Experimental measurement of the dissolution parameters of some actinide oxides and specific dose calculation for ^{239}Pu

P. Fritsch, B. Ramounet, S. Matton and J. Delforge
CEA, DSV/DRR/SRCA/Laboratoire de Radiotoxicologie, BP12, 91680 Bruyères le Châtel, France.

INTRODUCTION

At this time, after inhalation exposure to actinide oxides, most dose calculations are performed using the simplest dissolution model of the human respiratory tract model proposed by ICRP 66. Without any knowledge of the specific dissolution parameters, these oxides are considered either as type M or type S compound. In the simplest model, once a fraction f_r (M : f_r=0.1, S : f_r =0.001) has dissolved readily with a half life of about 10 minutes, the remaining dissolves at a constant rate s_s (M : s_s=0.005, S : s_s =0.0001).

Recently, we have developed new assays for experimental measurement of f_r and s_s *in vivo* and *in vitro* which were applied to different actinide oxides such as PuO_2 and a (U, Pu)O_2 (MOX) made according to a MIMAS process which contained 5 % Pu (1-2). These assays provide statistical variation of the dissolution parameters as standard deviation. The aims of this study were 1) to provide the most suitable dissolution parameters measured either *in vivo* or *in vitro* which could be used for dose calculation in human, 2) to perform dose calculation for the two oxides, PuO_2 and MOX considering ^{239}Pu only.

DISSOLUTION PARAMETER MEASUREMENTS

Aerosols of actinide oxide powders were studied. The aerodynamic median activity diameter (AMAD) of aerosols generated with our specific device (3) was 2.4 µm, σg=1.7 for PuO_2 and 2.2 µm σg=1.7 for MOX. Rats were exposed to the aerosols which were collected in a cascade impactor for *in vitro* dissolution study.

Groups of at least 4 rats were killed at different times during the first year after exposure. The calculation of f_r and s_s for plutonium is based on a linear correlation analysis of the total amount of the actinide transferred to blood as a function of the cumulated retention of actinide oxides in lungs.

The dissolution parameters of the aerosols in a serum simulating medium were measured *in vitro* for 3 months. Because different dissolution rate were measured for the first month and for 3 months, the results obtained *in vitro* suggest that s_s has to be considered as a variable depending on time after inhalation.

Table I compares the dissolution parameters f_r and s_s measured *in vivo* and *in vitro* for 3 month incubation time.

	In vitro		*In vivo*	
	f_r	s_s	f_r	s_s
PuO_2	**1.6 E-3** ± 1.0 E-4	**4.9 E-6** ± 3.1 E-6	**1.2 E-2** ± 1.1 E-3	**2.9 E-5** ± 5.2 E-5
MOX	**3.3 E-2** ± 3.1 E-2	**4.1 E-5** ± 2.3 E-5	**9.8 E-4** ± 6.3 E-4	**5.1 E-5** ± 1.2 E-5

Table I comparative value of the dissolution parameters of plutonium from PuO_2 and MOX measured either *in vitro* or *in vivo.*
Mean values ± standard deviation.

DOSE CALCULATION

Dose calculation were performed using our own software programs. These software programs are based on the recommendations of ICRP and a differential calculation approach. This allow us to provide exact solution for both the human respiratory tract models (CIPR 66) and the complex plutonium systemic model (CIPR 67). In the case of the respiratory tract model, calculation were performed each steps of about20seconds were used for the first 10 days and steps of 2 minutes were used later on. In the case of the systemic model, step of x minutes were used over a 50 year duration. First, doses delivered to the different respiratory tract compartments were calculated and a file containing the amount of radionuclide daily dissolved was written. Second, tables of cumulated daily doses to the different tissues considered for 50 years was generated into memory. Then, the doses due to particle dissolution was easily calculated after reading the file taking into account the different time intervals between the time considered and 50 years after exposure. Tables II compares doses obtained with our software programs, LUDEP 2.0 and ICRP CD ROM for type S aerosol containing ^{239}Pu. Default aerosol parameters were used, i.e. AMAD = 5, µm, σg = 2.5.

	LUDEP 2.0		DSV		ICRP CD ROM
	Sv eq*	Sv Wp**	Sv eq*	Sv Wp**	Sv Wp**
ET1			Neglegted		
ET2	7.96E-05	7.96E-05	7.93E-05	7.93E-05	
LN(ET)	1.41E-04	1.41E-07	1.42E-04	1.42E-07	
Total	2.21E-04	7.94E-05	2.21E-04	7.94E-05	8.0E-5
BB(bas)	5.80E-06	9.57E-07	5.85E-6	9.74E-07	
BB(sec)	6.50E-05	1.07E-05	6.35E-05	1.06E-05	
bb(sec)	3.31E-05	1.10E-05	3.20E-05	1.06E-05	
AI	6.92E-05	2.31E-05	6.93E-05	2.31E-05	
LN(TH)	4.88E-04	4.88E-07	4.88E-04	4.88E-07	
Total	6.61E-04	4.62E-05	6.58E-04	4.58E-05	4.7E-5

Table I : comparison of the committed equivalent doses delivered to the different compartments of the respiratory tract as defined by ICRP for a 50 year duration after inhalation exposure to type S ^{239}Pu after using the 3 software programs.
* actual equivalent dose, ** weighted equivalent dose from compartment radiosensibility.

Whatever the software program used, very similar results were obtained especially in the different respiratory tract compartments as defined in ICRP 66. Table III and IV show different equivalent and effective doses due to the dissolution of a type S particles calculated either using ICRP CD ROM or our software program.

Target	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Committed equivalent doses										
Bone surface	1.1E-10	2.3E-09	1.5E-08	5.2E-07	5.9E-06	1.5E-05	3.4E-05	5.4E-05	8.2E-05	9.1E-05
Red marrow	1.4E-11	2.3E-10	1.5E-09	5.1E-08	5.4E-07	1.2E-06	2.3E-06	3.1E-06	4.2E-06	4.5E-06
Liver	2.1E-11	3.7E-10	2.4E-09	8.6E-08	1.1E-06	3.0E-06	7.4E-06	1.2E-05	1.7E-05	1.9E-05
Gonads	5.0E-12	3.2E-11	1.6E-10	5.3E-09	6.7E-08	1.8E-07	4.5E-07	7.2E-07	1.1E-06	1.2E-06
Committed effective doses										
Lungs	1.0E-07	5.0E-07	1.6E-06	3.2E-06	4.4E-06	4.9E-06	5.3E-06	5.5E-06	5.5E-06	5.6E-06
Organs*	4.8E-12	7.5E-11	4.8E-10	1.7E-08	1.9E-07	4.8E-07	1.1E-06	1.7E-06	2.4E-06	2.6E-06
DPUI	**1.0E-07**	**5.0E-07**	**1.5E-06**	**3.2E-06**	**4.6E-06**	**5.4E-06**	**6.4E-06**	**7.2E-06**	**8.0E-06**	**8.3E-06**

Table III : evolution of doses as a function of time after acute inhalation exposure. to type S ^{239}Pu. Values obtained using ICRP DROM. * sum of effective doses delivered to bone surface, red marrow, liver and gonads.

Target	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Committed equivalent doses										
Bone surface	1.7E-10	2.2E-09	1.4E-08	5.1E-07	6.0E-06	1.6E-05	3.7E-05	5.9E-05	9.2E-05	1.0E-04
Red marrow	1.6E-11	2.2E-10	1.4E-09	4.7E-08	4.9E-07	1.1E-06	2.1E-06	3.0E-06	4.1E-06	4.4E-06
Liver	2.7E-11	3.6E-10	2.3E-09	8.5E-08	1.1E-06	3.2E-06	8.0E-06	1.3E-05	2.0E-05	2.2E-05
Gonads	1.7E-12	2.2E-11	1.4E-10	5.1E-09	6.8E-08	1.9E-07	4.9E-07	8.0E-07	1.2E-06	1.4E-06
Committed effective doses										
Lungs	9.7E-08	4.9E-07	1.5E-06	3.1E-06	4.4E-06	4.9E-06	5.2E-06	5.4E-06	5.5E-06	5.5E-06
Organs*	5.4E-12	7.1E-11	4.5E-10	1.6E-08	1.9E-07	4.8E-07	1.1E-06	1.8E-06	2.7E-06	2.9E-06
DPUI	**9.7E-08**	**4.9E-07**	**1.5E-06**	**3.2E-06**	**4.8E-06**	**5.3E-06**	**6.3E-06**	**7.1E-06**	**8.1E-06**	**8.4E-06**

Table IV : evolution of doses as a function of time after acute inhalation exposure. to type S ^{239}Pu. Values obtained using DSV software program. * sum of effective doses delivered to bone surface, red marrow, liver and gonads.

At this time, our software do not take into account neither doses due to particle transport and particle dissolution within the gastrointestinal tract. In fact, except for the first days after inhalation, doses delivered to

the gastrointestinal wall are negligible in term of contribution to the total committed effective doses. At later times the doses delivered to tissues other than those here considered, bone surface, red marrow, liver and gonads, present less than 2% of the total effective dose. Thus, our calculation provide doses close to those obtained taking into account the gastrointestinal model, the remainder and irradiation by low LET.

Some small differences, were observed especially for the longest times after exposure. This could be due to some approximation used in the calculation during these longest times.

Table V and VI compare the equivalent doses delivered to the different respiratory tract compartments obtained using LUDEP and DSV software program.

	LUDEP 2.0		DSV	
	Sv Eq*	Sv Wp**	Sv Eq*	Sv Wp**
ET1	1.45E-06	1.45E-09	Neglegted	
ET2	8.26E-05	8.24E-05	8.56E-05	8.56E-05
LN(ET)	2.06E-04	2.06E-07	2.71E-04	2.71E-07
Total	2.90E-04	8.27E-05	3.57E-04	8.56E-05
BB(bas)	5.78E-06	9.62E-07	5.84E-06	9.73E-07
BB(sEc)	6.45E-05	1.07E-05	6.32E-05	1.05E-05
bb(sEc)	3.34E-05	1.11E-05	3.27E-05	1.09E-05
AI	7.82E-05	2.60E-05	8.61E-05	2.87E-05
LN(TH)	7.53E-04	7.53E-07	1.01E-03	1.01E-06
Total	9.35E-04	4.96E-05	1.20E-03	5.21E-05

Table V : comparison of the committed equivalent doses delivered to the different compartments of the respiratory tract as defined by ICRP 66 for a 50 year duration after inhalation exposure to ^{239}Pu from PuO_2 using LUDEP and DSV software programs and the specific dissolution parameters (f_r= 1 E-02, s_s=2 E-05) measured *in vivo*.

* actual equivalent dose, ** weighted equivalent dose from compartment radiosensibility.

	LUDEP 2.0		DSV	
	Sv Eq*	Sv Wp**	Sv Eq*	Sv Wp**
ET1	1.45E-06	1.45E-09	Neglegted	
ET2	8.34E-05	8.32E-05	8.31E-05	8.31E-05
LN(ET)	2.08E-04	2.08E-07	2.09E-04	2.09E-07
Total	2.92E-04	8.34E-05	2.92E-04	8.31E-05
BB(bas)	5.83E-06	9.70E-07	5.84E-06	9.73E-07
BB(sEc)	6.51E-05	1.08E-05	6.32E-05	1.05E-05
bb(sEc)	3.37E-05	1.12E-05	3.27E-05	1.09E-05
AI	7.89E-05	2.63E-05	7.91E-05	2.63E-05
LN(TH)	7.60E-04	7.60E-07	7.60E-04	7.60E-07
Total	9.51E-04	5.01E-05	9.41E-04	4.95E-05

Table VI : comparison of the committed equivalent doses delivered to the different compartments of the respiratory tract as defined by ICRP 66 for a 50 year duration after inhalation exposure to ^{239}Pu from MOX using LUDEP and DSV software programs and the specific dissolution parameters (f_r= 1 E-03, s_s=5 E-05) measured *in vivo*.

* actual equivalent dose, ** weighted equivalent dose from compartment radiosensibility.

The similar results show that the doses calculated using specific dissolution parameters for PuO_2 and MOX are very close to those obtained for a type S compound. Only a 5 to 15 % increase of doses delivered to lungs and extra thoracic compartments was observed for both powders.

Table VII and VIII show the doses due to plutonium dissolution using the specific parameters for PuO_2 and MOX.

Target	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Committed equivalent doses										
Bone surface	1.7E-09	2.1E-08	1.1E-07	1.4E-06	7.3E-06	1.5E-05	3.0E-05	4.5E-05	6.7E-05	7.4E-05
Red marrow	1.6E-10	2.0E-09	1.1E-08	1.3E-07	5.8E-07	1.0E-06	1.6E-06	2.2E-06	2.9E-06	3.1E-06
Liver	2.7E-10	3.4E-09	1.8E-08	2.4E-07	1.4E-06	3.1E-06	6.5E-06	9.7E-06	1.4E-05	1.6E-05
Gonads	1.7E-11	2.1E-10	1.1E-09	1.5E-08	8.6E-08	1.9E-07	4.0E-07	6.1E-07	8.9E-07	9.8E-07
Committed effective doses										
ET	2.2E-09	1.5E-08	6.5E-08	6.7E-07	1.8E-06	2.1E-06	2.1E-06	2.1E-06	2.1E-06	2.1E-06
Lungs	9.7E-08	4.8E-07	1.5E-06	3.1E-06	4.4E-06	5.0E-06	5.6E-06	5.9E-06	6.2E-06	6.3E-06
Organs*	5.4E-11	6.7E-10	3.5E-09	4.5E-08	2.3E-07	4.6E-07	9.8E-07	1.3E-06	1.9E-06	2.1E-06
DPUI	**9.9E-08**	**5.0E-07**	**1.6E-06**	**3.8E-06**	**6.5E-06**	**7.6E-06**	**8.6E-06**	**9.4E-06**	**1.0E-05**	**1.1E-05**

Table VII : evolution of doses as a function of time after acute inhalation exposure. to ^{239}Pu from PuO_2. Values obtained using DSV software program and the specific dissolution parameters (f_r= 1 E-02, s_s=2 E-05) measured *in vivo*.

* sum of effective doses delivered to bone surface, red marrow, liver and gonads.

Target	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Committed equivalent doses										
Bone surface	1.7E-10	2.2E-09	1.3E-08	3.2E-07	3.4E-06	8.6E-06	2.1E-05	3.3E-05	5.3E-05	6.0E-05
Red marrow	1.6E-11	2.1E-10	1.2E-09	3.0E-08	2.8E-07	6.1E-07	1.2E-06	1.7E-06	2.4E-06	2.6E-06
Liver	2.7E-11	3.5E-10	2.0E-09	5.4E-08	6.4E-07	1.8E-06	4.5E-06	7.3E-06	1.1E-05	1.3E-05
Gonads	1.7E-12	2.1E-11	1.2E-10	3.3E-09	3.8E-08	1.1E-07	2.7E-07	4.5E-07	7.2E-07	8.0E-07
Committed effective doses										
ET	2.2E-09	1.5E-08	6.5E-08	6.6E-07	1.8E-06	2.0E-06	2.1E-06	2.1E-06	2.1E-06	2.1E-06
Lungs	9.7E-08	4.9E-07	1.5E-06	3.1E-06	4.4E-06	5.0E-06	5.5E-06	5.7E-06	5.9E-06	5.9E-06
Organs*	5.4E-12	6.9E-11	4.0E-10	1.0E-08	1.1E-07	2.7E-07	6.3E-07	9.9E-07	1.5E-06	1.7E-06
DPUI	**9.9E-08**	**5.0E-07**	**1.6E-06**	**3.8E-06**	**6.3E-06**	**7.3E-06**	**8.2E-06**	**8.8E-06**	**9.5E-06**	**9.7E-06**

Table VIII : evolution of doses as a function of time after acute inhalation exposure. to ^{239}Pu from MOX. Values obtained using DSV software program and the specific dissolution parameters (f_r= 1 E-03, s_s=5 E-05) measured *in vivo*.

* sum of effective doses delivered to bone surface, red marrow, liver and gonads.

In both cases, the maximal equivalent dose is delivered to extra thoracic compartments. Thus, according to ICRP 60, the dose calculation for the remainder has to be changed. The effective dose delivered to ET corresponds is calculated taking into account a weighting factor of 0.025. This induced a 20% and nearly a 15% increase of the DPUI value for ^{239}Pu from PuO_2 and MOX respectively compared with a type S compound.

CONCLUSION

In vitro dissolution assays are considered to provide intermediate values between default and absorption parameters measured *in vivo* after inhalation exposure (4). Our results suggest that similar s_s values could be obtained *in vivo* and *in vitro*. By contrast, quite different f_r values were measured. This was probably due to the very complex and changing particle microenvironment during the early times following particle deposition in the different respiratory tract compartments. Such a complex environment is difficult to be simulated *in vitro*. Preliminary results show a 10 fold decrease of the s_s value of plutonium from PuO_2 and MOX between 1 and 3 months after the beginning of the dissolution experiment. In fact, *in vitro* assays might be useful to estimate the range of s_s variation as a function of time after inhalation exposure. For this purpose dissolution assays for at least 6 months are in progress.

The specific values of s_s for PuO_2 and MOX are lower than that of a type S. In such conditions, even for a f_r value as large as 1% (PuO_2), the maximal equivalent dose is delivered to ET. The results show for ^{239}Pu,

similar DPUI for PuO_2 and MOX with quite different evolution of committed effective doses out of the respiratory tract as a function of time post inhalation. These DPUI will be increased 1) for isotopes with an energy larger than ^{239}Pu i.e. ^{238}Pu and ^{241}Am, 2) if the s_s value decreases as a function of time after inhalation exposure. Further studies are in progress to provide DPUI for the different plutonium isotopes and ^{241}Am contained in PuO_2 and MOX and to estimate the effect of s_s time variation on calculated doses.

For ^{239}Pu, most of the dose delivered to ET is due to particle sequestration.in ET2 which correspond to a fraction 0.0005 of the particles deposited in this compartment. ICRP 66 mentioned : "There is no direct evidence that particles are retained in the epithelia of the oropharynx and larynx, which are regarded as being the principal tissues at risk in ET2, and are therefore treated as the target tissues. Nevertheless, a retention compartment in ET2 is included in the model."… This "…will tend to overestimate the detriment since the oropharynx and larynx are regarded as being of higher sensitivity than the nasal passage". For some actinide oxides, the over estimate could be as large as 30% of DPUI. Because of the uncertainties mentioned in ICRP 66 as concern ET2, new experiments are needed to provide the suitable parameters.

REFERENCES

1. B. Ramounet, S. Matton, F. Guezingar-Liebard, M-C. Abram, G. Rateau, G. Grillon and P. Fritsch, *Comparative biokinetics of Pu and Am after inhalation of PuO_2 and mixed oxides $(U,Pu)O_2$ in the rat.* Int. J. Radiat. Biol. (in press).
2. S. Matton, G. Rateau and P. Fritsch, in vitro dissolution parameters *of PuO_2 and mixed oxides $(U,Pu)O_2$ inaerosols*. Int. J. Radiat Biol. (submitted).
3. S. André *Design of a new inhalation device for rodents and primates.* J. Aerosol. Sci., 20, 647-656 (1989).
4. E. Ansoborlo, M.H. Hengé-Napoli, V. Chazel, R. Gibert and R.A. Guilmette, *Review and critical analysis of available in vitro dissolution tests.* Health Phys. 77, 638-645 (1999).