

MASTER
Effect of Physico-chemical Properties on Metabolism of
Transuranium Oxide Aerosols Inhaled by Beagle Dogs

Douglas K. Craig, Ph.D., James F. Park, D.V.M., and Jack L. Ryan, M.S.*

Biology Department
Battelle
Pacific Northwest Laboratories
Richland, Washington 99352

ABSTRACT

The oxides of four transuranium isotopes (^{238}Pu , ^{239}Pu , ^{241}Am and ^{244}Cm), prepared by identical methods of calcining the oxalate at 750°C for two hours, had different physico-chemical properties. For all four oxides the density ranges from 9.8 to 11.4 g cm^{-3} and initial ultrafilterability (suspended fraction of activity $<24 \text{ \AA}$) varied from 0.002% for $^{239}\text{PuO}_2$ to 2.24% for $^{238}\text{PuO}_2$. Dogs were exposed by nose-only techniques to aerosols generated by nebulizing water suspensions of the oxides. The dogs were sacrificed at intervals from one week to about a year postexposure. The rate of translocation of material from lung to other tissues increased from ^{239}Pu to ^{238}Pu to ^{241}Am to ^{244}Cm , possibly reflecting the decrease in mean particle size from an MMD of $0.7 \text{ }\mu\text{m}$ for $^{239}\text{PuO}_2$ to $0.6 \text{ }\mu\text{m}$ for $^{238}\text{PuO}_2$ to $0.4 \text{ }\mu\text{m}$ for $^{241}\text{AmO}_2$ to $0.1 \text{ }\mu\text{m}$ for $^{244}\text{CmO}_x$. Accumulation of the isotopes in the liver and skeleton as a percentage of final body burden was 1% ^{239}Pu and 7 to 23% for ^{238}Pu at about a year postexposure, while at 270 days postexposure, values were 40% for ^{241}Am and 40 to 30% for ^{244}Cm .

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*Chemical Technology Department.

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INTRODUCTION

Maximum permissible concentrations (MPC) of radionuclides in air and water to which human beings might be exposed are established on the basis of the known or assumed metabolism of soluble and insoluble compounds containing each radionuclide. The MPCs of the transuranium elements were derived to a large extent from studies involving single intravenous injections of monomeric isotopes in citrate solutions to beagle dogs (Mays and Dougherty, 1972), on the basis of which the skeleton was established as the critical organ for these materials. Since experimental studies with isotopes and elements other than ^{239}Pu were limited in number, the actual values for the MPCs were largely derived from the ^{239}Pu data, making adjustments for the differences in physical decay rates, modes and energies.

The biological behavior of $^{239}\text{PuO}_2$ inhaled by beagle dogs was shown by Bair (1962, 1967 and 1968) and Park, et al (1972) to differ considerably from that of the plutonium citrate. This insoluble oxide was translocated only slowly from the lung once the rapid clearance phase via the ciliary escalator and GI tract was complete. Subsequent translocation occurred mainly to the thoracic lymph nodes (LN), the fractional distribution between lung, thoracic LN, liver and skeleton being roughly 0.10, 0.50, 0.15 and 0.05 ten years postexposure (Park et al, 1972), much of the balance being in the abdominal lymph nodes. Death of these dogs was due to pulmonary-fibrosis induced respiratory insufficiency (at the higher deposition levels) and pulmonary neoplasia.

These studies established the lung as the critical organ for inhaled, insoluble transuranium oxides. Even though the highest concentration (and therefore, presumably, dose rate) of ^{239}Pu was in the thoracic lymph nodes

and these were often nearly totally destroyed, no neoplasia or other serious consequence of this fact seems to have occurred. Also, neither osteosarcomas nor carcinomas of the liver have been seen in dogs that inhaled $^{239}\text{PuO}_2$.

The first suspicion that it might not be appropriate to apply results obtained with $^{239}\text{PuO}_2$ to predict the postinhalation biological disposition of other insoluble transuranium oxides arose when changes in solubility as a function of time were observed for $^{238}\text{PuO}_2$ stored in water following preparation in identical fashion to the $^{239}\text{PuO}_2$ (Park et al, 1974). No similar changes were observed with $^{239}\text{PuO}_2$ even after four years of storage in water and it retained its crystallinity, whereas the ^{238}Pu was shown by X-ray diffraction to have become completely amorphous in nine months.

A similar higher in vitro solubility of respirable $^{238}\text{PuO}_2$ compared to $^{239}\text{PuO}_2$ has recently been reported by Raabe et al (1973) in a system designed to eliminate the effect of particle size. Also, dogs which had been exposed to $^{238}\text{PuO}_2$ prepared by firing plutonium oxalate at 350°C in 1967 started dying with osteosarcomas, as much as 50% of their final body burden being found in the skeleton.

The reason for the observed changes in ultrafilterability of $^{238}\text{PuO}_2$ with time in water suspension is not known, though it has recently been ascribed to the tearing loose of recoil nuclei following alpha decay (Fleischer, 1975). It could also be a radiolytic effect or, simply a particle size effect. We do know that $^{238}\text{PuO}_2$ powder can be stored in a dry state indefinitely without displaying an elevated ultrafilterability when it is placed in suspension, nor does it lose its crystallinity under these conditions.

The differences in biological disposition reported by Bair and Park (1968) for $^{239}\text{PuO}_2$ as a function of calcination temperature are probably due to differences in physical properties such as particle size distribution, specific surface area, completeness of oxidation, etc. The differences in tissue distribution 90 days postexposure are within the range of variability observed for dogs all exposed to the same material.

The purpose of the present study was to compare the biological disposition as a function of time postinhalation exposure of beagle dogs to the dioxides of ^{238}Pu , ^{239}Pu , ^{241}Am and ^{244}Cm . As far as possible, we also wished to characterize the physico-chemical properties of materials prepared in identical fashion and to attempt to relate these to their observed biological behavior.

METHODS

Preparation of Actinide Oxides

^{238}Pu (80% isotopic purity) and ^{239}Pu (weapons grade) were both purified by anion exchange in nitric acid (Ryan and Wheelwright, 1959). ^{241}Am resulting from beta decay of ^{241}Pu in weapons grade plutonium was recovered by dibutylbutyl phosphonate extraction from the aqueous raffinate from tributyl phosphate extraction of plutonium. It was purified by removal of Pu by anion exchange (Ryan and Wheelwright, 1959) followed by final purification by displacement development chromatography on cation exchange columns using ammonium diethylenetriaminepentaacetate as eluant (Wheelwright, 1964, and Wheelwright, 1969). ^{244}Cm was obtained from Oak Ridge National Laboratory, and ^{240}Pu was removed from it by anion exchange in nitric acid immediately (<1 day) before precipitation of the trivalent (ascorbic acid was used as a reductant to product trivalent ^{239}Pu and

^{238}Pu) actinide oxalates from 0.2 to 0.5M HNO_3 , and the oxalates were washed free of HNO_3 and fired at 750°C in air for two hours. The oxides were allowed to cool slowly in air to insure that the stoichiometry closely approached CmO_2 in the curium case (Chikalla and Eyring, 1969). These conditions were chosen because they are the same as those selected for preparation of the Fast Flux Test Facility fuel. The day before an exposure, 5 to 100 milligrams of material was thoroughly shaken up in 30 to 1000 ml of triple distilled water. The suspension was then allowed to settle for 10 minutes before decanting for use the top 3.5 cm, as described by Craig et al (1972, 1973). This procedure was designed to eliminate large, non-respirable particles before aerosolizing the material.

Characterization of Materials

Density Determinations. The density of the $^{239}\text{PuO}_2$ was determined by Hanford Engineering Development Laboratory Analytical Laboratories as 10.16 g/cm^3 by an He displacement technique. The densities of the $^{238}\text{PuO}_2$, $^{239}\text{PuO}_2$, $^{241}\text{AmO}_2$, and $^{244}\text{CmO}_2$ were all determined pycnometrically within 40 hours or less of their preparation. A specially designed pycnometer of about 2 ml total capacity was used, and the densities of $^{238}\text{PuO}_2$ and $^{239}\text{PuO}_2$ were determined on the 400 mg scale, but because of personnel exposure problems (γ rays and neutrons) the densities of $^{241}\text{AmO}_2$ and $^{244}\text{CmO}_2$ were determined on the 100 mg scale. Carbon tetrachloride was used as pycnometer fluid since radiolysis in the cases of the shorter-lived isotopes produced severe bubbling in water. In the cases of $^{238}\text{PuO}_2$, $^{239}\text{PuO}_2$ and $^{244}\text{CmO}_2$, the pycnometer was removed from a rapidly stirred CCl_4 bath at 25°C , dried, and weighed as quickly as possible. With $^{238}\text{PuO}_2$ and $^{244}\text{CmO}_2$ this thermostating was an absolute necessity because

of radiolytic heat generation, and the failure to do the $^{241}\text{AmO}_2$ measurement in the same manner is probably the cause of the lower result in that case. All the measurements were repeated several times, and the density of powdered UO_2 was also determined on the 100 mg scale.

Particle Size Determination. The particle size distribution of the unmodified, freshly calcined powders of $^{238}\text{PuO}_2$ and $^{239}\text{PuO}_2$ were determined using an MSA Particle Size Analyzer. This device combines gravity sedimentation and five possible centrifugation speeds, 300, 600, 1200, 1800 or 3600 rpm, the suspended powder being placed in calibrated capillary tubes. A minimum of about 400 mg of powder is required and external dose rates from ^{241}Am and ^{244}Cm precluded use of this technique for sizing them.

Inhalation Exposures

The techniques used for the nose-only exposure of beagle dogs to radioactive aerosols (Figure 1) have been described in detail elsewhere (Bair and Dilley, 1967; Craig et al, 1972 and 1973; modified system: Craig, Buschbom and Decker, 1975). Data from five different experiments involving the exposure of 60 dogs were used for this paper. These are summarized in Table 1, from which it will be seen that 13 dogs exposed to $^{239}\text{PuO}_2$ were sacrificed when death was imminent out to 385 days postexposure. Data on 8 of 12 dogs sacrificed out to 270 days postexposure to each of $^{241}\text{AmO}_2$ and $^{244}\text{CmO}_2$ are available. Six dogs were exposed to freshly prepared $^{238}\text{PuO}_2$ and two were sacrificed at 29, 54 and 78 days postexposure to compare the disposition with that of apparently monomeric ^{238}Pu (Park et al, 1974). Data from one of the 29-day postexposure dogs were lost. A further 10 dogs were exposed to $^{238}\text{Pu}^{16}\text{O}_{2.0}$ (PPO) specially prepared for radionuclide

thermal generators for use on board space vehicles. These were sacrificed 8, 30, 56 and 90 days postexposure.

The radionuclide distribution in the tissues of the animals following sacrifice was determined by standard techniques. Samples that gave count rates of less than twice background were recycled for further processing and alpha spectrometric studies. Data for the low level ^{241}Am and ^{244}Cm animals that have been sacrificed are not yet available for this reason, something that also applies to much of the excreta analyses. Tissue distributions are, therefore, expressed as the percentage of final body burden in all cases.

RESULTS

Details of the times of purification of the material and its preparation for the inhalation exposures are given in Table 2. The ^{239}Pu purification involved separation of ^{241}Am , the decay product of one of the contaminants of this weapons-grade plutonium, viz ^{241}Pu , while ^{240}Pu has to be removed from the $^{244}\text{CmO}_2$. There were no actinide impurities in the ^{241}Am , the contaminants being mainly rare earth elements. The physical half-life in years and some of the more significant source material data is also given in Table 2. Measured densities of the powdered oxides, together with the theoretical densities and measured lattice parameters of each freshly-calcined material are presented in Table 3. These latter data were obtained using a GE X-Ray diffractometer and showed that we were definitely exposing dogs to curium dioxides.

Table 4 gives the calcined suspension characteristics, measured as soon as possible after material preparation in order to reduce the influence of self-inflicted radiation damage, spallation or radiolytic effects

in water suspension. It was not possible to get particle size distributions conducted for $^{241}\text{AmO}_2$ and $^{244}\text{CmO}_2$ in the same way as was done for the plutonium isotopes (Figure 2), mainly because of external dose rate considerations.

Characteristics of the aerosols used for the dog inhalation exposures are presented in Table 5. Tissue distribution data for each of the four transuranium dioxides, expressed as percentage of final body burden, are presented in Figures 3 through 6. For the two plutonium isotopes, data for lung, thoracic lymph nodes, liver and skeleton are plotted. Since the percentage ^{241}Am and ^{244}Cm found in the lymph nodes was negligible, while appreciable quantities were present in dog muscles, this latter tissue has been substituted for lymph nodes in Figures 5 and 6.

Table 6 summarizes the percentage of the final body burden translocated to the gonads of the dogs for each isotope.

DISCUSSION

On the basis of UO_2 density determination on the same scale, it appears that the experimental error resulting from radiolytic heating and the small scale of the experiment (100 mg of oxide represents only about 0.01 ml of pycnometer fluid displaced) is no more than $\pm 10\%$ in the case of $^{241}\text{AmO}_2$ and $^{244}\text{CmO}_2$, $\pm 5\%$ in the case of $^{238}\text{PuO}_2$, and $\pm 2\%$ in the case of $^{239}\text{PuO}_2$. It must be realized, of course, that the densities obtained on such finely divided materials will always be somewhat lower than the theoretical values since wetting of the surfaces cannot be perfect.

X-ray diffraction patterns of the four oxides were obtained the day after their preparation with ThO_2 present as an internal standard, and lattice parameters and theoretical densities were determined from the data.

The values were corrected for radiation damage to the lattice from the time of preparation using available data (Fuger, 1975). The lattice parameters, theoretical densities, and pycnometrically determined densities are shown in Table 3 and are compared to literature values. Since it is well known that the lattice parameters increase as the oxide to metal ratios of actinide oxides decrease below 2.00 and $\text{CmO}_{1.98}$ is reported to have a lattice parameter of 5.372 Å (Keller, 1971), it is apparent that the oxide prepared here is very close to $\text{CmO}_{2.00}$. This would appear to be the case for the other transuranium oxides as well, taking into account the fact that the americium dioxide density determination was carried out without thermostatically controlling the temperature.

The characteristics of the water suspensions of the transuranium dioxides given in Table 4 reveal an important discrepancy. Other things being equal, the ratio of the initial activity concentration (total) to that of the supernatant decanted after an appropriate settling time (respirable fraction) should give an indication of the initial mass distribution of the powder with respect to particle size. The $^{239}\text{PuO}_2$ suspensions do not fit, since this material is much coarser than, for example the $^{238}\text{PuO}_2$ (see Figure 2). It appears likely that the low ratio of 1.18 for total to respirable suspension concentration was due to a failure to adequately "wet" the $^{239}\text{PuO}_2$ powder, permitting some of the large particles that would normally have settled out to remain on the surface. Aerosols generated from this supernatant suspension had mean size distribution parameters AMAD = 4.2 μm , GSD = 2.1. The aerosol thus contained a large fraction (>60%) of particles that should have settled through more than 3.5 cm of water in 10 minutes.

This discrepancy should not have had any effect upon the other measured physical parameters, with the possible exception of density. The ultrafilterability of the $^{239}\text{PuO}_2$ is exceedingly low, a fact which is matched by the very slight translocation of this isotope to dog tissues other than the thoracic lymph nodes. These contained a mean (3 dogs) about 18% of the final body burden at about a year postexposure, with 80% still in the lungs. Both ^{244}Cm and ^{241}Am were translocated to the liver and skeleton more rapidly than ^{238}Pu , even though the latter displayed a much higher initial ultrafilterability. Data from only one dog sacrificed a year postexposure is available and this had nearly 23% of the final body burden in the skeleton, 6.5% in the liver and 9.5% in the thoracic lymph nodes. There was 56% left in the lungs at this time.

^{244}Cm is translocated extremely rapidly to the liver and skeleton, about 30% and 20% of the final body burden being in these organs by the tenth postexposure day. These values increased to 40% and 30%, respectively, by 270 days postexposure. Although the initial translocation of ^{241}Am from the lung was slower, as expected on the basis of its seventy-fold lower initial ultrafilterability, the liver and skeleton each contained about 40% of the final body burden by 270 days postexposure.

Accumulation of ^{241}Am and ^{244}Cm in the thoracic lymph nodes was significantly lower than was the case for ^{238}Pu , mean values at 270 days postexposure being about 1% and 0.5%, respectively. This compares with the 9.5% value observed in the one dog that had been sacrificed one year postexposure to $^{238}\text{PuO}_2$. The indication is that AmO_2 and CmO_2 particles are being solubilized and transported in the blood to other tissues more rapidly than is the case with the $^{238}\text{PuO}_2$, despite the apparently larger ultrafilterability of the latter.

Another significant difference between $^{238}\text{PuO}_2$ and these isotopes concerns the relative amounts accumulating in the liver and skeleton. The percentages in the liver of the dogs exposed to $^{241}\text{AmO}_2$ and $^{244}\text{CmO}_2$ remain higher than the skeleton values throughout the experimental period, whereas there is a 3-fold greater accumulation of ^{238}Pu in the skeleton than in the liver. This observation also applies to ^{239}Pu at longer postexposure times (Park, 1972).

Turning to the aerosol data presented in Table 5, it is apparent that there are considerable differences in the size distributions of the material that the dogs inhaled, even though the materials were all prepared in the same way. However, even though there were significant differences in the particle size parameters of the two forms of $^{238}\text{PuO}_2$, the tissue distributions in animals sacrificed at about the same times postexposure are indistinguishable. They have, therefore, been lumped together to give a larger data base for the $^{238}\text{PuO}_2$ -exposed dogs.

We have reported changes in the apparent solubility of $^{238}\text{PuO}_2$ in water suspension in the past (Park et al, 1974), the ultrafilterability increasing as a function of time in suspension from $0.17 \pm 0.04\%$ at 1 day to $15.8 \pm 0.70\%$ at 65 days post suspension. However, one of the difficulties experienced with this technique is that it is difficult to duplicate results from one preparation to another, as illustrated by the difference between 0.17% and the value of 2.24% reported in Table 4. We have observed similar differences in the ultrafilterability of $^{244}\text{CmO}_2$, the highest observed value one day after placing the powder in suspension being 3.3% . Ultrafilterability values for $^{239}\text{PuO}_2$ have always been extremely low, $<0.2\%$.

It seems likely that differences in ultrafilterability for different isotopes of the same element will serve to indicate differences in their

biological behavior. For different elements, even though they are all dioxides initially, this may not be true. On the basis of its physical half-life, actual particle size and ultrafilterability, $^{241}\text{AmO}_2$ would have been expected to be less translocatable than $^{238}\text{PuO}_2$. However, it is a different element and may undergo chemical change to Am_2O_3 or other more soluble compounds.

The $^{244}\text{CmO}_2$ has a considerably smaller real particle size than any of the other three materials, a count median diameter of $0.02\ \mu\text{m}$ compared with values in the range 0.1 to $0.2\ \mu\text{m}$. This could account for the observed higher ultrafilterability and translocation rates. On the other hand, curium dioxide is also relatively unstable and might be changing to a different compound that is translocated more rapidly.

Finally, some values for the percentage of final body burden accumulating in the gonads of these dogs is given in Table 6. These data show that only very small quantities of these transuranium oxides end up in the gonads, the highest values being attained by the ^{238}Pu one year postexposure. Interestingly, less ^{244}Cm was found in the gonads than ^{241}Am and there was no apparent increase in quantity as a function of time for this isotope.

CONCLUSIONS

The observations that have been reported here must all be considered interim in so far as they have been made on ongoing experiments. Both the $^{238}\text{PuO}_2$ and the $^{239}\text{PuO}_2$ observations are on dogs that have died of radiation pneumonitis or been sacrificed to obtain tissue distribution data as parts of a lifespan, low-level effects study. The $^{241}\text{AmO}_2$ and $^{244}\text{CmO}_2$ studies were designed to yield distribution and excretion data for these materials to help decide whether or not life-span effects studies were

required. There are 3 dogs, scheduled for sacrifice 810 days postexposure, still alive in each study. Thus, the data presented serve only to indicate trends, out to one year postexposure, in so far as these might be related to the measured physicochemical parameters of these transuranium oxides. To use the data for dose and dose distribution calculations it is necessary to derive the initial alveolar deposition for each dog, something that will not be possible until all the excreta samples have been radiochemically analyzed.

Although there are some discrepancies, it does appear that initial ultrafilterability and the aerosol particle size distribution give an indication as to the rate of translocation of these transuranium dioxides from the lung to other tissues in dogs. Thus $^{238}\text{PuO}_2$ has a much higher initial ultrafilterability than $^{239}\text{PuO}_2$ and is much more transportable. Curium-244 dioxide has a much smaller real particle size and a higher initial ultrafilterability than $^{241}\text{AmO}_2$. It is more rapidly transported from the lung to liver and bone than any of the other three transuranium oxides, though apparently not to the gonads.

It is clear that each transuranium isotope must be considered independently, even for the same element. Bair (1967) showed that the method of preparation of plutonium-239 dioxide was of significance, probably due to differences in the resulting particle size distribution and nature of the particles formed. It is possible that biological half-lives in the lung may have to be related to initial size distributions and solubilities in order to adequately define dose and dose distributions from measured initial depositions.

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TABLE 1. NUMBER OF DOGS SACRIFICED AT VARIOUS TIMES
POSTEXPOSURE TO TRANSURANIUM OXIDE AEROSOLS

Sacrifice Time in Days Postexposure	$^{238}\text{PuO}_2$		$^{239}\text{PuO}_2$	$^{241}\text{AmO}_2$	$^{244}\text{CmO}_2$
	Expt. 160B	Expt. 158A	Expt. 140	Expt. 170	Expt. 166
7 to 15	-	1	3	2 of 3	2 of 3
29 to 30	1 of 2*	3	3	2 of 3	2 of 3
54 to 60	2	3	-	-	-
78	2	-	-	-	-
90	-	3	-	2 of 3	2 of 3
140	-	-	4	-	-
270	-	-	-	2 of 3	2 of 3
358 to 385	-	1	3	-	-

*x of y indicates x dogs analyzed to date
y dogs exposed

TABLE 2. OXIDE PREPARATION AND PHYSICAL CHARACTERISTICS

<u>Item</u>	<u>$^{238}\text{PuO}_2$</u>	<u>$^{239}\text{PuO}_2$</u>	<u>$^{241}\text{AmO}_2$</u>	<u>$^{244}\text{CmO}_2$</u>
1. Date Purified	Mar. '72	1.7.75*	Early '74	Jan. '74
2. Date Oxalate Fired	10.4.72	1.10.75	6.17.74	1.7.74
3. Temperature (°C)	750	750	750	750
4. Duration (hours)	2	2	2	2
5. Half Life	87.8 y	24400 y	458 y	18.1 y
6. Wt.% Principal Isotope	80.89	94.21	100	83.32
7. Principal Contaminant	^{239}Pu	^{240}Pu		^{246}Cm
8. Wt.% Princ. Contaminant.	14.98	5.35		4.11

*Originally purified in May, 1970 for dog exposure in 1970 and 1971.
The physical characteristics were measured on the repurified material.

TABLE 3. DENSITIES AND LATTICE PARAMETERS^(a)

Compound	Pycnometrically Determined Density (g/cm ³)	Lattice Parameter (Å)	Theoretical Density (g/cm ³)	Literature Lattice Parameter (Å)
²³⁸ PuO ₂	10.82	5.396±0.001	11.41	5.3950-5.3953 ^(b)
²³⁹ PuO ₂	10.38	5.3929±0.0004	11.47	5.3950-5.3953 ^(b)
²⁴¹ AmO ₂	9.84	5.3722±0.0004	11.69	5.3743 ^(c)
²⁴⁴ CmO ₂	11.4	5.360±0.001	11.90	5.357 5.362 ^(b)

(a) Corrected for lattice damage to time of preparation.

(b) Fuger, 1975.

(c) J. A. Fahey, R. P. Turcotte, T. D. Chikalla, Inorg. Nucl. Chem. Lett., 10: 459 (1974).

TABLE 4. CALCINED SUSPENSION CHARACTERISTICS

Characteristic	$^{238}\text{PuO}_2$	$^{239}\text{PuO}_2$	$^{241}\text{AmO}_2$	$^{244}\text{CmO}_2$
1. Powder Mass (mg)	5	97.8	100	10
2. Water Volume (ml)	35	30	30	100
3. Mass Conc. (mg ml ⁻¹)	0.143	3.26	3.33	0.10
4. Specific Activity (mCi mg ⁻¹)	12.02	0.0725*	3.242	69.5
5. Initial Suspension Activity Conc. (mCi ml ⁻¹)	1.719	0.236	10.796	6.950
6. Powder Size Distribution				
(i) MMD (μm)	8.2	15.5	--	--
(ii) GSD	1.88	1.81	--	--
(iii) 10 Wt.% <d ₁₀ (μm)	3.5	7.2	--	--
(iv) 50 Wt.% <d ₅₀ (μm)	9.0	20.8	--	--
(v) 90 Wt.% <d ₉₀ (μm)	19.2	29.0	--	--
7. Supernatant Conc. (Respirable Fraction) (μCi ml ⁻¹)	235	200	2610	2110
8. Ratio Total:Respirable	7.31	1.18	4.14	3.29
9. Initial Ultrafilterability, %	2.24±0.12	0.0002± 0.00004	0.0062± 0.005	0.42±0.021

Note: AMAD = Activity median aerodynamic diameter
 GSD = Geometric standard deviation
 MMD = Mass median diameter

*This value is for PuO₂ containing 94.21% ²³⁹Pu and 5.35% ²⁴⁰Pu, the latter having a half-life of 6540 years. Aerosols generated from this suspension had parameters AMAD = 4.19±.34 μm, GSD = 2.10±.13.

TABLE 5. INHALATION EXPOSURE AEROSOL CHARACTERISTICS

	$^{238}\text{PuO}_2$		$^{239}\text{PuO}_2$	$^{241}\text{AmO}_2$	$^{244}\text{CmO}_2$
	Exp. 160B	Exp. 158A			
1. Date of Exposures	10.5.72	11.30.72	Late '70 & thru 1971	6.18.74	1.8.74
2. Total Number of Dogs Involved	5	10 + 1	13	15	12 & 3
3. Suspension Concs. ($\mu\text{Ci ml}^{-1}$)	(H) 410 (M) (L)	245 23.5 2.50	500 50 5	188.0 14.8 0.18	151.6 17.3 2.42
4. Aerosol Concs. (nCi l^{-1})	(H) 63.4 (M) (L)	158 27.2 3.91	1100 100 10	336.0 42.12 0.66	106.1 12.62 1.25
5. Aerosol Particle Size Distribution					
			(H&M Conc.)*		(All Conc.)
(i) AMAD (μm)	2.19 \pm .19	1.88 \pm .13	2.34 \pm .36	1.40 \pm .09	0.48 \pm .05
(ii) GSD	2.25 \pm .08	1.73 \pm .12	1.89 \pm .24	1.69 \pm .05	2.13 \pm .27
(iii) MMD (μm)	0.65 \pm .06	0.55 \pm .04	0.70 \pm .10	0.40 \pm .03	0.12 \pm .01
(iv) CMD (μm)	0.09 \pm .01	0.23 \pm .04	0.23 \pm .11	0.17 \pm .02	0.02 \pm .01

Note: (H) = High Level of Exposure
(M) = Medium Level of Exposure
(L) = Low Level of Exposure
CMD = Count Median Diameter

*L Values: AMAD = 0.73 \pm .10 μm ; GSD = 2.41 \pm .22, MMD = 0.20 \pm .03 μm ,
CMD = 0.20 \pm .01 μm .

TABLE 6. TRANSLOCATION OF TRANSURANIUM OXIDES TO THE GONADS -
PERCENTAGE OF FINAL BODY BURDEN

<u>Days Postexposure</u>	<u>$^{238}\text{PuO}_2$</u>	<u>$^{239}\text{PuO}_2$</u>	<u>$^{241}\text{AmO}_2$</u>	<u>$^{244}\text{CmO}_2$</u>
7 to 15	.014 (5)	.0007 (3)	.0083 (2)	.0053 (1)
28 to 30	.022 (4)	.0067 (3)	.013 (2)	.0048 (3)
55	.056 (5)			
75 to 90	.0023 (5)		.019 (3)	.0030 (3)
140		.0008 (4)		
270			.058 (3)	.0011 (3)
370 to 390	.12 (1)	.014 (3)		

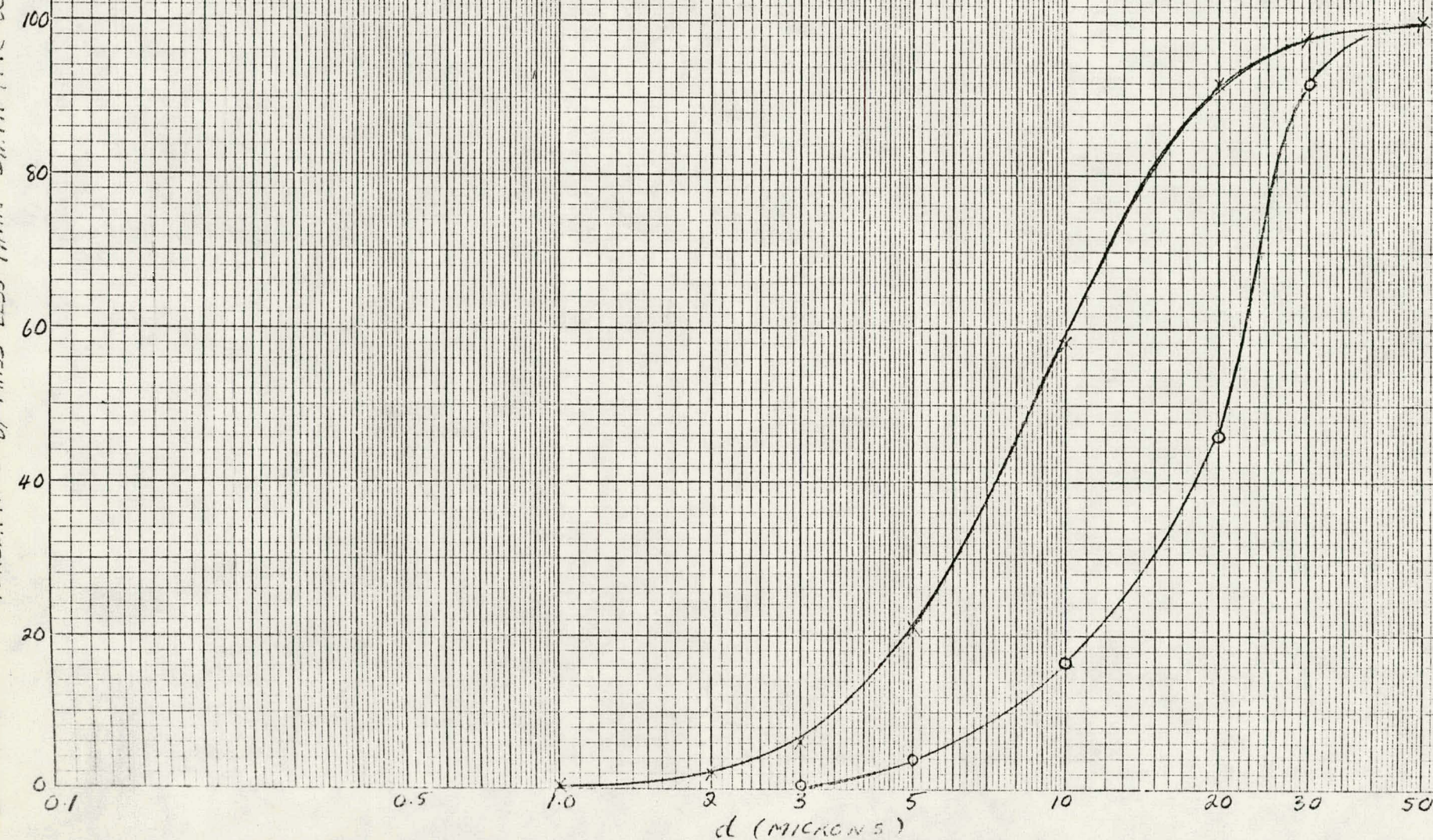
Note: Figures in brackets prepresent number of dogs.

LIST OF FIGURES

- Figure 1. Schematic of Exposure Box used for Nose-Only Inhalation Exposure of Beagle Dogs.
- Figure 2. Particle Size Distribution of Freshly Calcined Plutonium Oxalates (750°C for 2 hours).
- Figure 3. Tissue Distribution of ^{238}Pu , Expressed as Percentage of Final Body Burden, as a Function of Days Postexposure to $^{238}\text{PuO}_2$.
- Figure 4. Tissue Distribution of ^{239}Pu , Expressed as Percentage of Final Body Burden, as a Function of Days Postexposure to $^{239}\text{PuO}_2$.
- Figure 5. Tissue Distribution of ^{241}Am , Expressed as Percentage of Final Body Burden, as a Function of Days Postexposure to $^{241}\text{AmO}_2$.
- Figure 6. Tissue Distribution of ^{244}Cm , Expressed as Percentage of Final Body Burden, as a Function of Days Postexposure to $^{244}\text{CmO}_2$.

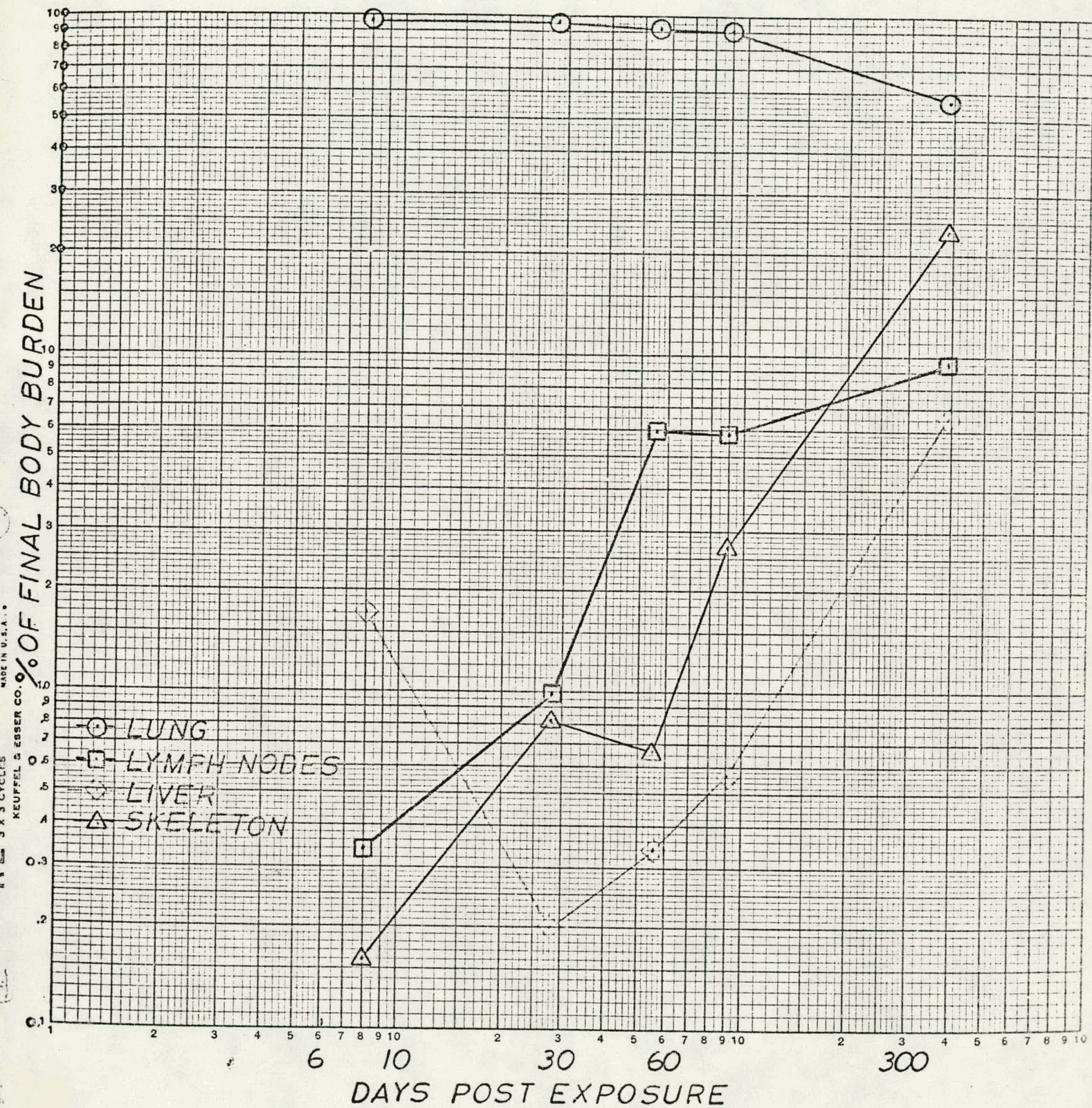
PARTICLE SIZE DISTRIBUTION OF FRESHLY CALCINED PLUTONIUM OXALATE
(750°C FOR 2 HOURS)

x ²³⁸ PuO₂
o ²³⁹ PuO₂ (MEAN OF 2 RUNS)



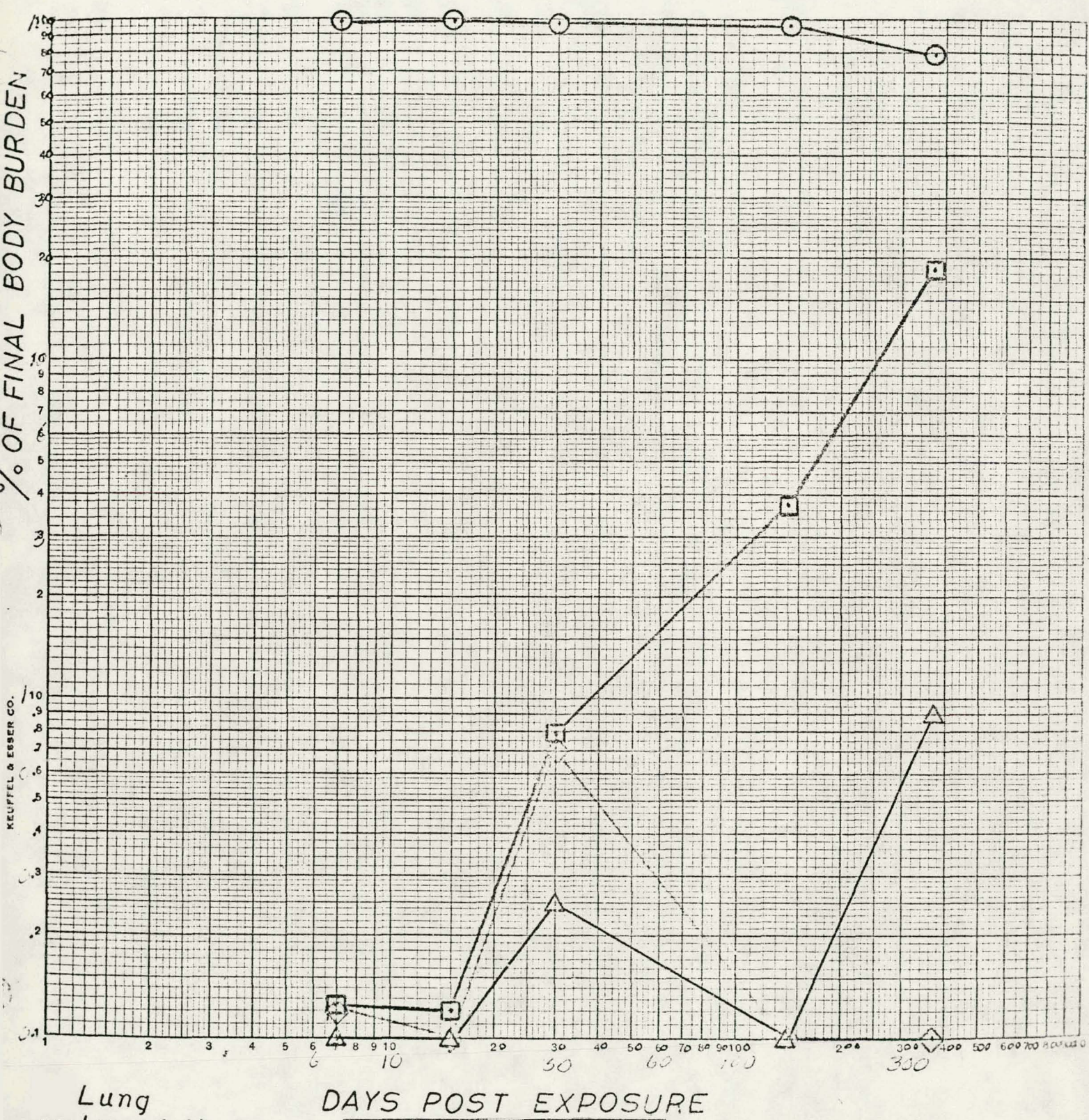
$^{238}\text{Pu O}_2$

EXPT. 158 JFP & 160 JFP



55/0

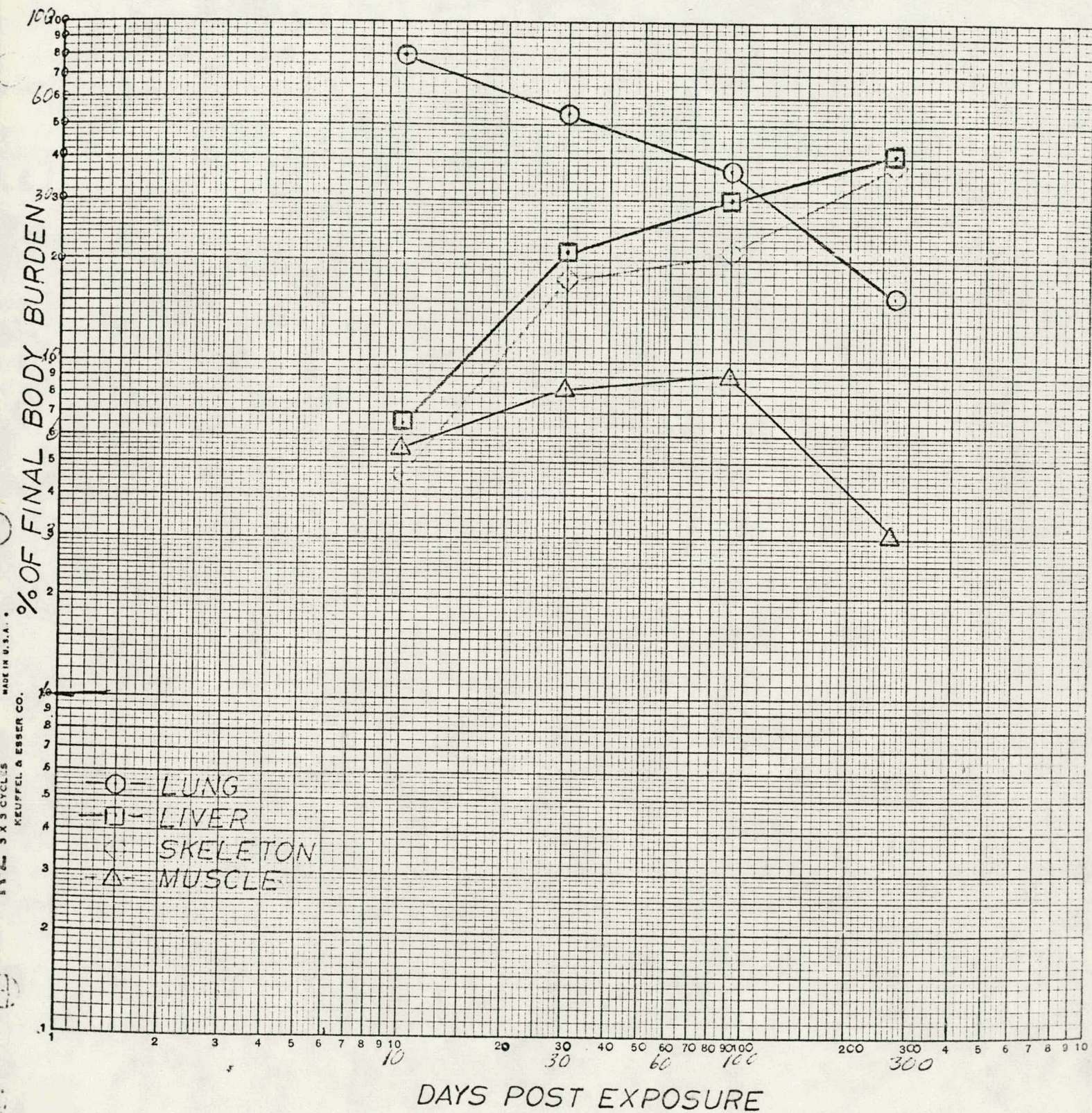
$^{239}\text{Pu O}_2$ - EXPT 140 JFP



Lung
 □ - Lymph Node
 ◇ - Liver
 △ - Skeleton

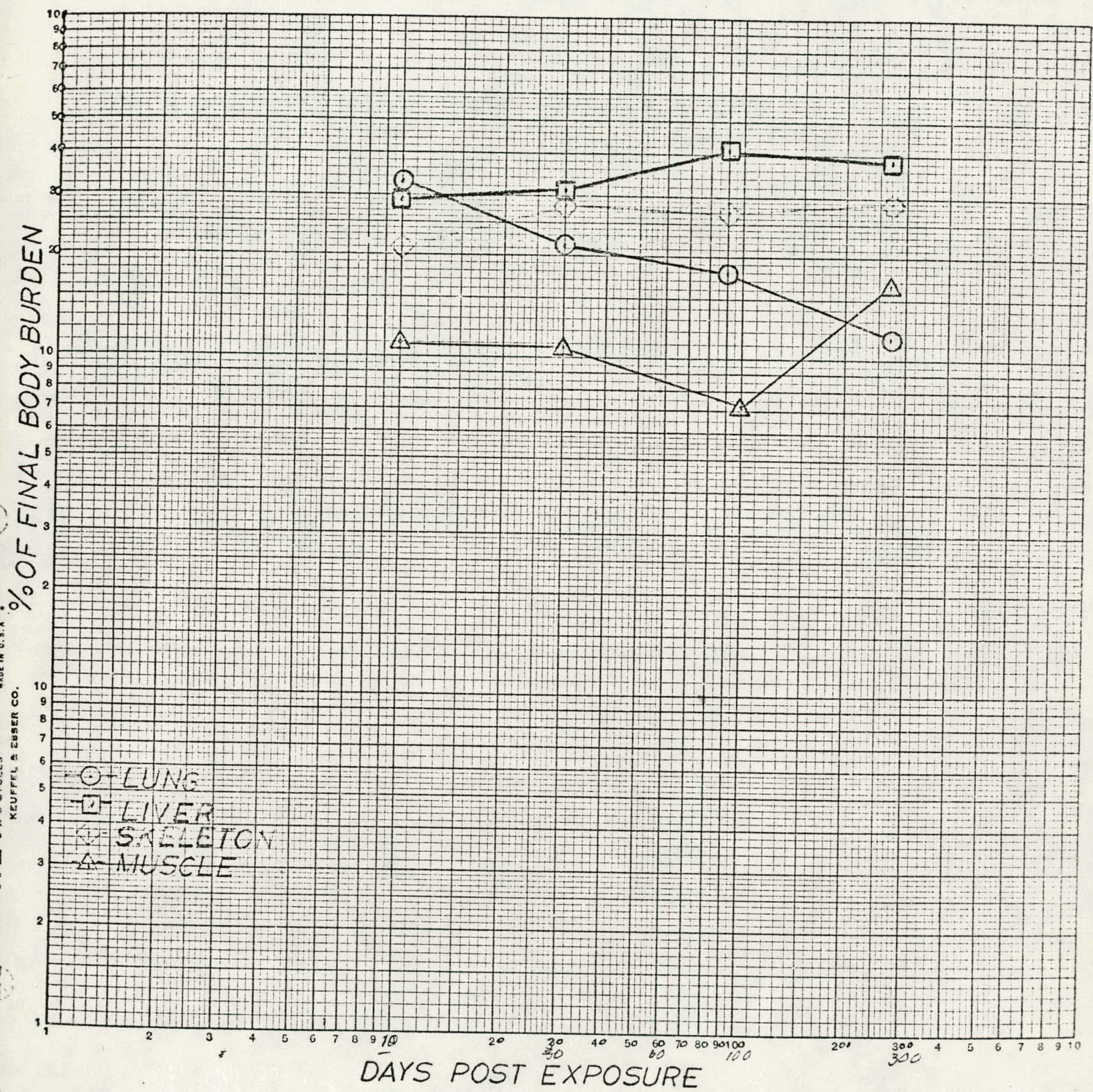
75/0

AMERICIUM - 241



7596

CURIUM - 244



REFERENCES

1. Bair, W. J., D. H. Willard, J. P. Herring and L. A. George II. Retention, translocation and excretion of inhaled $^{239}\text{PuO}_2$. Health Phys. **8**, 639 (1962).
2. Bair, W. J. and J. F. Park. Comparative disposition of four types of plutonium dioxides inhaled by dogs. In: Radiation Protection (edited by W. S. Snyder et al), Part 1, p. 181, Pergamon Press, Oxford (1968).
3. Bair, W. J. and J. V. Dilley. Pulmonary clearance of $^{59}\text{Fe}_2\text{O}_3$ and $^{51}\text{CrO}_3$ in rats and dogs exposed to cigarette smoke. In: Proc. Second International Symposium on Inhaled Particles and Vapours, Pergamon Press, Oxford (1967).
4. Chikalla, T. D. and L. Eyring, J. Inorg. Nucl. Chem., **31**, 85 (1969).
5. Craig, D. K., R. L. Buschbom and J. R. Decker. The aerodynamic equivalent size distribution of inhaled and exhaled polydispersed aerosols in beagle dogs. Presented at the AIH Conference, Minneapolis, MN, June 6, 1975, and submitted for publication.
6. Craig, D. K., J. M. Thomas, J. R. Decker and J. F. Park. Alveolar disposition of $^{239}\text{PuO}_2$ aerosols in beagle dogs as a function of respiration and aerosol parameters. Health Phys. **22**: 845-855 (1972).
7. Craig, D. K., R. L. Buschbom and J. P. Herring. Relationships between nebulizer suspension concentration, concentration and size distribution of $^{239}\text{PuO}_2$ aerosols generated for animal inhalation experiments. Health Phys. **24**: 637-644 (1973).
8. Fahey, J. A., R. P. Furcotte and T. D. Chikalla. Thermal expansion of the actinide dioxides. Inorg. Nucl. Chem. Letters **10**: 459-465 (1974).
9. Fleischer, Robert L. On the "dissolution" of respirable PuO_2 Particles. Health Phys. **29**: 69-73 (1975).

10. Fuger, J. MTP Int. Rev. Sci., Ser. Two, 7: 151-194 (1975).
11. Inorganic Chemistry, Series Two, Volume 7. Lanthanides and Actinides.
Ed. K. W. Bagnall, Butterworths (London), University Park Press
(Baltimore) 5, Effects of Radioactivity in Actinide Chemistry, by J.
Fuger, pp. 152-194. (1972)
12. Keller, C. "The Chemistry of the Transuranium Elements," Verlag Chemie
GmbH, Weinheim/Berstr., Germany, pp. 538-543, (1971).
13. Mays, C. W. and T. F. Dougherty. Progress in the beagle studies at the
University of Utah. Health Phys. 22: 793-801 (1972).
14. Park, J. F., D. L. Catt, D. K. Craig, R. J. Olson and V. H. Smith.
Solubility changes of ^{238}Pu Oxide in water suspensions and effect on bio-
logical behavior after inhalation by beagle dogs. In Proceedings of the
Third International Radiation Protection Association Conference, Washing-
ton, D. C., Sept. 9-14, 1973, pp. 719-724, CONF-730907-Pt. 1. (1974)
15. Park, J. F., W. J. Biar and R. H. Busch. Progress in beagle dog studies
with transuranium elements at Battelle-Northwest. Health Phys. 22:
803-810 (1972).
16. Raabe, O. G., G. M. Kanapely and H. A. Boyd. Studies of the in vitro
solubility of respirable particles of ^{238}Pu and ^{239}Pu oxides and an acci-
dentally released aerosol containing ^{239}Pu . In: Inhalation Toxicology
Research Institute Annual Report for 1972. LF 46: 24-30. (1973)
17. Ryan, J. L. and E. J. Wheelwright, "The Recovery, Purification and
Concentration of Plutonium by Anion Exchange in Nitric Acid," HW-55893,
January 2, 1959.
18. Wheelwright, E. J., "Cation-Exchange Purification of Am-241 on a Macro
Scale," HW-83956, September 4, 1964.
19. Wheelwright, E. J., Ion Exch. Process Ind., Pap. Conf., 202 (1969).