

RADIATION DOSE ESTIMATES AND HAZARD EVALUATIONS
FOR INHALED AIRBORNE RADIONUCLIDES

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TABLE OF CONTENTS

	<u>Page</u>
Executive Summary	1
An Improved Technique for Aerosolization of Dry Powders of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials	5
Infrared Spectra of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials	11
<i>In Vitro</i> Solubility of Aerosols of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials	19
Deposition, Retention and Dosimetry of Inhaled Mixed Uranium Plutonium Oxides (Heat-Treated at 750°C) in Fischer-344 Rats, Beagle Dogs and Cynomolgus Monkeys	35
Deposition, Retention and Dosimetry of Inhaled Mixed Uranium-Plutonium Oxides (Heat-Treated at 1750°C) in Fischer-344 Rats, Beagle Dogs and Cynomolgus Monkeys	47
Deposition, Retention and Dosimetry of Inhaled Plutonium Dioxide (Heat-Treated at 850°C) in Fischer-344 Rats, Beagle Dogs and Cynomolgus Monkeys	55
Comparison of Inhalation Studies Using Three Forms of Aerosols Produced in a Mixed (U-Pu) Oxide Fuel Fabrication Facility	61
Summary of Biological Effects Following Inhalation of Industrial Mixed Oxides (Uranium-Plutonium) or PuO ₂ in Rats	67
Appendix A - Status of Animals in Inhalation Studies	73
Appendix B - Personnel Contributing to Research	85

LIST OF FIGURES

'An Improved Technique for Aerosolization of Dry Powders of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials.'

- Figure 1. Generator used for the production of particulate aerosols from dry powders based on a modified DeVibiss[®] dry powder blower and a Vortex-Genie[®] shaker..6
- Figure 2. Simplified diagram of test system used in the development of the modified dry powder aerosol generator.....7
- Figure 3. Concentration of UO₂ aerosols generated at varying flow rates and constant 51.5 Hz shaking frequency.....8
- Figure 4. Concentration of UO₂ aerosols generated at three different and constant flow rates and varying shaking frequencies.....8
- Figure 5. Variations in particle size distribution characteristics of UO₂ aerosols generated at different shaking frequencies.....9

'Infrared Spectra of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials.'

- Figure 1. Infrared absorption spectrum of a bulk powder sample of PuO₂ heat-treated at 850°C and mixed with UO₂ and organic binders.....13
- Figure 2. Infrared spectrum of powdered (U,Pu) O_x produced by centerless grinding of fuel pellets which have been sintered at 1750°C in a reducing atmosphere.....14
- Figure 3. Infrared absorption spectrum of an aerosol of mixed PuO₂ and UO₂ powders used in the inhalation exposure of laboratory animals.....14
- Figure 4. Two possible modes of binding for bidentate CO₃²⁻ chemisorbed on the surface of a metal oxide particle.....15

'In Vitro Solubility of Aerosols of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials.'

- Figure 1. Dissolution of Pu and Am from aerosol samples of 1750°C heat-treated mixed uranium-plutonium oxides in 0.1 M HCl.....22
- Figure 2. Comparison of rates of Pu, Am, and U dissolution from aerosol samples of mixed PuO₂ and UO₂ containing organic binders in 0.1 M HCl.....26
- Figure 3. Comparison of Pu dissolution from aerosol samples of four industrial fuel materials in a serum simulant solution containing DTPA.....28
- Figure 4. Comparison of Pu dissolution from aerosol samples of four industrial fuel materials in 0.1 M HCl.....28
- Figure 5. Comparison of Pu dissolution from aerosols of four industrial fuel materials in 2 M HNO₃.....29
- Figure 6. Comparison of U dissolution from aerosols of three industrial materials in serum simulant solution containing DTPA.....30

Figure 7. Comparison of U dissolution from aerosols of three industrial fuel materials in 0.1 M HCl.....	30
Figure 8. Comparison of U dissolution from aerosols of three industrial fuel materials in 2 M HNO ₃	31
<p>'Deposition, Retention and Dosimetry of Inhaled Mixed Uranium-Plutonium (Heat-Treated at 750°C) in Fischer 344 Rats, Beagle Dogs and Cynomolgus Monkeys.'</p>	
Figure 1. The ranges of values of activity median aerodynamic diameter (AMAD in μm) and geometric standard deviation (σ _g) observed for exposure aerosols are shown in relation to the ICRP Task Group in Lung Dynamics lung deposition curves.....	38
Figure 2. Lung retention of plutonium in rats, dogs, and monkeys exposed to 750°C heat-treated mixed UO ₂ and PuO ₂ aerosols obtained from the ball milling process at HEDL.....	42
<p>'Deposition, Retention and Dosimetry of Inhaled Mixed Uranium-Plutonium Oxides (Heat-Treated at 1750°C) in Fischer 344 Rats, Beagle Dogs and Cynomolgus Monkeys.'</p>	
Figure 1. Lung retention of Pu and Am in Beagle dogs exposed to mixed U-Pu oxides heat-treated at 1750°C.....	52
Figure 2. Lung retention of Pu and Am in monkeys exposed to aerosols of mixed U-Pu oxides heat-treated at 1750°C.....	52
<p>'Deposition, Retention and Dosimetry of Inhaled Plutonium Dioxide (Heat-Treated at 850°C) in Fischer 344 Rats, Beagle Dogs and Cynomolgus Monkeys.'</p>	
Figure 1. Lung retention of Pu and Am in Beagle dogs exposed to aerosols of 850°C heat-treated PuO ₂ obtained from the V-blending process at B&W.....	59
Figure 2. Lung retention of Pu and Am in monkeys exposed to aerosols of 850°C heat-treated PuO ₂ obtained from the V-blending process at B&W.....	59
<p>'Comparison of Inhalation Studies Using Three Forms of Aerosols Produced in a Mixed (U,Pu) Oxide Fuel Fabrication Facility.'</p>	
Figure 1. Lung retention of Pu following inhalation of three aerosols by Beagle dogs and Cynomolgus monkeys, expressed as percent initial lung burden.....	63

LIST OF TABLES

'An Improved Technique for Aerosolization of Dry Powders of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials.'

Table 1. Aerosol concentrations of powders generated using the powder generator with the 45.5-54.5 Hz shaker.....9

'Infrared Spectra of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials.'

Table 1. Industrial mixed uranium-plutonium oxide fuel materials collected for laboratory studies.....12

'In Vitro Solubility of Aerosols of Industrial Uranium and Plutonium Mixed-Oxide Nuclear Fuel Materials.'

Table 1. Composition of simulated serum ultrafiltrate (SUF) used to study the dissolution of industrial mixed uranium, plutonium oxides.....20

Table 2. Dissolution *in vitro* of industrial mixed uranium and plutonium oxide fuel materials in synthetic serum ultrafiltrate solution containing DTPA..23

Table 3. Dissolution *in vitro* of industrial mixed uranium and plutonium oxide fuel materials in 0.1 M HCl.....24

Table 4. Dissolution *in vitro* of industrial mixed uranium and plutonium oxide fuel materials in 2 M HNO₃.....25

'Deposition, Retention and Dosimetry of Inhaled Mixed Uranium-Plutonium Oxides (Heat-Treated at 750°C) in Fischer 344 Rats, Beagle Dogs and Cynomolgus Monkeys.'

Table 1. Particle size distribution of aerosols of 750°C heat-treated mixed uranium and plutonium oxides sampled during the ball milling operation at HEDL and inhalation exposures of laboratory animals.....38

Table 2. Initial lung burden values of Fischer 344 rats, Beagle dogs and subhuman primates exposed by inhalation to aerosols of UO₂ + PuO₂ heat-treated at 750°C obtained from the ball milling process at HEDL.....40

Table 3. Organ content of Pu and Am expressed as percent initial lung burden in dogs and monkeys exposed to 750°C heat-treated mixed UO₂ and PuO₂ aerosols obtained from the ball milling operation at HEDL.....44

Table 4. Organ content of Pu in rats exposed to 750°C heat-treated mixed UO₂ and PuO₂ aerosols obtained from the ball milling operation at HEDL.....45

'Deposition, Retention and Dosimetry of Inhaled Mixed Uranium-Plutonium Oxides (Heat-Treated at 1750°C) in Fischer 344 Rats, Beagle Dogs and Cynomolgus Monkeys.'

Table 1.	Particle size distribution of aerosols of 1750°C heat-treated, mixed U-Pu oxides obtained from HEDL and used in the inhalation exposures of Fischer 344 rats, Beagle dogs and monkeys.....	48
Table 2.	Initial lung burden values of Fischer 344 rats, Beagle dogs and non-human primates exposed by inhalation to aerosols of 1750°C heat-treated mixed U-Pu oxides obtained from the centerless grinding operation at HEDL.....	49
Table 3.	Organ content of Pu and Am expressed as percent initial lung burden for rats exposed to aerosols of 1750°C heat-treated mixed U-Pu oxides obtained from the pellet grinding process at HEDL.....	50
Table 4.	Organ content of Pu and Am for dogs and monkeys exposed via inhalation to aerosols of mixed U-Pu oxides heat-treated at 1750°C from the pellet grinding process at HEDL.....	51
Table 5.	Retention half-times of Pu and Am in the lungs of dogs and monkeys exposed to 1750°C heat-treated mixed uranium and plutonium oxides from the pellet grinding process at HEDL.....	52

'Deposition, Retention and Dosimetry of Inhaled Plutonium Dioxide (Heat-Treated at 850°C) in Fischer 344 Rats, Beagle Dogs and Cynomolgus Monkeys.'

Table 1.	Particle size distribution of aerosols of 850° heat-treated PuO ₂ obtained from B&W and used in the inhalation exposures of rats, dogs and monkeys...	56
Table 2.	Initial lung burden values of Fischer 344 rats, Beagle dogs and non-human primates exposed via inhalation to aerosols of 850°C heat-treated PuO ₂ obtained from the V-blending process at B&W.....	57
Table 3.	Organ content of Pu and Am expressed as percent sacrifice body burden for rats exposed to aerosols of 850°C heat-treated PuO ₂ obtained from the V-blending operation at B&W.....	58
Table 4.	Retention half-times of Pu and Am in the lungs of dogs and monkeys exposed to inhalation aerosols of 850°C heat-treated PuO ₂ obtained from the V-blending process at B&W.....	59
Table 5.	Organ distribution of Pu and Am in dogs and monkeys exposed by inhalation to aerosols of 850°C heat-treated PuO ₂ obtained from the V-blending process at B&W.....	60

'Comparison of Inhalation Studies Using Three Forms of Aerosols
Produced in a Mixed (U,Pu) Oxide Fuel Fabrication Facility.'

Table 1.	Comparison of percent initial lung burden retained and slope with calculated half-time (days) of lung retention for Beagle dogs and Cynomolgus monkeys for three aerosols from mixed-oxide fuel fabrication.....	62
Table 2.	Comparison of the effects of 2-years after inhalation exposure datum point being added to data used to produce Table 1.....	62
Table 3.	Distribution of Pu in selected tissues of the Beagle dog and Cynomolgus monkey at several sacrifice times after inhalation exposure.....	63
Table 4.	Excretion of Pu from Beagle dogs and Cynomolgus monkey following inhalation of three aerosols containing Pu.....	64
'Summary of Biological Effects Following Inhalation of Industrial Mixed Oxides (Uranium-Plutonium) or PuO ₂ in Rats.'		
Table 1.	Rats exposed to mixed-oxide aerosols that died before scheduled sacrifice times.....	68-69
Table 2.	Comparison of lung tumor incidence in rats exposed to various transuranic radionuclide aerosols.....	71

EXECUTIVE SUMMARY

This annual progress report details the research conducted in the project, "Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides." The report is composed of a series of research papers, each presenting the status of specific areas of the total research effort. An attempt has been made to include substantial detail in each paper to indicate clearly the state of the research and to provide interpretations of the results where possible. The reader is advised that in many cases these interpretations are preliminary; and final, more complete interpretations and comparison must await the completion of individual research projects.

The objective of this project is to conduct confirmatory research on aerosol characteristics which may modify the biological fate, patterns of radiation dose and predicted health consequences of airborne radioactivity which may be released in normal operations or under accident conditions in the nuclear fuel cycle. It involves physical, chemical and biological characterization of aerosols actually present in different segments of the nuclear fuel cycle. Since it involves actual aerosols produced in industrial operations, this work provides a key link between studies with idealized, laboratory-produced aerosols and derived radiation protection standards and hazard analyses. Industrially-collected aerosol materials are re-aerosolized in the laboratory to determine the patterns of deposition, retention and translocation in laboratory animals as a function of time after an inhalation exposure. The aerosols used for these studies are characterized using a number of physical and chemical techniques to determine possible differences between the aerosol and the corresponding bulk material which might help to explain the observed patterns seen in the animals after exposure. Multiple species (rats, dogs and monkeys) are being used to strengthen the eventual extrapolation to man. Although current studies are concentrated on the biological characterization of mixed (UO_2 , PuO_2) fuel elements, later studies may utilize materials from other sources of industrial operations involving the handling of nuclear fuel material as well as from the pilot processes involved in fabrication of processing of advanced fuel forms.

This progress report begins with a presentation on an improved technique for the aerosolization of dry powders of industrial uranium and plutonium mixed-oxide powders for use in animal inhalation exposures. The system used represents an evolution of the system previously employed but represents a significant improvement in the maintenance of a uniform activity concentration for periods of up to 20 minutes. Uniform activity concentration is important in the conduct of inhalation exposure of animals in that it provides less variation in the activity deposited in the respiratory tract of animals making the attainment of specified initial lung burden more precise.

The next presentation details one aspect of our continuing effort to characterize the aerosols produced during normal mixed-oxide fuel fabrication. This characterization, using infrared spectral analysis, is specifically intended to complement X-ray diffraction techniques in order to detect, identify and quantify the relative quantities of amorphous chemical forms of uranium or plutonium which would not be characterized by X-ray diffraction techniques alone. The results of these efforts have shown the presence of the surface of aerosol particles of adsorbed H_2O and CO_3^{2-} . The major significance of the presence of an oxidized or hydrated surface layer on these aerosols lies in the probable effect these forms can have on the *in vivo* solubility of the material. The potential impact of these modifier surface characteristics is pursued in the next presentation in which the *in vitro* solubility studies being conducted are described. The studies show that dissolution occurs initially at a rapid rate which is probably related to the

chemical form of the U and Pu at the surface followed by a substantially slower dissolution at longer times. These studies have also shown that U dissolves more rapidly than Pu for the mixed oxide treated at 750°C, whereas the mixed oxide treated at 1750°C results in the formation of a solid solution of U and Pu which dissolves at a modified rate for both U and Pu. The presentation discusses the potential effect on the radiation dose to lung which these different solubility rates may have, as well as the impact and importance of these rates on bioassay procedures designed to elucidate the burden of such materials following inhalation.

The next presentation in this report is the first of three which specifically address the biological studies underway. In these studies, conducted under identical experimental protocols, inhalation exposures of rats, dogs and monkeys were accomplished to one of three aerosol materials collected at industrial facilities. These radiation dose pattern studies can best be denoted by the temperature of treatment employed in the fuel fabrication process from which samples of the aerosol created in the safety enclosures were drawn. Since these studies were initiated at different times, the comparisons and conclusions drawn from the results to date represent preliminary analyses of the data.

The first study utilized an aerosol of mixed U and Pu oxides treated at 750°C. The results from this study indicate that the *in vivo* solubility of both U and Pu was relatively low in all three species. However, the retention of this material in lung is different for the three species of animal; the Beagle dog cleared about 80% of the initial lung burden with a half-time of about 1700 days, whereas the Cynomolgus monkey and Fischer-344 rat cleared 66 and 25% of the initial lung burden, respectively, with a half-time of about 340 days. In addition, the rate of lung clearance of Am appears to have been more rapid than the rate for Pu in all three species indicating greater solubility of Am in this aerosol. The report describes in detail comparisons of the retention, distribution and excretion of Pu and Am determined in this work with similar data following inhalation of PuO₂ by researchers in other laboratories.

The second presentation in this series on biological studies details the status of the radiation dose pattern study in which inhalation exposures were conducted using an aerosol of mixed U-Pu oxides treated at 1750°C. This material is a solid solution of U-Pu as shown by X-ray diffraction. Lung clearance of this material is different for dogs and monkeys, being more rapid for the latter. Interestingly, the rates of lung clearance for Pu and Am do not appear different in any single species for this material.

The last of the three presentations for the radiation dose pattern studies details the results to date following inhalation of PuO₂ treated at 850°C. This study, conducted using PuO₂ prior to mixing with UO₂ in the fuel fabrication process, provides a key link between inhalation studies conducted at this Institute and at other laboratories using laboratory-produced, idealized aerosols of PuO₂ and the studies carried out in this project using aerosols as they exist in the industrial environment. Since this study, initiated as the last in the sequence of three, it has not reached sufficient maturity to allow more than very preliminary comparisons. Again, the rate of lung clearance appears different for dogs compared to monkeys and the overall solubilization of Pu in lung is low.

The next presentation was prepared to draw comparisons among the three radiation dose pattern studies at common times after inhalation exposure. The comparison focuses on the similarities and differences in lung retention and tissue distribution of Pu among the three studies. The similarities and differences highlighted in the presentation clearly indicate the need for coherent structure of a biomathematical model to be applied to the final results from these studies. This effort represents the next major stage in this project.

The final presentation summarizes the biological effects which have appeared in the Fischer-344 rats as a result of inhalation of these materials. The high incidence of lung tumors in rats with initial lung burdens ranging from 67 to 230 nCi is contrasted to published reports of lung tumor incidence data in rats following inhalation of Pu and Cf. None of these latter studies reported incidences as high as 87% at comparable radiation dose to lung. An interesting feature of the histological types of lung tumors found in rats in these studies was the occurrence of three cases of malignant mesothelioma, an unusual tumor type in rats and usually associated with implantation or inhalation of fibers or polycyclic hydrocarbons. It is difficult to fully evaluate the significance of the high tumor incidence and the several tumor types observed in these studies due to the relatively few numbers of animals involved. Additional studies are being planned to address the specific dose response relationships in Fischer-344 rats to assist in resolution of this question.

This report concludes with summary tables listing the status of all animals in the three radiation dose pattern studies.

AN IMPROVED TECHNIQUE FOR AEROSOLIZATION OF DRY POWDERS OF INDUSTRIAL
URANIUM AND PLUTONIUM MIXED-OXIDE NUCLEAR FUEL MATERIALS

ABSTRACT

The interpretation of results of inhalation studies of industrial mixed-oxide nuclear fuel aerosols using laboratory animals requires that sufficient concentrations of aerosols be generated for exposures lasting from 5-30 minutes. An aerosol generator system incorporating a modified DeVilbiss powder blower and a mechanical shaker was tested on various powders including UO_2 , U_3O_8 , ammonium diuranate, Fe_2O_3 , fibrous glass and methylene blue. Results of these tests indicated that the system generated concentrations of aerosols ranging from 0.1 to 1 μg per cm^3 of generator air for periods up to 20 minutes. Aerosols of UO_2 were generated with particle size distributions in the respirable range.

PRINCIPAL INVESTIGATOR

A. F. Bidaon

To assess the potential biological hazard to humans following inhalation of aerosols containing mixed oxides of uranium and plutonium, a prime requisite is the conduct of inhalation studies in animals to define the radiation dose to specific organs and tissues. The applicability of results from such studies is enhanced if the aerosol characteristics closely approximate, in both physical and chemical form, the actual aerosols produced by the industrial process. It was, therefore, necessary to develop a method to generate aerosols from bulk material that duplicated the physical characteristics of aerosols sampled on site.

A generator system suitable for extensive animal studies must generate an aerosol with the desired particle size distribution characteristics for a period of time useful for conducting the inhalation exposures. Typically, this is 5 to 30 minutes. Further, these characteristics must be reproducible to allow data to be compared within a multi-animal study. Another desirable characteristic is that the system generate a relatively uniform aerosol concentration so that total activity delivered to the animal can be conveniently related to total inhalation exposure time.

The generator system described in an earlier Annual Report¹ has been modified and employed to generate aerosols of uranium dioxide. The major modification was the incorporation of a lower frequency (= 50 Hz) shaker into the system to replace the sonic agitator used previously. The modified generator was tested on various powders including UO_2 , ammonium diuranate, U_3O_8 , Fe_2O_3 , fibrous glass and methylene blue. Results of these tests indicated that the modified system generated higher concentrations of aerosols with particle size distributions in respirable range. Further, the modified generator operated with improved reproducibility for longer periods of time and will be used in future exposures.

MATERIALS AND METHODS

The aerosol generator assembly is shown in Figure 1. It consists of a DeVilbiss powder blower which has been modified to allow the aerosol to escape from the generator bottle without undergoing a right-angle bend.¹ This modified powder blower has been attached to a Vortex-Genie[®] shaker which includes a rubber collar on an eccentric shaft as shown in Figure 1. This shaker provides a shaking frequency range from 45.5 to 54.5 Hz. In a typical aerosol generation, the powder blower bottle is filled with 300 to 700 mg of dry powder and firmly attached to the rubber collar on the shaker. Dry metered air is introduced as shown in the drawing and the aerosol output is delivered to the

sampling system through flexible tubing. The shaking frequency is measured using a stroboscopic light. A schematic diagram of the test apparatus used to develop this generator system is shown in Figure 2. In this system, the output aerosol from the powder blower was passed through a ^{85}Kr discharger into a sampling chamber. The sampling chamber was the balance point for the entire system in which air flows were adjusted such that no net pressure existed in the chamber. This assured that the sampling devices actually sampled a steady state aerosol concentration. Aerosols were passed into the sampling chamber and sampled by membrane filters, seven-stage Mercer style² cascade impactors and a point-to-plane electrostatic precipitator (ESP) as described by Morrow and Mercer.³

The majority of the testing of this generator was performed with uranium compounds. These tests were conducted to provide a set of operating conditions that would be applicable to animal inhalation exposures of mixed uranium dioxide and plutonium dioxide aerosols or to aerosols of ammonium diuranate and U_3O_8 compounds found in refined uranium ores produced by uranium mills. A few tests were conducted using other materials which served to define the range of application of this generator. Ferric oxide and fibrous glass were chosen as representative environmental samples and methylene blue was chosen as a representative and conveniently used organic material.

The procedure for quantitative analysis of Fe_2O_3 deposited on membrane filters and cascade impactor stages included dissolving the sample in 1 ml of concentrated HCl with warming and dilution to 20 ml with distilled H_2O . Five ml of this sample were then mixed with 0.5 ml of 3M NH_4SCN . The concentration of the iron complex was then determined by absorbance at the 475 nm peak.

The specimen containing methylene blue was dissolved in distilled water and the concentration determined by the absorbance at the 655 nm absorption peak. The amount of fiberglass prepared according to the method of Pickrell *et al.*⁴ was determined gravimetrically as deposited on filters.

Powders used in these studies were obtained from commercial sources. Commercial grade U_3O_8 was obtained from K&K Laboratories, Plainview, NY; Fe_2O_3 was obtained from the Matheson, Coleman and Bell Company and methylene blue was obtained from Eastman Chemical Company. Ammonium diuranate was prepared in the laboratory from uranyl nitrate obtained from the Fisher Scientific Company. A weighed amount of $\text{UO}_2(\text{NO}_3)_2 \cdot 6 \text{H}_2\text{O}$ was dissolved in 20 ml of distilled water and ammonium diuranate was precipitated by adjusting the pH to 7.0 to 7.5 with 15% NH_4OH with stirring at room temperature. The resulting yellow precipitate was allowed to stir at room temperature for 16 hours, filtered, washed with 15% ammonium hydroxide, alcohol and air dried.

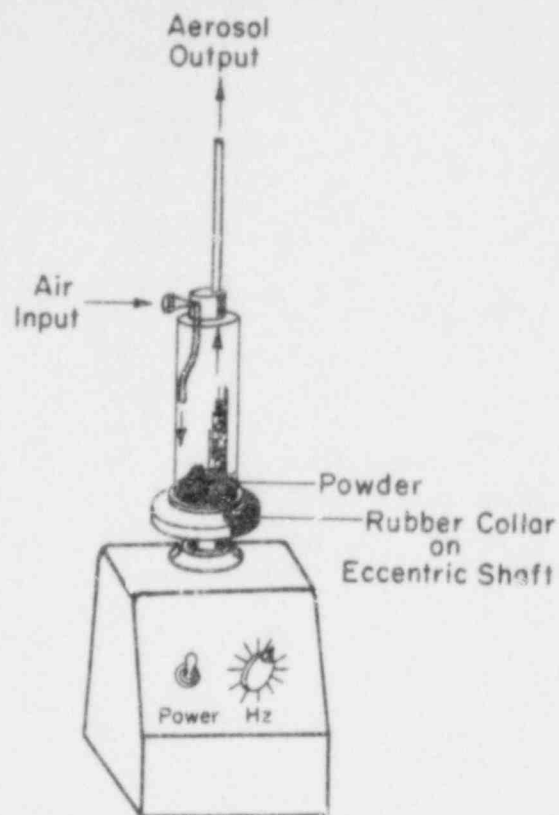


Figure 1. Generator used for the production of particulate aerosols from dry powders based on a modified DeVilbiss dry powder blower and a Vortex-Genie[®] shaker. Shaking frequency was variable from 45.5 Hz to 54.5 Hz.

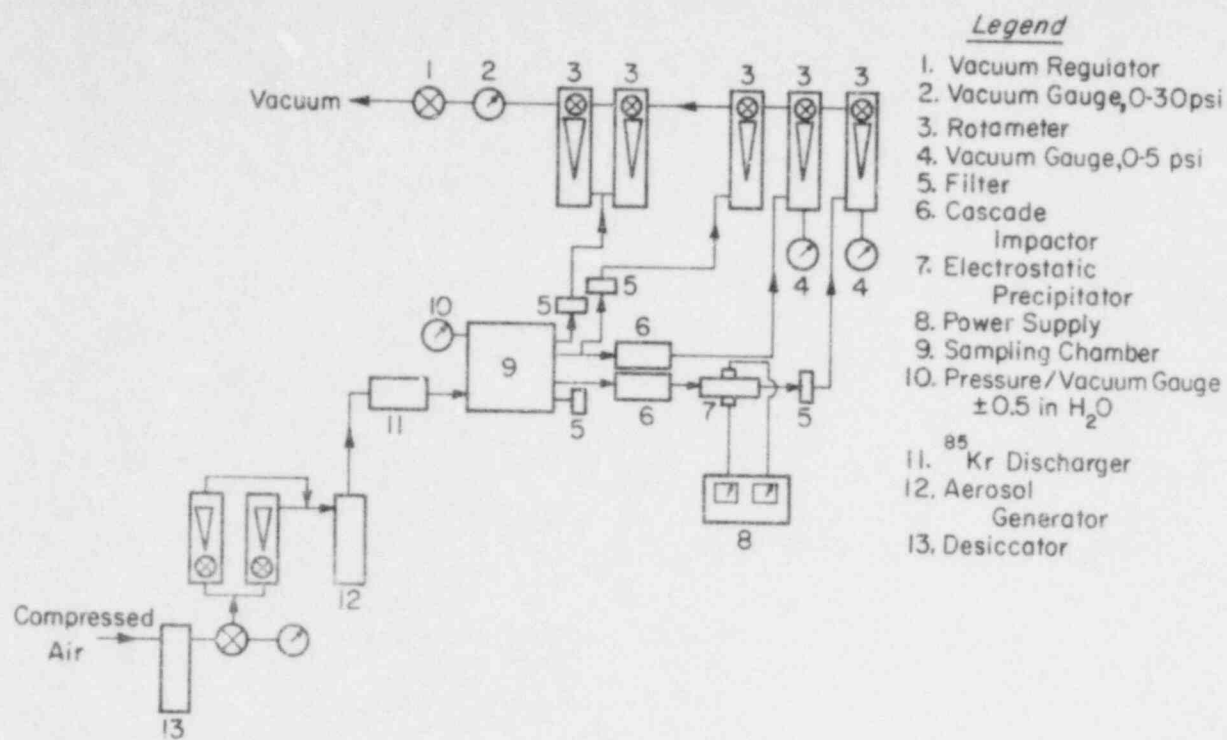


Figure 2. Simplified diagram of test system used in the development of the modified dry powder aerosol generator.

All generation runs were conducted using 300 to 700 mg of material except for the generation of fiberglass aerosols. Since gravimetry was used for determination of the characteristics of the fiberglass aerosols, larger amounts, 10 to 20 grams, were placed in the aerosol generator.

RESULTS AND DISCUSSION

Results of studies to describe the aerosol output versus generator input air flow rate are shown in Figure 3. The aerosol generation concentration was linear with generator input air flow rate. This was true for aerosols generated between 0 and 5 minutes after initiation of the run and it was also true for aerosols generated over an entire 20 minute run. It was noted that deviation from linearity occurred at an input air flow rate of 2.5 l/min for generations lasting 20 minutes. This was attributed to depletion of respirable material loaded into the generator bottle after operation at this relatively high flow rate before the end of a 20 minute period. The shaking frequency was maintained at a constant 51.5 Hz for these studies.

Results of studies to determine the aerosol output as a function of shaking frequency are shown in Figure 4. The aerosol concentration was found to vary linearly with shaking frequency at generation air flow rates of 1.0 l/min or greater; but was found to be independent of shaking frequency at airflow rates of 0.5 l/min or less. Uranium dioxide aerosol concentrations may be achieved in the 0.1 to 0.9 $\mu g/cm^3$ range by proper selection of generator operating conditions.

Variations in particle size distribution for uranium dioxide aerosols generated using this system are shown in Figure 5. It is shown in the figure that some slight variability can be achieved in a predictable linear manner in the particle size distribution of uranium dioxide aerosols generated from dry powders. The results of aerosol generation experiments using powders other than

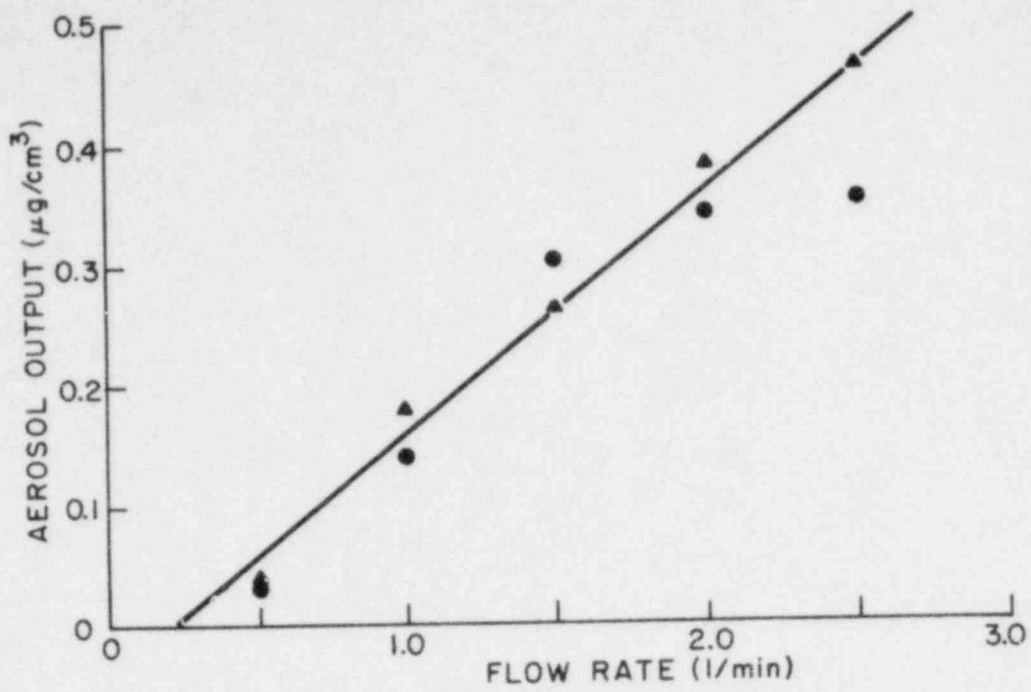


Figure 3. Concentration of UO_2 aerosols generated at varying flow rates and constant 51.5 Hz shaking frequency. Generation time of 0-5 minutes, ▲; 0-20 minutes, ●.

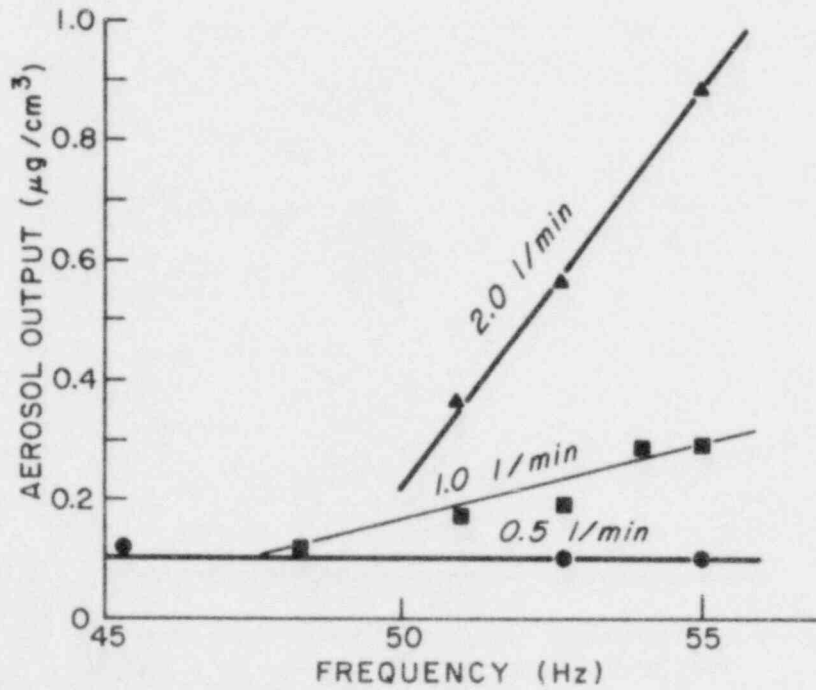


Figure 4. Concentration of UO_2 aerosols generated at three different and constant flow rates and varying shaking frequencies.

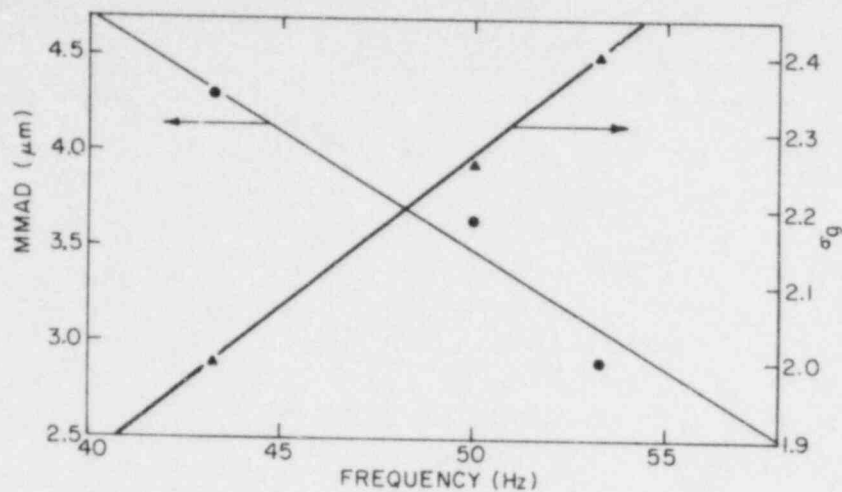


Figure 5. Variations in particle size distribution characteristic of UO_2 aerosols generated at different shaking frequencies. MMAD = mass median aerodynamic diameter in micrometers, σ_g = geometric standard deviation.

Table 1
Aerosol Concentrations of Powders Generated Using the Powder Generator
With the 45.5-54.5 Hz Shaker

Powder	Flow Rate (l/min)	Generation Frequency (Hz)	Generation Time (min)	Concentration ($\mu\text{g}/\text{cm}^3$ generation air)
Ammonium Diuranate	2.0	50.0	0- 5	0.147
	2.0	50.0	5-10	0.153
	2.0	50.0	10-15	0.123
	2.0	50.0	15-20	0.117
				$\bar{X} = 0.14 \pm 0.02$ SD
U_3O_8	2.0	50.0	0-20	0.106
	2.0	50.0	0- 5	0.330
	2.0	50.0	5-10	0.275
	2.0	50.0	10-15	0.196
	2.0	50.0	15-20	0.177
				$\bar{X} = 0.24 \pm 0.07$ SD
Fe_2O_3	2.0	50.0	0-20	0.250
	2.0	50.0	0-20	0.166
	2.0	50.0	0-20	0.198
	3.0	50.0	0-20	0.327
	3.0	50.0	0-20	0.351
Fibrous Glass	4.0	50.0	0-20	1.04
	10.0	50.0	0-10	0.538
	10.0	50.0	10-20	0.390
	10.0	50.0	20-30	0.258
				$\bar{X} = 0.4 \pm 0.1$ SD
Methylene Blue	1.0	50.0	0- 5	0.034
	2.0	50.0	0- 5	0.128
	3.0	50.0	0- 5	0.187

UO₂ are summarized in Table 1, for a range of aerosol generation flow rates, shaking frequencies and total generation times. Aerosol particle size distribution characteristics for these other powders were not determined.

Results summarized in Table 1 indicate that the aerosol concentrations produced by the generator within a 20 to 30 minute generation time at constant flow rate and shaking conditions varied within 15 to 30% for a given material, particularly for uranium compounds. Similar reproducibility was found for aerosols generated over a 20 minute period using Fe₂O₃ and fiberglass. Results for generation of methylene blue aerosols do not indicate linearity between aerosol flow rate and aerosol concentration. Particle size distribution characteristics of UO₂ aerosols were constant at constant flow rates and shaking frequencies. The mass median aerodynamic diameter (MMAD) was constant within ± 1 μm and the geometric standard deviation was constant within ± 0.5 when UO₂ aerosols were generated at different shaking frequencies and different flow rates.

To date aerosol particle size distributions have not been determined for aerosols of all materials but the determinations have been made for uranium dioxide aerosols which is most relevant to mixed-oxide nuclear fuel aerosol generations. It has not been determined that aerosols generated from fiberglass indeed were distributed as single particles rather than chain or clumped aggregates. This matter will not be pursued in this project.

CONCLUSIONS

The combined results showed that concentrations of respirable uranium dioxide aerosols changed linearly with flow rate up to = 1/min, for generation times of up to 20 minutes. This modified generator has been shown to be an improvement over previous designs for the purpose of generating aerosols of mixed oxide nuclear fuel materials. In addition, a variety of types of powders have been generated. The advantages of this improved design include: relatively small size providing optimal conditions for use in glove box enclosures, the simplicity of design and the low cost of the system. The primary disadvantage of this system is its size which limits its applicability for long-term exposures of laboratory animals. Future work in the development of this generator will include determination of particle size distribution characteristics of other uranium compounds and particle size information related to a wider range of operating conditions.

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INFRARED SPECTRA OF INDUSTRIAL URANIUM AND PLUTONIUM MIXED-OXIDE NUCLEAR FUEL MATERIALS

ABSTRACT

Mixed uranium and plutonium oxide fuel pellets have been made for the Fast Flux Test Facility (FFTF) located near Richland, WA. Powders and aerosols which are representative of four of the fuel pellet fabrication steps have been studied by infrared spectroscopy. It was found that the surfaces of aerosol particles had adsorbed commonly occurring atmospheric molecules or their ions, e.g., H_2O and CO_3^{2-} . Evidence suggesting that the surfaces of particles included a partially hydrolyzed form of plutonium dioxide was found, along with evidence suggesting that aerosols produced from powder ground from substoichiometric fuel pellets were oxidized at the surface of the particles. The implications of these observations for interpretation of results of in vitro solubility and biological experiments are discussed.

PRINCIPAL INVESTIGATOR

A. F. Eidson

Mixed uranium and plutonium oxide powders are processed to produce fuel pellets of uniform size, density and oxygen-to-metal ratio to conform to design specifications of the Fast Flux Test Facility (FFTF) near Richland, WA. The primary purpose of the studies described here is to delineate physical and chemical factors which might be of importance in determining the biological fate of these mixed-oxide powders if they are inhaled in the event of an accidental release. The characterization scheme uses a variety of analytical methods including a number of solid state, non-destructive techniques which have been selected to minimize extensive sample preparation or chemical interconversion, thus allowing the material to be studied in its original form. Results of studies related to isotopic composition, elemental composition, chemical form and crystalline properties have been reported in the previous Annual Progress Report.¹ This paper reports progress of infrared spectroscopic analysis.

It is probable that industrial nuclear fuel materials contain amorphous chemical forms of uranium or plutonium which cannot be detected by X-ray diffraction techniques. Infrared spectra of these materials have been measured to detect, identify and determine the relative quantities of these amorphous forms. The approach used in the infrared spectroscopic analysis involved intercomparisons of spectra of industrial nuclear fuel materials collected at selected process stages to determine any differences which could be related to the process stage. Further, comparisons were made between the spectra of each bulk powder and the corresponding aerosols generated from the bulk powder and collected during the inhalation exposure of laboratory animals. The purpose of these comparisons was to determine if the aerosols generated from powders were representative of the bulk powders in chemical form.

MATERIALS

Materials which were analyzed in these studies are shown in Table 1. A detailed description of the materials selected for study was given in the last Annual Progress Report.^{2,3} A brief summary of that description will be given here to aid in this discussion.

Table 1

Industrial Mixed Uranium-Plutonium Oxide Fuel Materials Collected for Laboratory Studies

Sampling Site ^a	Chemical Composition	Temperature History of PuO ₂	Process Step	Selected for Inhalation Study or Dissolution Study <i>In Vitro</i>
B&W ^b	PuO ₂	850°C	Sieving	NO
B&W	PuO ₂	850°C	V-Blending	Multi-species Inhalation and <i>In Vitro</i> Dissolution Studies
HEDL ^c	UO ₂ + PuO ₂	750°C	Sieving	No
HEDL	UO ₂ + PuO ₂	750°C	Ball Milling	Multi-species Inhalation and <i>In Vitro</i> Dissolution Studies
B&W	UO ₂ + PuO ₂ + Binders	850°C	Pellet Pressing	Pilot Study in Rats and <i>In Vitro</i> Dissolution Studies
HEDL	(U,Pu)O _{1.96}	1750°C	Pellet Grinding	Multi-species Inhalation and <i>In Vitro</i> Dissolution Studies
B&W	(U,Pu)O _{1.96}	1750°C	Pellet Grinding	No
HEDL	(U,Pu)O _{1.96}	1750°C	Whole Sintered Ceramic Pellets	No

^aAll PuO₂ was prepared at HEDL prior to shipment to B&W for further processing.

^bBabcock and Wilcox Fuel Fabrication Facility, Apollo, PA.

^cHanford Engineering and Development Laboratory, Richland, WA.

The material listed in Table 1 as B&W, PuO₂, 850°C V-blending is PuO₂ powder prepared at HEDL by calcination of the plutonium oxalate salt in air at 750°C. This powder was transported to the B&W facility, heated to 850°C and mixed with other lots using a V-blender. This material will be referred to as "B&W PuO₂" for simplicity in this report.

The material listed as HEDL, UO₂ + PuO₂, 750°C, ball milling is a powder composed of PuO₂ prepared as described above without subsequent heating to 850°C. The PuO₂ was mixed with UO₂ powder, sieved, then milled in a ball mill. This material will be referred to as "HEDL 750°".

The powder listed as B&W, UO₂ + PuO₂ + Binders, 850°C consists of mixed-oxide powders that have been mixed with organic binders at B&W and prior to fuel pellet pressing. This material will be referred to as "B&W mixed-oxides with binders".

The powder listed as (U,Pu)O_{1.96} 1750°C pellet grinding was produced by the centerless grinding of pressed and sintered fuel pellets. The pellets were sintered at 1750°C in a reducing atmosphere to form the substoichiometric oxide shown. This material will be referred to as "HEDL 1750°." The particle size distribution characteristics of each aerosol generated from these powders were similar to those measured at the industrial sites. A discussion of this similarity in aerosol particle size distributions and the relationship to lung deposition patterns was given in the previous Annual Progress Report.⁴

METHODS

A mixture of 250 mg desiccated KBr and 0.2 mg mixed-oxide bulk powder was made by grinding in a mortar and pestle in a glove box. Specimens of aerosolized materials were prepared in a similar manner. The particulates which had been deposited on membrane filters during animal inhalation exposures were scraped from the filter material using a glass slide. A correction for the contribution of removed filter material to the infrared spectrum was made using the spectrum of pure filter material. Infrared spectra were measured using a Perkin-Elmer Model 621 grating spectrophotometer. Samples were stored with desiccant in sealed jars.

RESULTS AND DISCUSSION

Representative infrared spectra of the bulk materials analyzed are shown in Figures 1 and 2. The spectrum of a specimen taken from the bulk powder of the B&W mixed-oxides with binders is shown in Figure 1. The broad, intense absorption in the $300\text{-}600\text{ cm}^{-1}$ region was assigned to the metal-oxygen (M-O) stretching frequencies of UO_2 and PuO_2 .⁵⁻⁷ The weak absorption bands at 920 cm^{-1} and 1380 cm^{-1} were assigned to species on the surface of the particles as will be discussed. All remaining bands in the spectrum were assigned to the Sterotex[®] and Carbowax[®] binders added to the mixed-oxide powders to facilitate the pellet pressing operation by comparisons with spectra of pure binders. The spectrum shown in Figure 2 is representative of all bulk materials listed in Table 1 which consist of mixed UO_2 and PuO_2 powders without binder material. The spectra are featureless in the region corresponding to the organic binder absorption. The spectra of all bulk powders contained no bands related to metal oxides other than those mentioned above.

Figure 2 shows the spectrum of the specimen of the HEDL 1750° powders. The most noteworthy difference between this spectrum and Figure 1 is the resolution of the M-O stretching band into two broad bands centered at $\approx 360\text{ cm}^{-1}$ and $\approx 550\text{ cm}^{-1}$. These bands have been assigned to the transverse optical and longitudinal optical resonances associated with the M-O stretching mode observed for both UO_2 and PuO_2 .^{6,7} The band at 1380 cm^{-1} was observed for this material as well as for the material shown in Figure 1. The spectrum of the HEDL 1750° was similar to that observed for the same type of powder obtained from the B&W facility.

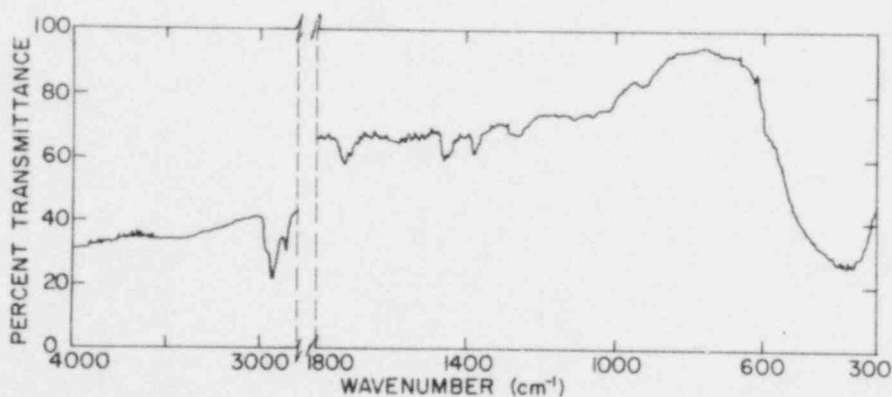


Figure 1. Infrared absorption spectrum of a bulk powder sample of PuO_2 heat-treated at 850°C and mixed with UO_2 and organic binders. Material was obtained from the pellet pressing operation at the Babcock and Wilcox Fuel Fabrication Facility,

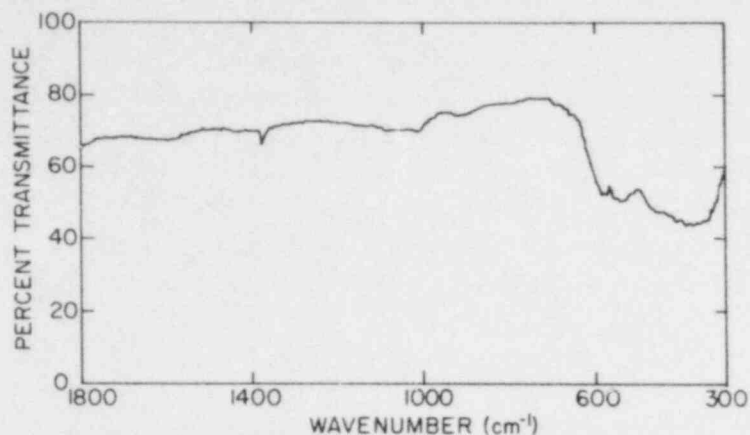


Figure 2. Infrared spectrum of powdered $(U,Pu)O_x$ produced by centerless grinding of fuel pellets which had been sintered at $1750^\circ C$ in a reducing atmosphere. Material was obtained from the Hanford Engineering and Development Laboratory, Richland, WA.

Figure 3 shows the spectrum from particulates collected from an aerosol generated from the HEDL 750° powder. This spectrum also contains the broad, intense band of the M-O stretching frequency. Additional bands were observed at 845 cm^{-1} , 920 cm^{-1} , 1380 cm^{-1} , 1550 cm^{-1} , and 1650 cm^{-1} . The broad band centered near 3400 cm^{-1} is commonly associated with water absorbed from the atmosphere by KBr. However, this absorption band was more intense in the spectra of the bulk powders than in the spectrum of pure KBr. This band has, therefore, been assigned to H_2O associated with a polymeric form of plutonium of the general form $[(HO)_{n-1}Pu-O-Pu(OH)_{n-1}]^{8-2n}$. The other bands in Figure 3 were assigned to either CO_3^{2-} or H_2O adsorbed on the surface of the aerosol particles by comparisons of the spectrum with those of the polymeric species and the spectra of other metal-carbonate surface species.^{8,9}

The spectrum shown in Figure 3 is representative of spectra of other aerosolized particulates studied. However, comparison of these spectra revealed slight variations in the positions and relative intensities of the bands. In general, the bands in other spectra between 800 and 1000 cm^{-1} were of the same frequency but were less intense. The bands between 1300 and 1800 cm^{-1} and in the 3500 cm^{-1} region were observed at approximately the same frequencies (within 30 cm^{-1}) with similar or lesser intensities. The reduced intensities of bands observed for some other samples were the result of the small masses of sample collected. Generation of more concentrated aerosols of industrial powders for further infrared studies is in progress.

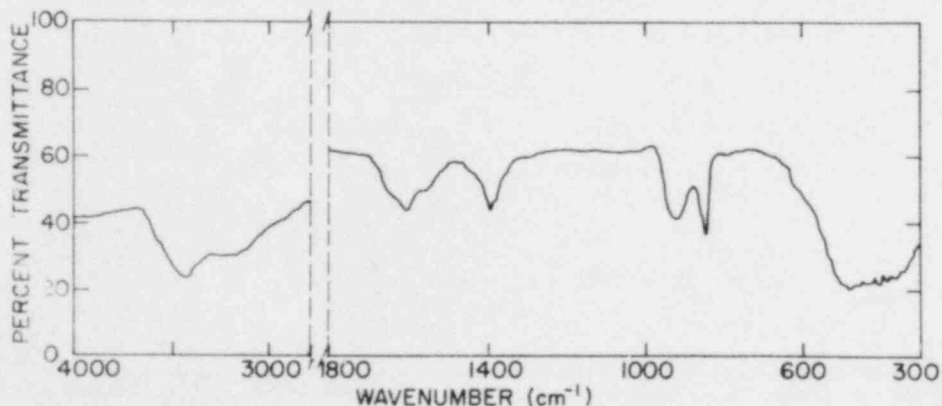


Figure 3. Infrared absorption spectrum of an aerosol of mixed PuO_2 and UO_2 powders used in the inhalation exposure of laboratory animals. Aerosol was generated from a powder of $750^\circ C$ heat-treated PuO_2 mixed with UO_2 and ball milled at the Hanford Engineering and Development Laboratory, Richland, WA.

The most notable result of the infrared analysis of these industrial materials was obtained by comparisons of the spectra of bulk powders and of particles collected from aerosols generated from the same powder. In addition to the low energy M-O stretching bands observed in the spectra of aerosol particulates, additional bands were found which were assigned to resonances of H_2O and CO_3^{2-} species adsorbed on the surface of the particles. These bands were of variable intensity for each material. The bands assigned to surface adsorbed species in the spectra of aerosol particulates were also observed in some spectra of bulk powders as weak bands.

The greater intensity of these adsorbed molecules in the spectra of aerosol particles was probably a result of the greater specific surface area of the more finely divided particles. The absorption band at 845 cm^{-1} corresponds to the out-of-plane bending (ν_2) mode of the CO_3^{2-} ion. The bands at 1380 cm^{-1} and 1550 cm^{-1} are assigned to the doubly degenerate asymmetric stretching (ν_3) mode of CO_3^{2-} , which was split upon surface adsorption. The degree of splitting of the degeneracy is related to the degree of covalency of the bond between the adsorbed CO_3^{2-} and the substrate. Accordingly, the infrared band at 1650 cm^{-1} was assigned to the same vibrational mode of a more strongly adsorbed carbonate species. The infrared bands observed in the 1300 to 1650 cm^{-1} region shown in Figure 3 are consistent with either bidentate structure for chemisorbed CO_3^{2-} shown in Figure 4. Absorption bands observed at ≈ 1050 and $\approx 1200\text{ cm}^{-1}$ in spectra of other aerosols suggest the presence of a monodentate species in addition to these bidentate forms.

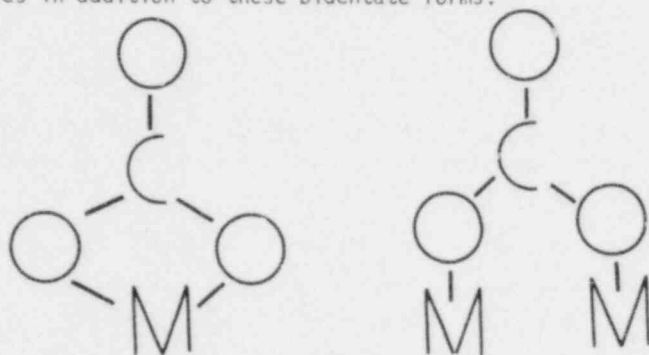


Figure 4. Two possible modes of binding for bidentate CO_3^{2-} chemisorbed on the surface of a metal oxide particle.

The bands shown in Figure 3 at 1600 and 830 cm^{-1} could not be assigned unambiguously. These bands were within the range of values observed for the bidentate carbonate species shown in Figure 4. However, the bending vibration mode (ν_2) of H_2O that occurs at 1595 cm^{-1} has been observed in the polymeric form of $Pu(OH)_n$ discussed above.⁸ This band could be due to H_2O being chemisorbed onto the surface of the mixed-oxide industrial particulates. Since the broad band in the 3400 cm^{-1} region has been assigned to adsorbed or occluded H_2O , the 1600 cm^{-1} band must include a contribution of adsorbed H_2O independent of any contribution of CO_3^{2-} to the same band. The most prominent and well resolved example of the 830 cm^{-1} band observed at 830 cm^{-1} in the spectra of all aerosol particulates (Figure 3) might have been assigned to an ionic or very weakly covalent monodentate form of adsorbed CO_3^{2-} . However, the band at 920 cm^{-1} indicates the presence of UO_3^5 or UO_2^{2+} on the UO_2 particles in the mixture.¹⁰ The intensity of this band suggests the formation of a uranyl carbonate species similar to the $UO_2(CO_3)_2$ ion that absorbs at 856 cm^{-1} .¹⁰

The partially hydrated surface layer containing adsorbed carbonates of the general form shown in Figure 4 and the possibility of a surface layer of UO_3 on the mixed oxide particles were not detected by X-ray diffraction measurements. This was probably the result of several contributing factors; (1) the mass of the surface layer was probably less than the detection limit ($\approx 0.5\%$) for

one crystalline phase in the presence of another by X-ray diffraction, (2) the close similarity in the crystallographic properties of PuO_2 and the most probable surface species⁸ and (3) the amorphous nature of the surface UO_3 which has been observed on UO_2 particles stored in air at 25°C.¹¹

The profile of the low frequency M-O stretching band in the 300 to 600 cm^{-1} region could not be correlated with the process stage of the powders with certainty. The apparent resolution of the M-O stretching band in the spectra of powders produced by the centerless grinding of fuel pellets was not sufficient to identify the powder as a product of the centerless grinding process. The assignment of the two components of the M-O stretching band to the transverse optical and longitudinal optical components has been made for pure UO_2 and the resolution of the band has been related to the stoichiometry of uranium compounds ranging from UO_2 to U_3O_8 .⁸ The greatest resolution was observed for UO_2 , the compound with the smallest oxygen-to-metal ratio.

An hypothesis based on an extrapolation of this trend to the $\text{MO}_{1.96}$ stoichiometry of sintered fuel pellets cannot be supported, however. It was noted⁶ that the assignment of these bands according to this theoretical model is uncertain when the specimen under study is a fine powder containing particles similar in size to the wavelength of the incident radiation ($\approx 20 \mu\text{m}$ for this absorption band). The effect of particle size and shape was observed to cause a broadening of the absorption band profile. All bulk powders listed in Table 1 could contain particles in the 20 μm size range, except those obtained from the ball milling and pellet pressing steps. These powders had been subjected to powder comminution steps to reduce the maximum particle size to 2 to 5 μm . Comparisons of the spectra of all bulk powders in the 300 cm^{-1} to 600 cm^{-1} region do not allow the identification of these two powders as unique with respect to particle size. Thus, the interpretation of the intense low energy infrared band should be limited to the confirmation of the presence of metal oxides in the specimen.

A determination of the relative amounts of organic binders and mixed actinide oxides in the bulk powder obtained from the pellet pressing operation was attempted. The spectrum shown in Figure 2 was compared with spectra of known mixtures of UO_2 , Sterotex, and Carbowax. It was found that the binders contained primarily Sterotex. The mass of Carbowax was relatively small, making a quantitative analysis by infrared spectroscopy uncertain. The relative intensities of the M-O band at 300 to 600 cm^{-1} and the Sterotex bands near 2900 cm^{-1} were used to estimate the amount of Sterotex present. This estimation proved to be highly uncertain as a result of the unknown effect of the particle size distribution of the commercial UO_2 powder used on the width of the U-O band and the possible contribution of a broad Sterotex absorption band centered at 600 cm^{-1} which overlapped the M-O band.

CONCLUSIONS

The primary conclusion made from these infrared studies is that the surfaces of particulates in aerosols that might be inhaled by a worker in a fuel fabrication facility contained adsorbed H_2O and CO_3^{2-} and probably exist in chemical forms representative of partial oxidation and hydrolysis of the metal oxides. The precise nature and geometry of binding of the surface species were not clear from the results available. The major significance of the presence of an oxidized or hydrated surface layer lies in the solubility of the inhaled particles. The rapid initial dissolution phase of aerosol particulates observed *in vitro*¹² (to be discussed in the following paper) might be the result of solvation of the partly hydrolyzed forms of PuO_2 and UO_2 . It is probable that this rapid initial dissolution would also occur in lung fluid.

A further conclusion based on these results relates to the chemical form of particulates in aerosols of the HEDL 1750° material generated from substoichiometric sintered fuel pellets. Although the fuel pellets and presumably powders ground from them consist of a solid solution of

(U,Pu) $O_{1.96}$, the presence of a partly hydrolyzed surface layer and the solubility of oxygen in uranium oxides⁶ suggest that the surfaces of aerosol particles probably consist of a partly hydrolyzed solid solution of (U,Pu) O_2 . This would indicate partial or complete reversal of the reduction that occurred during the pellet sintering step.

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IN VITRO SOLUBILITY OF AEROSOLS OF INDUSTRIAL URANIUM AND
PLUTONIUM MIXED-OXIDE NUCLEAR FUEL MATERIALS

ABSTRACT

In vivo solubility is an important property of mixed-oxide nuclear fuels for prediction of biological behavior of inhaled aerosols. Studies of the dissolution of Pu, Am and U from four nuclear fuel materials in 0.1 M HCl, 2 M HNO₃ and a serum simulant solution are described. The combined results of these studies showed that: (1) dissolution occurred at a rapid rate initially and slowed at longer times, (2) greater percentages of U dissolved than Pu or Am, (3) the U dissolution rate from all materials except that produced by pellet grinding was faster than the Pu dissolution rate and (4) the dissolution rates of U and Pu generally reflected the physical composition of the UO₂-PuO₂ matrix. The implications of these results for interpretation of the biological behavior of inhaled mixed-oxide aerosols are discussed.

PRINCIPAL INVESTIGATOR

A. F. Eidson

INTRODUCTION

In vivo solubility is an important physical property of mixed UO₂ and PuO₂ fuel materials in determining the biological fate of inhaled aerosols. Insoluble particles generally are cleared from the lung by mechanical clearance mechanisms and excreted via the gastrointestinal tract. Some insoluble particles are also cleared from lung to the tracheobronchial lymph nodes. Solubilization of particles remaining in lung determines the quantities of uranium or plutonium available for deposition in liver and bone tissue or for chelation therapy.

One objective of the *in vitro* solubility studies described here is to provide data from studies lasting 30 to 60 days which might be used to predict the biological fate of inhaled actinide oxides over a longer period of time. Another objective is to allow a correlation of solubility with results of other physical and chemical analyses discussed earlier in this report and in the previous Annual Progress Report.¹ These solubility studies, then, represent a key step of the entire project; that of predicting the biological fate of inhaled industrial aerosols based on their physical properties.

To achieve these objectives, a series of *in vitro* solubility experiments were conducted concurrently with inhalation experiments using rats, dogs and monkeys described later in this report. Aerosols collected during the inhalation exposure of laboratory animals were subjected to dissolution in three solvents. The three solvents used in these dissolution studies were 2 M HNO₃, 0.1 M HCl and a salt solution designed to simulate blood serum ultrafiltrate (SUF). The SUF formulation was designed to simulate the composition of blood serum and to provide a comparison with studies of a plutonium aerosol released under accident conditions.² A chelating agent, diethylenetriamine-pentaacetic acid (DTPA) was added to prevent precipitation of dissolved plutonium ions in the experimental apparatus. Nitric acid was used as a solvent since the actinide dioxides under consideration are known to be quite insoluble. The nitric acid was able to cause appreciable amounts of each actinide to be dissolved in a short period of time. The use of 0.1 M HCl provides a comparison in a common solvent³ between the dissolution rate of industrial mixed oxides and those produced in the laboratory.

MATERIALS AND METHODS

Table 1

The mixed oxides studied were the same as those described in detail in the previous paper in this report (pp. 11-18). The mineral acids used were ACS grade reagents obtained from the Fischer Scientific Company. No further preparation was performed. The composition of the SUF solvent is detailed in Table 1. All constituents were reagent grade.

Particulates of each aerosol used in the exposure of laboratory animals were collected by a membrane filter. A segment of this filter was cut and placed on a Millipore[®] membrane filter (0.1 μ m pore size) and a second filter of identical type was placed over the sample. The filter sandwich containing the specimen was secured by compression of an O-ring near the periphery by a circular teflon clamp. This assembly was then placed in 200 ml of solvent.³ This *in vitro* system allowed for retention of particulates between the two filters while allowing free diffusion of the solvent and solute. The same assembly was used for all studies except those using SUF as a solvent in which the aerosol specimen was sandwiched between two Nucleopore[®] membrane filters of 0.1 μ m pore size.

The solvent was changed every hour for the first 6 hours. Beyond this time, the solvent was changed periodically throughout the experiment. The duration of experiments using 0.1 M HCl and SUF as solvents was 30 days. The experiments in 2 M HNO₃ lasted 60 days.

Radiochemical Analysis

The 200 ml portions of each solvent collected during the experiments were analyzed for Pu, Am and U. Solutions of 2 M HNO₃ were used directly for analysis without pretreatment. Aliquots of 0.1 M HCl solutions were adjusted to 2 M with nitric acid and used for further analysis. Pretreatment of SUF solutions was found to be necessary as a result of the interference of DTPA and other salts in the solution with the separation of Pu and Am by solvent extraction. The analytical procedures used were similar to those developed for the analysis of Pu, Am and U in biological samples.⁴ Since these procedures have been described in detail, only a brief description will be given here.

The 200 ml SUF solution was evaporated to dryness at 90°C in an oven. The residue was heated to 500°C in a muffle furnace for 8 hours, wet-ashed with concentrated HNO₃ and 30% H₂O₂ and evaporated to dryness. The residue was again heated in a muffle furnace at 500°C for 8 hours, removed from the furnace and allowed to cool to room temperature. Twenty-five ml of 3 M HF in concentrated HNO₃ was added and the mixture was heated to dryness on a heating plate at 180°C. Two ml of an aqueous solution of 0.2 M H₃BO₃ was added to the residue along with 100 ml 2 M HNO₃. The solution was heated at 180°C until clear. The solution was allowed to cool and the volume was adjusted to 120 ml with 2 M HNO₃. This procedure was also used to analyze the filter sandwich containing the undissolved fraction of the particulates.

Composition of Simulated Serum Ultrafiltrate (SUF) Used to Study the Dissolution of Industrial Mixed Uranium, Plutonium Oxides (pH = 7.6)

Salt	Molar Concentration
NaCl	0.116
NH ₄ Cl	0.010
NaHCO ₃	0.27
Glycine	0.005
Na ₃ Citrate	0.0002
CaCl ₂	0.0002
L-cysteine	0.001
H ₂ SO ₄	0.0005
Na ₂ HPO ₄	0.0012
DTPA ^a	0.0002
ABAC ^b	5 x 10 ⁻⁵ %

^aDiethylenetriaminepentaacetic acid, not present in blood serum.

^bAlkylbenzylidimethylammonium chloride added as an antibacterial agent.

Uranium Determination

An aliquot of the sample in dissolved nitric acid was used directly for the determination of total uranium by fluorimetry. No separation of U from Pu or Am was necessary since Pu is not fluorescent in any oxidation state and Am is known to be present in negligible amounts by mass.¹

Analysis for total uranium content of each solvent sample and the undissolved material remaining in the filter sandwich was accomplished by fluorimetry after fusion of an aliquot in a 2% LiF-98% NaF salt mixture.⁵ Fluorescence intensity was measured using a Jarrel-Ash Model 2600 reflex fluorimeter calibrated with a standard solution of U_3O_8 . Appropriate standard solutions and blank samples were employed to ensure the accuracy and precision of the uranium determinations.

Plutonium and Americium Alpha Activity Determination

Separation of Pu and Am was achieved by extraction of an aliquot of the nitric acid solution with an extractant scintillation solution.⁵ The D_2EHPA in the cocktail specifically extracts > 99% of the Pu (IV) and U into the organic phase upon shaking.⁶

Plutonium and americium activities were determined by liquid scintillation. The Pu and U dissolved in the organic extractant phase was counted in a Packard Tri-Carb liquid scintillation counter, using the total Pu alpha activity counting mode with a counting efficiency of 98%. The average blank background observed for Pu was 22.0 ± 0.1 cpm. The alpha activity of U was insignificant in comparison to that of Pu, although the mass of U was known to be greater than that of Pu.¹ This was the result of the fact that only natural or depleted uranium was used in these mixed oxides designed for use in breeder reactors.

Americium alpha activity was determined in a manner similar to that used for plutonium. An aliquot of the aqueous phase from which Pu had been extracted quantitatively was shaken with Aquasol[®] in a liquid scintillation counting vial until a gel was obtained. The ^{241}Am activity was determined using the same liquid scintillation counter adjusted for optimal detection of ^{241}Am . The counting efficiency was 98%. The average blank background observed for ^{241}Am was 36.9 ± 0.3 cpm.

Calculations

The initial quantity of Pu, Am and U present on the filter segment was determined by summing the total amount of each isotope in each solvent sample plus the quantity measured in the filter sandwich at the conclusion of the study according to equation (1).

$$A_i = A_f + \sum_{j=1}^n A_j \quad (1)$$

The initial amount of actinide is A_i ; A_j is the amount of actinide determined in each solvent sample in the same units, A_f is the amount of actinide in the filter sandwich at the conclusion of the experiment and n is the total number of times the solvent was changed during the experiment. Quantities of A were expressed as nCi alpha activity for $^{238,239,240}Pu$ and ^{241}Am isotopes¹ or as μg U. The observed fraction undissolved (F_{obs}) was expressed as a percentage of the initial quantity, A_i , and was calculated by equation (2).

$$\% F_{obs_j} = \frac{A_i - \sum_{j=1}^n A_j}{A_i} \times 100 \quad (2)$$

The values of $\% F_{obs_i}$ were plotted versus time. A negative exponential equation was fitted to the data using a non-linear, least squares technique. The fitted curve was of the form

$$\% F_{calc} = \alpha_1 e^{-\lambda_1 t} + \alpha_2 e^{-\lambda_2 t} + \dots + \alpha_n e^{-\lambda_n t} \quad (3)$$

where F_{calc} is the calculated fraction undissolved at elapsed time (t) in hours. The percentages of the total sample dissolved, α_1 , and the corresponding dissolution rate constants, λ_1 , associated with each component of the fitted curves were obtained. The fitted curves (Eq. 3) λ_1 were evaluated at $\alpha_1 t = 0$ hours to check the predicted initial percentages versus the true value (100%). The mean of the predicted initial percentage for all curves was $98.8 \pm 1.2\%$.

Representative graphs of the rate of Pu and Am dissolution in 0.1M HCl from an aerosol generated during the grinding of fuel pellets are shown in Figure 1 to illustrate the interpretation of the results of these calculations. The two component fitted function calculated for Pu dissolution according to equations (1)-(3) was

$$\% F_{calc} = 3e^{-2.0 \times 10^{-1}t} + 97e^{-3.3 \times 10^{-5}t} \quad (4)$$

The precision of the data is indicated by the range of values from duplicate experiments. The exponents shown in equation (4) correspond to dissolution half-times of 3.5 hours and 880 days. Therefore, the curve represents the dissolution of 3% of the Pu initially present with a half-time of 3.5 hours followed by the dissolution of 97% with a half-time of 880 days.

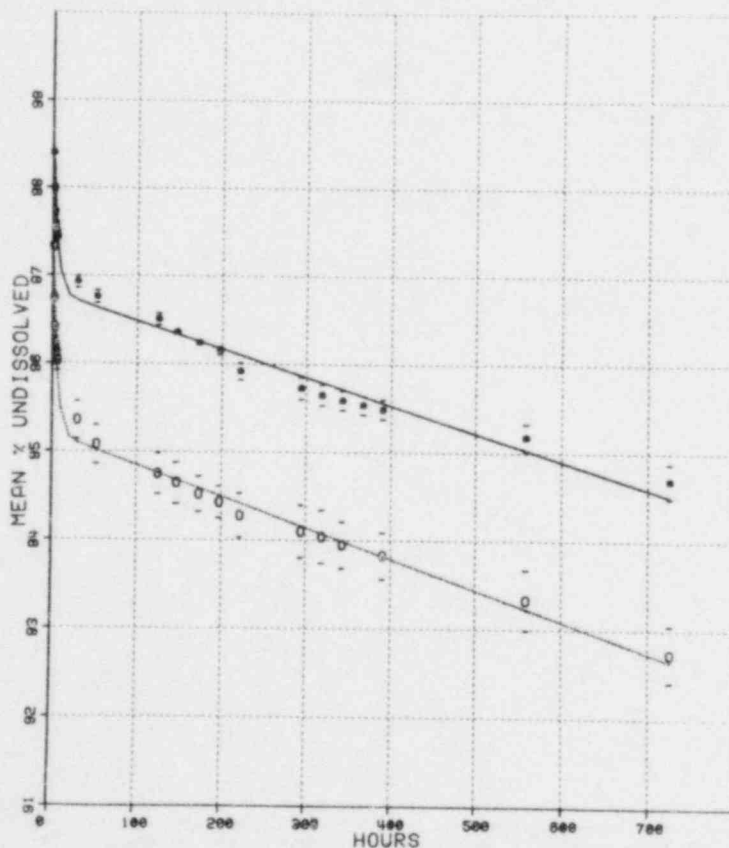


Figure 1. Dissolution of Pu (*) and Am (o) from aerosol samples of 1750°C heat-treated mixed uranium-plutonium oxides in 0.1 M HCl. Mean and range of measurements from duplicate experiments are indicated.

RESULTS AND DISCUSSION

Results of calculations using equations (1) to (3) from studies conducted in three solvents; the serum simulant solution (SUF), 0.1 M HCl and 2 M HNO₃ are summarized in Tables 2 to 4. The precision of calculated values was determined from duplicate experiments conducted in both 0.1 M HCl and SUF. The precision of values reported from 2 M HNO₃ studies was derived from four replicate experiments. The precision was found to be lowest for very rapid and very slow dissolution. This is illustrated by Figure 1 and the tables. The precision of Pu and Am measurements as reflected by the range of values shown in the figure limits the precision of the fitted slope. The precisions of calculated half-times of the very rapid dissolution which occurred within the first 6 hours of the study were determined to be ± 0.01 day in 0.1 M HCl and 0.3 day in 2 M HNO₃. Such high precision was artifactual and the 0.3 day value shown in the table is the more reliable one, as estimated from the frequency of measurement. Since the sampling frequency during this portion of the experiment was one change of solvent per hour, the lower limit of precision for the dissolution half-time is 0.1 day (2.4 hour). At this sampling frequency, 2.4 measurements per half-time of 0.1 day can be obtained. In the case of more rapid dissolution, where two or fewer measurements per half-time were obtained (Table 3), greater precision was not warranted. Thus, the limit of precision of dissolution half-time values in these experiments was estimated to be ± 0.1 day.

Table 2

Dissolution *In Vitro* of Industrial Mixed Uranium and Plutonium Oxide Fuel Materials in Synthetic Serum Ultrafiltrate Solution Containing DTPA^a

Composition, Temperature History, Process Step, Source	Nuclide	Dissolution Component ^b			
		I		II	
		α_1 (%)	$T_{1/2}$ (days)	α_2 (%)	$T_{1/2}$ (days)
PuO ₂ , 850°C V-Blending, B&W ^c	Pu ^d	e	e	100 ± 0.1	20000 ± 9000
	Am ^d	e	e	99.6 ± 0.2	6100 ± 900
PuO ₂ + UO ₂ , 750°C, Ball Milling, HEDL ^f	Pu	0.3	1.4	99.6	15000
	Am	1.7	1.2	98.0	20000
	U	33	1.6	62.7	400
PuO ₂ + UO ₂ + Binders, 850°C Pellet Pressing, B&W ^c	Pu	0.1	0.8	99.9	21000
	Am	0.3	0.7	99.4	5400
	U	22	1.7	74.5	300
(Pu,U)O _x , 1750°C, Pellet Grinding, HEDL ^f	Pu	4.6	1.5	95.4	29000
	Am	5.4	0.8	93.3	8300
	U	23	0.8	74.3	11000

^aDiethylenetriaminepentaacetic acid, not present in blood serum.

^bTwo component exponential dissolution equation of the form

$$\% \text{ Undissolved} = \alpha_1 e^{-\lambda_1 t} + \alpha_2 e^{-\lambda_2 t}$$

^cBabcock & Wilcox Fuel Fabrication Facility, Apollo, PA.

^dMean ± standard deviation of values from duplicate experiments.

^eOnly single component observed.

^fHanford Engineering and Development Laboratory, Richland, WA.

Table 3

Dissolution *In Vitro* of Industrial Mixed Uranium and Plutonium Oxide Fuel Materials in 0.1 M HCl

Composition, Temperature History, Process Step, Source	Nuclide	Dissolution Component ^a			
		I		II	
		α_1 (%)	$T_{1/2} \pm 0.3$ (days)	α_2 (%)	$T_{1/2}$ (days)
PuO ₂ , 850°C, V-Blending, B&W ^b	Pu	0.1	0.1	99.9	12000
	Am	0.1	0.2	99.6	5100
PuO ₂ + UO ₂ , 750°C, Ball Milling, HEDL ^c	Pu	0.5	0.1	99.6	1300
	Am	0.5	0.1	96.0	2800
	U	6.3	0.1	90	85
PuO ₂ + UO ₂ + Binders, 850°C, Pellet Pressing, B&W ^b	Pu	0.2	0.2	99.7	6700
	Am	0.4	0.1	99.2	6100
	U	24	0.2	77	130
(Pu,U)O _x , 1750°C, Pellet Grinding, HEDL ^c	Pu ^d	1.9 ± 0.3	0.1 ± 0.1	96.8 ± 0.1	880 ± 90
	Am	1.5 ± 0.3	0.1 ± 0.3	95.2 ± 0.3	770 ± 60
	U ^d	3.4 ± 0.3	0.2 ± 0.1	91 ± 1	360 ± 90

^aTwo component exponential dissolution equation of the form

$$\% \text{ Undissolved} = \alpha_1 e^{-\lambda_1 t} + \alpha_2 e^{-\lambda_2 t}$$

^bBabcock & Wilcox Fuel Fabrication Facility, Apollo, PA.^cHanford Engineering and Development Laboratory, Richland, WA.^dMean ± standard deviation of values from duplicate experiments.

In the case of extremely slow dissolution, the precision of calculated half-times was determined by the detection limit and precision of the analytical method for the particular element. As shown in Figure 1, the variability in the fitted line would become greater as the slope approaches zero. Thus, the precision of a dissolution half-time of greater than 1000 days based on measurements during a 30 to 60 day period would be expected to be low. Results of duplicate studies of dissolution of Pu and Am from PuO₂ in SUF (Table 3) indicate that the precision of dissolution half-times greater than 1000 days was approximately 50%. The precision of calculated half-time values in the 10 to 1000 day range was approximately 15% (Tables 3 and 4) and in the 1 to 10 day range was found to be approximately 20% (Table 4). A statistical treatment of these data has been designed to provide more refined estimates of the relationships between the frequency and precision of measurement on the calculated dissolution half-times is in progress. The results of this statistical treatment will be discussed when they are completed.

Table 4

Dissolution *In Vitro* of Industrial Mixed Uranium and Plutonium Oxide Fuel Materials in 2 M HNO₃

Composition, Temperature History, Process Step, Source	Nuclide	Dissolution Component ^a			
		I		II	
		α_1 (%)	$T_{1/2}$ (days)	α_1 (%)	$T_{1/2}$ (days)
PuO ₂ , 850°C, V-Blending, B&W ^b	Pu	0.5	1.4	99	2600
	Am	1.2	1.4	99	2500
PuO ₂ + UO ₂ , 750°C, Ball Milling, HEDL ^c	Pu	1	0.5	98	95
	Am	4	1.4	95	130
	U ^d	46	e	54	26
PuO ₂ + UO ₂ , + Binders, 850°C, Pellet Pressing, B&W ^b	Pu	1	1.0	99	420
	Am	1	1.7	98	660
	U ^d	22	0.1	81	25
(Pu,U)O ₂ , 1750°C, Pellet Grinding, HEDL ^c	Pu ^f	13 ± 1	1.6 ± 0.3	80 ± 2	72 ± 7
	Am ^f	23 ± 2	1.8 ± 0.3	72 ± 2	70 ± 10
	U ^{d, f}	18 ± 1	0.2 ± 0.3	84 ± 3	25 ± 3

^aTwo-component exponential dissolution equation of the form

$$\% \text{ Undissolved} = \alpha_1 e^{-\lambda_1 t} + \alpha_2 e^{-\lambda_2 t}$$

^bBabcock & Wilcox Fuel Fabrication Facility, Apollo, PA.^cHanford Engineering & Development Laboratory, Richland, WA.^dUranium dissolution did not exhibit exponential dissolution during entire study, values estimated from data obtained during first 100 hours of the study.^eVery rapid, estimated to be < 0.01 days.^fMean ± standard deviations of values calculated from four replicated experiments.

The origin of the rapid initial dissolution phase is probably related to several properties of the aerosol: (1) particle size distribution; (2) specific surface area and (3) surface composition. Polydisperse aerosols which contained a fraction of small particles would be expected to dissolve more rapidly initially until the smaller particles were completely dissolved. This factor was probably not a major one, since similar rapid initial dissolution rates have been observed for monodisperse ²³⁹PuO₂ aerosols as well. Similarly, an aerosol composed of particulates having a rough surface would be expected to dissolve rapidly until the surfaces of the particles were smoothed. The third and possibly most important factor, was discussed in the previous paper in this report in relation to the infrared and surface analysis results which suggested the presence of a partially hydrated surface layer formed by the adsorption of atmospheric water and carbon dioxide on the surfaces of particulates.

The relative dissolution properties of Pu, Am and U for one material are illustrated in Figure 2. The major fraction of Pu and Am (Table 3) dissolved with a half-time of 6000 to 7000 days while 77% of the U dissolved with a half-time of 130 days. The similarity in Pu and Am dissolution rates reflects the fact that Pu and Am are incorporated within the same crystalline matrix.¹ The mass

contribution of AmO_2 to this matrix in all materials studied was 0.1% to 0.5%. Under these conditions, the dissolution rate of AmO_2 was governed by the dissolution rate of PuO_2 as the major constituent in the crystalline phase. This similarity in long term dissolution rates of Pu and Am was found to hold true in general within the limits of precision discussed above. The major exceptions to this observation were the relative Pu and Am dissolution rates observed for both the B&W PuO_2 and the B&W mixed oxides with binders in the serum simulant solution (Table 2). A discussion of these exceptions must await a more refined statistical treatment of the significance of dissolution half-times greater than 10,000 days.

The dissolution behavior of uranium was found to be dependent on the nature of the mixed-oxide materials in all three solvents. A much greater percentage of uranium than plutonium or americium dissolved from the HEDL 1750° materials in the early dissolution component in all these solvents. Approximately 9% to 30% of the U dissolved during this time while only approximately 1 to 4% Pu and Am dissolved during the same time as shown in Tables 2 and 4 and Figure 2. During the slower dissolution phase, uranium dissolved much more rapidly than plutonium or americium in both 0.1M HCl and the serum simulant solution. The dissolution of uranium in 2 M HNO_3 at later times did not follow the exponential behavior shown in other solvents, particularly after nearly complete dissolution. This will be discussed separately. The dissolution behavior of Pu, Am and U in mixed oxides which were obtained from fabrication steps prior to sintering at 1750°C indicate that the UO_2 dissolved independently of the PuO_2 - AmO_2 matrix. This behavior is in agreement with the results of X-ray diffraction studies showing that these powders and aerosols consisted of admixtures of PuO_2 and UO_2 .¹

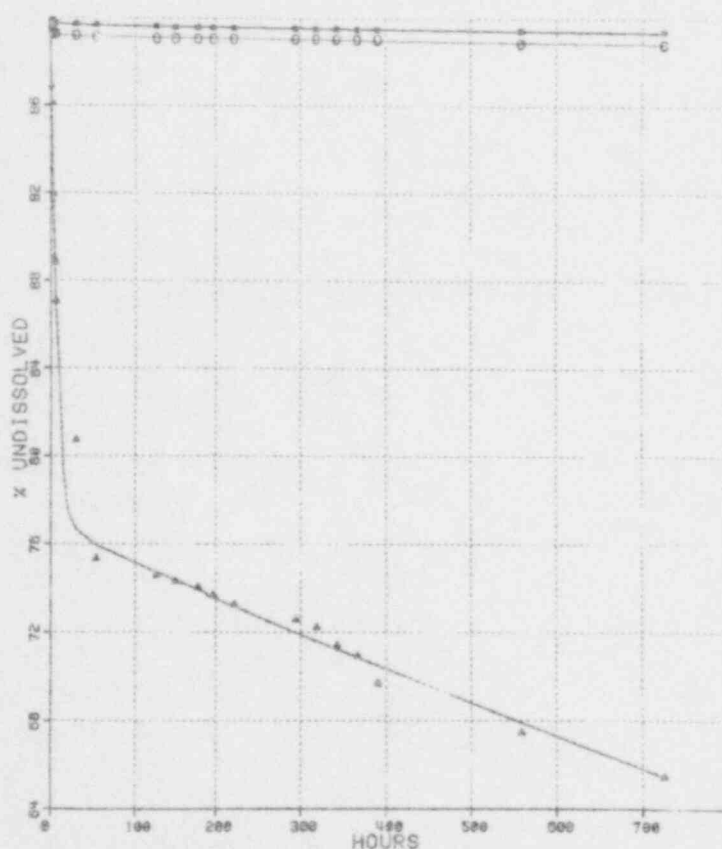


Figure 2. Comparison of rates of Pu, Am and U dissolution from aerosol samples of mixed PuO_2 and UO_2 containing organic binders in 0.1 M HCl. Pu (*), Am (o), U (Δ).

The HEDL 1750° material which had been sintered to form a solid solution of UO_2 and PuO_2 ¹ exhibited unique dissolution properties in all three solvents. The effect of this solid solution was to modify the dissolution behavior of both PuO_2 and UO_2 . Greater percentages of Pu and Am in this material were dissolved in the early dissolution component in all three solvents relative to values observed for other materials. Results indicate that, for the slower dissolution component, the dissolution rates for Pu and Am were unchanged in the serum simulant solution while that of U was decreased. The dissolution rates of Pu and Am were increased in 0.1 M HCl and 2 M HNO_3 while the U dissolution rate was decreased. These results indicate that in the solid solution, in which UO_2 represents 87% of the mass, the rate of Pu and Am dissolution in the slower component was governed by the more rapid dissolution of UO_2 from the matrix. At the same time, the dissolution rate of UO_2 was modified by the more slowly dissolving PuO_2 constituent. The one exception to this observation was observed in 2 M HNO_3 (Table 4) in which the dissolution half-time of uranium was the same for all materials within the precision of the measurements. These results support the hypothesis that the major component of the matrix (by mass) modified the dissolution rate of all other components with the rate of the major component slightly modified in turn.

One major objective of the use of three solvents in these *in vitro* studies was to provide data which could be used to predict the biological fate of the inhaled actinides. The dissolution rate curves of Pu and U contained in the industrial aerosols studied in the three solvents were compared. Plutonium and uranium were chosen for the comparison as a result of their quite different dissolution rates. Since the dissolution behavior of Am was shown to be similar to that of Pu and since the radiochemical analysis for Pu was more precise than that for Am, the dissolution rate of Pu was taken to be representative of both Pu and Am for these comparisons.

Figures 3 to 5 show the relative dissolution rates of Pu from the four fuel materials in common solvents. As shown in Figure 3, the HEDL 1750° material dissolved differently than the other materials in serum simulant solution. The early dissolution of this material was the primary cause of the unique behavior of this material in this solvent. Plutonium dissolved at similar rates from all four materials at later times within the precision of the measurements as discussed above. The three materials which consisted of PuO_2 without UO_2 or in an admixture with UO_2 dissolved similarly in this solvent. The slight difference in the profile of the 750°C heat-treated ball milled material noted in the figure represented only 0.2% difference in comparison to the percentage of Pu dissolved from the B&W materials during the same time. This difference is not expected to be biologically significant.

When 0.1 M HCl was used as a solvent, differences in dissolution behavior among the four materials were more apparent as shown in Figure 4. The Pu dissolution from aerosols of the solid solution of PuO_2 and UO_2 (HEDL 1750°) was again unique, particularly within the first 24 hours. At later times, the dissolution rate was slightly faster than that of the HEDL 750° material. Figure 5 shows the Pu dissolution curves measured for the four materials in 2 M HNO_3 . The dissolution rate constants of the materials were different within the first 200 hours of the experiment, while after 200 hours the dissolution rates of Pu from the HEDL 750° material and the HEDL 1750° material were similar. The use of both 0.1 M HCl and 2 M HNO_3 provides insights related to the correlation of material properties of one aerosol to relative Pu dissolution rates. However, the prediction of possible radiation dose patterns or modes of retention and translocation in laboratory animals or humans based on dissolution studies conducted in these solvents alone should not be made.

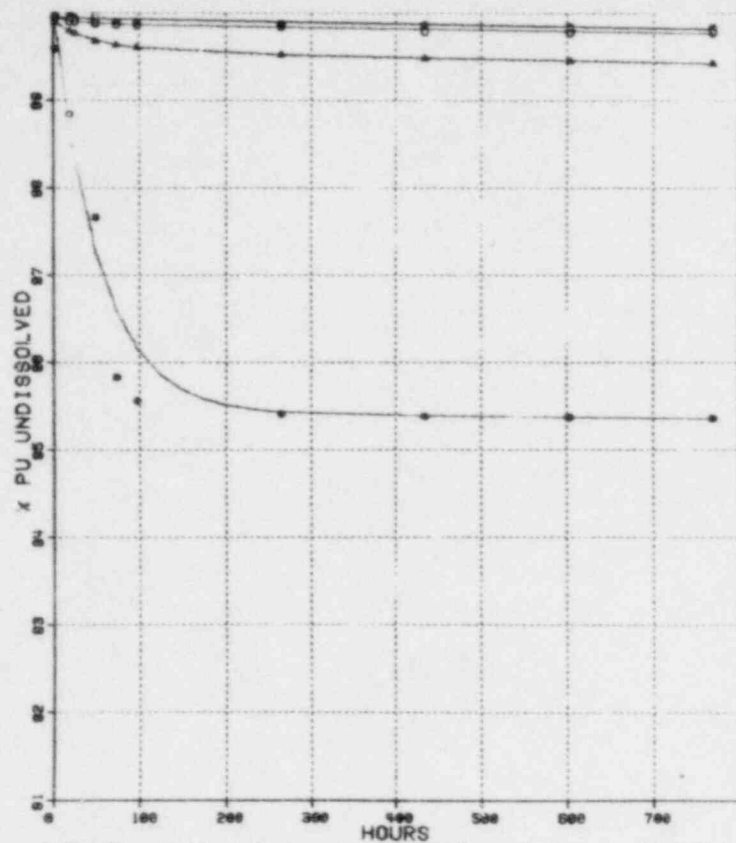


Figure 3. Comparison of Pu dissolution from aerosol samples of four industrial fuel materials in a serum simulant solution containing DTPA. B&W PuO_2 (*), B&W mixed oxides with binders (o), HEDL 750° (Δ), HEDL 1750° (\diamond).

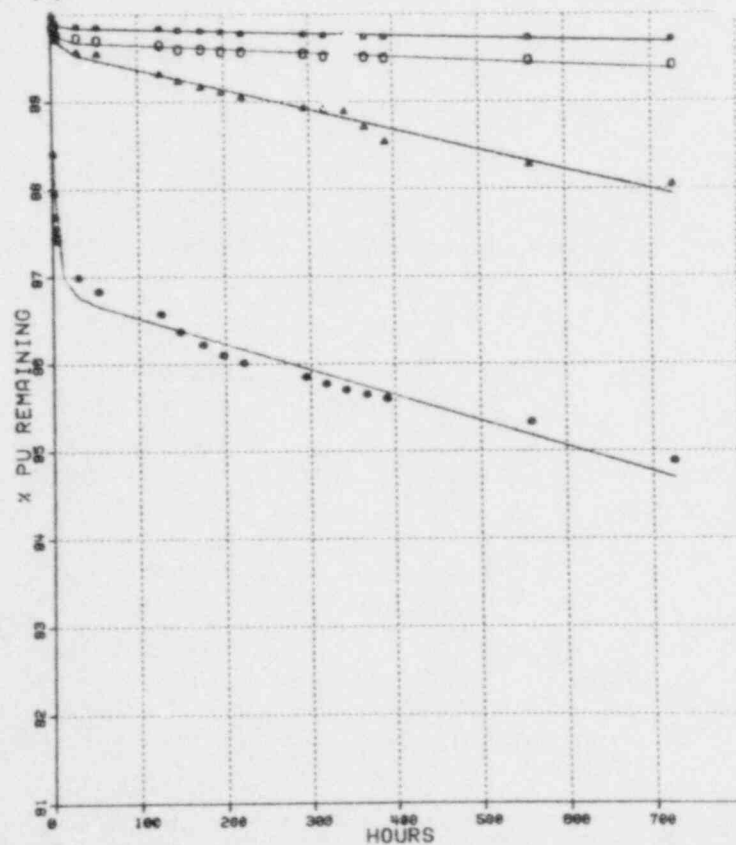


Figure 4. Comparison of Pu dissolution from aerosol samples of four industrial fuel materials in 0.1 M HCl. B&W PuO_2 (*), B&W mixed oxides with binders (o), HEDL 750° (Δ), HEDL 1750° (\diamond).

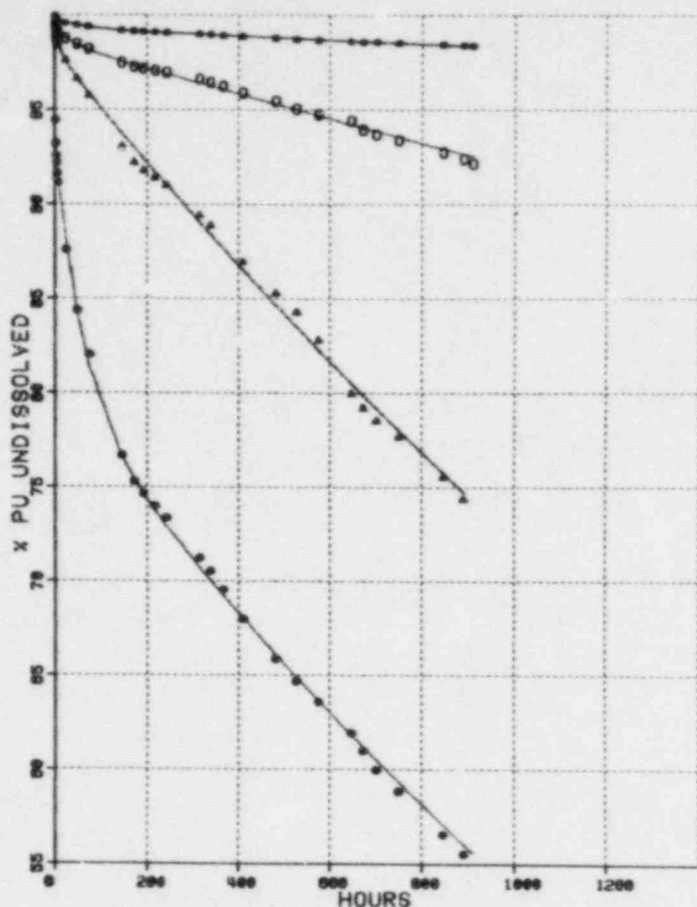


Figure 5. Comparison of Pu dissolution from aerosols of four industrial fuel materials in 2 M HNO_3 . B&W PuO_2 (*), B&W mixed oxides with binders (o), HEDL 750° (Δ), HEDL 1750° (\oplus).

Figures 6 to 8 show the dissolution behavior of uranium from the three materials which contained UO_2 . The plutonium and uranium dissolution profiles in SUF, shown in Figures 3 and 6, respectively, illustrate that larger percentages of U than Pu dissolved using this solvent. The rates observed after 200 hours for these materials illustrate that the dissolution of U from the solid solution matrix (HEDL 1750°) was retarded with respect to the two materials composed of mixed PuO_2 and UO_2 powders. The relative percentages and corresponding U dissolution rates of these mixed powders were similar. This observation supports the hypothesis that when PuO_2 and UO_2 were present as a single crystalline phase, the dissolution rate of U was changed from the dissolution rate of U in the pure UO_2 phase.

A similar observation may be made for the U dissolution curves determined in 0.1 M HCl as shown in Figure 7. Comparison of the dissolution rates at later times shows that the U dissolved from the two mixed-oxide materials at the same rate within the precision of the experiment and the rate was slightly retarded in the sample of the HEDL 1750° solid solution. Again, the Pu and U clearly dissolved independently in the PuO_2 and UO_2 admixtures (Figure 4 and Table 3) while the U and Pu dissolution rates were more consistent when dissolved from a solid solution.

The dissolution behavior of U in 2 M HNO_3 did not follow the exponential rate as described by equation (3) observed in other solvents during the course of the study. The profile of the curve did show a two-component exponential dissolution curve during the first 600 hours of the experiment. As the percentage of U remaining undissolved approached 40%, the dissolution rate accelerated such that uranium dissolution was nearly complete by 1400 hours. The values reported in Table 4 for the U dissolution rates from all materials were estimated using data from the first 200 hours of the experiment only. Calculations using equation (3) based on these estimated values, indicated that approximately 16% of the initial uranium would have remained undissolved at 1400 hours if dissolution followed an exponential rate law.

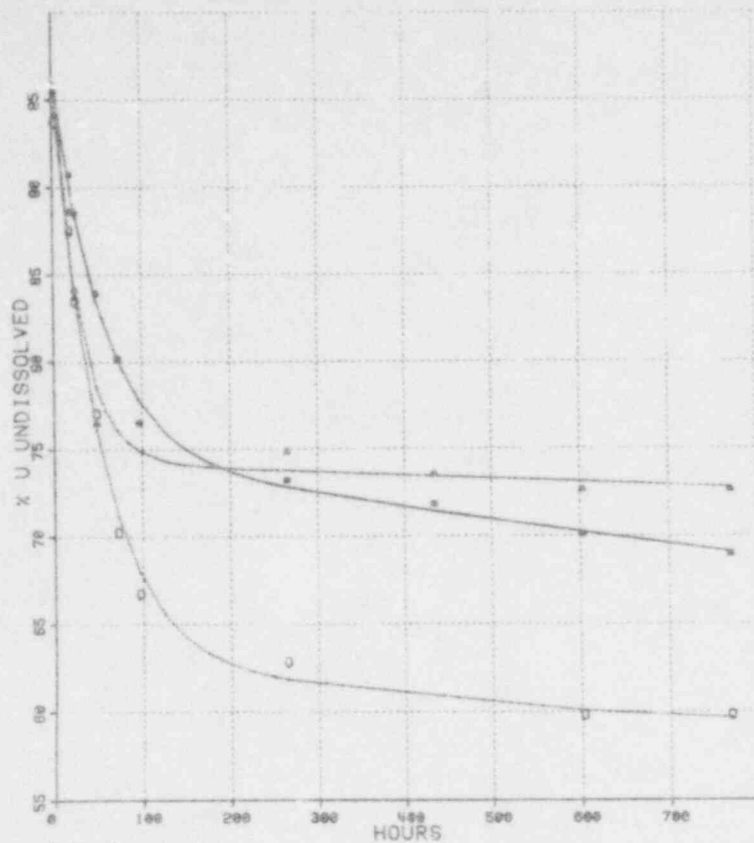


Figure 6. Comparison of U dissolution from aerosols of three industrial fuel materials in a serum simulant solution containing DTPA. B&W mixed oxides with binders (*), HEDL 750° (o), HEDL 1750° (Δ).

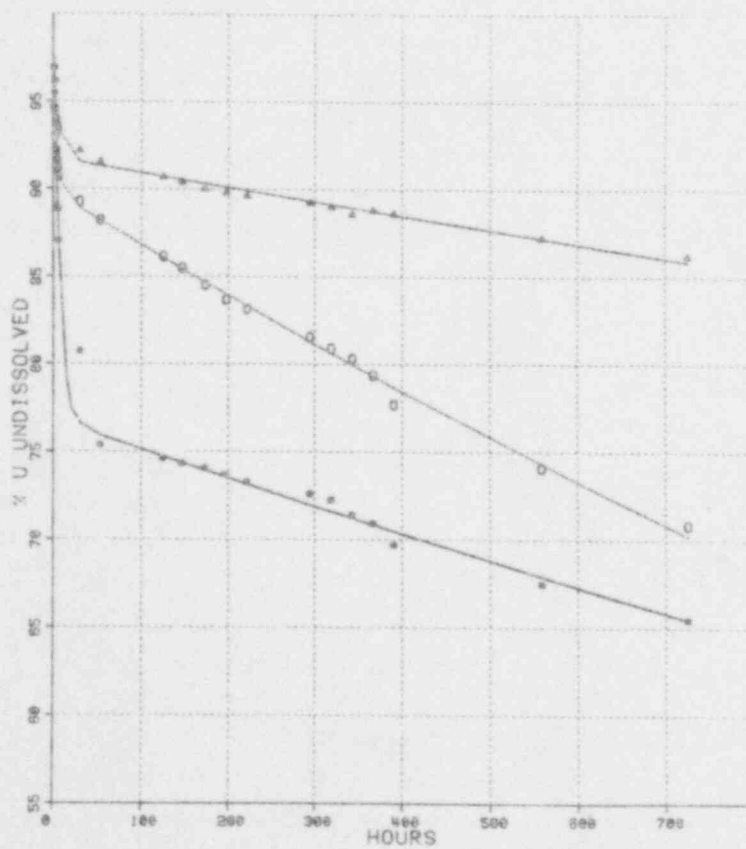


Figure 7. Comparison of U dissolution from aerosols of three industrial fuel materials in 0.1 M HCl. B&W mixed oxides with binders (*), HEDL 750° (o), HEDL 1750° (Δ).

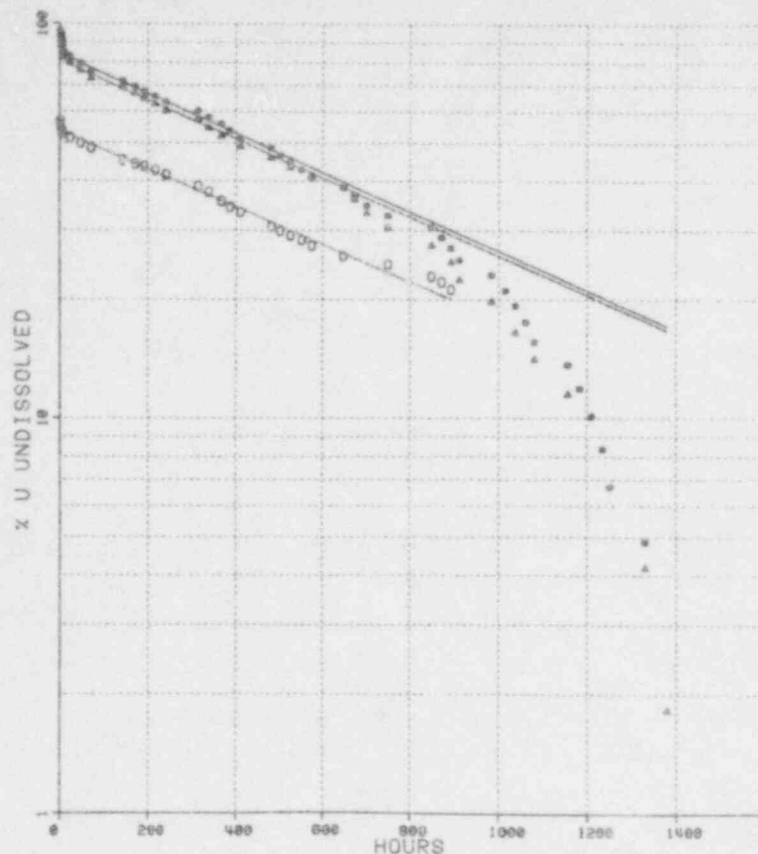


Figure 8. Comparison of U dissolution from aerosols of three industrial fuel materials in 2 M HNO_3 . HEDL 1750° (*), HEDL 750° (o), B&W mixed oxides with binders (Δ).

The observation of accelerated dissolution rates is significant both in interpretation of biological implications of inhaled mixed oxides and the mechanism of particulate dissolution. The acceleration in dissolution rates of polydisperse aerosol particles has been predicted and the behavior at later times shown in Figure 9 may be interpreted according to this theory. At early times after dissolution, the rapid dissolution was probably the result of the (1) dissolution of a partly hydrolyzed and oxidized surface layer as discussed above, (2) rapid dissolution of material from the highly irregular surfaces of the particle and (3) dissolution of very small particles. These factors may have contributed singly or in concert to the rapid dissolution rate observed. After the first 24 hours, the dissolution rate slowed and corresponded to the predicted dissolution profile of a monodisperse aerosol.⁷ These industrial aerosols would not be expected to approach true monodispersity. However, the trend toward the creation of smoothed particles of more uniform and larger size would be expected as the fraction dissolved increased. As dissolution continued, the remaining particles decreased in size to the point where the specific surface area of the particles became the controlling factor in the dissolution rate. Mercer's theory predicts this point to occur at approximately 45% dissolved for a monodisperse aerosol. It is noteworthy that this occurred for U and not Pu in all samples, suggesting that in the HEDL 1750° material, Pu also dissolved nearly completely also but remained in a less soluble form. The experiment using HEDL 750° material was terminated at 892 hours as a result of a leak of particles from the filter assembly.

Biological Implications

Some indications of potential biological behavior were suggested by results of these *in vitro* studies. The utility and significance of the rapid early dissolution component must be practically

limited to the determination of the fraction of each actinide which might be dissolved within a few days after inhalation. For example, the dissolution behavior of Pu, Am and U contained in B&W mixed oxides with binders in 0.1 M HCl (Table 3) shows that Pu and Am dissolve very rapidly with a half-time of 2 to 4 hours. However, only 0.2 to 0.4% of the initial amount dissolved at this rate while the remaining > 99% dissolved much more slowly as shown in Figure 2. This observation was made for this material in all solvents. The biological implications of the behavior of this material are that rapid initial dissolution would probably contribute to a very minor degree in clearance of Pu and Am from the lung if inhaled, resulting in correspondingly small translocation to other tissues such as liver and bone and therefore, little likelihood for a successful chelation therapy approach.

The dissolution behavior of uranium from this same material on the other hand, shows that 24% of the initial uranium present dissolved with a half-time of 4 hours and the remaining 77% dissolved much more rapidly than Pu or Am. One would predict on the basis of these *in vitro* results, that if this material were deposited in lung, significant quantities of uranium would be cleared from lung via solubilization followed by tissue deposition and urinary excretion while only minute quantities of soluble Pu and Am would be cleared from lung. In general, the fraction of any Pu or Am that dissolved shortly after deposition could be amenable to a chelation therapy approach.

The slower dissolution component could be useful in the prediction of accumulated radiation dose to lung. The variability in the estimates of dissolution half-time values described above does not reduce the utility of the estimate, since values > 10^4 days are much greater than the lung retention half-time of approximately 10^3 days in Beagle dogs exposed to industrial materials (this report, pp.61 -65). As such, slowly dissolving Pu and Am isotopes can be considered insoluble for the purpose of predicting the metabolism of material deposited in lung.

The dissolution behavior of uranium in 2 M HNO_3 suggests that if an aerosol of a more soluble form of mixed-oxide fuel were deposited in lung, the uranium dissolution rate could be expected to increase at some time after deposition when the fraction remaining undissolved approached approximately 40%. Although such a change in dissolution rate has yet to be demonstrated in animals, predictions of the biological behavior in humans based on animal studies should consider this possibility for more soluble forms of inhaled actinides.

These *in vitro* dissolution studies further indicate that the dissolution of PuO_2 and UO_2 occur independently in the materials composed of mixed powders, but that their dissolution rates were modified when the two compounds were in a solid solution (HEDL 1750° material). The Pu dissolution rate was unchanged or increased while the U dissolution rate was unchanged or slightly decreased. If similar differences in the solubilities of PuO_2 and UO_2 are confirmed by animal studies, an interpretation of bioassay results to estimate the initial lung burden of an accidentally exposed worker should include data that reflects Pu, Am and U excretion rates if a valid estimate is to be made.

It must be noted that the above discussion of the relationships between the chemical forms of mixed-oxide fuels and their dissolution properties includes information obtained from experiments using three different solvents. No single experiment yielded information that adequately described the general dissolution behavior and as a result, the discussion became more complete through the use of all three solvents. The results discussed in this report will be compared with data from concurrent radiation dose pattern studies using laboratory animals. The results of these comparisons will be used to evaluate the three solvent systems for the purpose of defining an *in vitro* solvent system that can serve as the best model of *in vivo* solubility of inhaled mixed-oxide aerosols.

CONCLUSIONS

The combined results of these *in vitro* dissolution studies using three solvents allow general conclusions to be made regarding the solubility of industrial nuclear fuel materials that might be released accidentally during fuel fabrication: (1) dissolution occurred at a rapid rate initially and slowed at longer times, (2) greater percentages of U dissolved than Pu or Am, (3) the U dissolution rate from all materials, except the HEDL 1750° material, was faster than the Pu dissolution rate, (4) the dissolution rates of U and Pu generally reflected the physical composition of the UO_2 - PuO_2 matrix. The utility of *in vitro* solubility tests in the prediction of *in vivo* behavior of inhaled industrial mixed-oxide aerosols must be demonstrated through the correlation of these data discussed in this report with results of studies under way in which rats, dogs and monkeys were exposed by inhalation to aerosols of the same materials. A selection of an optimal *in vitro* test system also must be based on these same data from animal studies.

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DEPOSITION, RETENTION AND DOSIMETRY OF INHALED MIXED URANIUM PLUTONIUM OXIDES
(HEAT-TREATED AT 750°C) IN FISCHER-344 RATS, BEAGLE DOGS AND CYNOMOLGUS MONKEYS

ABSTRACT

A study was conducted to provide information regarding the patterns of radiation doses and their implications with respect to possible health consequences of an inhalation exposure to one form of U and Pu oxide aerosols found in the industrial workplace. The material used was a mixture of UO_2 and 750°C heat-treated PuO_2 obtained from the ball milling operation at the Hanford Engineering and Development Laboratory. The alpha specific activity of this mixed-oxide was 23 mCi/g. Fischer-344 rats, Beagle dogs and Cynomolgus monkeys received inhalation exposures to aerosols generated from dry mixed-oxide powders. The particle size distribution characteristics of the aerosols ranged from 1.5 to 2.5 μ m activity median aerodynamic diameter and from 1.3 to 1.8 in geometric standard deviation. Based on comparisons of these values with those of aerosols sampled at the industrial site, these aerosols were judged to be suitable simulators of aerosols which could be released in this fuel fabrication step. Plutonium from this $UO_2 + PuO_2$ admixture was seen to behave biologically in dogs like PuO_2 from laboratory produced aerosols in terms of its rate of clearance from the lung and its resulting distribution in other tissues. The material was relatively insoluble in the lungs of all species, although monkeys and rats appeared to clear plutonium from their lungs much faster than dogs. Tissue distribution data suggest that most of the plutonium and americium left the lungs by mechanical means. The faster clearance of plutonium from the lungs of monkeys and rats and the lesser tendency for plutonium particles to accumulate in their lymph nodes as compared to dogs suggests that reliance on dog data alone may tend to overestimate the risk of radiation-induced injury in human inhalation cases.

PRINCIPAL INVESTIGATORS

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The primary objective of this study is to provide information regarding the biological fate, associated patterns of radiation dose and their implications with respect to possible health consequences of an inhalation exposure to one form of mixed uranium and plutonium oxide aerosol found in the industrial workplace. Results of this study will be integrated with results of similar studies using other materials found in the industrial mixed U, Pu oxide fuel fabrication process as outlined in an earlier report.¹ The material used for these inhalation studies was a mixture of UO_2 and 750°C heat-treated PuO_2 obtained from the ball milling operation at Hanford Engineering and Development Laboratory (HEDL). This mixture has been found to consist of an admixture of 22% PuO_2 and 78% UO_2 by weight. The UO_2 contained depleted uranium and the PuO_2 included different amounts of isotopes ranging from ^{238}Pu to ^{241}Pu with ^{241}Am present as a decay daughter of ^{241}Pu . The specific activity of the mixed oxides with regard to alpha radiation was found to be 23 mCi/g and for beta radiation, 180 mCi/g. This material was considered to be representative of the materials handled in fabrication steps after mixing of PuO_2 with UO_2 and preceding the addition of organic binders for the pellet pressing and grinding steps. A detailed description of the fuel fabrication process may be found in an earlier report.² The X-ray diffraction analyses have shown that the mixed oxides present in the V-blending and ball milling steps have the same crystal properties. Therefore, the results of the inhalation exposure studies described for this one material will be taken as

typical for all aerosols of materials in a similar stage of processing unless another material is found to be unique in some property which would warrant biological study.

Results of radiochemical analyses of selected tissue and excreta samples for Pu content are now complete for this 2 year study. They are presented and intercompared in the report that follows. Analysis of uranium data from tissues and excreta is not complete for this study and will be presented in a later report.

MATERIALS AND METHODS

Aerosol Generation and Characterization

Aerosols were generated for the inhalation exposure of laboratory animals using the dry powder aerosol generation system described in a previous report.³ Briefly, the system included a DeVilbiss dry powder blower containing the mixed-oxide powder which was subjected to sonic agitation. The aerosol was generated by a moving air stream, passed through a ⁸⁵Kr deionizer to reduce particle agglomeration and then through a tube to the exposure chamber. Each exposure aerosol was characterized in regard to concentration and particle size distribution using membrane filters, cascade impactors and a point-to-plane electrostatic precipitator. The alpha activity on the membrane filters and on each impactor stage was determined by ZnS scintillation counting methods. A lognormal distribution function was fitted to each set of impactor data by a least squares method and the activity median aerodynamic diameter (AMAD) in microns and the geometric standard deviation of the distribution (σ_g) were determined. The point-to-plane electrostatic precipitator (ESP) samples were analyzed by transmission electron microscopy and electron diffraction techniques.

Experimental Protocols

General descriptions of the inhalation exposure procedures, schedules for excreta collections and animal sacrifice procedures are described in model protocols for these studies given in a previous Annual Report.⁴ The protocols also include the lists of tissues to be taken at necropsy for radiochemical and autoradiographic and histopathologic examination. A brief summary is included here.

Thirty-six Fischer-344 rats, 18 male and 18 female, 8 to 9 weeks of age, were exposed via inhalation to aerosols generated from the industrial mixed UO₂ and PuO₂ powder to achieve a desired initial lung burden of 50 nCi. The value of the desired initial lung burden was chosen to provide a comparison with concurrent longevity studies involving inhalation of ²³⁹PuO₂ aerosols by Syrian hamsters.⁵ Fifteen animals were included in the study as unexposed controls.

Eighteen purebred Beagles from the ITRI colony, nine male and nine female, 15 to 40 months of age, received individual inhalation exposures to aerosols generated from a dry powder to achieve a desired initial lung burden of 0.07 μ Ci/kg body weight. This initial lung burden was chosen to correspond with concurrent longevity studies using ²³⁹PuO₂.⁶

Nine subhuman primates were exposed to aerosols generated in the same way to achieve the same initial lung burden, 0.07 μ Ci/kg, desired for Beagle dog exposures. The exposed population included three Rhesus monkeys and six Cynomolgus monkeys. All monkeys were male with the exception of one female Cynomolgus monkey. Ages of monkeys were more difficult to determine since they were caught in the wild. However, ages were estimated based on body weight at the time of exposure. All monkeys were 2 to 4.5 years at the time of exposure except two Rhesus monkeys which were 5 to 7 years old. These two animals were sacrificed at 4 hours and 4 days after inhalation exposure. The remaining Rhesus monkey is being held in reserve as described below.

Rats were exposed collectively by placing individual animals into plastic exposure tubes through which their noses projected and then inserting these tubes into a multi-port exposure manifold which

formed the end of the aerosol generation train. This resulted in a nose and head exposure for these animals. Dogs and monkeys were exposed individually and by nose only. This was accomplished by placing a latex exposure mask over the individual's muzzle and allowing its nose to project into an exposure chamber which formed the end of the aerosol production train. As was the case in the other radiation dose pattern studies of mixed-oxide fuel materials, additional animals were included in each exposure group without being assigned to a particular sacrifice group. These animals are being held in reserve for substitution into a particular sacrifice group in the event of the death of animals prior to the assigned sacrifice date and to provide a small group for the observation of any biological effects produced at times later than 2 years after inhalation exposure.

Excreta collections including feces, urine and cage wash samples were made on a routine basis for all species. For rats, composite urine, feces and cage wash samples were collected every 3 days from three animals in the 64-day sacrifice group. Composite collections were also made every 3 days from three animals in the 2-year sacrifice group through 64 days after exposure followed by 3 day composite collections at 12, 18 and 24 weeks and at 6-month intervals thereafter. Daily collections were made on all dogs and monkeys through 21 days after exposure followed by 3 day composite collections at 12, 18 and 24 weeks and at 6-month intervals thereafter. Animals to be collected were maintained in individual metabolism cages for the duration of the collections. Rats and monkeys not being collected were maintained individually in cages and dogs were returned to their kennels between composite 3-day collections.

Animals were randomly scheduled for sacrifice at 4 hours, 4 days, 64 days and 1, 1.5 and 2 years after inhalation exposure. Animals were sacrificed in groups of five rats, two dogs (one male and one female) and one monkey at each scheduled sacrifice time. Rats were sacrificed with an intraperitoneal injection of sodium pentobarbital, weighed prior to necropsy and individual organs weighed at necropsy. Dogs and monkeys were sacrificed by exsanguination performed under sodium pentobarbital anesthesia and a complete postmortem examination was performed on each animal. Tissues subject to radiochemical analysis and to histopathologic and autoradiographic study are detailed in a previous report.⁴ Tissue samples were obtained at necropsy according to the model protocol with the modification that gonad, adrenal and thyroid tissues of animals sacrificed at 1 year and later after exposure were analyzed using low level radiochemical analysis techniques.

Radiochemical, Histological and Autoradiographic Analyses

Procedures used for radiochemical analysis of tissue and excreta samples collected during these studies are described in detail in a previous Annual Progress Report.⁷ Briefly, these procedures involved alternate dry and wet ashing to obtain a clear acid digest solution. Plutonium was separated from americium by extraction from the aqueous solution with an extractant cocktail containing (2-ethylhexyl)phosphoric acid dissolved in toluene. The activities of Pu and Am were measured separately by liquid scintillation counting techniques. Standard procedures were used for histologic and autoradiographic analysis of tissue samples.

RESULTS AND DISCUSSION

Analysis of Exposure Aerosols

Results of analyses of the exposure aerosols are described in detail in a previous Annual Progress Report⁸ and are summarized in Table 1. As shown, the particle size distribution characteristics, AMAD and σ_g , of the exposure aerosols agree with those of aerosols sampled during a normal ball milling operation at HEDL. Figure 1 shows the range of all AMAD and σ_g values observed for industrial mixed-oxide aerosols generated in the laboratory in relation to the ICRP lung deposition model proposed by the ICRP Task Group on Lung Dynamics.^{9,10}

Table 1

Particle Size Distribution of Aerosols of 750°C Heat-Treated Mixed Uranium and Plutonium Oxides Sampled During the Ball Milling Operation at HEDL and Inhalation Exposures of Laboratory Animals

Species or Process Step	AMAD (μm)	σ_g
Rat	2.3	1.7
Dog	2.2 ± 0.3^a	1.8 ± 0.2^a
Monkey	1.5 ± 0.3^b	1.6 ± 0.3^b
Ball Milling ^c	1.9 ± 0.4^d	1.5 ± 0.07^d

^aMean \pm standard error of 21 measurements.

^bMean \pm standard error of nine measurements.

^cRaabe, O. G., G. J. Newton, C. J. Wilkinson, S. V. Teague and R. C. Smith, "Plutonium Aerosol Characterization Inside Safety Enclosures at a Demonstration Mixed-Oxide Fuel Fabrication Facility," *Health Phys.*, 35: 649, 1978.

^dMean \pm standard error of six measurements.

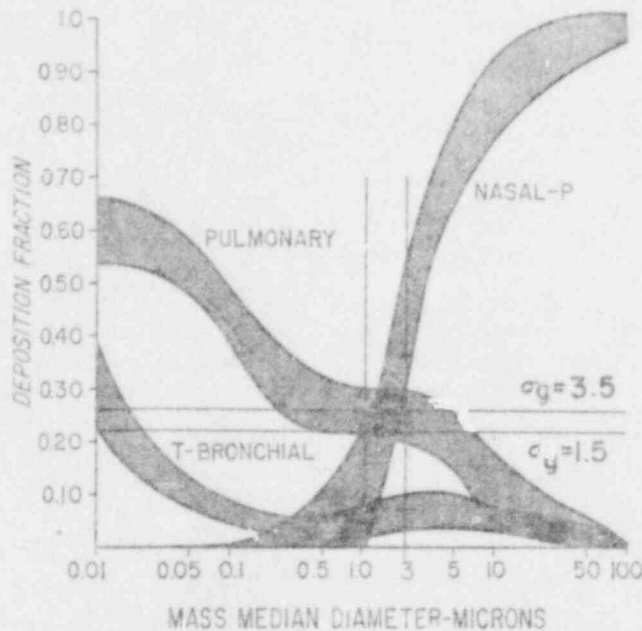


Figure 1. The ranges of values of activity median aerodynamic diameter (AMAD in μm) and geometric standard deviation (σ_g) observed for exposure aerosols are shown in relation to the ICRP Task Group on Lung Dynamics lung deposition curves.^{8,9} Similar fractions of all aerosols inhaled by animals in these studies would have been deposited in the pulmonary region according to the model.

A comparison of the values given in Table 1 with Figure 1 shows that the aerosols regenerated in the laboratory from industrial powders and aerosols sampled at the industrial site had particle size distribution characteristics such that similar pulmonary deposition fractions would be expected when inhaled. Based on this comparison, the aerosols inhaled by laboratory animals were judged to be suitable simulators of aerosols of dry powders which could be accidentally released in this fuel fabrication step. This conclusion holds for the 750°C heat-treated mixed oxides discussed here as well as for the aerosolized materials described in the following two sections of this report.

Determination of Initial Lung Burden Values

Future assessment of potential biological effects that may result from mixed-oxide inhalation will be based on mathematical models of radiation dose absorbed by critical organs. These mathematical models require the use of accurate values of initial lung burdens and the related retention functions for lung and other critical organs. Therefore, methods used to determine the initial lung burdens and retention functions for the three species of laboratory animals will be described in detail. Subsequent reports on these studies will describe the mathematical methods to be used in the final interpretation of the results currently being collected.

In the context of these studies, the initial lung burden represents the amount of inhaled material that was deposited initially in the pulmonary region. In accord with the lung model proposed by the ICRP Task Group on Lung Dynamics, the pulmonary region is considered to be the non-ciliated portion of the respiratory tract beyond the terminal bronchioles.⁸ Relatively insoluble materials deposited above this region in the nasopharyngeal or tracheobronchial regions are cleared rapidly by mucociliary activity during the first three to five days after exposure, swallowed, passed unabsorbed through the gastrointestinal tract and excreted in the feces.

The initial lung burden of a relatively insoluble material, having been deposited in the non-ciliated parenchymal areas of the lung, is retained for a much longer period of time. Since the industrial mixed-oxide materials being studied in this project are relatively insoluble in body fluids, they are retained in the lung for prolonged periods of time and provide both a source of irradiation to the adjacent pulmonary tissues and a reservoir for the slow absorption of these radionuclides into the systemic circulation and subsequent deposition in other organs.

The initial lung burdens for dogs and subhuman primates were calculated for individual animals based on the results of radiochemical analyses of tissues obtained at necropsy and of excreta samples obtained from each animal between the inhalation exposure and sacrifice.

The general strategy for calculating initial lung burdens from these tissue and excreta analyses involved several assumptions based on the known behavior of inhaled, relatively insoluble particles described above. The first was that all of the activity in the excreta collected during the first 4 days came from the clearance of the nasopharyngeal and tracheobronchial regions. A second assumption was that negligible absorption from the pulmonary region occurred during this time period. Any radionuclide found in body tissues other than the lung at times greater than 4 days after the inhalation exposure was assumed to have originated from the pulmonary region. Likewise, any radionuclide excreted in the urine or feces after day 4 was also assumed to have originated from the pulmonary region.

On these bases, the lung burden at 4 days after exposure was reconstructed by summing the radionuclide burden found at death in all body organs (the sacrifice body burden) and all urine and feces excreted from day 4 to death using the following equation:

$$LB(4) = SBB + 1.2 \int_4^{t_d} EX(t) dt \quad (1)$$

where $LB(4)$ = lung burden at 4 days in nCi, SBB = sacrifice body burden in nCi, $EX(t)$ = total excretory rate of urine and feces expressed as nCi per day for each radionuclide being studied as a function of time, t , after the inhalation exposure and t_d = time of death expressed as days after the inhalation exposure. The factor of 1.2 is included to take into account the excreted activity contained in cage wash. Previous studies performed at ITRI of the deposition, retention and excretion of $^{238}\text{PuO}_2$ and $^{241}\text{AmO}_2$ aerosols in the Beagle dog indicated that the amount of activity found in the cage washes of these animals was equal to approximately 20% of the activity excreted in urine plus feces for any given time period.

The total excretory rate function, $EX(t)$, used in equation (2) was of the following general form:

$$EX(t) = A_1 e^{-\lambda_1 t} + A_2 e^{-\lambda_2 t} + A_3 e^{-\lambda_3 t} \quad (2)$$

where A_1 = amount of activity in nCi excreted with the rate constant λ_1 in day^{-1} . This equation was fitted to individual sets of data using a nonlinear least squares technique. Some sets of data required equations of less than three components for adequate fits to the data.

For the calculations presented here, the initial lung burden and the 4 day lung burden were considered to be equal. Since lung burden in this context dealt only with material deposited initially in the non-ciliated pulmonary region, this appeared to be a reasonable approximation since relatively insoluble materials are retained with biological half times of several hundred days in this region.

Initial lung burden values for all dogs and monkeys sacrificed and analyzed to date in these studies are summarized in Table 2. The initial lung burden values for animals sacrificed at 4 hours or 4 days after exposure were assumed to be equivalent to the lung burdens measured at

Table 2
Initial Lung Burden Values of Fischer-344 Rats, Beagle Dogs and
Subhuman Primates Exposed by Inhalation to
Aerosols of $UO_2 + PuO_2$ Heat Treated at $750^\circ C$
Obtained From the Ball Milling Process at HEDL^a

Species	Animal Number	Initial Lung Burden (nCi)		
		Pu	Am	Total
Fischer-344 Rats	217E	59 (1.9-380) ^b	c	--
Beagle Dog	871D	490	56	550
Beagle Dog	219C	589	190	1800
Beagle Dog	635B	660	68	650
Beagle Dog	817T	2100	240	2300
Beagle Dog	804A	1200	150	1400
Beagle Dog	799B	780	260	1000
Beagle Dog	826T	630	170	800
Beagle Dog	802D	1700	480	2200
Beagle Dog	821T	330	310	640
Beagle Dog	811A	2200	430	2600
Beagle Dog	825S	1200	220	1400
Rhesus Monkey	917	440	33	480
Rhesus Monkey	918	310	33	340
Cynomolgus Monkey	21	560	79	640
Cynomolgus Monkey	26	250	96	350
Cynomolgus Monkey	22	93	66	160
Cynomolgus Monkey	24	160	67	230
Cynomolgus Monkey	27	310	190	500

^aSee tables in Appendix C of this report.

^bMedian (range).

^cNot available at this time.

death. For animals sacrificed within 4 hours after exposure, radionuclides deposited on the ciliated bronchial regions of the lung may have contributed to the sacrifice lung burden. To minimize this error, each lung lobe was excised at the point where each lobar bronchus joined the right or left main bronchus. In the animals sacrificed at 4 days after exposure, clearance of the bronchial region should have been essentially complete and the sacrifice lung burden should have provided an accurate measure of the initial lung burden. All other initial lung burdens were calculated using equation (1).

Initial lung burdens of the ten rats sacrificed at 4 hours and 4 days after exposure were assumed to be equivalent to the lung burdens measured at sacrifice. For the remaining 26 rats, the approach used was similar to that described above for the dogs and monkeys. However, excreta collections were only made for six of these rats, three that were sacrificed at 64 days and three that were sacrificed at 2 years. Initial lung burdens for these six rats were determined using their individual sacrifice body burdens and excreta data. Initial lung burdens for the remaining 20 rats were determined as follows: Excretion rate functions of the form shown in equation (2) were fitted to the excreta data for each of the six rats for which excreta collections were made and individual 4-day lung burdens were calculated. The corresponding whole-body retention functions were calculated according to the following relationship:

$$BB(t) = \frac{LB(4) - \int_0^{t_d} EX(t)dt}{LB(4)} \quad (3)$$

where $BB(t)$ = whole body retention as a fraction of the 4-day lung burden, $LB(4)$ = lung burden at 4 days after exposure, $EX(t)$ = excretory rate function described in equation (2) above, and t_d = days after the inhalation exposure.

The whole-body retention functions computed in this way were averaged to obtain the following equation:

$$\overline{BB}(t) = 0.74e^{-0.013t} + 0.26e^{-0.001t} \quad (4)$$

This average retention function was used to estimate the initial lung burdens of the animals for which excreta collections were not made. These lung burdens were estimated from the following relationship:

$$ILB = LB(4) = \frac{SBB}{\overline{BB}(t)} \quad (5)$$

The median and range of initial lung burden values calculated for individual animals is given in Table 2.

Lung retention of plutonium for this material in dogs, monkeys and rats is shown in Figure 2. The retention curves represent the percentage of the initial lung burden remaining in lung as a function of time after inhalation exposure throughout the 2 years of the study. The letters represent individual data points in the case of the monkeys and the mean of two points in the case of the dogs. Two component exponential functions of the form $A_1e^{-\lambda_1 t} + A_2e^{-\lambda_2 t}$ were fit to each set of data utilizing a nonlinear least squares method and the resulting regression lines superimposed on the data points. No data points are shown in the case of the rats, as this curve represents a composite retention function determined as explained above.

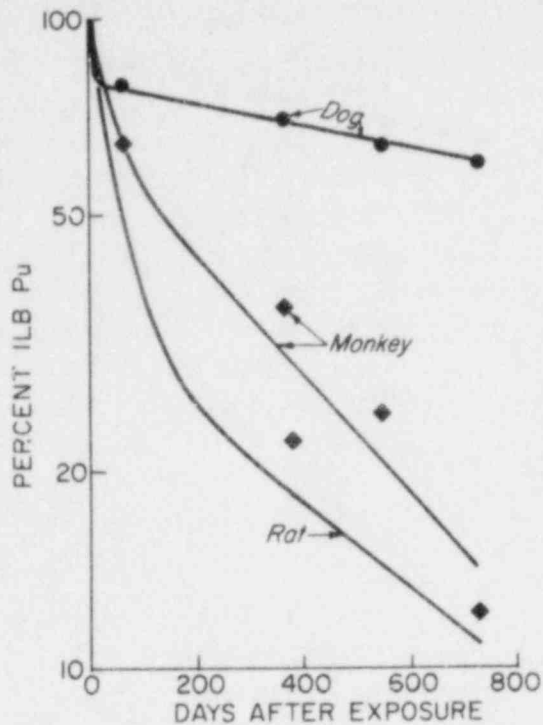


Figure 2. Lung retention of plutonium in rats, dogs and monkeys exposed to 750°C heat-treated mixed UO₂ and PuO₂ aerosols obtained from the ball milling process at HEDL.

There is an obvious difference in the clearance of plutonium from the lungs of dogs as compared to monkeys and rats which seem to clear the material in a similar manner. The slopes of the long-term components of these curves indicate that dogs cleared 80% of the initially deposited plutonium from their lungs with a half-time of about 1700 days while monkeys cleared 66% with a half-time of 330 days and rats cleared 26% with a half-time of 350 days.

Table 3 shows the retention and translocation of alveolar deposited plutonium and americium from this material in the dogs and monkeys for lung, tracheobronchial lymph nodes, liver and skeleton. All numbers in the table represent the percentage of the initial lung burden present in the particular organ at that time.

At 2 years after inhalation exposure, the dogs had about 60% of their initial lung burden remaining in lung. This is in excellent agreement with data from a study in which Beagle dogs were exposed by inhalation to polydisperse aerosols of laboratory produced ²³⁹PuO₂.¹¹ Initial alveolar deposition of plutonium in the Battelle dogs ranged from 0.2-3.3 μCi as compared with 0.6-2.2 μCi for the dogs in this study. Also, comparing americium and plutonium in lung for both dogs and monkeys, it appears that americium left the lung more rapidly than plutonium in both species.

Accumulation of plutonium in tracheobronchial lymph nodes of dogs increased with time, reaching levels of 7-9% of the initial lung burden at 1.5-2 years after exposure. The results of Park *et al.* show about 10% at this time. Comparable amounts of americium were also translocated to dog tracheobronchial lymph nodes; however, the accumulation of both plutonium and americium in the lymph nodes of monkeys was much smaller.

At 2 years after exposure, 1-2% of the initial lung burden of plutonium and americium was found in the liver of dogs, but very little of either isotope was found in the liver of monkeys. That monkeys and dogs differ with respect to hepatic retention of plutonium and americium has been demonstrated in the literature. Stover shows a hepatic retention half-time of about 3800 days for Beagles injected with ^{239}Pu citrate at dose levels up to $0.096 \mu\text{Ci/kg}$.¹² Similarly, Lloyd has demonstrated a retention half-time of 3500 days for ^{241}Am citrate in the Beagle dog.¹³ The primate liver, on the other hand, appears to clear these two isotopes much more rapidly. A study in which Cynomolgus monkeys were injected either intramuscularly or intravenously with ^{241}Am citrate yielded a retention half-time in the liver of 70 days, Durbin *et al.*,¹⁴ while 28 days was the value demonstrated by Guilmette *et al.*¹⁵ for intravenous injection of baboons with ^{241}Am citrate. In a study using adult macaques injected at a dose level of $0.3 \mu\text{Ci/kg}$ of $^{238}\text{Pu(IV)}$ citrate, Durbin *et al.*¹⁶ has demonstrated that ^{238}Pu clears from the simian liver at a rate comparable to that of ^{241}Am . With such rapid hepatic clearance, it is not surprising that we do not see as much of a buildup of these isotopes in the liver of primates as in the liver of dogs.

The 2 year skeletal values show that only very small amounts of either isotope were translocated in the case of both dogs and monkeys. Park *et al.* reported similar values at 2 years after exposure: Liver: < 1% ILB; Skeleton: ~ 1% ILB. Skeletal burdens of dogs and monkeys were estimated from activity levels found in one femur and one humerus according to the equation:

$$S = K(F + H) \quad (6)$$

where S = total skeletal burden of an isotope in nCi, K = a constant relating the activity in nCi deposited in one femur (F) plus one humerus (H) to the total skeletal burden. The value of K for plutonium isotopes, as determined from the analyses of total skeletons of 35 Beagle dogs containing ^{238}Pu , was found to be 12 ± 1 nCi in one femur plus one humerus. The same value was determined from the skeletons of 52 Beagle dogs which contained ^{241}Am . The values shown in Table 3 for skeleton suggest that americium was deposited in bone to a greater extent than plutonium for both dogs and monkeys. This is consistent with the apparent greater rate at which americium left the lung over plutonium in both these species.

Table 3 shows that very little translocation of solubilized material from the lung to other organs occurred. This suggests that most of this material was cleared via mechanical means. The tracheobronchial lymph nodes of the dog were the only organs that accumulated substantial amounts of plutonium or americium and this is due mostly to accumulation of particles by these lymph nodes.

Table 4 gives the distribution of plutonium in terms of percent of initial lung burden for these same tissues for rats. Rats, like dogs and monkeys, showed very little translocation of solubilized plutonium to liver and skeleton. The skeletal values in this table were constructed by summing the activity in the skull, femur, humerus and remaining carcass. The skeletal value for 4 days after exposure was omitted from the table as it was unrealistically high due to some residual contamination in the skull at this early time after exposure. Rats also showed very little accumulation of plutonium in the tracheobronchial lymph nodes even at 2 years after inhalation exposure.

Data from James *et al.*¹⁷ in which rats and hamsters were exposed via inhalation to mixed uranium and plutonium oxide aerosols from an industrial nuclear fuel fabrication facility showed a slightly faster clearance of plutonium from the lungs of rats. Their data show that about 5% of the initially deposited plutonium remained in the lung at 2 years after inhalation exposure as compared to 10% shown in Table 4. However, it must be noted that they arrived at their long-term retention equations by the external counting of the 60 KeV gamma from the ^{241}Am present in the mixed-oxide on the assumption (based on their data) that americium and plutonium leave the lung at the same rate.

Table 3

Organ Content of Plutonium and Americium Expressed as a Percent of Initial Lung Burden in
Dogs and Monkeys Exposed to 750°C Heat-Treated Mixed UO₂ and PuO₂ Aerosols
Obtained From the Ball Milling Operation at HEDL

Organ	Time After Exposure	% Initial Lung Burden			
		Beagle Dog ^a		Subhuman Primate ^b	
		Pu	Am	Pu	Am
Lung	4 days	100	100	100	100
	64 days	80	56	65	52
	1 year	70	29	36	11
	1.5 years	64	31	24	8.8
	2 years	60	46	15	3.6
Tracheobronchial Lymph Nodes	4 days	0.11	0.04	0.01	< 0.01
	64 days	0.65	0.59	0.22	0.20
	1 year	7.4	2.7	3.8	1.5
	1.5 years	7.1	7.2	c	c
	2 years	9.0	6.6	1.6	0.39
Liver	4 days	0.03	0.77	< 0.01	0.25
	64 days	0.07	0.30	0.02	0.26
	1 year	0.12	0.07	0.06	0.01
	1.5 years	0.06	0.13	0.03	< 0.01
	2 years	1.4	1.3	0.04	0.01
Skeleton	64 days	0.21	7.5	0.05	0.84
	1 year	0.16	0.91	0.27	1.9
	1.5 years	0.15	0.36	0.11	0.60
	2 years	0.12	0.65	< 0.01	0.87

^aValues represent mean of two dogs at each sacrifice time.

^bValues represent a single animal at each sacrifice time.

^cData not available.

Table 4
Organ Content of Plutonium in Rats Exposed
to 750°C Heat Treated Mixed UO₂ and PuO₂
Aerosols Obtained From the
Ball Milling Operation at HEDL

Organ	Time After Exposure	% ILB Pu ^a
Lung	4 days	100 ^b
	63 days	50 ± 12
	1 year	18 ± 1.0
	1.5 years	14 ± 1.0
	2 years	10 ± 1.0
TBLN ^c	4 days	1.9 ± 2.2
	63 days	< 0.01
	1 year	0.24 ± 0.23
	1.5 years	0.05 ± 0.06
	2 years	< 0.01
Liver	4 days	0.40 ± 0.39
	63 days	0.02 ± 0.01
	1 year	0.03 ± 0.01
	1.5 years	0.12 ± 0.11
	2 years	< 0.01
Skeleton	4 days	0.31 ± 0.41
	1 year	0.63 ± 0.29
	1.5 years	0.13 ± 0.10
	2 years	0.87 ± 1.1

^aMean ± 1 standard deviation.

^bExactly 100% by definition.

^cTracheobronchial lymph nodes.

Data shown in Table 3 for dogs and monkeys indicate that americium might be leaving the lung faster than plutonium in these species and the same may be true for rats. This question will be explored more thoroughly in a later report upon completion of analysis of americium content in rat tissue and excreta samples. The initial plutonium lung burdens of the rats used in the experiment by James *et al.* was about 32 nCi as compared to the value of 59 nCi shown in Table 2, also, James found less than 1% of the initial lung burden of the plutonium deposited in these rats in liver or skeleton at 180 days after exposure which is in agreement with the conclusions drawn here (Table 4) that very little of the plutonium from this inhaled material is translocated to other organs of the body.

These results demonstrate, among other things, the importance of using data from more than one species of animal when attempting to determine the potential risk to humans from these inhaled materials. In this case, the faster clearance of plutonium from the lungs of monkeys and rats and the lesser tendency of plutonium particles to accumulate in their lymph nodes suggests that reliance on dog data alone may tend to overestimate the risk of radiation-induced injury in human inhalation cases.

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DEPOSITION, RETENTION AND DOSIMETRY OF INHALED MIXED URANIUM-PLUTONIUM OXIDES
(HEAT-TREATED AT 1750°C) IN FISCHER-344 RATS, BEAGLE DOGS AND CYNOMOLGUS MONKEYS

ABSTRACT

Fischer-344 rats, Beagle dogs and Cynomolgus monkeys were exposed by inhalation to aerosols produced during the centerless grinding of industrially produced nuclear fuel pellets heat treated at 1750°C. In rats, 91% of the sacrifice body burden of plutonium and 69% of the sacrifice body burden of americium was found in the lungs at 2 years after inhalation exposure. Lung retention curves determined for dogs and monkeys showed that both americium and plutonium are cleared much more rapidly from the monkey lung than from the dog lung. For example, the lung retention half-time of inhaled industrial plutonium in dogs was determined to be about 700 days, while for monkeys, it was only 400 days. Dogs tended to accumulate larger amounts of plutonium and americium in their tracheobronchial lymph nodes than did monkeys and they also showed an accumulation of these isotopes in liver which monkeys did not exhibit. These obvious differences in which plutonium and americium are distributed and retained in different species of animals have an important impact on our use of animal data to estimate potential risk to humans from these industrial fuel materials.

PRINCIPAL INVESTIGATORS

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Aerosols produced during the centerless grinding of industrially produced mixed uranium and plutonium oxide nuclear fuel pellets were chosen for extended radiation dose pattern studies for two reasons. The centerless grinding process was shown to be a dusty operation with gross alpha activity aerosol concentrations reaching as high as 1700 $\mu\text{Ci/l}$ inside glove box enclosures where this operation was performed. Therefore, this operation poses a potentially significant hazard to nearby workers in the event of a loss of glove box integrity. Also, this material has a different temperature history than the other aerosols sampled in that the pellets were sintered at 1750°C before beginning the grinding process. It was hypothesized that the higher temperature treatment might make a significant difference in the biological behavior of this material as opposed to the other materials which had temperature histories of 750 to 850°C. The actual industrial fabrication process and the results of the on-site sampling efforts during which this material was obtained are discussed elsewhere.^{1,2}

MATERIALS AND METHODS

Three species of animals were exposed once, by inhalation, to aerosols formed in the centerless grinding process. The species were the Fischer-344 rat (40 animals exposed), the Beagle dog (18 animals exposed) and the Cynomolgus monkey (7 animals exposed). Two Rhesus monkeys already on hand at the Institute completed the desired total of 9 monkeys. Since these Rhesus were older than the Cynomolgus monkeys, they were sacrificed at early times (4 hours and 4 days after exposure).

The rats, dogs and monkeys used in this study were similar in age, weight and sex to those used in parallel studies and described earlier in this report, pp. 35-46. Animals were exposed via inhalation to aerosols of this material using a dry powder aerosol generation technique³ to achieve a desired initial lung burden of 50 nCi per animal for rats and 0.07 μCi per kilogram body weight for dogs and monkeys. The values of the desired initial lung burdens were chosen to provide data

for comparison with concurrent longevity studies involving inhalation of $^{239}\text{PuO}_2$ aerosols by Syrian hamsters,⁴ dogs and monkeys.⁵ Individual monkeys and dogs were exposed, nose-only, to the aerosol by means of a latex exposure mask which allowed the animal's nose to project into a chamber located at the end of the aerosol generation train. Rats were exposed as a group of 40 animals through the use of an exposure manifold into which exposure tubes containing the individual animals were inserted. Animals were sacrificed at 4 hours, 4 days, 64 days, 1, 1.5 and 2 years after exposure. There were five rats, two dogs and one monkey in each sacrifice group, with the remaining animals held in reserve to replace animals that died prior to the scheduled sacrifice date and also to provide information on possible long-term biological effects. A more complete explanation of the exposure of rats, dogs and monkeys detailing the exposure apparatus, post-exposure excreta collections and tissues collected for radiochemical and histopathological analysis may be found in the appendices of a previous Annual Report.⁶

RESULTS AND DISCUSSION

Results of the characterization of aerosols inhaled by the animals are shown in Table 1. The table shows the activity median aerodynamic diameter (AMAD) and the geometric standard deviation (σ_g) of the aerosol to which each species was exposed. For dogs and monkeys, these represent the mean of the values observed individually for all animals of that species. These parameters were determined for actual exposure aerosols by measuring the alpha activity on successive stages of a cascade impactor and fitting a lognormal distribution to the results. In general, the assumption that the aerosol particle sizes were distributed lognormally proved to be a good one as no bimodal distributions or other departures from lognormality were encountered.

In each case, these aerosols were found to have similar particle size characteristics to those obtained during actual sampling runs at the industrial facility and thus similar pulmonary deposition fractions would be expected when inhaled. An explanation of the criteria used to make this judgment can be found elsewhere in this report, pp. 35-46. This was an important finding, as one of the pre-requisites for conducting these experiments was the regeneration of aerosols from the bulk powders which closely resembled those generated during the production process.

Initial lung burdens received by dogs and monkeys were calculated as the sum of the total body burden of the isotope at death and the total excretory output of the animal from 4 days after inhalation exposure to death as shown in equation (1).

$$LB(4) = ILB = SBB + 1.2 \int_4^{t_d} EX(t) dt \quad (1)$$

In this equation, LB(4) is the alveolar burden on day 4 after exposure which is assumed to be equal to the initial lung burden (ILB), SBB is the sacrifice body burden or body burden at death and EX(t) is a total excretory function of the form:

$$EX(t) = A_1 e^{-\lambda_1 t} + A_2 e^{-\lambda_2 t} \quad (2)$$

Table 1

Particle Size Distribution of Aerosols of 1750°C Heat Treated, Mixed Uranium and Plutonium Oxides Obtained from HEDL and Used in the Inhalation Exposures of Fischer-344 Rats, Beagle Dogs and Monkeys

Species	AMAD (μm)	σ_g
Rat	2.3	1.7
Dog	2.5 ± 0.4^a	1.8 ± 0.2^a
Monkey	2.4 ± 0.2^b	1.7 ± 0.4^b

^aMean and standard error based on 21 measurements.

^bMean and standard error based on 9 measurements.

where A_1 = amount of activity in nCi excreted with the rate constant λ_1 in days⁻¹. It is assumed, based on previous experience, that by day 4 after exposure, clearance of material initially deposited in the upper airways which is not considered a part of the deep lung burden, is essentially complete. Values of $Ex(t)$ were determined for individual animals using equation (2). The functions were fitted to the excreta data from individual animals using a nonlinear least squares technique. The factor of 1.2 in equation (1) is included to take into account the excreted activity recovered when washing the cages. Previous studies performed at the ITRI of the deposition, retention and excretion of ²³⁸PuO₂ and ²⁴¹AmO₂ aerosols in the Beagle dog indicated that the activity of these two isotopes found in the cage washes of these animals was equal to approximately 20% of the activity excreted in urine plus feces for any given time period.

Table 2 summarizes initial lung burdens of plutonium and americium deposited in rats, dogs and monkeys as calculated by equation 1. Values given for rats are the median and range of the radiochemically determined lung burdens of animals sacrificed at 4 hours and 4 days after exposure. These values may be compared with the desired initial lung burdens of 50 nCi in rats and 0.07 μ Ci/kg body weight in dogs and monkeys if one remembers that the weight of the average dog was 10 kg and that of the average monkey 4 kg.

Table 2

Initial Lung Burden Values of Fischer-344 Rats, Beagle Dogs and Nonhuman Primates Exposed by Inhalation to Aerosols of 1750°C Heat-Treated Mixed Uranium and Plutonium Oxides Obtained From the Centerless Grinding Operation at HEDL

Species	Animal Number	Initial Lung Burden (nCi)		Total
		Pu	Am	
Rat	--	43 (12-84) ^a	7.8 (2.1-15) ^a	51
Beagle Dog	6	2400	6300	8700
Beagle Dog	643A	1380	460	1800
Beagle Dog	777D	1500	320	1800
Beagle Dog	640S	940	300	1200
Beagle Dog	641S	4000	1300	5300
Beagle Dog	796S	1500	370	1900
Beagle Dog	783B	870	390	1300
Beagle Dog	789A	850	260	1100
Beagle Dog	961B	870	220	1100
Beagle Dog	797S	1550	360	1900
Beagle Dog	798T	2700	820	3500
Beagle Dog	820U	1200	540	1700
Cynomolgus Monkey	36	190	73	260
Rhesus Monkey	900	2000	95	2100
Cynomolgus Monkey	35	300	83	380
Cynomolgus Monkey	39	290	97	390
Rhesus Monkey	914	180	24	200

^aMedian (range).

The distribution of americium and plutonium among the organs known to accumulate appreciable levels of activity in the rat is presented in Table 3. Only data expressed as a percentage of sacrifice body burden is available at this time for rats. Upon completion of analyses of excreta samples for plutonium and americium, initial lung burdens in individual rats will be calculated in a manner similar to that described for dogs and monkeys with the resulting expression of tissue distribution in terms of percentage of initial lung burden. The data suggest very low solubility of the plutonium from this material in the lung, with greater than 90% of the body burden at two years after exposure residing in the lung. Americium appeared to be somewhat more soluble, with 69% of the sacrifice body burden in the lung at two years after exposure. This difference in solubility is also reflected in the relative amounts of each isotope translocated to liver and skeleton. *

Table 3

Organ Content of Pu and Am Expressed as Percent of Sacrifice Body Burden for Rats Exposed to Aerosols of 1750°C Heat-Treated, Mixed Uranium and Plutonium Oxides Obtained From the Pellet Grinding Process at HEDL

Organ	Time After Exposure	% SBB Pu (nCi) ^a	% SBB Am (nCi) ^a
Lung	4 hr	28 ± 21	24 ± 26
	4 da	81 ± 9.3	78 ± 9.2
	64 da	93 ± 5.4	82 ± 7.9
	1 yr	91 ± 5.3	68 ± 14
	1.5 yr	95 ± 2.0	69 ± 18
	2 yr	91 ± 2.5	b
TBLN ^c	4 da	0.08 ± 0.08	d
	64 da	d	d
	1 yr	1.2 ^e	d
	1.5 yr	1.4 ^e	1.5 ± 0.89
	2 yr	2.4 ± 0.91	b
Liver	4 da	0.04 ± 0.03	0.44 ± 0.24
	64 da	0.20 ± 0.24	0.98 ± 0.67
	1 yr	0.34 ± 0.17	2.7 ± 0.71
	1.5 yr	0.19 ± 0.04	2.1 ± 1.5
	2 yr	0.72 ^e	b
Skeleton	4 da	10 ± 6.4	17 ± 8.3
	64 da	5.6 ± 5.5	16 ± 7.1
	1 yr	6.1 ± 3.0	25 ± 9.0
	1.5 yr	3.4 ± 1.2	23 ± 14
	2 yr	5.9 ± 3.0	b

^aMean ± 1 standard deviation.

^bData not available at this time.

^cTracheobronchial lymph nodes.

^d< 0.01% of sacrifice body burden.

^eOne observation only.

Table 4 gives the tissue distribution of plutonium and americium in the dog and monkey at various times after inhalation exposure. Values are expressed as percentages of the initial lung burden. Two important conclusions can be drawn from this table. First, the magnitude of the buildup of plutonium and americium in the tracheobronchial lymph nodes (TBLN) of dogs may be compared with that of the monkey. Even though data are not yet available for the monkeys sacrificed at 2 years after exposure, the values at 1 and 1.5 years suggest that the accumulation of both plutonium and americium in TBLN of monkeys is much less than for dogs during these times. In the case of liver, there was a gradual increase with time of the plutonium and americium burdens in the dog. This trend was absent in the monkeys, since there appeared to be a decrease with time. This is in agreement with the present knowledge regarding the rather rapid clearance of certain actinides from the liver of monkeys as compared with that of dogs (this report, pages 42 - 45).

Table 4

Organ Content of Plutonium and Americium for Dogs and Monkeys Exposed Via Inhalation to Aerosols of Mixed Uranium and Plutonium Oxides Heat-Treated at 1750°C From the Pellet Grinding Process at HEDL

Organ	Time After Exposure	% Initial Lung Burden			
		Dog ^a		Monkey	
		Pu	Am	Pu	Am
Lung	4 hr	100	100	100	100
	4 da	100	100	100	100
	64 da	71	65	81	39
	1 yr	53	34	44	13
	1.5 yr	42	44	38	19
	2 yr	38	31	b	b
TBLN ^d	4 hr	c	c	c	c
	4 da	0.39	0.35	0.06	0.36
	64 da	0.36	0.30	0.49	0.22
	1 yr	4.2	3.3	0.67	0.36
	1.5 yr	14	11	2.9	1.5
	2 yr	13	16	b	b
Liver	4 hr	0.02	0.07		
	4 da	0.04	0.16	0.11	1.4
	64 da	0.18	0.36	0.04	0.10
	1 yr	0.63	0.40	0.01	c
	1.5 yr	1.2	2.0	0.14	c
	2 yr	1.8	1.9	b	b
Skeleton	4 hr	c	c	c	c
	4 da	c	c	c	c
	64 da	0.20	1.4	c	c
	1 yr	0.43	c	c	c
	1.5 yr	0.77	1.2	c	c
	2 yr	0.91	0.89	b	c

^aMean of two animals.

^bData not available at this time.

^c< 0.01% ILB.

^dTracheobronchial lymph nodes.

Skeletal values of plutonium and americium in the dog also gradually increased with time after exposure, while in the monkey very little of either isotope can be found at any time. The skeletal burdens in Table 5 were estimated from activity levels found in one femur and one humerus according to the equation

$$S = K(F + H)$$

where S = total skeletal burden of an isotope in nCi, K = a constant relating the activity in nCi deposited in one femur (F) plus one humerus (H) to the total skeletal burden. The value of K for plutonium isotopes as determined from the analyses of total skeletons of 35 Beagle dogs containing ^{238}Pu was found to be 12 ± 1 nCi in one femur plus one humerus. The same value was determined from the skeletons of 52 Beagle dogs which contained ^{241}Am .

Figures 1 and 2 show the retention of plutonium and americium in lung as a function of time after exposure for dogs and monkeys, respectively. Data points represent the mean of two animals in the case of dogs, or individual animals in the case of the monkeys at each sacrifice time. Data for dogs is complete through 2 years after exposure; for monkeys data is available at the time of

Table 5

Retention Half-Times of Plutonium and Americium in the Lungs of Dogs and Monkeys Exposed to 1750°C Heat-Treated Mixed Uranium and Plutonium Oxides From the Pellet Grinding Process at HEDL

Species	Isotope	Fraction	Retention Half-Time (days)
Beagle Dog	Plutonium	0.75	710
Beagle Dog	Americium	0.66	630
Monkey	Plutonium	0.90	400
Monkey	Americium	0.43	320

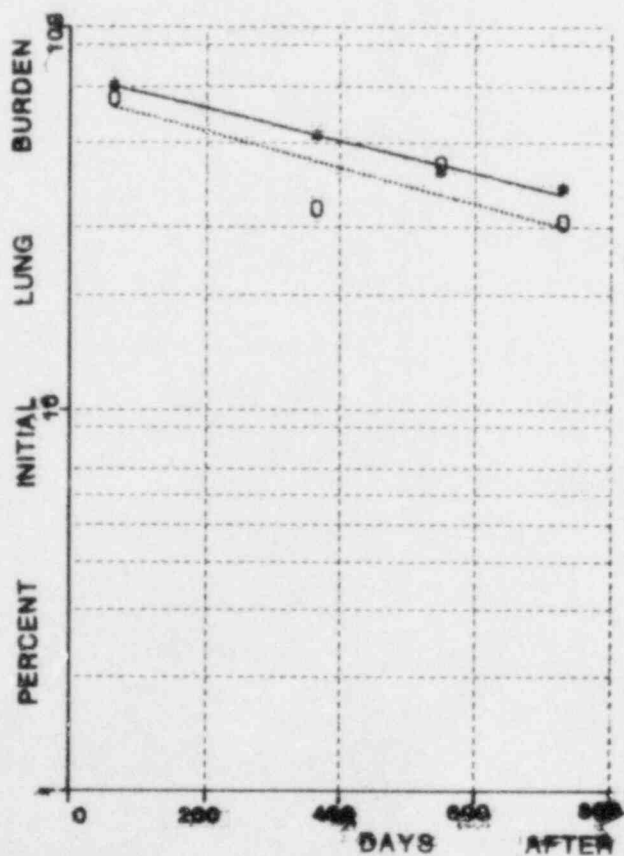


Figure 1. Lung retention of Pu(*) and Am(o) in Beagle dogs exposed to mixed uranium and plutonium oxides heat-treated at 1750°C.

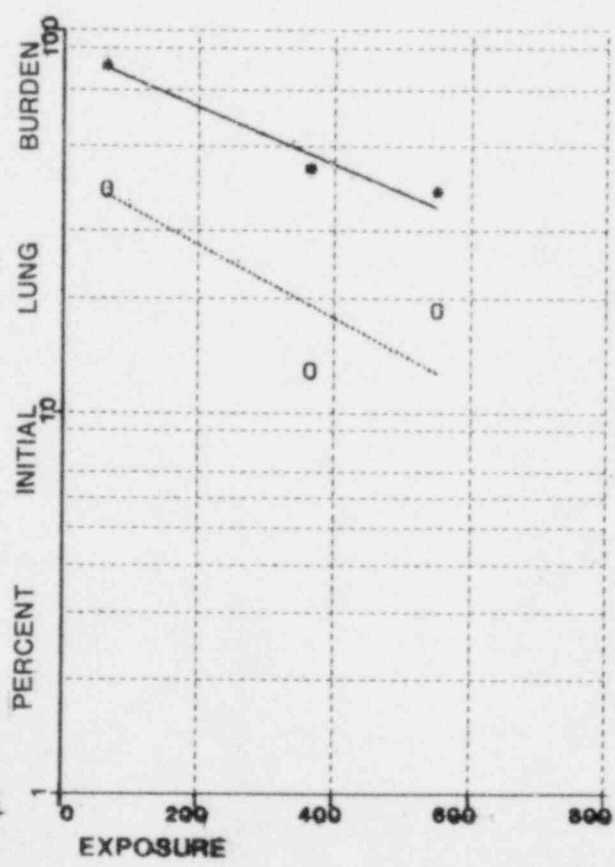


Figure 2. Lung retention of Pu(*) and Am(o) in monkeys exposed to aerosols of mixed uranium and plutonium oxides heat-treated at 1750°C.

this report only through 1.5 years. Single component negative exponential functions were fitted to the data from 64 days after exposure through 2 years and are represented by the straight lines drawn through the points. Values four days after exposure were assumed to be 100% as described above and were not included. Table 5 gives the retention half-times calculated from these curves along with the associated fraction of initially deposited material retained with these half-times. Retention of plutonium and americium in the dog lung appears to be very similar with about 70% of both isotopes leaving the lung with a half-time of about 700 days. For monkeys, the slopes of the retention curves for plutonium and americium are similar, but there appears to be a significant difference in the amount of each isotope leaving the lung during the first few days. Overall, the long-term clearance of these two isotopes appears to be much faster from the monkey lung than from the dog lung.

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*Available for purchase from the NRC/GPO Sales Program, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, and/or the National Technical Information Service, Springfield, VA 22161.

DEPOSITION, RETENTION AND DOSIMETRY OF INHALED PLUTONIUM DIOXIDE (HEAT-TREATED AT 850°C)
IN FISCHER-344 RATS, BEAGLE DOGS AND CYNOMOLGUS MONKEYS

ABSTRACT

Fischer-344 rats, Beagle dogs and Cynomolgus monkeys were exposed by inhalation to aerosols of $^{239}\text{PuO}_2$ heat-treated at 850°C produced during the V-blending process stage in the fabrication of nuclear fuel composed of mixed oxides of uranium and plutonium.

Information available through 1.5 years after exposure shows definite differences in the distribution and retention of this material in different species. For example, monkeys clear both plutonium and americium from this material from their lungs more quickly than do dogs. Also, the tracheobronchial lymph nodes of dogs accumulate a large percentage of the initially deposited lung burden of Pu and Am at longer times after exposure whereas monkeys and rats do not. The lack of an appreciable buildup of plutonium or americium in the liver of rats and monkeys indicates that either there is negligible dissolution of these isotopes in the lung or else they were cleared from the liver with relatively short half-times. The fact that a buildup of both isotopes was seen in the liver of dogs along with the known differences in the clearance of plutonium from dog liver as compared with monkey and rat liver suggest the latter.

PRINCIPAL INVESTIGATORS

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A radiation dose pattern study is under way which utilizes PuO_2 collected from the V-blending process stage in the fabrication of nuclear fuel composed of mixed oxides of U and Pu. This PuO_2 represents an early stage of fuel fabrication in which a lot of PuO_2 is thoroughly blended with powder from other lots to insure uniformity of feedstocks. After the heat treatment at 850°C and blending, the PuO_2 is mixed and blended with UO_2 to form input feed for mixed-oxide fuel fabrication. This study provides a key link between the other studies in this project that involve mixed oxides of uranium and plutonium and other on-going studies at this Institute which employ idealized, spherical, laboratory-produced aerosols of single actinide radionuclides.

MATERIALS AND METHODS

Three animal species were exposed by inhalation to aerosols of this material using dry powder generation techniques. The three species were the Fischer-344 rat (40 animals), the Beagle dog (18 animals), and the monkey (six Cynomolgus and three Rhesus). Animals were scheduled for sacrifice at 4 hours, 4 days, 64 days and 1, 1.5 and 2 years after inhalation exposure. Animals were sacrificed in groups of five rats, two dogs and one monkey at each scheduled sacrifice time. The three Rhesus monkeys included in the study were already on hand at the Institute. Two of these were assigned to the earlier sacrifice times (4 hours and 4 days), and one was held in reserve. As was the case in the other radiation dose pattern studies of mixed-oxide fuel materials, additional animals were included in each exposure group without being assigned to a particular sacrifice group. These animals are being held in reserve for substitution into a particular sacrifice group in the event of the death of animals prior to the assigned sacrifice date and to provide a small group for the observation of any biological effects produced by inhalation of the aerosol at times later than 2 years after exposure. A detailed description of the exposure process, excreta collection necropsy schedules and a listing of tissues collected for radiochemical and histopathological analysis may be found in a previous Annual Report.¹

RESULTS AND DISCUSSION

A summary of the results of characterization of exposure aerosols for each species of animal is given in Table 1. The table shows the activity median aerodynamic diameter (AMAD) and the geometric standard deviation (σ_g) of the aerosol to which each species was exposed. In the case of the dogs and monkeys, these values represent the mean of the values observed for each individual animal of that species. Since the rats were exposed as a group rather than individually, only one set of values is given. These parameters were determined for actual exposure aerosols by determining the alpha activity on successive stages of a cascade impactor and fitting a lognormal distribution function to the results. In general, the assumption that the aerosol particle size was distributed lognormally proved to be a good one as no multi-modal distributions or other significant departures from lognormality were encountered.

In each case, these aerosol parameters were found to be similar to those determined during actual sampling runs at the industrial facility as discussed previously in this report (pp. 35-46) and in a previous Annual Report.² This was an important finding, as one of the pre-requisites for conducting these experiments was to be able to regenerate aerosols from the bulk powders which closely resembled those generated during the production process.

Initial lung burdens received by dogs and monkeys were calculated by summing the total body burden of the isotope at death and the total excretory output of the animal from four dogs after inhalation exposure to death as shown in equation (1).

$$LB(4) \equiv ILB = SBB + 1.2 \int_0^4 EX(t) dt \quad (1)$$

In this equation, LB(4) is the alveolar burden on day 4 after exposure which is assumed to be equal to the initial lung burden (ILB), SBB is the sacrifice body burden or body burden at death and EX(t) is a total excretory function of the form:

$$EX(t) = A_1 e^{-\lambda_1 t} + A_2 e^{-\lambda_2 t} \quad (2)$$

where A_1 = amount of activity in nCi excreted with the rate constant λ_1 in days⁻¹. It is assumed, based on previous experience, that by day 4 after exposure, clearance of material initially deposited in the upper airways which is not considered a part of the deep lung burden, is essentially complete. Values of EX(t) were determined for individual animals using equation (2). The functions were fitted to the excreta data from individual animals using a nonlinear least squares technique. The factor of 1.2 in equation (1) is included to take into account the excreted activity recovered when washing the cages. Previous studies performed at ITRI of the deposition, retention and excretion of ²³⁸PuO₂ and ²⁴¹AmO₂ aerosols in the Beagle dog indicated that the amount of activity found in the cage washes of these animals was equal to approximately 20% of the activity excreted in urine-plus-feces for any given time period.

Table 1

Particle Size Distribution of Aerosols of 850°C Heat-Treated PuO₂ Obtained From B&W and Used in the Inhalation Exposures of Rats, Dogs and Monkeys

Species	AMAD (μm)	σ_g
Rat	2.2	2.00
Dog	2.2 ± 0.1 ^a	1.8 ± 0.06 ^a
Monkey	2.2 ± 0.2 ^b	1.8 ± 0.06 ^b

^aMean and standard error of 21 measurements.

^bMean and standard error of 9 measurements.

Table 2 gives initial lung burdens of plutonium and americium deposited in dogs and monkeys as calculated by equation 1. Values given for rats are the median and range of radiochemically determined lung burdens of animals sacrificed at 4 hours and 4 days after exposure.

The distribution of americium and plutonium among the organs of interest for rats is presented in Table 3. The low values for lung at 0 and 4 days after exposure are due to the amounts of these isotopes found in the gastrointestinal tract and upper airways during the first few days after exposure. After 4 days, most of the plutonium body burden was found in the lung through 1.5 years after exposure. Little of either isotope was found in the tracheobronchial lymph nodes or liver through 1.5 years. High skeletal burdens of americium throughout are somewhat puzzling and must await the analysis of further data for elucidation. Skeletal burdens are calculated from relevant bone data as described in this report, page 43.

Figures 1 and 2 show the retention in lung of plutonium and americium from this material in the dog and the monkey, respectively. The points represent the mean of two animals in the case of dogs and individual animals in the case of monkeys. Single component negative exponential functions of the form $Ae^{-\lambda t}$ were fit to the point sets using a nonlinear least squares technique. The retention half-times calculated from the slopes of these curves along with the respective fractions of deposited material retained with these half-times are summarized in Table 4. Only the points from 64 days after exposure and beyond were utilized in producing these curves. The 4 hour and 4 day

Table 2

Initial Lung Burden Values of Fischer-344 Rats, Beagle Dogs and Nonhuman Primates
Exposed by Inhalation to Aerosols of 850°C Heat-Treated PuO₂
Obtained From the V-Blending Process at B&W^a

Species	Animal Number	Initial Lung Burden (nCi)		Total
		Pu	Am	
Rat	-	75 (32-124) ^b	4.7 (1.8-7.3) ^b	80
Beagle Dog	2220-01	100	97	1400
Beagle Dog	2224-01	850	160	1000
Beagle Dog	2221-01	190	81	270
Beagle Dog	2224-03	1000	74	1100
Beagle Dog	2218-03	4500	380	4900
Beagle Dog	2220-03	3300	190	3500
Beagle Dog	2218-01	1200	140	1300
Beagle Dog	2223-02	660	120	780
Beagle Dog	2222-01	1100	120	1200
Beagle Dog	2222-02	2800	280	3100
Monkey	2254-01	8000	250	8300
Monkey	2265-01	500	38	540
Monkey	2254-02	55	9.5	65
Monkey	2254-03	150	93	240
Monkey	2253-01	250	160	410

^aBabcock and Wilcox Nuclear Fuel Fabrication Facility, Apollo, PA.

^bMedian (range).

Table 3

Organ Content of Pu and Am Expressed as Percent of Sacrifice Body Burden for
Rats Exposed to Aerosols of 850°C Heat-Treated PuO₂
Obtained From the V-Blending Operation at B&W

Organ	Time After Exposure	% SBB ^a Pu	% SBB ^a Am
Lung	4 hrs	15 ± 3.4	25 ± 22
	4 days	80 ± 5.5	71 ± 7.0
	67 days	96 ± 2.2	77 ± 6.0
	1 yr	97 ± 0.47	66 ± 12
	1.5 yr	94 ± 7.2	d
Tracheobronchial lymph nodes	4 days	b	0.15 ^c
	67 days	1.9 ± 2.5	d
	1 yr	1.1 ± 0.68	1.4 ± 0.01
	1.5 yr	1.1 ± 0.83	d
Liver	4 days	0.17 ± 0.19	0.43 ^c
	67 days	0.04 ± 0.03	1.7 ± 1.9
	1 yr	0.08 ± 0.02	1.6 ± 1.0
	1.5 yr	0.11 ^c	d
Skeleton	4 days	15 ± 4.7	23 ± 5.6
	67 days	1.9 ± 2.0	15 ± 7.3
	1 yr	1.6 ± 0.71	29 ± 11
	1.5 yr	4.0 ± 6.0	d

^aSacrifice body burden.

^b< 0.01% SBB.

^cValue for one animal only.

^dData not available.

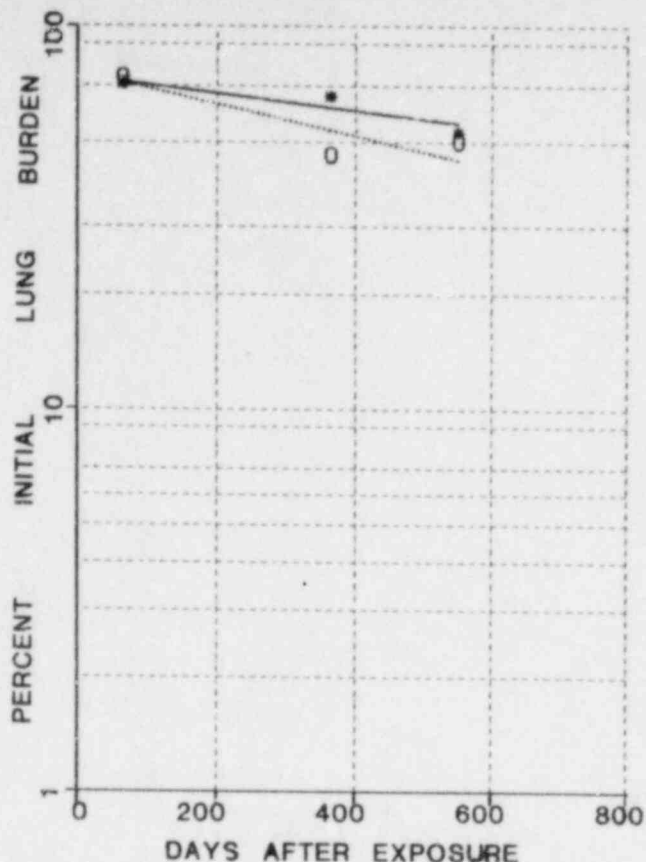


Figure 1. Lung retention of plutonium (*) and americium (o) in Beagle dogs exposed to aerosols of 850°C heat-treated PuO₂ obtained from the V-blending process at B&W.

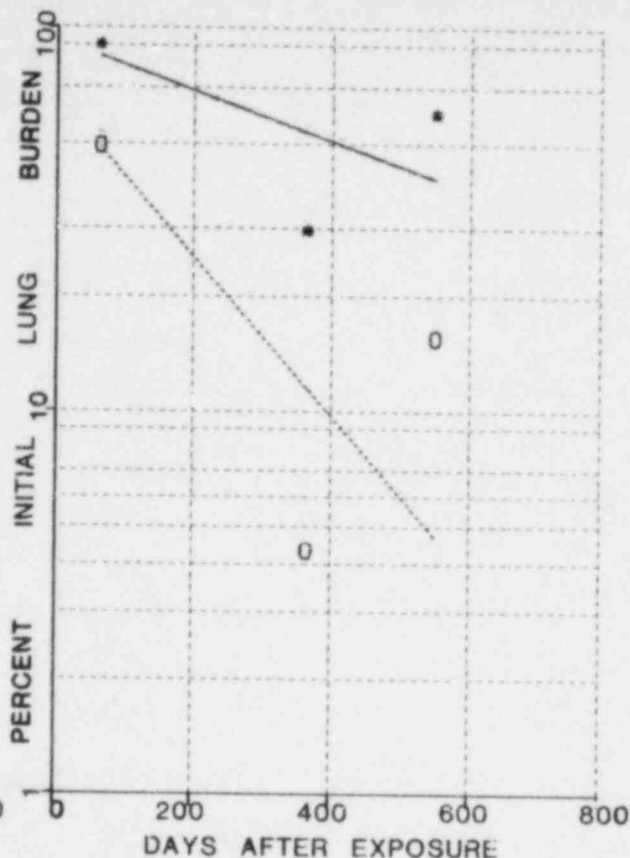


Figure 2. Lung retention of plutonium (*) and americium (o) in monkeys exposed to aerosols of 850°C heat-treated PuO₂ obtained from the V-blending process at B&W.

points were defined to be 100%. Two trends are immediately apparent from Figures 1 and 2. First, both plutonium and americium leave the monkey lung much more rapidly than they leave the dog lung. Second, it appears as though americium was cleared from the lung slightly faster than plutonium in both dogs and monkeys. This trend was more pronounced in monkeys than it was in dogs.

Table 5 gives the distribution of plutonium and americium in lung, tracheobronchial lymph nodes, liver and skeleton in terms of percentage of initial lung burden for dogs and monkeys. A careful examination of Table 5 reveals the same trends that have been observed with the two mixed-oxide materials that are the subject of the previous two papers in this report. A greater accumulation of plutonium and americium was observed in the lymph nodes of the dog than in the lymph nodes of the monkey. Evidence of a small but increasing liver burden with time was observed in dogs, although no such trend was seen in monkeys. The skeleton of both dogs and monkeys contained only traces of both isotopes. Further information is becoming available that will aid in the interpretation of these trends.

Table 4

Retention Half-Times of Plutonium and Americium in the Lungs of Dogs and Monkeys Exposed by Inhalation to Aerosols of 850°C Heat-Treated PuO₂ Obtained From the V-Blending Process at B&W

Species	Isotope	Fraction	T _{1/2} (days)
Dog	Pu	0.74	1300
Dog	Am	0.76	720
Monkey	Pu	0.93	460
Monkey	Am	0.66	140

Table 5

Organ Distribution of Pu and Am in Dogs and Monkeys Exposed by Inhalation to Aerosols of 850°C Heat-Treated PuO₂ Obtained From the V-Blending Process at B&W

Organ	Time After Exposure	% Initial Lung Burden			
		Beagle Dog ^a		Nonhuman Primate ^b	
		Pu	Am	Pu	Am
Lung	4 hr	100	100	100	100
	4 days	100	100	100	100
	64 days	71	74	90	49
	1 yr	65	46	30	4.3
	1.5 yr	53	51	60	15
Tracheobronchial Lymph Nodes	4 days	0.21	0.14	c	c
	64 days	0.41	0.48	0.38	c
	1 yr	21	20	13	0.87
	1.5 yr	19	18	5.3	1.3
Liver	4 days	0.02	0.16	c	0.59
	64 days	c	0.06	c	c
	1 yr	0.08	0.18	c	c
	1.5 yr	0.27	0.28	0.04	c
Skeleton	4	c	c	c	c
	64 days	c	c	c	c
	1 yr	0.51	c	c	c
	1.5 yr	c	c	c	c

^aMean of two animals.

^bValues reported for a single animal per sacrifice group.

^c< 0.01 %ILB.

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*Available for purchase from the NRC/GPO Sales Program, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, and/or the National Technical Information Service, Springfield, VA 22161.

COMPARISON OF INHALATION STUDIES USING THREE FORMS OF AEROSOLS PRODUCED
IN A MIXED (U-Pu) OXIDE FUEL FABRICATION FACILITY

ABSTRACT

A preliminary comparison has been made of lung retention, tissue distribution and mode of excretion of Pu following inhalation by Beagle dogs and Cynomolgus monkeys of three aerosols produced in the fabrication of mixed oxide nuclear fuels. The aerosols differed in at least two respects; thermal history and presence or absence of uranium. Two of the aerosols were mixed oxides of U and Pu treated at 750° or 1750°C and one aerosol was PuO₂ treated at 850°C. Inhalation exposure of both species to these aerosols followed by serial sacrifice of animals at 4 and 64 days, 1, 1.5 and 2.0 years allows separate compilation of data for each species and each aerosol. The information obtained to date indicates specific differences between the lung retention of dogs and monkeys for at least one aerosol (750°C). Tissue distribution, especially accumulation and retention of Pu in liver is different for dogs compared to monkeys. Excretion of Pu from both species for all three aerosols is predominately via the feces indicating the relatively insoluble nature of the aerosols.

PRINCIPAL INVESTIGATOR

J. A. Mewhinney

Three aerosol forms generated during normal operation of a mixed (U-Pu) oxide nuclear fuel fabrication facility have been used in separate, but identical, inhalation studies using three species of laboratory animals. These studies were designed to provide a measure of the lung retention, tissue distribution and excretion of these materials to permit estimation of the radiation dose pattern to specific organs and tissue. The results of these studies can then be employed to develop risk estimates for conditions in which human inhalation exposure may occur. The key factor in these studies is the use of aerosols that closely resemble in all physical and chemical respects the aerosols generated during normal plant operation and therefore the aerosol likely to be released in accidents involving human exposure. Throughout this paper the three aerosols (and therefore the three radiation dose pattern studies) will be referred to as 750°C mixed oxides of U and Pu, 1750°C mixed oxides of U and Pu and 850°C PuO₂.

MATERIALS AND METHODS

The specific details of the materials, methods, experimental design and progress of these studies have been presented.^{1,2} Common to all studies is the inhalation exposure of three animal species (Fischer-344 rat, Beagle dog and Cynomolgus monkey) with serial sacrifice of animals at preselected times after inhalation exposure to determine the lung retention, tissue distribution and excretion. Direct comparison of results for a single aerosol form and for a given species is facilitated by the commonality of experimental protocols.

Since the studies were started at different times, not all comparisons are complete. For example, the 850°C study has no data available for the 2-year sacrifice times. Thus, lung retention comparisons among the three studies were only possible through 1.5 years after inhalation exposure. The comparison of lung retention for dogs and monkeys for each aerosol type was accomplished by fitting a single component negative exponential function to the data for 64 days, 1 and 1.5 years after inhalation. For those studies or parts of studies for which lung retention data were available at 2.0 years after inhalation, that datum point was added to the earlier data and another curve

fitted to all the data. Statistical comparison of the slopes of the fitted function was accomplished using a one-way analysis of variance to test whether two slopes were different. The criterion for difference between slopes was at the 95% confidence level.

RESULTS

The fitted parameters of lung retention for dogs and monkeys through 1.5 years are given in Table 1. A comparison of the effect of addition of the datum point at 2.0 years after inhalation upon the fitted parameters of lung retention is given in Table 2. Figure 1 illustrates the lung retention data from 64 to 547 days after inhalation with the fitted single negative exponential function for dogs and monkeys for each aerosol. For ease of comparison, the Pu content in selected tissues of dogs and monkeys is reproduced in Table 3 expressed as the percent of the initial lung burden (ILB). The mode of excretion of Pu from dog and monkey following inhalation of the three aerosols is depicted in Table 4 expressed as percentage of the ILB present in urine or feces.

Table 1

Comparison of Percent of Initial Lung Burden Retained and Slope With Calculated Half-Time (Days) of Lung Retention for Beagle Dog and Cynomolgus Monkeys for Three Aerosols From Mixed-Oxide Fuel Fabrication

Aerosol (°C)	Dog			Monkey		
	%	λ	$T_{1/2}$	%	λ	$T_{1/2}$
750	83	0.460×10^{-3}	1500	75	2.06×10^{-3}	350
1750	76	1.06×10^{-3}	650	87	1.61×10^{-3}	430
850	75	0.553×10^{-3}	1250	79	1.12×10^{-3}	615

Table 2

Comparison of the Effect of 2-Years After Inhalation Exposure Datum Point Being Added to Data Used to Produce Information in Table 1

Aerosol (°C)	%	λ	$T_{1/2}$	Comment
<u>Dog</u>				
750	83	0.460×10^{-3}	1500	w/o 730 datum
750	82	0.438×10^{-3}	1600	w 730 datum
1750	76	1.05×10^{-3}	650	w/o 730 datum
1750	74	0.959×10^{-3}	700	w 730 datum
<u>Monkey</u>				
750	75	2.06×10^{-3}	350	w/o 730 datum
750	77	2.19×10^{-3}	300	w 730 datum

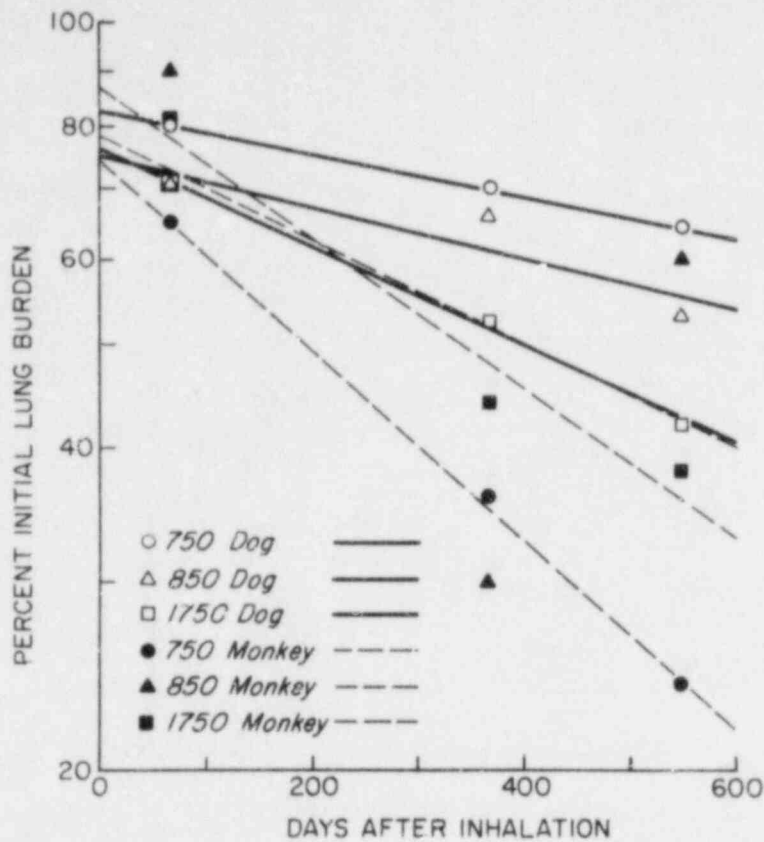


Figure 1. Lung retention of Pu following inhalation of three aerosols by Beagle dogs and Cynomolgus monkeys expressed as percent of initial lung burden.

Table 3

Distribution of Pu in Selected Tissues of the Beagle Dog and Cynomolgus Monkey at Several Times After Inhalation Exposure. Data Expressed as Percent of Initial Lung Burden. Temperature Refers to Thermal History of Inhaled Aerosols.

DPE	Dog			Monkey		
	750°C	1750°C	850°C	750°C	1750°C	850°C
	<u>TBLN</u>					
64	0.65	0.35	0.41	0.22	0.49	0.38
365	7.4	4.2	21	3.8	0.67	13
547	7.1	14	18	-	2.9	5.3
729	9.0	13		1.6		
	<u>LIVER</u>					
64	0.07	0.18	0.02	0.02	0.04	< 0.01
365	0.12	0.63	0.08	0.06	0.01	< 0.01
547	0.06	1.2	0.27	0.03	0.14	< 0.01
730	1.4	1.8		0.04		
	<u>LIVER</u>					
64	0.21	0.39	0.05	0.05	< 0.01	< 0.01
365	0.16	0.43	0.52	0.27	< 0.01	< 0.01
547	0.15	0.77	0.05	0.11	< 0.01	< 0.01
730	0.12	0.92		< 0.01		

Table 4

Excretion of Pu From Beagle Dogs and Cynomolgus Monkey Following Inhalation of Three Aerosols Containing Pu. Data Expressed as Percent of the Initial Lung Burden (mean of two dogs \pm 1 SD)

DPE	750°C				1750°C				850°C			
	Dog		Monkey		Dog		Monkey		Dog		Monkey	
	U	F	U	F	U	F	U	F	U	F	U	F
64	0.13 \pm 0.07	16 \pm 3.2	0.11	29	0.35 \pm 0.08	23 \pm 9.0	0.91	13	0.06 \pm 0.01	24 \pm 15	2.1	4.6
365	0.96 \pm 0.47	17 \pm 1.9	6.1	44	0.74 \pm 0.18	35 \pm 4.2	2.2	44	0.56 \pm 0.33	10 \pm 5.3	7.1	40
547	2.8 \pm 3.0	37 \pm 20	2.8	60	0.92 \pm 0.67	21 \pm 3.0	2.7	46	0.52 \pm 0.23	23 \pm 1.6	7.6	21
730	1.5 \pm 0.15	26 \pm 9.9	0.34	72	1.3 \pm 0.22	36 \pm 11						

DISCUSSION

The fraction of the initial lung burden which may be ascribed to long-term retention in lung was not different ($p < 0.05$) for dogs and monkeys which received inhalation exposure to the same aerosol, nor was there a difference among animals of the same species exposed to the three different aerosols (Table 1). The calculated lung retention half-times for dogs were always greater than for monkeys exposed to the same aerosol. However, statistical analysis of the slope of the fitted functions indicate that only for the 750°C aerosol was the dog lung retention different from that of the monkey. As can be noted in Figure 1, the single negative exponential function provides a good description of each set of data for lung retention with the single exception of the 850°C aerosol inhaled by monkeys. The large scatter of the data in this latter case negate meaningful comparisons. The inclusion, where possible, of the additional datum point for lung retention at 2.0 years after inhalation did not alter the above comparisons and conclusions.

When retention in dog lungs was considered alone, dogs that inhaled the 1750°C aerosol had significantly shorter lung retention half-times compared to the 750 or 850°C materials which were not different from each other. This was true whether the 2-year data were included or excluded. Comparing the lung retention in monkeys in the same manner showed no significant differences in the retention half-times among the three aerosols.

Some trends were noted in the tissue distribution of Pu in dogs and monkeys. The dogs have tended to accumulate larger fractions of the initial lung burdens in tracheobronchial lymph nodes than have the Cynomolgus monkey (Table 3). As has been reported for both Cynomolgus monkeys and baboons,³ the retention of actinide elements deposited in liver is substantially shorter than in the Beagle dog. This pattern is confirmed in these studies, most notably for the 1750°C aerosol where slightly larger fractions of the initial lung burden were transported from lung to liver and skeleton. Although the quantity of Pu reaching the skeleton of both monkeys and dogs was comparable for a given aerosol, the quantity found in liver was much lower for monkey than for dogs due to longer retention times in liver for dogs than for monkeys.

The mode of excretion of Pu from lung may be noted in Table 4 wherein the percent of the initial lung burden present in urine and feces is tabulated. For all three aerosols, fecal excretion predominated throughout the 2-year experimental period. Urinary excretion was quite low, indicating

the relatively insoluble nature of these aerosols. For the 1750°C aerosol, slightly larger fractions of the initial lung burden were translocated to liver and skeleton but this increased translocation did not result in significantly increased urinary excretion.

This preliminary comparison of data from the three radiation dose pattern studies serves two purposes. While the data are incomplete at this date, these comparisons indicate several trends in the data which will be followed. These comparisons also indicate that while trends or indications exist that the final analysis can best be carried out using computer modeling of the data to provide coherence of the data within a framework of total materials balance. With the experimental and mathematical rigor of modeling, the maximum information can be extracted from these studies.

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SUMMARY OF BIOLOGICAL EFFECTS FOLLOWING INHALATION OF INDUSTRIAL
MIXED OXIDES (URANIUM-PLUTONIUM) OR PuO₂ IN RATS

ABSTRACT

Tumors have been observed in the lungs of Fischer-344 rats after inhalation of aerosols composed of mixed oxides of Pu and U or PuO₂. Radiation doses calculated for the rats exposed to aerosols of 750 or 850°C heat-treated (U,Pu)O₂ indicate that these mixed oxides are apparently more efficient in producing lung tumors than laboratory produced single actinide oxides at the dose levels studied.

PRINCIPAL INVESTIGATORS

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Although the primary purpose of this project is not the determination of the biological effects of inhaled industrially produced radionuclides, effects have been observed in the lungs of some rats held for long-term observation. The observation and reporting of these effects is an important link between studies done using laboratory produced aerosols and studies using aerosols as actually found in nuclear fuel fabrication facilities.

METHODS

Radiation Dose Calculation

Methods used to obtain initial lung burden values and lung retention functions for these studies have been previously reported.^{1,2} The retention information and initial lung burdens used for dose calculations have been updated from these reports. Sufficient data are not yet available to determine lung doses for two of the studies.

Radiation dose in rads was calculated from the equation:

$$\text{cumulative dose (rads)} = \frac{51.2 \bar{E} f g A}{W} \int_0^{t_d} B(t) dt \quad (1)$$

where: 51.2 = conversion factor, \bar{E} = energy per disintegration in MEV, f = absorbed fraction of energy, g = fractional yield of emission, A = initial lung burden in μCi , W = lung weight in grams, $B(t)$ = lung retention expressed as a fraction of the initial lung burden as a function of time after inhalation exposures. Since the lung weights of animals with severe pulmonary radiation damage and/or lung tumors may be significantly changed with respect to their prediseased weights, the value of W is estimated in the case of these animals as a fraction of their body weight (0.0038 for males and 0.0051 for females). The values were determined from control animals sacrificed between 84 and 500 days of age.

The dose to lung was calculated separately for Am and Pu and the two values summed to arrive at total dose to lung for each animal that died. Results of the calculations are shown in Table 1 for each animal where sufficient data are available.

Two rats died at relatively early times after inhalation exposure (212, 284 days) due to radiation pneumonitis and pulmonary fibrosis. One rat was euthanized 207 days after exposure because of a large subcutaneous fibrosarcoma. It is unlikely that this tumor resulted from radiation exposure since the latent period was very short, no radionuclide was in the subcutaneous tissues and subcutaneous fibrosarcomas are common spontaneous tumors in this strain of rat.

Table 1

Rats Exposed to Mixed-Oxide Aerosols that Died Before Scheduled Sacrifice Times

Animal Number	Exposure Aerosol	Survival (DPE) ^b	ILB ^a (nCi)	Cumulative Lung Dose to Death (rads)	Significant Lesions
1933 20	UO ₂ + PuO ₂ ^c + Binder ^c	491	180	10 000	Squamous cell carcinoma, squamous cell papilloma, lung
1933 21	"	453	130	5 800	Squamous cell papilloma, lung
1933 23	"	819	109	4 100	Adenocarcinoma, lung
1933 25	"	636	156	5 600	Squamous cell carcinoma, lung
1933 29	"	369	51	1 900	Large lung mass (not examined histologically)
1933 31	"	216	74	1 900	Adenocarcinoma, lung
1933 32	"	501	120	7 500	Squamous cell carcinoma, lung
2086 4	UO ₂ + PuO ₂ ^d	415	97	2 600	Malignant mesothelioma, squamous cell carcinoma, lung
2086 5	"	493	67	2 300	Squamous cell carcinoma, lung
2086 8	"	207	80	1 500	Fibrosarcoma, subcutis
2086 19	"	627	169	8 000	Adenocarcinoma, lung
2086 24	"	284	385	14 000	Radiation pneumonitis, pulmonary fibrosis
2086 25	"	212	321	9 900	Radiation pneumonitis, pulmonary fibrosis
2086 26	"	497	298	16 000	Squamous cell papillomas, lung
2086 28	"	553	101	4 400	Squamous cell carcinoma, lung
2086 29	"	542	138	6 400	Pulmonary fibrosis
2086 31	"	663	157	7 300	Squamous cell carcinoma, lung
2086 32	"	499	144	5 800	Squamous cell carcinoma, lung
2086 34	"	438	7.2	190	Adenocarcinoma, lung
2086 39	"	711	230	9 800	Squamous cell carcinoma, lung
2100 15	(U,Pu)O ₂ ^e	427	f	-	Adenocarcinoma, lung
2100 17	"	577	f	-	Squamous cell carcinoma, lung
2100 20	"	557	f	-	Squamous cell carcinoma, lung; malignant mesothelioma
2100 23	"	564	f	-	Lymphocytic leukemia
2100 27	"	607	f	-	Squamous cell carcinoma, lung; malignant mesothelioma
2100 32	"	415	f	-	Adenocarcinoma, lung
2100 36	"	527	f	-	Squamous cell carcinoma, lung
2100 38	"	517	f	-	Squamous cell carcinoma, lung; hemangiosarcoma, lung
2100 39	"	520	f	-	Squamous cell carcinoma, lung

Table 1 (Continued)

Animal Number	Exposure Aerosol	Survival (DPE) ^b	ILB ^a (nCi)	Cumulative Lung Dose to Death (rads)	Significant Lesions
2217 1	PuO ₂ ^g	598	f	-	Squamous cell carcinoma, lung; adenocarcinoma, lung
2217 4	"	528	f	-	Squamous cell papilloma
2217 14	"	700	f	-	Squamous cell carcinoma, lung
2217 15	"	511	f	-	Squamous cell carcinoma, lung; adenocarcinoma, lung
2217 17	"	692	f	-	Squamous cell carcinoma, lung; adenocarcinoma, lung
2217 18	"	693	f	-	Squamous cell carcinoma, lung; adenocarcinoma, lung
2217 29	"	395	f	-	Hemangiosarcoma, lung
2217 30	"	589	f	-	Hemangiosarcoma, lung
2217 31	"	522	f	-	Hemangiosarcoma, pleura
2217 39	"	597	f	-	Squamous cell carcinoma, lung
2217 49	"	404	f	-	Fibrosarcoma, pleura

^aInitial lung burden of Pu and Am combined, calculated for each animal using sacrifice lung burden and standard retention curve for each radionuclide.

^bDays after exposure.

^cPuO₂ heat-treated at 850°C before mixing with UO₂ and organic binder material, powder obtained from the pellet processing operation at the Babcock and Wilcox plant.

^dPuO₂ calcined at 750°C before mixing with UO₂, powder obtained from the ball milling operation at the Hanford Engineering and Development Laboratory.

^eUO₂ and PuO₂ heat-treated at 1750°C in a reducing atmosphere to produce substoichiometric solid solution, powder obtained from the centerless grinding operation at the Hanford Engineering and Development Laboratory.

^fDetermination of retention functions not completed for determination of initial lung burdens or radiation dose.

^gPuO₂ heat-treated at 850°C, powder obtained from the V-blending process operation at the Babcock and Wilcox plant.

Thirty-three rats died with lung tumors at times ranging from 216 to 819 days after inhalation exposure. Of those animals with calculated doses, the initial lung burdens ranged from 7.2 to 298 nCi and lung doses ranged from 190 to 16,000 rads. One of these tumors was not examined histologically.

Two general morphologic types of primary lung tumors were found, adenocarcinoma and squamous cell tumors. The adenocarcinomas were characterized by large, anaplastic, cuboidal cells with basilar nuclei which formed small tubular or acinar structures. In some tumors, the acini were occasionally lined by keratinized squamous epithelium giving an adeno-squamous appearance. Some tumors had foci that were papillary, or mucinous in nature or were solid sheets of anaplastic cells. In some cases the tumor cells obliterated normal lung architecture, invading vessels, airways, pleura and the thoracic cavity. None of the carcinomas metastasized outside the thoracic cavity. In some cases the adenocarcinomas were found in the same lungs with squamous cell tumors.

The squamous cell tumors were either benign or malignant. The benign tumors were solitary masses which, on occasion, achieved 2 cm diameter and compressed adjacent lung parenchyma but did not invade it. Most of the masses were composed of necrotic cells which were sloughed from a thin border of keratinized squamous epithelium at the periphery of the mass. Although these tumors were cystic in nature, they would be classified as squamous cell papillomas using the classification system for rat lung tumors propounded by the International Agency for Research on Cancer.³

The malignant squamous cell tumors were designated squamous cell carcinomas. All were malignant based on cytologic criteria and, in some cases, invasion of adjacent structures. In no case did they metastasize outside the thoracic cavity. About one-third of the squamous cell tumors of all types were multiple or found in the lung with other lung tumor types.

Eight rats had sarcomas of the lung or pleura. Four were hemangiosarcomas primary in the lung and one was a fibrosarcoma of the pleura. Malignant mesotheliomas were found in three cases, always in association with squamous cell carcinoma of the lung. Mesotheliomas are uncommon tumors in the rat and are associated with the implantation or inhalation of fibers or polycyclic hydrocarbons. Inhalation of radioactive materials has only once been reported to cause mesothelioma and that was with inhalation of $^{238}\text{Pu}(\text{NO}_3)_4$.⁴ This finding leaves the possibility that other non-radioactive carcinogens may be present in the mixed-oxide powders obtained from industrial facilities.

An important observation in these studies is the apparent relatively high efficiency of inhaled mixed-oxide aerosols for inducing lung tumors. From Table 1 (Appendix) it can be seen that 13 of 15 rats in the 67 to 230 nCi initial lung burden range had lung tumors. The two animals with higher initial lung burdens had greatly shortened life spans and died with radiation pneumonitis. Some of those with lower initial lung burdens also had lung tumors but the range of initial lung burdens values were scattered and the number of rats few.

This lung tumor incidence of 87% was compared with the lower incidence reported in the literature for groups of rats exposed to various laboratory produced aerosols⁴⁻⁷ of plutonium and californium (Table 2). The comparison was made among groups of rats with as similar initial lung burden values as possible. In no case, regardless of the initial lung burden of the group, was the incidence of lung tumor as high as 87%. There are numerous possible reasons for the differences lung tumor incidences among these groups. This does indicate, however, that further study is needed to verify hazard estimates for mixed-oxide aerosols that are based on biologic dose response data for single isotope actinide aerosols produced in the laboratory.

Table 2

Comparison of Lung Tumor Incidence in Rats Exposed
to Various Transuranic Radionuclide Aerosols

Compound	Amount Deposited in Lungs (nCi)	Lung Tumor Incidence (%)	Reference
$^{244}\text{CmO}_2$	450 ± 300	32	5
$^{233}\text{Pu}(\text{NO}_3)_4$	70 ± 27	46	4
$^{239}\text{PuO}_2$	180 ± 54	53	6
$^{239}\text{Pu}(\text{NO}_3)_4$	142 ± 47	57	4
$^{238}\text{PuO}_2$	220 ± 97	60	7
Mixed Oxides	130 ± 45	87	This report

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*Available for purchase from the NRC/GPO Sales Program, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, and/or the National Technical Information Service, Springfield, VA 22161.

APPENDIX A

Status of Inhalation Studies

List of Tables

Aerosols of PuO_2 Heat-Treated at 750°C , Mixed with UO_2 and Ball Milled at HEDL - Beagle Dogs, Monkeys and F-344 Rats.....	75
Aerosols of $(\text{U,Pu})_{1.96}$ Heat-Treated at 1750°C , from the Pellet Grinding Operation at HEDL - Beagle Dogs, Monkeys and F-344 Rats.....	78
Aerosols of PuO_2 Heat-Treated at 850°C , from the V-Blending Operation at Babcock and Wilcox - Beagle Dogs, Monkeys and F-344 Rats.....	81
Aerosols of PuO_2 Mixed with UO_2 and Organic Binders Heat-Treated at 850°C , from the Pellet Pressing Operation at Babcock and Wilcox - F-344 Rats (Pilot Study).....	84

Status of Inhalation Studies of Aerosols of PuO₂ Heat Treated at 750°C, Mixed With UO₂ and Ball Milled
at HEDL in Beagle Dogs, Monkeys and Fischer-344 Rats

Species	Tattoo	Radiobiology Number	Sex	Exposure		Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments	
				Date	Age (days)	Weight (kg)	AMAD (μm) ± 1 SD		σ _g ± 1 SD	Date			DPE
Beagle Dog	871D	1935-01	M	76344	708	9.90	2.19 ± 0.26	1.91 ± 0.04	0	76344	0	S	
"	219C	1935-02	M	76344	3629	10.05	2.15 ± 0.09	1.74 ± 0.01	4	76348	4	S	
"	635B	1935-03	M	76344	1656	11.35	1.84 ± 0.06	1.68 ± 0.06	4	76348	4	S	
"	821T	1936-02	F	76345	884	8.45	1.58 ± 0.22	1.65 ± 0.27	549	76345	551	S	
"	217E	1937-01	M	76349	3648	8.05	2.41 ± 0.01	1.70 ± 0.03	0	76349	0	S	
"	817T	1937-02	F	76349	892	8.20	2.04 ± 0.05	1.74 ± 0.03	64	77047	64	S	
"	823S	1937-03	F	76349	886	7.20	2.50 ± 0.04	1.77 ± 0.04				928	Long Term Reserve
"	812A	1937-04	M	76349	896	9.25	2.33 ± 0.09	1.73 ± 0.02				928	" " "
"	803A	1938-01	M	76350	910	10.5	2.10 ± 0.02	1.67 ± 0.03				927	" " "
"	810U	1938-02	F	76350	901	8.0	2.61 ± 0.08	2.38 ± 0.08				927	" " "
"	811B	1938-03	M	76350	897	10.2	2.67 ± 0.02	1.62				927	" " "
"	804A	1938-04	M	76350	910	10.9	2.47 ± 0.04	1.58 ± 0.04	64	77049	65	S	
"	828T	1939-01	F	76351	872	6.95	2.18	1.66				926	Long Term Reserve
"	811A	1939-02	M	76351	898	12.8	2.18 ± 0.18	1.71 ± 0.08	730	78349	729	S	
"	799B	1939-03	M	76351	929	11.65	2.34	1.73	365	77350	364	S	
"	825S	1940-01	F	76352	889	9.3	2.22 ± 0.11	1.73 ± 0.08	730	78352	731	S	
"	826T	1940-02	F	76352	884	11.0	1.79 ± 0.10	1.81 ± 0.07	365	77353	367	S	
"	802D	1940-03	M	76352	915	8.3	2.35 ± 0.05	1.96 ± 0.23	549	78170	549	S	
Rhesus Monkey	917	2087-01	M	77039	5 - 7 years	4.85	1.61 ± 0.06	1.62 ± 0.01	0	77039	0	S, B	
Cynomolgus Monkey	25	2087-02	M	77039	3.5- 4.5 years	3.15	1.53 ± 0.05	1.53 ± 0.05				872	Long Term Reserve
"	21	2088-01	M	77040	5 - 7 years	4.35	1.10 ± 0.42	1.34 ± 0.03	64	77104	64	S	
"	26	2088-02	M	77040	3.5- 4.5 years	3.65	1.37 ± 0.04	1.56 ± 0.08	365	78040	365	S, B	
"	24	2088-03	M	77040	3.5- 4.5 years	3.60	1.22 ± 0.02	1.55 ± 0.01	549	78222	547	S, B	
Rhesus Monkey	918	2089-01	M	77041	5 - 7 years	4.40	1.61 ± 0.01	1.53 ± 0.04	4	77045	4	S, B	
Cynomolgus Monkey	27	2089-02	M	77041	3.5- 4.5 years	3.35	1.41 ± 0.04	1.56 ± 0.01	730	79040	729	S	
"	22	2089-03	F	77041	3.0- 3.5 years	2.45	1.25 ± 0.03	1.59 ± 0.04	Long Term Reserve	78056	380		D, B Gastric torsion, not radiation related
Rhesus Monkey	897	2090-01	M	77046	5 - 7 years	4.60	2.13 ± 0.04	2.30 ± 0.10	" " "	78211	530		D, B Fibrinous pleuritis caused by <i>Pasteurella</i> sp.

750°C Heat Treated PuO₂, UO₂ - HEDL (cont'd)

Species	Tattoo	Radiobiology Number	Sex	Exposure			Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
				Date	Age (weeks)	Weight (kg)	AMAD (μ m) \pm 1 SD	10 g \pm 1 SD		Date	DPE		
Fischer-344 Rats		2086-01	M	77042	9 -10	weeks	2.32 \pm 0.01	1.77 \pm 0.01	0	77042	0	S	
"	"	2086-02	M	"	"	"	"	"	365	78044	367	S	
"	"	2086-03	M	"	"	"	"	"		79017	705	D	
"	"	2086-04	M	"	"	"	"	"		78094	415	D	D, Malignant mesothelioma of thorax and squamous cell carcinoma of lung
"	"	2086-05	M	"	"	"	"	"		78170	493	D	D, Squamous cell carcinoma of the lung
"	"	2086-06	M	"	"	"	"	"	4	77046	4	S	
"	"	2086-07	M	"	"	"	"	"	365	78044	367	S	
"	"	2086-08	M	"	"	"	"	"		77249	207	E	E, Fibrosarcoma subcutis, not radiation related
"	"	2086-09	M	"	"	"	"	"	730	79043	731	S	
"	"	2086-10	M	"	"	"	"	"	4	77046	4	S	S, Unexposed control
"	"	2086-11	M	"	"	"	"	"	365	78044	367	S	
"	"	2086-12	M	"	"	"	"	"	0	77042	0	S	
"	"	2086-13	M	"	"	"	"	"	0	77042	0	S	
"	"	2086-14	M	"	"	"	"	"	64	77105	63	S	
"	"	2086-15	M	"	"	"	"	"	4	77046	4	S	
"	"	2086-16	M	"	"	"	"	"	4	77046	4	S	
"	"	2086-17	M	"	"	"	"	"	4	77046	4	S	
"	"	2086-18	M	"	"	"	"	"	64	77105	63	S	
"	"	2086-19	M	"	"	"	"	"		78304	627	D	D Adenocarcinoma, lung
"	"	2086-20	M	"	"	"	"	"	64	77105	63	S	
"	"	2086-21	F	"	"	"	"	"	547	78223	546	S	
"	"	2086-22	F	"	"	"	"	"	730	79043	731	S	
"	"	2086-23	F	"	"	"	"	"	0	77042	0	S	
"	"	2086-24	F	"	"	"	"	"		77326	284	D	D, Radiation pneumonitis and pulmonary fibrosis
"	"	2086-25	F	"	"	"	"	"		77254	212	D	D, Radiation pneumonitis and pulmonary fibrosis
"	"	2086-26	F	"	"	"	"	"		78174	497	D	D, Squamous cell papillomas, lung
"	"	2086-27	F	"	"	"	"	"	365	78044	367	S	
"	"	2086-28	F	"	"	"	"	"		78230	553	D	D Squamous cell carcinoma, lung
"	"	2086-29	F	"	"	"	"	"		78219	542	D	D Pulmonary fibrosis
"	"	2086-30	F	"	"	"	"	"	730	79043	731	S	

750°C Heat Treated PuO₂, UO₂ - HEDL (cont'd)

Species	Tattoo	Radiobiology Number	Sex	Date	Exposure Age (weeks)	Weight (kg)	Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
							AMAD (µm) ± 1 SD	G ₀ ± 1 SD		Date	DPE		
Fischer-344 Rats		2086-31	F	77042	9 -10 weeks		2.32 ± 0.01	1.77 ± 0.01		78340	663		D Squamous cell carcinoma, lung
"	"	2086-32	F	"	"	"	"	"		78176	499		D, Squamous cell carcinoma, lung
"	"	2086-33	F	"	"	"	"	"	547	78223	546		S
"	"	2086-34	F	"	"	"	"	"		78115	438		D, Adenocarcinoma, lung
"	"	2086-35	F	"	"	"	"	"	0	77042	0		S
"	"	2086-36	F	"	"	"	"	"	365	78044	367		S
"	"	2086-37	F	"	"	"	"	"	64	77105	63		S
"	"	2086-38	F	"	"	"	"	"	64	77105	63		S
"	"	2086-39	F	"	"	"	"	"		79023	711		D Squamous cell carcinoma, lung
"	"	2086-40	F	"	"	"	"	"	730	79043	731		S

B: Primate caught in the wild, age estimated from body weight at exposure.
 D: Spontaneous death.
 E: Euthanized
 S: Sacrificed.

Status of Inhalation Studies of 1750°C Heat Treated (U,Pu)O_{1.96} Aerosols from the Pellet Grinding
Operation at HEDL in Beagle Dogs, Monkeys and Fischer-344 Rats

Species	Tattoo	Radiobiology Number	Sex	Exposure		Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
				Date	Age (days)	Weight (kg)	AMAD (μm) ± 1 SD		U ²³⁵ g ± 1 SD	Date		
Beagle Dog	634A	2118-01	M	77083	1761	12.95	2.6	2.35	0	77083	0	S
" "	643A	2118-02	M	77083	1725	9.80	2.37 ± 0.01	1.70 ± 0.01	4	77087	4	S
" "	777D	2118-03	M	77083	1167	9.50	2.51 ± 0.01	1.75 ± 0.02	64	77147	64	S
" "	640S	2119-01	F	77084	1745	10.25	2.24 ± 0.02	1.62 ± 0.01	0	77084	0	S
" "	641S	2119-02	F	77084	1730	11.40	1.27 ± 0.01	1.66 ± 0.01	4	77088	4	S
" "	796S	2119-03	F	77084	1037	10.00	2.62 ± 0.08	1.64 ± 0.04	64	77147	63	S
" "	783B	2120-01	M	77088	1102	8.65	2.39 ± 0.01	1.65 ± 0.01	365	78088	365	S
" "	789A	2120-02	M	77088	1069	10.25	2.31 ± 0.02	1.70 ± 0.01	547	78270	547	S
" "	883C	2120-03	M	77088	763	9.75	2.35 ± 0.00	1.69 ± 0.01				823 Long Term Reserve
" "	961B	2122-01	M	77090	524	12.00	3.06 ± 0.04	1.78 ± 0.01	729	79089	729	S
" "	797S	2122-02	F	77090	1035	8.30	2.65 ± 0.04	1.61 ± 0.01	365	78090	365	S
" "	798T	2122-03	F	77090	1034	8.60	2.56 ± 0.11	1.65 ± 0.07	547	78272	547	S
" "	791A	2123-01	M	77091	1063	9.30	2.41 ± 0.01	1.71 ± 0.01				710 Long Term Reserve
" "	802U	2123-02	F	77091	1020	9.20	2.86 ± 0.08	1.78 ± 0.01	729	79092	731	S
" "	853T	2124-01	F	77091	895	9.55	2.93 ± 0.02	1.92 ± 0.01		78207	481	D, Long Term Reserve, Radiation Pneumonitis and Pulmonary Fibrosis
" "	863C	2124-02	M	77095	856	10.15	2.80 ± 0.18	1.67 ± 0.06				815 Long Term Reserve
" "	803S	2124-03	F	77095	1021	9.35	2.64 ± 0.04	1.76 ± 0.04				815 " " "
" "	888S	2124-04	F	77095	753	8.20	2.87 ± 0.07	1.74 ± 0.02		79163	797	D
Cynomolgus Monkey	36	2256-01	M	77236	3.5- 4.5 years	3.30	1.96 ± 0.01	1.61 ± 0.01	365	78236	365	S, B
Rhesus Monkey	900	2257-01	M	77237	5 - 7 years	7.45	2.30 ± 0.04	1.67 ± 0.06	0	77237	0	S, B
Cynomolgus Monkey	35	2257-02	M	77237	3.5- 4.5 years	3.70	2.54 ± 0.09	1.69 ± 0.01	64	77301	64	S, B
" "	39	2257-03	M	77237	3.5- 4.5 years	3.05	2.40 ± 0.06	1.72	547	79053	546	S, B
" "	38	2257-04	M	77237	3.5- 4.5 years	3.20	2.40 ± 0.05	1.70 ± 0.04	729			674 B
Rhesus Monkey	914	2258-01	M	77238	5 - 7 years	6.95	2.33 ± 0.03	1.75 ± 0.03	4	77242	4	S, B
Cynomolgus Monkey	34	2258-02	M	77238	3.5- 4.5 years	3.75	2.49 ± 0.02	1.74 ± 0.02				673 C, Long Term Reserve
" "	31	2258-03	M	77238	3.5- 4.5 years	3.75	2.37 ± 0.07	1.68 ± 0.04				673 B, " " "
" "	44	2258-04	M	77238	5 - 7 years	4.65	2.79 ± 0.01	1.73 ± 0.01				673 B, " " "

1750°C Heat Treated (U,Pu)_{1.96} - HEDL
[cont'd] [front and back]

1750°C Heat Treated (U,Pu)_{1.96} - HEDL (cont'd)

Species	Tattoo	Radiobiology Number	Sex	Date	Exposure Age		Weight (kg)	Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
					Weeks	Days		AMAD (μm) ± 1 SD	Conc (μg) ± 1 SD		Date	DPE		
Fischer-344 Rat		2100-01	F	77055	9	-10	weeks	2.30 ± 0.05	1.70 ± 0.01	547	78237	547	S	
"	"	2100-02	F	"	"	"	"	"	"	0	77055	0	S	
"	"	2100-03	F	"	"	"	"	"	"	730	79058	733	S	
"	"	2100-04	F	"	"	"	"	"	"	64	77119	64	S	
"	"	2100-05	F	"	"	"	"	"	"	365	78055	365	S	
"	"	2100-06	M	"	"	"	"	"	"	64	77119	64	S	
"	"	2100-07	F	"	"	"	"	"	"	365	78055	365	S	
"	"	2100-08	F	"	"	"	"	"	"	64	77119	64	S	
"	"	2100-09	F	"	"	"	"	"	"	0	77055	0	S	
"	"	2100-10	M	"	"	"	"	"	"	4	77059	4	S	
"	"	2100-11	F	"	"	"	"	"	"	547	78237	547	S	
"	"	2100-12	F	"	"	"	"	"	"	730	79058	733	S	
"	"	2100-13	F	"	"	"	"	"	"		78198	508	0	
"	"	2100-14	F	"	"	"	"	"	"	365	78055	365	S	
"	"	2100-15	F	"	"	"	"	"	"		78117	427	D	Adenocarcinoma, lung
"	"	2100-16	F	"	"	"	"	"	"	4	78059	4	S	
"	"	2100-17	F	"	"	"	"	"	"		78267	577	D	Squamous cell carcinoma, lung
"	"	2100-18	F	"	"	"	"	"	"	0	77055	0	S	
"	"	2100-19	F	"	"	"	"	"	"	730	79058	733	S	
"	"	2100-20	F	"	"	"	"	"	"		78247	557	D	Squamous cell carcinoma, lung; malignant mesothelioma
"	"	2100-21	M	"	"	"	"	"	"	64	77119	64	S	
"	"	2100-22	M	"	"	"	"	"	"	365	78055	365	S	
"	"	2100-23	M	"	"	"	"	"	"		78254	564	D	Lymphocytic leukemia
"	"	2100-24	M	"	"	"	"	"	"	0	77055	0	S	
"	"	2100-25	M	"	"	"	"	"	"	0	77055	0	S	
"	"	2100-26	M	"	"	"	"	"	"	0	77055	0	S	
"	"	2100-27	M	"	"	"	"	"	"		78297	607	D	Squamous cell carcinoma, lung; malignant mesothelioma
"	"	2100-28	M	"	"	"	"	"	"		77055	0	D	Died during exposure
"	"	2100-29	M	"	"	"	"	"	"		77055	0	D	Died during exposure
"	"	2100-30	F	"	"	"	"	"	"	4	77059	4	S	

1750°C Heat Treated (U,Pu)_{1.96} - HEDL (cont'd)

Species	Tatton	Radiobiology Number	Sex	Date	Exposure		Weight (kg)	Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
					Age (weeks)			AMAD (μm) \pm 1 SD	^{17}g \pm 1 SD		Date	DPE		
Fischer-344 Rat		2100-31	M	77055	9	-10	weeks	2.30 \pm 0.05	1.70 \pm 0.01	730	79058	733		S
"	"	2100-32	M	"	"	"	"	"	"		78105	415		D, Adenocarcinoma, lung
"	"	2100-33	M	"	"	"	"	"	"	547	78237	547		S
"	"	2100-34	M	"	"	"	"	"	"	64	77119	64		S
"	"	2100-35	M	"	"	"	"	"	"	4	77059	4		S
"	"	2100-36	M	"	"	"	"	"	"		78217	527		D Squamous cell carcinoma, lung
"	"	2100-37	M	"	"	"	"	"	"	4	77059	4		S
"	"	2100-38	M	"	"	"	"	"	"		78207	517		D Squamous cell carcinoma, lung; hemangiosarcoma, lung
"	"	2100-39	M	"	"	"	"	"	"		78210	520		D Squamous cell carcinoma, lung
"	"	2100-40	M	"	"	"	"	"	"	547	78237	547		S

B: Primate caught in the wild, age estimated from body weight at exposure.

D: Spontaneous death.

E: Euthanized.

S: Sacrificed.

Status of Inhalation Studies of 850°C Heat Treated PuO₂ Aerosols from the V-Blending Operation
At Babcock and Wilcox in Beagle Dogs, Monkeys and Fischer-344 Rats

Species	Tattoo	Radiobiology Number	Sex	Date	Exposure Age (days)	Weight (kg)	Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
							AMAD (μm) ± 1 SD	g ± 1 SD		Date	DPE		
Beagle Dog	791D	2218-01	M	77193	1166	8.15	2.42	1.91	365	78193	365		S
"	902A	2218-02	M	77193	806	8.85	2.27 ± 0.01	1.90 ± 0.06				718	Long Term Reserve
"	974U	2218-03	F	77193	602	7.85	2.35 ± 0.08	1.81 ± 0.03	64	77257	64		S
"	839S	2219-01	F	77194	1058	8.85	2.07 ± 0.04	1.74 ± 0.06		77196	2		D, Hypoxia induced cardiac arrest
"	837S	2220-01	F	77195	1059	9.65	2.01 ± 0.04	1.73 ± 0.02	0	77195	0		S
"	843T	2220-02	F	77195	1055	9.70	2.16 ± 0.06	1.79 ± 0.07	729	79194	729		S
"	789C	2220-03	M	77195	1176	12.15	2.02 ± 0.01	1.76 ± 0.04	64	77259	64		S
"	838S	2221-01	F	77196	1061	10.55	2.19 ± 0.04	1.76 ± 0.04	4	77200	4		S
"	800B	2221-02	M	77196	1140	9.10	2.10 ± 0.01	1.76 ± 0.02				715	Long Term Reserve
"	912A	2221-03	M	77196	762	12.35	2.27 ± 0.01	1.75 ± 0.01				715	" " "
"	841U	2222-01	F	77200	1061	6.10	2.24 ± 0.05	1.83 ± 0.03	547	79017	547		S
"	792B	2222-02	M	77200	1168	12.95	2.19 ± 0.02	1.83 ± 0.02	547	79017	547		S
"	901T	2222-03	F	77200	817	10.20	2.03	1.69				711	Long Term Reserve
"	794A	2223-01	M	77201	1163	9.35	2.23 ± 0.01	1.76 ± 0.02	729	79201	730		S
"	852S	2223-02	F	77201	1017	6.85	2.20 ± 0.06	1.76 ± 0.05	365	78256	370		S
"	974V	2223-03	F	77201	610	9.10	2.35 ± 0.02	1.80 ± 0.02				710	Long Term Reserve
"	695B	2224-01	M	77202	1627	10.85	2.12 ± 0.04	1.76 ± 0.10	0	77202	0		S
"	857W	2224-02	F	77202	985	10.50	2.29 ± 0.01	1.87 ± 0.06				709	Long Term Reserve
"	897A	2224-03	M	77202	833	11.40	2.14 ± 0.04	1.83 ± 0.01	4	77206	4		S
Rhesus Monkey	883	2253-01	M	77234	5 - 7 years	7.20	2.00 ± 0.03	1.70 ± 0.04	547	79054	550		S, B
Cynomolgus Monkey	37	2253-02	M	77234	3.5- 4.5 years	3.90	2.08 ± 0.01	1.77 ± 0.03				677	B, Long Term Reserve
"	40	2253-03	M	77234	3.5- 4.5 years	3.80	2.13 ± 0.01	1.74 ± 0.01	729	79234	730		B
Rhesus Monkey	891	2254-01	M	77235	5 - 7 years	8.25	2.43 ± 0.07	1.82 ± 0.05	0	77235	0		B
Cynomolgus Monkey	33	2254-02	M	77235	2.0- 3.5 years	2.55	2.16 ± 0.01	1.76 ± 0.06	64	77299	64		B
"	41	2254-03	M	77235	3.5- 4.5 years	3.70	2.59 ± 0.04	1.85 ± 0.03	365	78235	365		B
"	45	2254-04	M	77235	5 - 7 years	4.05	2.25 ± 0.02	1.76 ± 0.05				676	B, Long Term Reserve
"	30	2255-02	M	77236	3.5- 4.5 years	3.90	2.15 ± 0.04	1.72 ± 0.05				675	B, " " "
Rhesus Monkey	874	2265-01	M	77238	5 - 7 years	4.35	2.01 ± 0.04	1.66 ± 0.06	4	77242	4		S, B

850°C Heat Treated PuO₂ - Babcock and Wilcox (cont'd)

Species	Tattoo	Radiobiology Number	Sex	Date	Exposure		Weight (kg)	Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
					Age (weeks)			AMAD (μm) ± 1 SD	σ _g ± 1 SD		Date	DPE		
Fischer-344 Rats		2217-01	M	77195	9	-10	weeks	2.21 ± 0.12	2.00 ± 0.09		79063	598		D Squamous cell carcinoma, lung; adenocarcinoma, lung
"		2217-02	M	"	"	"	"	"	"	0	77195	0		S
"		2217-03	M	"	"	"	"	"	"	64	77262	67		S
"		2217-04	M	"	"	"	"	"	"		78358	528		D Squamous cell papilloma
"		2217-05	M	"	"	"	"	"	"	4	77199	4		S
"		2217-06	M	"	"	"	"	"	"	547	79015	550		S
"		2217-07	M	"	"	"	"	"	"	365	78195	365		S
"		2217-08	M	"	"	"	"	"	"	547	79015	550		S
"		2217-09	M	"	"	"	"	"	"	64	77262	67		S
"		2217-10	M	"	"	"	"	"	"	4	77199	4		S
"		2217-11	M	"	"	"	"	"	"	0	77195	0		S
"		2217-12	M	"	"	"	"	"	"	365	78195	365		S
"		2217-13	M	"	"	"	"	"	"	64	77262	67		S
"		2217-14	M	"	"	"	"	"	"		79165	700		D Squamous cell carcinoma, lung
"		2217-15	M	"	"	"	"	"	"		78341	511		D Squamous cell carcinoma; adenocarcinoma; lung
"		2217-16	M	"	"	"	"	"	"		77195	0		D + Died during exposure
"		2217-17	M	"	"	"	"	"	"		79157	692		D Squamous cell carcinoma; adenocarcinoma; lung
"		2217-18	M	"	"	"	"	"	"		79158	692		D Squamous cell carcinoma; adenocarcinoma; lung
"		2217-19	M	"	"	"	"	"	"	547	79015	550		S
"		2217-20	M	"	"	"	"	"	"		77195	0		D + Died during exposure
"		2217-21	F	"	"	"	"	"	"	365	78195	365		S
"		2217-22	F	"	"	"	"	"	"	547	79015	550		S
"		2217-23	F	"	"	"	"	"	"	730	79197	732		S
"		2217-24	F	"	"	"	"	"	"	64	77262	67		S
"		2217-25	F	"	"	"	"	"	"	0	77195	0		S
"		2217-26	F	"	"	"	"	"	"	64	77262	67		S
"		2217-27	F	"	"	"	"	"	"	365	78195	365		S
"		2217-28	F	"	"	"	"	"	"	4	77199	4		S
"		2217-29	F	"	"	"	"	"	"	365	78225	365		S Hemangiosarcoma, lung
"		2217-30	F	"	"	"	"	"	"		79054	589		D Hemangiosarcoma, lung
"		2217-31	F	"	"	"	"	"	"		78352	522		D Hemangiosarcoma, pleura

850°C Heat Treated PuO₂ - BW (cont'd)
[front]

850°C Heat Treated PuO₂, UO₂ and Organic
Binders [back]

850°C Heat Treated PuO₂ - Babcock and Wilcox (cont'd)

Species	Tattoo	Radiobiology Number	Sex	Date	Exposure Age (weeks)	Weight (kg)	Exposure Aerosol		Sacrifice DPE	Projected Death		Active DPE 6/30/79	Comments
							AMAD (µm) ± 1 SD	mg ± 1 SD		Date	DPE		
Fischer-344 Rats		2217-32	F	77195	9 -10	weeks	2.21 ± 0.12	2.00 ± 0.09	0	77195	0	S	
"	"	2217-33	F	"	"	"	"	"	4	77199	4	S	
"	"	2217-34	F	"	"	"	"	"	730	79197	732	S	
"	"	2217-35	F	"	"	"	"	"	730	79197	732	S	
"	"	2217-36	F	"	"	"	"	"	547	79015	550	S	
"	"	2217-37	F	"	"	"	"	"	365	78195	365	S	
"	"	2217-38	F	"	"	"	"	"	730	79197	732	S	
"	"	2217-39	F	"	"	"	"	"		79062	597	D	Squamous cell carcinoma, lung
"	"	2217-40	F	"	"	"	"	"	4	79199	4	S	
"	"	2217-46	F	"	"	"	"	"	0	77195	0	S	
"	"	2217-49	F	"	"	"	"	"		78234	404	D	Fibrosarcoma, pleura

B: Primate caught in the wild, age estimated from body weight at exposure.

D: Spontaneous death.

E: Euthanized.

S: Sacrificed.

Status of Inhalation Studies of 850°C Heat Treated PuO₂, Mixed with UO₂ and Organic Binders
(Pellet Pressing at Babcock and Wilcox) in Fischer-344 Rats (Pilot Study)

Species	Tattoo	Radiobiology Number	Sex	Date	Exposure		Exposure Aerosol		Projected Sacrifice DPE	Death		Alive DPE 6/30/79	Comments
					Age (weeks)	Weight (kg)	AMAD (μm) ± 1 SD	g ± 1 SD		Date	DPE		
Fischer-344 Rat		1933-01	M	76348	9 -10	weeks	1.73 ± 0.06	2.60 ± 0.07	0	76348	0	S	
"	"	1933-02	M	"	"	"	"	"	0	76348	0	S	
"	"	1933-03	M	"	"	"	"	"	0	76348	0	S	
"	"	1933-04	F	"	"	"	"	"	0	76348	0	S	
"	"	1933-05	F	"	"	"	"	"	0	76348	0	S	
"	"	1933-06	F	"	"	"	"	"	8	76356	8	S	
"	"	1933-07	F	"	"	"	"	"	8	76356	8	S	
"	"	1933-08	F	"	"	"	"	"	8	76356	8	S	
"	"	1933-09	F	"	"	"	"	"	8	76356	8	S	
"	"	1933-10	F	"	"	"	"	"	8	76356	8	S	
"	"	1933-11	M	"	"	"	"	"	16	76364	16	S	
"	"	1933-12	M	"	"	"	"	"	16	76364	16	S	
"	"	1933-13	F	"	"	"	"	"	16	76364	16	S	
"	"	1933-14	F	"	"	"	"	"	16	76364	16	S	
"	"	1933-15	F	"	"	"	"	"	16	76364	16	S	
"	"	1933-16	M	"	"	"	"	"	64	77046	64	S	
"	"	1933-17	F	"	"	"	"	"	64	77046	64	S	
"	"	1933-18	F	"	"	"	"	"	64	77046	64	S	
"	"	1933-19	F	"	"	"	"	"	32	77014	32	S	
"	"	1933-20	F	"	"	"	"	"		78108	491	D	Squamous cell carcinoma, squamous cell papilloma, lung
"	"	1933-21	F	"	"	"	"	"		78070	453	D	Squamous cell papilloma, lung
"	"	1933-22	M	"	"	"	"	"	64	77046	64	S	
"	"	1933-23	M	"	"	"	"	"		79071	819	E	Adenocarcinoma, lung
"	"	1933-24	M	"	"	"	"	"	32	77014	32	S	
"	"	1933-25	M	"	"	"	"	"		78253	636	D	Squamous cell carcinoma, lung
"	"	1933-26	M	"	"	"	"	"	32	77014	32	S	
"	"	1933-27	M	"	"	"	"	"	64	77046	64	S	
"	"	1933-28	M	"	"	"	"	"	32	77014	32	S	
"	"	1933-29	M	"	"	"	"	"		77351	369	D	Large lung mass (not examined histologically)
"	"	1933-30	M	"	"	"	"	"	32	77014	32	S	
"	"	1933-31	M	"	"	"	"	"		77192	210	D	Adenocarcinoma, lung
"	"	1933-32	F	"	"	"	"	"		78118	501	D	Squamous cell carcinoma, lung

D: Spontaneous death.

S: Sacrificed.

E: Euthanized

APPENDIX B

Personnel Contributing to the Research

Senior and Associate Staff

J. A. Mewhinney, PhD	Radiobiologist
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It should be emphasized that a listing such as this is rarely comprehensive in acknowledging all the individuals who have made important contributions to the research. In the unnamed category are the many highly skilled animal care, maintenance, shop, administrative and secretarial personnel whose efforts are essential to the continuation of a productive and meaningful research project.

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16. ABSTRACT (200 words or less) <p>This report details progress in studies of aerosol characteristics which may modify the biological fate, patterns of radiation dose and predicted health consequences of airborne radioactivity which may be released in normal operations or under accident conditions in the nuclear fuel cycle. Initial efforts in this project have been focused on the fabrication of nuclear fuel elements and the potential influence of radionuclide mixtures on the observed effects. Results of laboratory characterization and solubility testing of field-collected samples of PuO₂ and mixtures of PuO₂ and UO₂ are discussed relative to their potential biological impact. The current status of studies involving Fischer-344 rats, Beagle dogs and Cynomolgus monkeys exposed by inhalation to either (1) PuO₂ heat-treated at 750°C mixed with UO₂, (2) (Pu,U) oxide heat-treated at 1750°C, or (3) PuO₂ heat-treated at 850°C is given. Study (1) is near completion at two years. Comparison of the tissue distribution and excretion data available to date indicates a biological behavior for all three inhaled materials that is generally comparable to that expected from existing data on inhaled laboratory-generated aerosols of ²³⁹PuO₂. Several lung tumors have been observed in the exposed rats to date. They are described briefly in relation to the calculated absorbed doses to lung.</p>					
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