on human and animal data. *Radiat. Prot. Dosim.* 53:255–258; 1994.

