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# Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides

Annual Progress Report
July 1982 - June 1983

Prepared by J. A. Mewhinney

Inhalation Toxicology Research Institute
Lovelace Biomedical and Environmental Research Institute

Prepared for
U.S. Nuclear Regulatory
Commission

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# PREVIOUS DOCUMENTS IN SERIES

1. Radiation Exposure and Risk Estimates for Inhaled Airborne Radioactive Pollutants Including Hot Particles, Annual Progress Report, 1976-1977, NUREG/CR-0010, 1978.

2. Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Progress Report, 1977-1976, NUREG/CR-0673, 1979.

3. Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Progress Report, 1978-1979, NUREG/CR-1458, 1980.

4. Comparison of Physical Chemical Properties of Powder and Respirable Aerosols of Industrial Mixed Uranium and Plutonium Oxide Fuels, NUREG/CR-1736, 1980.

5. <u>In Vitro</u> Dissolution of Respirable Aerosols of Industrial Uranium and Plutonium Mixed Oxide Nuclear Fuels, NUREG/CR-2171, 1981.

6. Particle Analysis of Mixed-Oxide Nuclear Fuel Materials by Energy Dispersive X-Ray Fluorescence, NUREG/CR-1871, 1981.

7. Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Progress Report, 1979-1980, NUREG/CR-2246, 1981.

8. Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Progress Report, 1980-1981, NUREG/CR-2512, 1982.

9. Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides, Annual Progress Report, 1981-1982, NUREG/CR-3313, 1983.

ABSTRACT

The objective of this project is to conduct confirmatory research on aerosol characteristics and the resulting radiation dose distribution in animals after inhalation and to provide prediction of health consequences in humans from airborne radioactivity that might be released in normal operations or under accident conditions during production of nuclear fuel composed of mixed oxides of uranium and plutonium. Two research reports summarize the progress of current research. The first paper details results from the completed radiation dose distribution studies in which dogs, monkeys and rats were exposed to either $UO_2$ + $PuO_2$ treated at 750°C, $(U,Pu)O_2$ treated at 1750°C, or $PuO_2$ treated at 850°C. This paper focuses on analysis of the data from the last animals sacrificed in the study and updates earlier analyses of lung retention, tissue distribution, and excretion.

The second paper details preliminary analyses of the lung retention in Fischer-344 rats exposed to either $(U,Pu)O_2$ or to $PuO_2$ at one of three levels of projected dose to lung for each aerosol. This paper presents the methods and the application of a rigorous statistical procedure allowing detection of similarities and differences in the lung retention of rats at different dose levels and for different aerosols. This preliminary work is necessary before final analyses of these data can be done when all animals have died. The paper presents complete development of the data to allow calculation of radiation dose to lung and other tissues for animals in these studies and will lead to the analysis of dose-response relationships.

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ACKNOWLEDGMENTS

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It should be emphasized that a listing such as this is rarely comprehensive in acknowledging individuals who have made important contributions to the research. In the unnamed catagory are the many highly skilled animal care, maintainance, shop, administrative, and secretarial personnel whose efforts are essential to the continuation of a productive research project. Research is performed in facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

## EXECUTIVE SUMMARY

This annual progress report, consisting of two research papers details research conducted in the project "Radiation Dose Estimates and Hazard Evaluations for Airborne Radionuclides". The two papers describe the status of the two major animal studies, one completed and one under way. An attempt has been made to describe the research in 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 completion of the individual research studies.

The objective of this research project is to conduct confirmatory research on aerosol characteristics that may modify the biological fate, patterns of radiation dose and predicted health consequences of airborne radioactivity that may be released in normal operations or under accident conditions in the nuclear fuel cycle. The project involves physical, chemical and biological characterization of aerosols present in different segments of the nuclear fuel cycle. Because 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 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 aerosols, and the corresponding bulk material that might help to explain the observed patterns in the animals after exposure. Multiple species (rats, dogs, and monkeys) are being used to strengthen the eventual extrapolation to man.

The first paper describes the incorporation of data describing the retention, translocation and excretion of the Pu component of three aerosol materials, $UO_2 + PuO_2$, $(U,Pu)O_2$ and $PuO_2$ obtained from dogs and monkeys sacrificed at up to 5.5 years after inhalation. Incorporation of these new data, covering long times after inhalation, allowed extension of the biomathematical model used to describe retention, distribution, and excretion of the Pu component from these aerosols with only minor changes to a few rate constants. These additional data also allow a more rigorous statistical treatment of the pulmonary retention, hepatic and skeletal uptake and retention to highlight similarities and differences when the aerosol form and the species of animal are intercompared.

The second paper reports the current status of dose-response studies in which Fischer-344 rats were exposed to achieve graded levels of projected dose to lung from retention of either $(U,Pu)O_2$ or $PuO_2$. An analysis of lung retention data from the several groups of rats exposed in these studies, using an F statistic to determine similarities and differences, has shown that the form of the aerosol material may influence retention of the Pu component. The analysis showed that the level of projected dose to lung did not influence lung retention of Pu. This analysis, although accomplished on incomplete data sets (73 animals remain alive), has formed the basis upon which subsequent determination of the absorbed radiation dose to lung and other tissues will be based upon completion of the study and incorporation of all data.

## 1. RETENTION AND DISTRIBUTION OF PU BY BEAGLE DOGS AND CYNOMOLGUS MONKEYS AFTER INHALATION OF INDUSTRIAL AEROSOLS

*PRINCIPAL INVESTIGATORS*

*J. A. Mewhinney*

*A. F. Eidson*

*Abstract — Beagle dogs and cynomolgus monkeys received inhalation exposure to one of three aerosols derived from industrial production of mixed U, Pu oxide nuclear fuels. Sacrifice of dogs and monkeys at times up to 5.5 years after inhalation have resulted in information on lung retention, tissue distribution, and modes of excretion at longer times after inhalation. Biomathematical models developed from data up to 4 years after inhalation have been extended to encompass these new data. That incorporation has not led to significant changes in the model parameters. These new data also have allowed a more rigorous statistical analysis to test for the potential role of aerosol form and animal species on the retention and distribution of Pu after inhalation of the three aerosols. Results of these analyses confirm earlier conclusions about similarities and differences among the different aerosols and the species used in the studies, i.e., the aerosol form does not influence lung retention of the Pu component of these aerosols, whereas significant differences in lung retention do exist when dogs are compared to monkeys.*

Three completed studies provide information about the biological fate, associated distribution of radiation dose to tissue, and the implications for potential health consequences of an inhalation exposure involving mixed U, Pu oxide nuclear fuels. Within each study, differentiated by different forms of aerosol used but conducted using a common protocol, Beagle dogs and cynomolgus monkeys inhaled either 750°C-treated $UO_2$+$PuO_2$, 1750°C-treated $(U,Pu)O_2$ or 850°C-treated $PuO_2$. In the original experimental protocol, two dogs and one monkey were to be sacrificed at each scheduled sacrifice (4 hour, 4 and 64 days, 1, 1.5, and 2 years after inhalation). Six additional dogs and three additional monkeys inhaled identical amounts of each of the three aerosols at the same time as all other animals in the study. These reserve animals could then be substituted at any sacrifice time should a designated animal succumb before the scheduled sacrifice. After the two-year sacrifice time for each study, sufficient reserve animals were available for an additional set of sacrifices (2 dogs and 1 monkey) at 4 years after inhalation for two of the three studies. In the study involving the 850°C-treated $PuO_2$ aerosol, only one dog was sacrificed at 4 years (because of an error) along with one monkey.

To bring the studies to an orderly conclusion, the four dogs and three monkeys still alive were sacrificed during November and December of 1982. Exact times to sacrifice for these animals and for all others in the studies can be found in Appendix A of this report. A summary of animals sacrificed at times equal to or greater than 4 years after inhalation is presented in Table 1-1.

Lung retention, tissue distribution, and mode of excretion of Pu have been quantified using data obtained by radiochemical analysis of tissue and excreta samples from animals that died after the 4-year sacrifices or from animals that were sacrificed during November and December of 1982.

This report updates an earlier one that described data available through 4 years after exposure (Ref. 1). The resulting additional data describing the retention, distribution, and excretion of Pu have been incorporated into the data base, and the biomathematical models have been extended in time. The result of incorporation of these new data has been to confirm earlier

Table 1-1. Disposition of Reserve Animals Living at Least 4 Years After Exposure in the Three Radiation Dose Pattern Studies

| Study Aerosol | 4-Year Sacrifices | | Died Before Scheduled Sacrifice | | Sacrificed to Terminate Study | | Totals | |
|---|---|---|---|---|---|---|---|---|
| | Dog | Monkey | Dog | Monkey | Dog | Monkey | Dog | Monkey |
| 750°C | 2 | 1 | 4 | 2 | 0 | 0 | 6 | 3 |
| 1750°C | 2 | 1 | 3 | 0 | 1 | 2 | 6 | 3 |
| 850°C | 1 | 1 | 2 | 1 | 3 | 1 | 6 | 3 |

conclusions that no differences can be discerned between dogs and monkeys in the lung retention of the Pu component of these aerosol forms. In contrast, for a single aerosol form, differences do exist in the retention, distribution, and excretion of the Pu component when dogs are compared to monkeys.

## METHODS

The inhalation exposure procedures and the physical chemical characteristics of the three aerosols used have been described (Ref. 2,3), as have the *in vitro* dissolution rates of Pu, Am, and U from these materials in several solvents (Ref. 4). The biomathematical model used to describe these data sets at times up to 4 years after inhalation has been reported (Ref. 1).

An additional statistical treatment of the biological data has been completed using the completed study data set for each aerosol and each species. The treatment is based on a nonlinear least squares regression fit of appropriate functions to data sets to determine the degree of similarity of data sets. The method is based on a generalized F statistic that uses the residual sums of squares of the fitted function to test the null hypothesis that two or more data sets describing retention of an element in an organ or tissue are from the same population. The results of this statistical treatment provide a firmer basis for comparing the data than does use of the biomathematical model alone.

The generalized F statistic is calculated as follows;

$$F = \frac{\dfrac{RSS_g - \sum RSS_i}{(m-1)p}}{\dfrac{\sum RSS_i}{n-mp}} \qquad \text{(Eq. 1-1)}$$

where $RSS_g$ = the residual sums of squares of the function fitted to the grouped data set,

$RSS_i$ = the sum of the residual sums of squares of the function fitted separately to each subset of data,

m = number of subsets of data in group,

n = total number of data points in grouped data set,

p = number of parameters in the fitted function.

Applying the generalized F test to linear models involves determining the critical F value from standard statistical tables with (m-1)p degrees of freedom in the numerator and n-mp degrees of freedom in the demoninator. This method is appropriate for comparisons of lung retention when a single-component exponential function is fitted to the data. To apply the generalized F test to the situation in which nonlinear models are used (as for the hepatic and skeletal uptake and retention), a modified critical value must be determined (Ref. 5). The corrected critical value is calculated as follows;

$$C^* = 1 + F_{(\alpha;q,n-p)} \frac{q}{n-mp} \qquad \text{(Eq. 1-2)}$$

where $F(\alpha;q,n\text{-}mp)$ = the tabulated F statistic for $\alpha$ level of confidence, with q degrees of freedom for the numerator and n-mp degrees of freedom for the denominator.

The test of the null hypothesis that the data subsets are from a single population (and therefore not different) is based on either a tabulated F value or a corrected critical value as appropriate. At the stated level of confidence, the null hypothesis cannot be rejected when the calculated F value is less than the appropriate tabulated F value or the corrected critical value.

## RESULTS

The subsets of Pu lung retention data for individual dogs exposed to one of the three aerosols were fitted to a single-component exponential function. The data for all dogs were then grouped and fitted to the same function. Lung retention data for monkeys exposed to the same aerosols were treated identicallly. Table 1-2 presents, 1) the fitted parameters, residual sums of squares, number of data points for each of these fits to the subsets of data; 2) the results of fitting the same function to the grouped Pu lung retention data for each species exposed to all three aerosols; 3) the results of fitting the combined data for both species; and, 4) the calculated F statisitic for the data and the tabular critical value of F for each of the combined data fits.

In a similar manner, the data describing uptake and retention of Pu in liver and skeleton of both dogs and monkeys were fitted by a functional form that has provided an adequate description of $^{241}Am$ hepatic uptake and retention of $^{241}Am$ in dogs after inhalation of $^{241}AmO_2$ (Ref. 6). The function was

$$\%ILB = A_1 e^{-\lambda_1 t} \quad 1 - e^{-\lambda_2 t} \qquad \text{(Eq. 1-3)}$$

Results of the analysis to determine whether either aerosol or species were important in hepatic uptake and retention are presented in Table 1-3, and the identical analyses for skeleton are presented in Table 1-4.

The combined data sets for dogs and monkeys with the individual fitted functions for each species for lung, liver, and skeleton are illustrated in Figures 1-1, 1-2 and 1-3, respectively.

Table 1-2. Analysis of Lung Retention of Pu After Inhalation of One of Three Aerosol Forms by Dogs or Monkeys

| Data Set | Fitted Parameters $A_1$ | $\lambda_1$ | Residual Sum of Squares | N | Calculated F | Critical F (95%) |
|---|---|---|---|---|---|---|
| | | | Dogs | | | |
| 750°C | 83.0 | -5.68E-04 | 1160 | 14 | | |
| 1750°C | 77.5 | -6.69E-04 | 1180 | 14 | | |
| 850°C | 86.4 | -6.34E-04 | 792 | 14 | | |
| Combined | 81.9 | -6.14E-04 | 3560 | 42 | 1.27 | 2.63 |
| | | | Monkeys | | | |
| 750°C | 70.3 | -1.19E-03 | 1220 | 7 | | |
| 1750°C | 48.7 | -2.01E-04 | 362 | 7 | | |
| 850°C | 60.7 | -3.97E-04 | 1180 | 7 | | |
| Combined | 53.6 | -3.48E-04 | 3560 | 21 | 1.10 | 3.06 |
| | | | Both Species | | | |
| Combined | 71.8 | -5.30E-04 | 10060 | 63 | 12.2 | 3.15 |

Table 1-3. Analysis of Liver Uptake and Retention of Pu After Inhalation of One of Three Aerosol Forms by Dogs and Monkeys

| Data Set | Fitted Parameters $A_1$ | $\lambda_1$ | $\lambda_2$ | Residual Sum of Squares | N | Calculated F | Critical F (95%) |
|---|---|---|---|---|---|---|---|
| | | | | Dogs | | | |
| 750°C | 0.0403 | 3.28E-03 | -0.458 | 3.01 | 14 | | |
| 1750°C | 0.389 | 1.62E-03 | -1.63 | 1.77 | 14 | | |
| 850°C | 0.0336 | 3.45E-03 | -43700 | 3.80 | 14 | | |
| Combined | 0.100 | 2.60E-03 | -0.230 | 11.9 | 42 | 2.12 | 1.43 |
| | | | | Monkeys | | | |
| 750°C | 0.514 | 6.19E-04 | -29.7 | 0.639 | 7 | | |
| 1750°C | 0.0416 | 1.81E-03 | -5.43 | 0.828 | 7 | | |
| 850°C | 0.00579 | 2.53E-03 | -1.58 | 0.806 | 7 | | |
| Combined | 0.0213 | 1.92E-03 | -5.45 | 3.97 | 21 | 1.49 | 2.50 |
| | | | | Both Species | | | |
| Combined | 0.0522 | 2.56E-03 | -1.21 | 27.2 | 63 | 14.2 | 1.15 |

Table 1-4. Analysis of Skeletal Uptake and Retention of Pu After Inhalation of Three Aerosol Forms by Dogs and Monkeys

| Data Set | Fitted Parameters $A_1$ | $\lambda_1$ | $\lambda_2$ | Residual Sum of Squares | N | Calculated F | Critical F (95%) |
|---|---|---|---|---|---|---|---|
| | | | | Dogs | | | |
| 750°C | 0.122 | 7.47E-04 | -98.8 | 0.561 | 14 | | |
| 1750°C | 0.929 | 2.99E-04 | -11800 | 1.38 | 14 | | |
| 850°C | 0.0281 | 1.63E-03 | -10.0 | 0.572 | 14 | | |
| Combined | 0.160 | 8.18E-04 | -3.71 | 11.1 | 42 | 20.5 | 1.39 |
| | | | | Monkeys | | | |
| 750°C | 0.0610 | 1.24E-03 | -4480 | 0.657 | 7 | | |
| 1750°C | 0.0663 | 1.02E-03 | -1.47 | 0.621 | 7 | | |
| 850°C | 0.213 | 4.11E-04 | -4.68 | 0.820 | 7 | | |
| Combined | 0.098 | 4.72E-04 | -3.33 | 2.97 | 21 | 0.83 | 2.50 |
| | | | | Both Species | | | |
| Combined | 0.139 | 7.00E-04 | -0.724 | 15.8 | 63 | 2.28 | 1.15 |

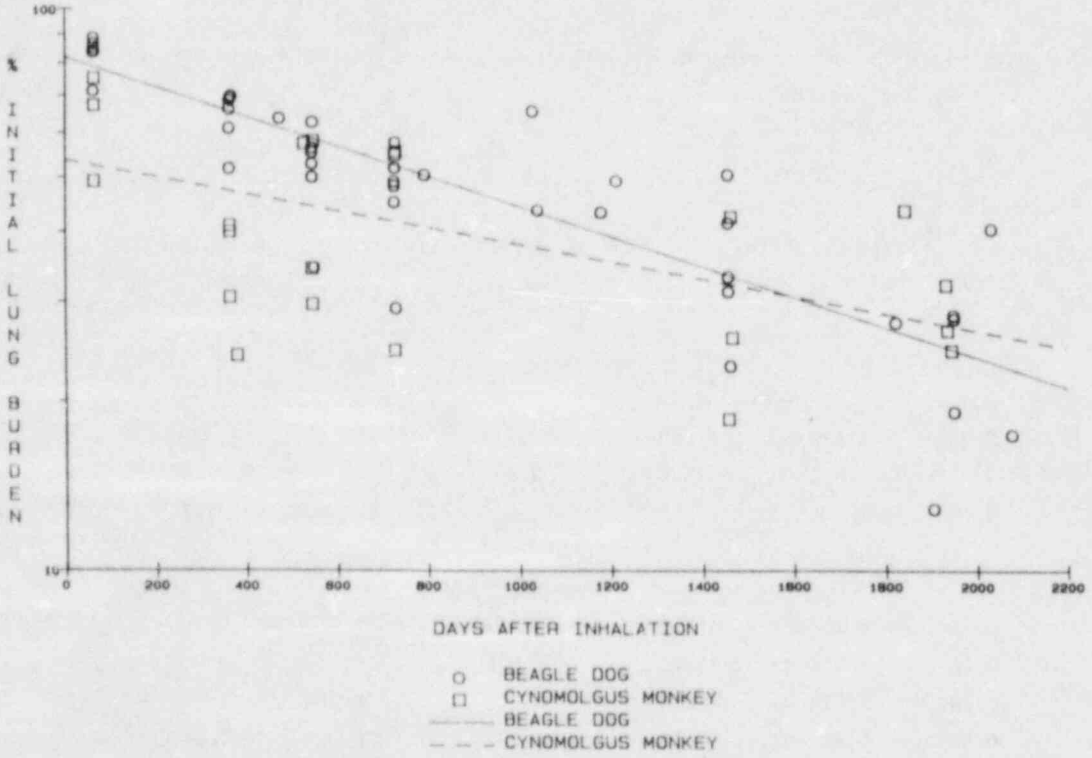


Figure 1-1. Lung retention of Pu in dogs and monkeys after inhalation of 750°C-treated $UO_2$ + $PuO_2$, 1750°C-treated $(U,Pu)O_2$ or 850°C-treated "pure" $PuO_2$. Each curve represents a non-linear least squares fit to the grouped data for a given species.

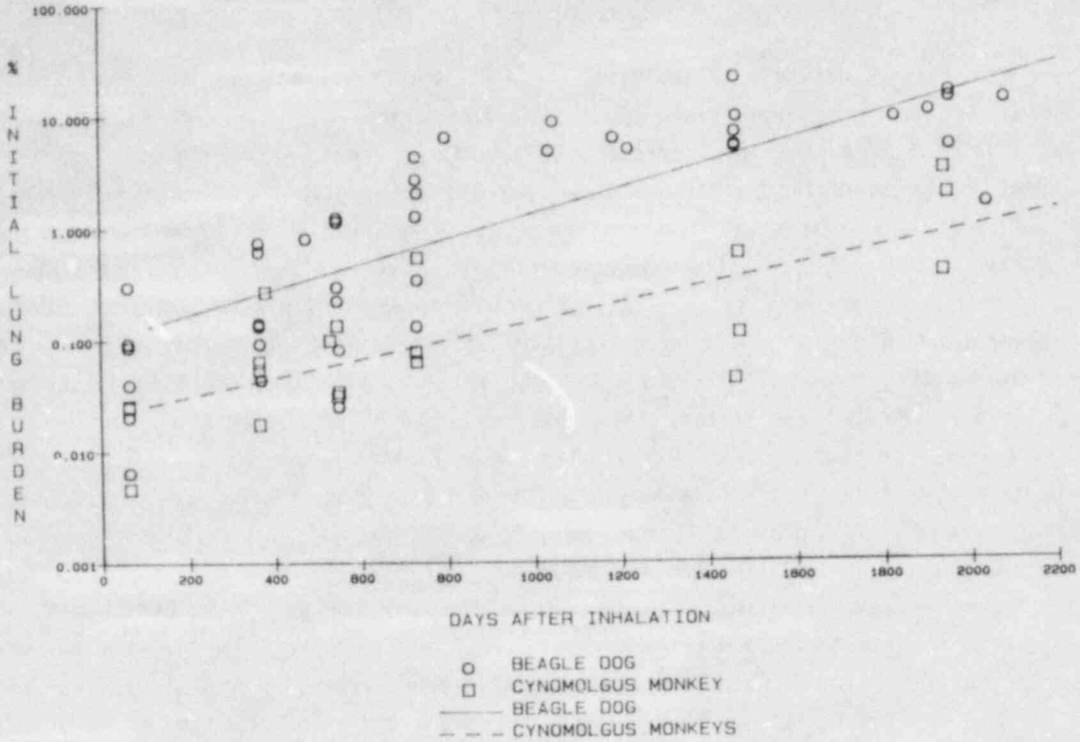


Figure 1-2. Uptake and retention of Pu in the liver of dogs and monkeys after inhalation of 750°C-treated $UO_2$ + $PuO_2$, 1750°C-treated $(U,Pu)O_2$ or 850°C-treated $PuO_2$. Each curve represents a non-linear least squares fit to the grouped data for a given species.

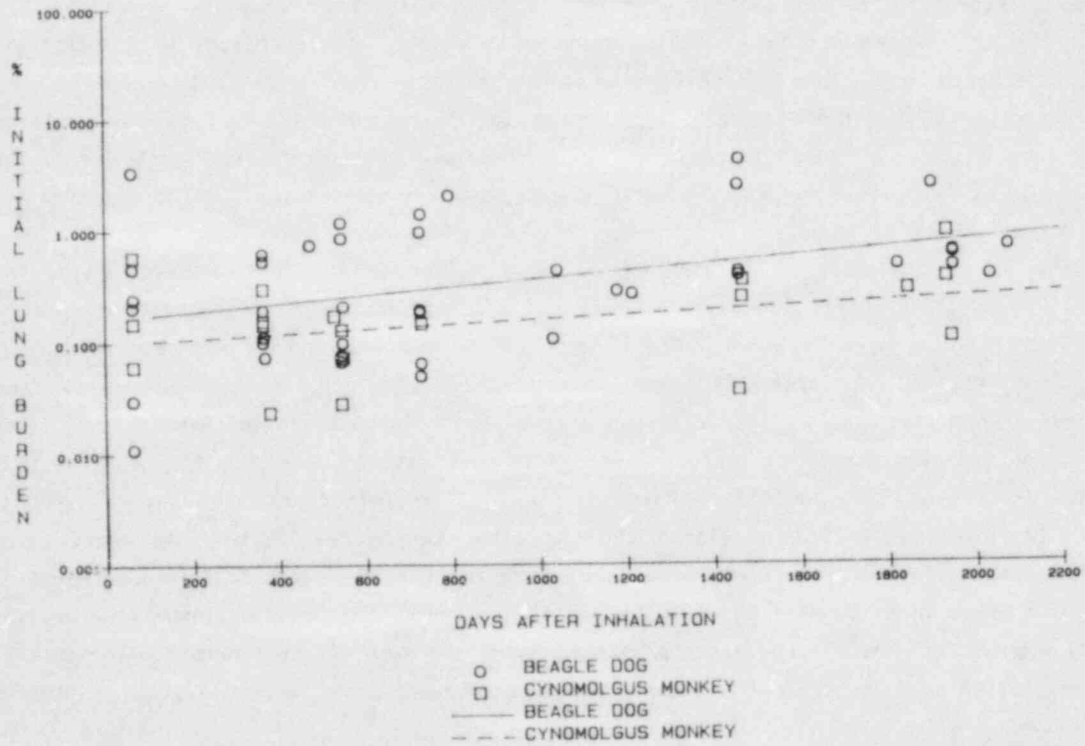


Figure 1-3. Uptake and retention of Pu in the skeleton of dogs and monkeys after inhalation of 750°C-treated $UO_2$ + $PuO_2$, 1750°C-treated $(U,Pu)O_2$ or 850°C-treated $PuO_2$. Each curve represents a non-linear least squares fit to the grouped data for a given species.

## DISCUSSION

These studies were designed to determine the distribution of radiation dose to tissues after inhalation of one of three industrial aerosols formed during fabrication of mixed uranium and plutonium oxide nuclear fuel. Three species of laboratory animals were exposed to each aerosol form in groups with scheduled sacrifice of Fischer-344 rats extending through two years after exposure and sacrifices through four years after exposure for Beagle dogs and cynomolgus monkeys. For the latter two species, additional reserve animals were placed on study to allow for substitution into the experiment in the event of unplanned deaths within the original experimental design. After the 4-year sacrifices were completed, the remaining reserve animals were kept on study with semiannual excreta collections obtained. At times ranging up to 2079 days (dogs) and 1947 days (monkeys) after inhalation, these reserve animals were sacrificed in the standard manner, and analysis of tissue and excreta samples for Pu content completed.

This report includes the preliminary anaylsis of data from these studies with completed experimental phases. The information from the Fischer-344 rat portion of the studies has been fully reported (Ref. 1) and will not be included herein.

The grouped Pu lung retention data for dogs and monkeys and the fitted curves are shown in Figure 1-1, with no distinction among the aerosol types. As shown in Table 1-2, the calculated F statistic for the fit to the combined data set for all aerosols inhaled by dogs was less than the critical value, confirming the earlier conclusion that the aerosol form did not lead to differences in lung retention. The same conclusion was apparent in the F test for lung retention in monkeys (Table 1-2). However, when the grouped data for dogs was compared with the grouped data for monkeys, the calculated F value was greater than the critical value, indicating that the null hypothesis could be rejected at the 95% confidence level. This confirmed the earlier conclusion based on data through four years after inhalation (Ref. 1) that the retention of Pu in lung was different in the two species of animals. It appears, from inspection of Figure 1-1, that the differences between species are due to differences in the percentages of the initial lung burden associated with long-term retention and the associated half-times of retention. The half-time of lung retention for all aerosols in dogs was approximately 1100 days, whereas the half-time in monkey was approximately 2000 days. Because of differences in the early phase of lung clearance, the percentage of the initial lung burden available for clearance with these long half-times was lower in monkeys than in dogs.

Data describing uptake and retention of Pu in liver of dogs and monkeys follow the same course. Figure 1-2 presents the data for dogs and monkeys and the associated fits of the function (Eq. 1-3) to each grouped data set. The results of the individual fits for each aerosol in each species are detailed in Table 1-3. When the liver uptake and retention of Pu in dogs were individually compared among the three aerosol forms, the F test indicated that the null hypothesis could not be rejected, that is, the three data sets were not from one population. Examination of the data indicated that the dogs exposed to the 1750°C-treated $(U,Pu)O_2$ aerosol had greater initial uptake of Pu than was evident for the other two aerosol forms. An exact conclusion regarding this difference in liver uptake and retention for this aerosol form cannot be made at this time. Using an F statistic at the 95% confidence level would always allow for a rejection of the null hypothesis when it was inappropriate in 5% of the cases (Type I error). For monkeys, the F test indicated that no differences among the three aerosol forms were influencing liver uptake and retention.

Differences were apparent when the grouped data for dogs and monkeys were compared. Figure 1-2 shows that the uptake of Pu in the liver of monkeys is less than for dogs at all times. This difference may be due to two factors. Less Pu is available for transport from lung to liver in monkeys at all times (Fig. 1-1), and the retention half-time for actinide elements in the liver of monkeys is reported to be less than for dogs (Ref. 7). The true retention half-times of Pu in liver of either dogs or monkey cannot be assessed from these studies because uptake of Pu is continuing through the time span of these experiments.

The fit of the function (Eq. 1-3) to the grouped data for uptake and retention of Pu in the liver of dogs is not entirely satisfactory. Examination of the data and fitted curve in Figure 1-2 shows that at times from 1000 to 1500 days after inhalation, the fitted curve underestimates the data. Plots of the residuals of the data to fitted curve show a definite pattern, indicating the function is not providing an unbiased estimate in the time frame. Attempts to weight the data to provide an improved fit were not fruitful. This phenomenon is still under investigation.

A similar analysis of the data for uptake and retention of Pu in the skeleton of dogs and monkeys (Fig 1-3 and Table 1-4) provided comparable results. That is, the fit to grouped skeletal uptake and retention data for all aerosols inhaled by dogs indicated that the data were not from a single population. Again, the data for the $(U,Pu)O_2$ aerosol appear to be different from those for the other two aerosols for the same reason cited above for the liver. When the data describing uptake and retention of Pu in the skeleton of monkeys were subjected to the F test, no difference among the aerosol forms was apparent.

With the potential for a Type I error in mind and the result of no difference indicated for monkeys, the data were grouped by species. Then the calculated F value was greater than the critical F value, indicating that a difference between the two species was evident in skeletal uptake and retention. To provide a check on the effect of inclusion of the data for the 1750°C-treated $(U,Pu)O_2$ aerosol upon the conclusion of a difference between species, the data for the 1750°C aerosol were excluded, and a second calculated F value was determined. This comparison still indicated a difference between species in skeletal uptake and retention.

## SUMMARY

The inclusion of additional data describing the retention, distribution, and excretion of Pu in dogs and monkeys at long times after inhalation of either 750°C-treated $UO_2 + PuO_2$, 1750°C-treated $(U,Pu)O_2$ or 850°C-treated $PuO_2$ has confirmed earlier conclusions regarding the fate of Pu in the lung, liver, and skeleton of these species. No effect of aerosol form on lung retention of the Pu component of these aerosols could be discerned within either of the two species, whereas differences were confirmed when the grouped data for each species were compared. The long-term lung retention of Pu present in all three aerosol forms appears to involve retention of a larger percentage of the initial lung burden in lung for somewhat shorter half-times in dogs than in monkeys. Uptake and retention of Pu in the liver and skeleton appears to be greater in the dog than in the monkey, regardless of the aerosol form. The greater initial uptake of Pu after inhalation of the $(U,Pu)O_2$ aerosol in dogs does not appear to account for the difference noted between species.

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## 2. DOSE-RESPONSE STUDIES IN FISCHER-344 RATS

PRINCIPAL INVESTIGATORS
J. A. Mewhinney
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*Abstract* — *Two studies are under way in which groups of Fischer-344 rats received inhalation exposure to either 1750°C-treated (U,Pu)$O_2$ or 850°C-treated $PuO_2$ aerosols to determine the relationship of radiation dose to biological response. In each study, groups of rats were exposed to achieve one of three initial lung burdens to produce doses of 25, 125, or 625 rads to lung during the median lifespan. Additional groups of rats are being maintained as controls. This report provides an updated summary of the current status of the animals in these studies. The major focus of this paper consists of a series of evaluations designed to determine the appropriateness of combining data describing the lung retention of the Pu component of these aerosols for the animals sacrificed at selected times after exposure with the lung retention measured at death in the animals in the dose-response groups. Additional evaluations are presented to determine if the lung retention data for the three levels of projected dose to lung groups can be combined and if all lung retention data for all levels of projected dose to lung and for both aerosols may be combined.*

The objective of this experiment is to determine the relationship of radiation dose to biological response after inhalation of one of two forms of aerosol produced during normal operation of an industrial facility fabricating mixed uranium-plutonium (U,Pu) nuclear fuel. One aerosol consisted of 1750°C-treated (U,Pu)$O_2$; the second aerosol consisted of 850°C-treated $PuO_2$. The rationale leading to the design and execution of the study has been presented previously (Ref. 1).

This report presents a summary of the current status of the study and a preliminary analysis of data describing the lung retention of the Pu component of the two aerosols. Specifically, a series of evaluations are reported that assist in the determination of the appropriateness of combining lung retention data from the radiation dose pattern (RDP) groups of animals with the animals that died or were euthanized in the dose-response (DR) studies. Similarly, the appropriateness of combining the lung retention data for the dose-response animals among the three levels of initial lung burden for each aerosol and for both aerosols is evaluated.

### METHODS

The experimental design for these studies is summarized in Table 2-1. Methods used in the statistical design, inhalation exposure, aerosol characterization, and determination of the initial lung burdens for each exposure group have been presented (Ref. 2). Lung content of Pu for each animal was expressed as a percentage of the initial lung burden determined from the mean lung content of Pu for eight rats from each exposure group sacrificed at seven days after inhalation exposure (Ref. 2). Cumulative percentage of survival after exposure was calculated by a life table method (Ref. 3).

The method used to evaluate the lung retention data for the several groups of animals has been described (this report, pp 2 to 10). Briefly, the residual sums of squares of the function fitted to data sets are compared using an F statistic to determine whether the two or

Table 7-1. Experimental Design of Dose-Response Studies in Fischer-344 Rats that Inhaled $(U,Pu)O_2$ or $PuO_2$

| Lung Dose (rad) | Initial Lung Burden $(U,Pu)O_2$ | Initial Lung Burden $PuO_2$ | Number of Animals $(U,Pu)O_2$ | Number of Animals $PuO_2$ |
|---|---|---|---|---|
| 625 | 0.013 | 0.020 | 52[a] | 52 |
| 125 | 0.0026 | 0.005 | 104(+24 RDP)[b] | 104(+24 RDP) |
| 25 | 0.00052 | 0.0008 | 156[c] | 156 |
| Control | 0 | 0 | 80[d] | 80 |

[a]Animal group = 40(DR*) + 8 (7 day sacrifice) + 4 (spares)
= 1 exposure run per aerosol

[b]Animal group = 80(DR) + 16 (7 day sacrifice) + 8 (spares) + 24 (RDP**)
= 2 exposure runs per aerosol

[c]Animal group = 120(DR) + 24 (7 day sacrifice) + 12 (spares)
= 3 exposure runs per aerosol

[d]Animal group = 80 (control)
= 2 exposure runs per aerosol

*DR = dose response animals.

**RDP = radiation dose pattern animals.

more data sets are from a single population. When the calculated F value is less than the critical value at the appropriate confidence level, the null hypothesis cannot be rejected. It is assumed, then, that the data sets are from one population and that a fit to the combined data sets is an appropriate representation of the data. When the opposite result is obtained, it indicates that the data sets must be treated separately.

Lung retention data for the RDP rats in both studies sacrificed through two years after inhalation exposure were fitted separately and then as a combined group. A two-component negative exponential function was fitted in each case using a nonlinear least squares routine in which the function was constrained to pass through 100% retention at 7 days after inhalation. This time corresponds to the time of determination of the initial lung burden by measurement of the lung content of Pu in eight animals sacrificed from each exposure group.

The same function was fitted to the combined lung retention data for the RDP and DR animals exposed to each aerosol separately and to the combined data for the two aerosols.

For rats that died or were euthanized in the dose-response studies involving exposure to one of three levels of initial lung burden for each aerosol, similar data were fitted to a single-component exponential function with no constraints. This was because the deaths of these animals occurred more than 150 days after inhalation. At 150 days or more, the early, rapid phase of clearance from lung measured in the sacrifice series was complete. Each dose group for each aerosol was fitted separately; then the three dose groups for a given aerosol were fitted as a single group. The data for all dose groups for both aerosols were then grouped, and an overall fit was obtained.

The sequence of statistical evaluations accomplished for this report were, 1) determine whether the lung retention of the Pu component of the two aerosols was similar or different when only the data for animals sacrificed at preselected times was considered; 2) determine whether the lung retention of the Pu component of the two aerosols was similar or different when the data for sacrificed animals was combined with data from the animals that died or were euthanized in the dose-response studies at the projected level of 125 rad to lung; 3) determine whether the lung retention data for the three dose levels for either aerosol could be combined into a single group; and, 4) determine whether the lung retention data for all dose levels and both aerosols could be combined.

## RESULTS

A summary of the current status of animals in the studies is presented in Table 2-2. The results of the life table analysis of rats in the studies as of 30 June 1983 is illustrated in Figure 2-1.

The values for the variables in the function fitted to the lung retention data, when only RDP animals were considered, are given in the first portion of Table 2-3, as are the values for the function fitted to the combined data. Also shown are the calculated and critical F values. These results are presented graphically in Figure 2-2. In the second portion of Table 2-3 the fitted values obtained when the RDP and DR animals were combined for each aerosol and when both data sets were combined are shown along with the calculated and critical F values. These results are illustrated in Figure 2-3.

Table 2-4 presents similar results of fitting a single exponential function to the lung retention measured in DR animals only at each of the levels of lung dose, followed by the individual values obtained when the data for the three levels are combined. The first portion of Table 2-4 presents the results for animals exposed to the $(U,Pu)O_2$ aerosol; the second portion gives the results for animals exposed to $PuO_2$. These results are illustrated graphically in Figures 2-4 and 2-5, respectively, for the two aerosols. The last portion of Table 2-4 presents the result for all DR groups combined into a single data set. The results of this overall combination of the DR lung retention data are illustrated in Figure 2-6.

Table 2-2. Status of Dose-Response Studies in Which Fischer-344 Rats Were Exposed to Graded Levels of Initial Lung Burden of Either $(U,Pu)O_2$ or $PuO_2$ (as of 30 June 1983)

| Aerosol | Projected Dose to Lung (rad)* | Days After Inhalation | Number of Animals Entered In Exp. | Number of Deaths | Number Surviving | Percent Survival |
|---|---|---|---|---|---|---|
| $(U,Pu)O_2$ | 25 | 1015 | 131 | 122 | 9 | 7 |
| | 125 | 1016 | 88 | 83 | 5 | 6 |
| | 625 | 1014 | 44 | 44 | 0 | 0 |
| | Control | 1014 | 80 | 76 | 4 | 5 |
| $PuO_2$ | 25 | 976 | 128 | 120 | 8 | 6 |
| | 125 | 975 | 88 | 81 | 7 | 8 |
| | 625 | 800 | 44 | 26 | 18 | 41 |
| | Control | 974 | 80 | 71 | 9 | 11 |
| | Over-exposed | 974 | 44 | 44 | 0 | 0 |

*Lung dose projected to 900 days after exposure.

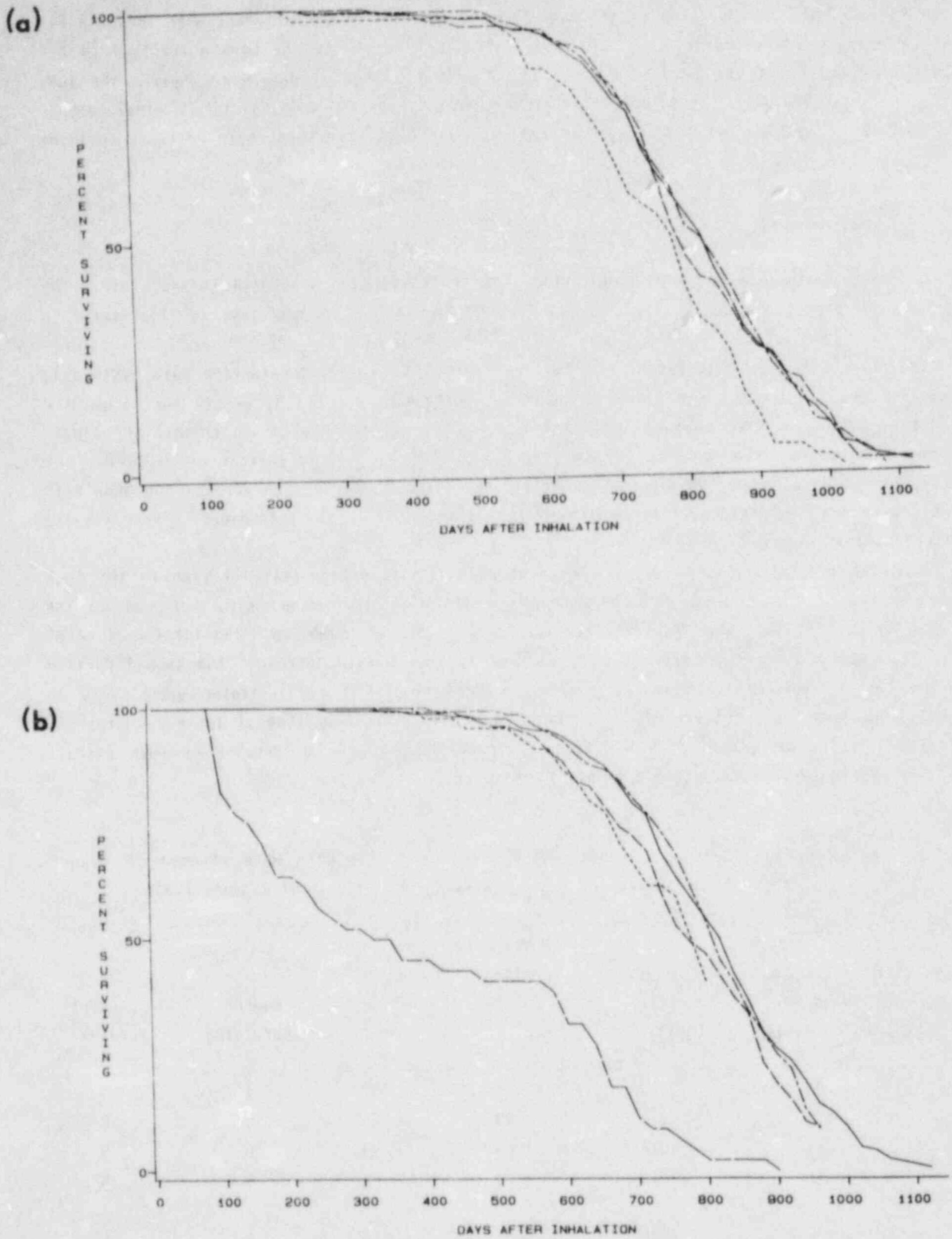


Figure 2-1. Cumulative percentage survival of rats exposed to graded levels of initial lung burden; (a) inhaled material was $(U,Pu)O_2$ and (b) inhaled material was $PuO_2$.

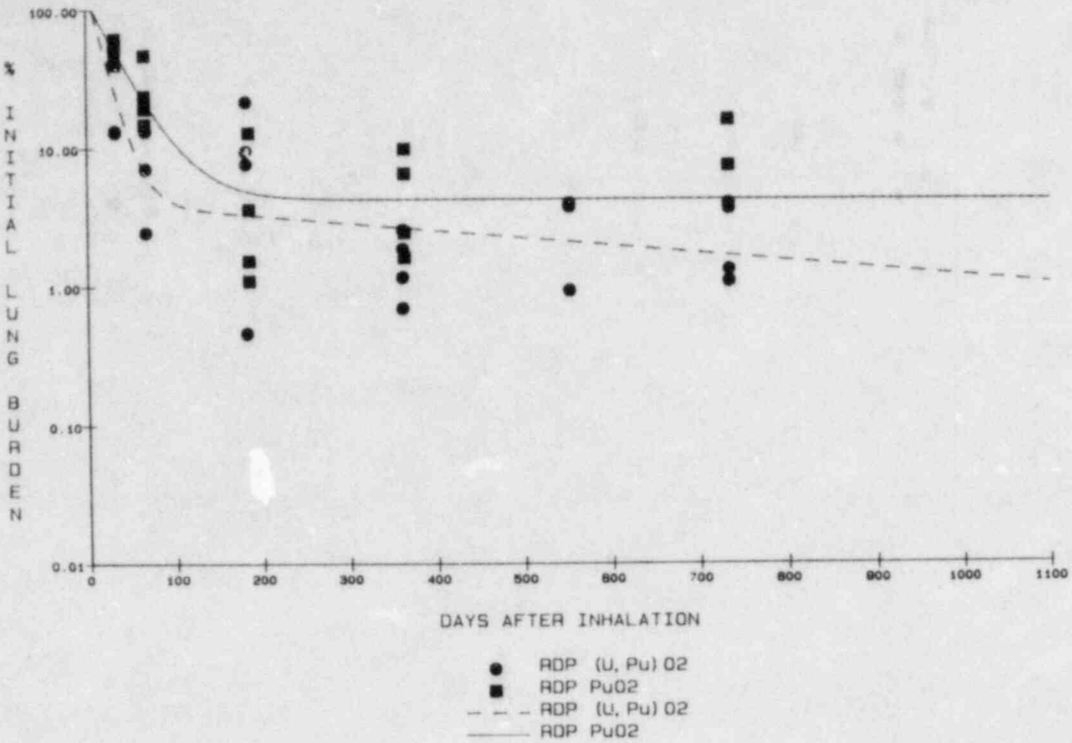


Figure 2-2. Lung retention of Pu component of $(U,Pu)O_2$ and $PuO_2$ in Fischer-344 rats sacrificed at selected times from 32 to 730 days after inhalation. Each curve represents the result of a non-linear least squares fit of a two-component exponential function to data for one aerosol.

Table 2-3. Analysis of Lung Retention in Dose-Response Studies in Which Fischer-344 Rats Were Exposed to Graded Levels of Projected Dose to Lung

| Data Set | Fitted Parameters $A_1$ | $\lambda_1$ | $A_2$ | $\lambda_2$ | Residual Sum of Squares | N | Calculated F | Critical Value |
|---|---|---|---|---|---|---|---|---|
| a. Animals from Radiation Dose Pattern Study | | | | | | | | |
| $(U,Pu)O_2$ | 146 | -5.96E-02 | 4.04 | -1.24E-03 | 3.54 | 27 | | |
| $PuO_2$ | 117 | -2.86E-02 | 4.23 | -3.89E-19 | 2.04 | 27 | | |
| Combined | 125 | -3.64E-02 | 3.00 | -9.81E-05 | 6.93 | 54 | 3.87 | 1.18 |
| b. Animals from Radiation Dose Pattern and 125-rad Dose Response Studies | | | | | | | | |
| $(U,Pu)O_2$ | 146 | -6.05E-02 | 4.20 | -5.89E-04 | 12.3 | 97 | | |
| $PuO_2$ | 117 | -2.66E-02 | 2.80 | -3.75E-05 | 16.4 | 99 | | |
| Combined | 125 | -3.75E-02 | 3.50 | -3.65E-04 | 29.6 | 186 | 1.79 | 1.04 |

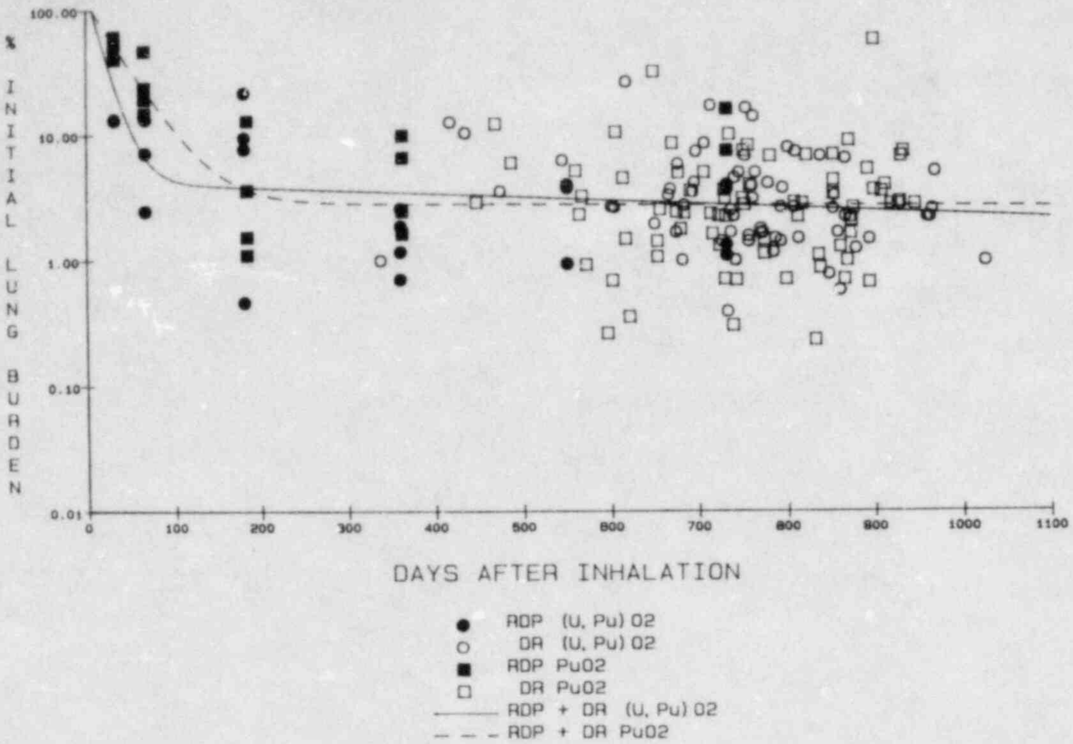


Figure 2-3. Lung retention of Pu component of $(U,Pu)O_2$ or $PuO_2$ in Fischer-344 rats sacrificed from radiation dose pattern (RDP) studies and rats that died or were euthanized in the 125-rad projected dose to lung group in the corresponding dose-response (DR) studies. Curves are the result of a fit to all data for RDP and DR studies for each aerosol independently.

Table 2-4. Analysis of Lung Retention in Dose-Response Studies in Which Fischer-344 Rats Were Exposed to Graded Levels of Projected Dose to Lung

| Data Set | Fitted Parameters $A_1$ | $\lambda_1$ | Residual Sum of Squares | N | Calculated F | Critical F |
|---|---|---|---|---|---|---|
| a. $(U,Pu)O_2$ | | | | | | |
| 25 rad | 6.93 | -7.88E-04 | 19.02 | 111 | | |
| 125 rad | 10.1 | -1.66E-03 | 8.082 | 70 | | |
| 625 rad | 61.0 | -3.27E-03 | 9.793 | 32 | | |
| Combined | 12.5 | -1.61E-03 | 38.90 | 213 | 2.81 | 2.41 |
| b. $PuO_2$ | | | | | | |
| 25 rad | 4.88 | -7.81E-04 | 35.60 | 108 | | |
| 125 rad | 2.56 | -6.54E-20 | 14.02 | 76 | | |
| 625 rad | 5.42 | -8.48E-20 | [illegible].231 | 17 | | |
| Combined | 4.68 | -6.92E-05 | 53.23 | 201 | 1.30 | 2.41 |
| All or Data combined | 7.39 | -1.11E-03 | 93.82 | 414 | 3.76 | 3.02 |

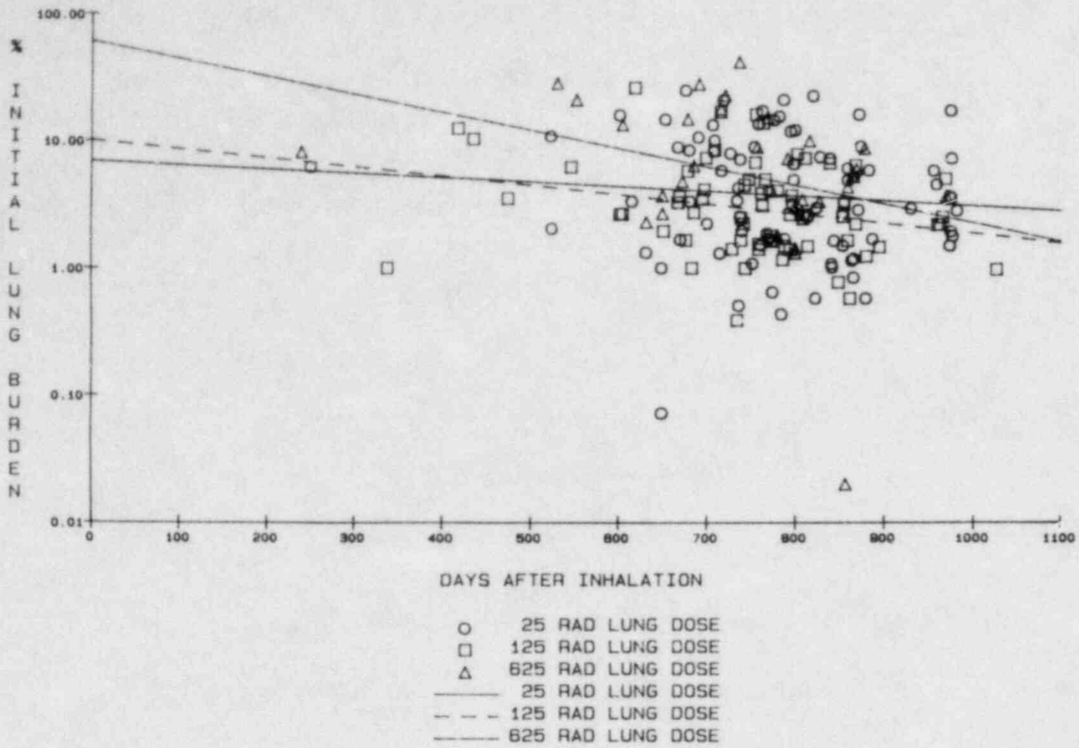


Figure 2-4. Lung retention of Pu component of $(U,Pu)O_2$ aerosol in Fischer-344 rats exposed in the DR studies at all three levels of projected dose to lung. Curves are the result of independant fits of a single-component exponential function to data for each of the three dose levels.

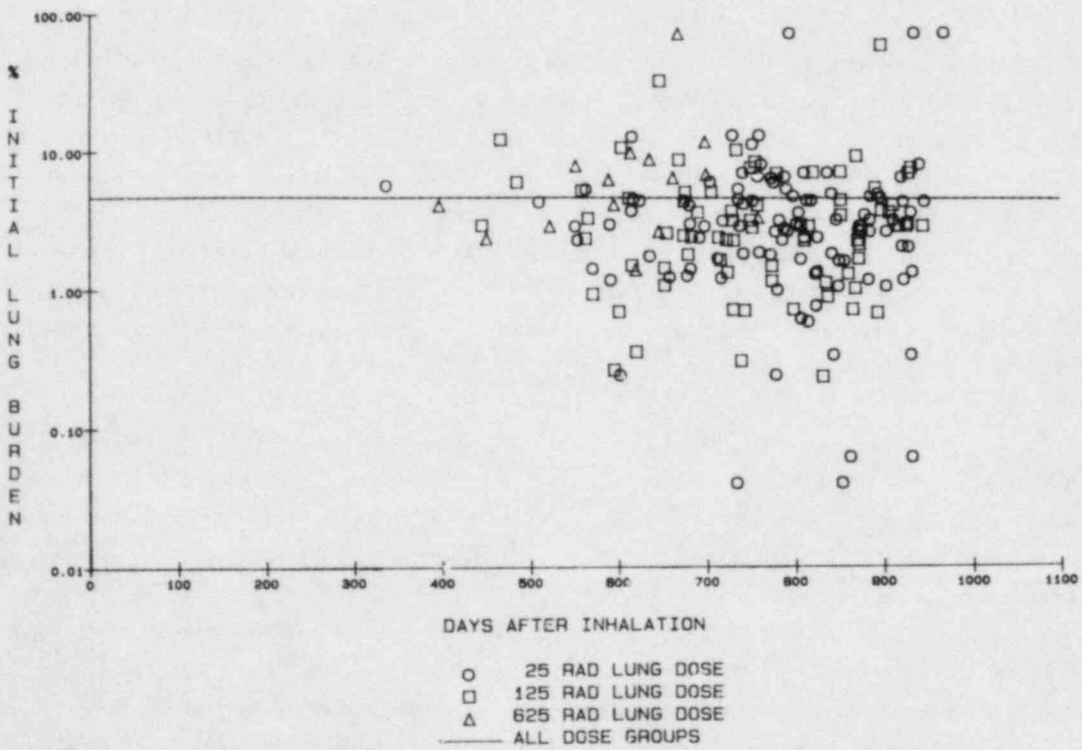


Figure 2-5. Lung retention of Pu component of $PuO_2$ aerosol in Fischer-344 rats exposed in the DR studies at all three levels of projected dose to lung. Curve is the result of fitting a single component exponential function to combined data from all three levels.

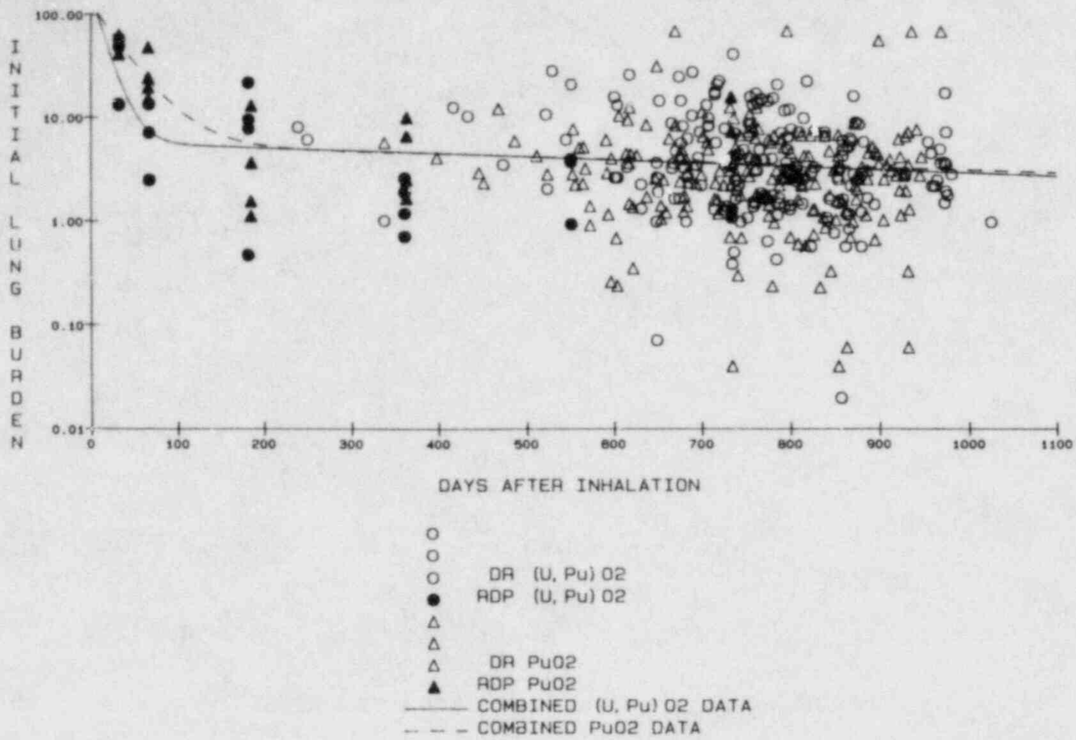


Figure 2-6. Lung retention of Pu component of $(U,Pu)O_2$ and $PuO_2$ aerosols in Fischer-344 rats exposed at all three levels of projected dose to lung in the DR studies combined with the RDP data. Curves are the result of fitting a two-component exponential function to data for each aerosol independently.

## DISCUSSION

The survival of rats in the dose-response study continues to indicate that no discernible differences exist between the experimental and control groups, with the single exception of the "over-exposed" group, which was replaced in the experiment. This survival pattern conforms to that desired in the original design of the experiment (Ref. 4). It also appears from the survival patterns that the study will be completed during the next fiscal year.

Lung retention of the Pu component of the two aerosols used in these dose-response studies is being characterized in two ways. First, to provide description of the time course of lung retention at early times after exposure, rats randomly selected from the groups exposed to each aerosol at the 125-rad projected dose to lung level were sacrificed at times from 32 to 730 days after inhalation.

The first concern stemming from the need for accurate description of the radiation dose absorbed in lung of animals in the DR studies is to determine the extent of similarity or differences in lung retention when the two groups of RDP animals (one for each aerosol) are compared. Table 2-3 lists the fitted parameters obtained when the lung retention data for each group were fitted separately to a two-component exponential function. Also given in Table 2-3 are the fitted parameters obtained when the two data sets were combined and the calculated F values and corrected critical values used to determine whether the two data sets are from a single population. Figure 2-2 shows the two data sets and the individual fitted curves for each. Because the calculated F statistic is greater than the critical value, the null hypothesis that the two data sets are from a single population can be rejected at the 95% confidence level. Thus, it would appear from the RDP lung retention data alone that some difference exists in the lung retention of the two aerosols.

The second and more nearly complete method for description of the lung retention of the Pu component in these aerosols is to combine the data from RDP animals with the data from the animals that died or were euthanized in the DR study at the same level of projected radiation dose to lung. Because the RDP and DR animals were exposed simultaneously and the RDP animals were randomly selected after the exposure, the combining of lung retention data for the two groups exposed to the identical aerosol should need no statistical confirmation. This combination of data for both the RDP and DR animals provides a complete description of lung retention during the experiment. Table 2-3 lists the values derived from fitting the RDP plus DR data sets individually for each aerosol and the values obtained when the RDP + DR data sets for both aerosols were combined. As shown in Table 2-3, the calculated value of the F statistic was greater than the corrected critical value for this latter combination, indicating that when the RDP + DR data sets for each aerosol were combined, the null hypothesis could be rejected at the 95% confidence level. This indicates that in the lung retention of Pu, differences do exist that may be ascribed to the inhaled aerosol form. Therefore, Figure 2-4 shows the RDP plus DR data sets for each aerosol and the two curves resulting from a fit to the data for each aerosol.

Another set of assessments was performed to determine if the level of projected lung dose caused a difference in lung retention among the three levels of projected lung dose for each aerosol. For this comparison, the lung retention data for each projected dose to lung group was fitted separately using a single exponential function. The results are shown in Table 2-4 for the two aerosols. Also shown are the fitted values and the calculated and critical F statistics for the curve fit in which the data for the three projected dose groups were combined for each aerosol. These results indicate that for the $(U,Pu)O_2$ aerosol, the different levels of projected dose to lung led to discernable differences in lung retention. In contrast, the results for the $PuO_2$ aerosol do not indicate that projected dose to lung influences lung retention of the Pu component. The data sets for the DR animals exposed to the $(U,Pu)O_2$ aerosol at three levels of projected dose to lung are shown in Figure 2-4, along with the curves representing the fits to the data for each level of projected dose to lung. The data sets and the resultant single curve fit for the $PuO_2$ aerosol are illustrated in Figure 2-5.

Considering the above results, an assessment was made to determine if the lung retention of the Pu component of the aerosols for the DR data was influenced by the form of the inhaled aerosol. Thus, the data for all DR animals for both aerosols and all projected dose to lung levels were combined, and the single component exponential function was fitted. The results are given in Table 2-4. The calculated F statistic was greater than the critical F statistic, leading to the conclusion that the entire data set was not from a single population. Thus, aerosol form, as well as projected dose to lung level, may have influenced lung retention for the DR animals.

The last assessment involved the combining of the RDP and DR data at all three dose levels for each aerosol and fitting them with a two-component exponential function. These two data sets were then combined, and an overall fit to all lung retention data was obtained. The results are given in Table 2-5 and illustrated in Figure 2-6. This assessment led to the conclusion that all lung retention data for both RDP and DR animals at all levels of projected dose to lung and for both aerosols cannot be combined into a single population of data. Therefore, the two curves shown in Figure 2-6 represent the fit to the separate data for each aerosol.

Although it is understood that the above assessments are made with incomplete data (73 animals remain alive, Table 2-2), it is unlikely that data from the relatively few animals to be included at termination of the experiment will have a profound influence in changing the conclusions. However, this will be rigorously checked at the appropriate time.

These preliminary results indicate that the level of projected dose to lung may have influenced lung retention of the Pu component of the two aerosols. Also, the aerosol form may

Table 2-5. Analysis of Lung Retention in Dose-Response Studies in Which Fischer-344 Rats Were Exposed to Graded Levels of Projected Dose to Lung

| Data set | Fitted Parameters $A_1$ | $\lambda_1$ | $A_2$ | $\lambda_2$ | Residual Sum of Squares | N | Calculated F | Critical Value |
|---|---|---|---|---|---|---|---|---|
| | All RDP + DR Animals | | | | All Dose Levels | | | |
| $(U,Pu)O_2$ | 149 | -6.55E-02 | 5.7 | -6.54E-04 | 44.19 | 240 | | |
| $PuO_2$ | 117 | -2.83E-02 | 4.2 | -5.41E-04 | 55.38 | 224 | | |
| Combined | 126 | -3.98E-02 | 5.0 | -6.23E-04 | 101.5 | 464 | 2.65 | 3.02 |

have an influence on lung retention, as noted when only the RDP data are compared, when only the DR data are compared, and when the RDP and DR data are combined. In view of these results, and subject to reanalysis when the studies are completed, it appears that separate retention functions will be required to provide an accurate description of the lung retention data for each aerosol.

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

## APPENDIX A
## Status of Inhalation Studies

STATUS OF INHALATION STUDIES OF AEROSOLS OF $PuO_2$ HEAT-TREATED AT 750°C MIXED WITH $UO_2$ AND BALL MILLED AT HEDL IN BEAGLE DOGS, MONKEYS AND FISCHER-344 RATS

| SPECIES | NUMBER TTOO | NUMBER RADIO | SEX | EXPOSURE DATE | EXPOSURE AGE (DAYS) | EXPOSURE WT. (KG) | EXP. AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DATE | DPE | ALIVE DPE 6-30-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BEAGLE DOG | 871D | 1935-01 | M | 76344 | 708 | 9.90 | 2.19 | 1.91 | 0 | 76344 | 0 | | S- |
| BEAGLE DOG | 219C | 1935-02 | M | 76344 | 3629 | 10.1 | 2.15 | 1.74 | 4 | 76348 | 4 | | S- |
| BEAGLE DOG | 635B | 1935-03 | M | 76344 | 1656 | 11.4 | 1.84 | 1.68 | 4 | 76348 | 4 | | S- |
| BEAGLE DOG | 821T | 1936-02 | F | 76345 | 884 | 8.5 | 1.68 | 1.65 | 549 | 78165 | 551 | | S- |
| BEAGLE DOG | 217E | 1937-01 | M | 76349 | 3648 | 8.1 | 2.41 | 1.70 | 0 | 76349 | 0 | | S- |
| BEAGLE DOG | 817T | 1937-02 | F | 76349 | 892 | 8.2 | 2.04 | 1.74 | 64 | 77047 | 64 | | S- |
| BEAGLE DOG | 823S | 1937-03 | F | 76349 | 886 | 7.2 | 2.50 | 1.77 | | 79297 | 1044 | | E-LTR |
| BEAGLE DOG | 812A | 1937-04 | M | 76349 | 896 | 9.3 | 2.33 | 1.73 | 1462 | 80350 | 1462 | | S- |
| BEAGLE DOG | 803A | 1938-01 | M | 76350 | 910 | 10.5 | 2.10 | 1.67 | | 80106 | 1217 | | D-LTR |
| BEAGLE DOG | 810U | 1938-02 | F | 76350 | 901 | 8.0 | 2.61 | 2.38 | 1462 | 80351 | 1462 | | S- |
| BEAGLE DOG | 811B | 1938-03 | M | 76350 | 897 | 10.2 | 2.67 | 1.62 | | 82237 | 2079 | | E-LTR |
| BEAGLE DOG | 804A | 1938-04 | M | 76350 | 910 | 10.9 | 2.47 | 1.58 | 64 | 77049 | 65 | | S- |
| BEAGLE DOG | 828T | 1939-01 | F | 76351 | 872 | 6.9 | 2.18 | 1.66 | | 81349 | 1825 | | E-LTR |
| BEAGLE DOG | 811A | 1939-02 | M | 76351 | 898 | 12.8 | 2.18 | 1.71 | 730 | 78349 | 729 | | S- |
| BEAGLE DOG | 799B | 1939-03 | M | 76351 | 929 | 11.7 | 2.34 | 1.73 | 365 | 77350 | 365 | | S- |
| BEAGLE DOG | 825S | 1940-01 | F | 76352 | 889 | 9.3 | 2.22 | 1.73 | 730 | 78352 | 731 | | S- |
| BEAGLE DOG | 826T | 1940-02 | F | 76352 | 884 | 11.0 | 1.79 | 1.81 | 365 | 77353 | 367 | | S- |
| BEAGLE DOG | 802D | 1940-03 | M | 76352 | 915 | 8.3 | 2.35 | 1.96 | 549 | 78170 | 549 | | S- |
| RHESUS MONKEY | 917 | 2087-01 | M | 77039 | 5-7YRS-B | 4.85 | 1.61 | 1.62 | 0 | 77039 | 0 | | S- |
| CYNOMOLGUS MONKEY | 25 | 2087-02 | M | 77039 | 3-5YRS | 3.15 | 1.53 | 1.53 | 1462 | 81048 | 1470 | | S- |
| CYNOMOLGUS MONKEY | 21 | 2088-01 | M | 77040 | 5-7YRS | 4.4 | 1.10 | 1.34 | 64 | 77104 | 64 | | S- |
| CYNOMOLGUS MONKEY | 26 | 2088-02 | M | 77040 | 3-5YRS-B | 3.7 | 1.37 | 1.56 | 365 | 78040 | 365 | | S- |
| CYNOMOLGUS MONKEY | 24 | 2088-03 | M | 77040 | 3-5YRS-B | 3.6 | 1.22 | 1.55 | 549 | 78222 | 547 | | S- |
| RHESUS MONKEY | 918 | 2089-01 | M | 77041 | 5-7YRS-B | 4.4 | 1.61 | 1.53 | 4 | 77045 | 4 | | S- |
| CYNOMOLGUS MONKEY | 27 | 2089-02 | M | 77041 | 3-5YRS-B | 3.4 | 1.41 | 1.56 | 730 | 79040 | 729 | | S- |
| CYNOMOLGUS MONKEY | 22 | 2089-03 | F | 77041 | 3-4YRS-B | 2.5 | 1.25 | 1.59 | | 78056 | 380 | | D-GASTRIC TORSION |
| RHESUS MONKEY | 897 | 2090-01 | M | 77046 | 5-7YRS-B | 4.6 | 2.13 | 2.30 | | 78211 | 530 | | D-FIB. PLEURITIS |
| FISCHER-344 RATS | | 2086-01 | M | 77042 | 9WKS | | 2.32 | 1.77 | 0 | 77042 | 0 | | S- |
| FISCHER-344 RATS | | 2086-02 | M | 77042 | 9WKS | | 2.32 | 1.77 | 365 | 78044 | 367 | | S- |
| FISCHER-344 RATS | | 2086-03 | M | 77042 | 9WKS | | 2.32 | 1.77 | | 79017 | 705 | | D- |
| FISCHER-344 RATS | | 2086-04 | M | 77042 | 9WKS | | 2.32 | 1.77 | | 78094 | 417 | | D-MAL. MESO THORAX |
| FISCHER-344 RATS | | 2086-05 | M | 77042 | 9WKS | | 2.32 | 1.77 | | 78170 | 493 | | D-SQU. CELL CARC. |
| FISCHER-344 RATS | | 2086-06 | M | 77042 | 9WKS | | 2.32 | 1.77 | 4 | 77046 | 4 | | S- |
| FISCHER-344 RATS | | 2086-07 | M | 77042 | 9WKS | | 2.32 | 1.77 | 365 | 78044 | 367 | | S- |
| FISCHER-344 RATS | | 2086-08 | M | 77042 | 9WKS | | 2.32 | 1.77 | | 77249 | 207 | | E-FIB. SUB. |
| FISCHER-344 RATS | | 2086-09 | M | 77042 | 9WKS | | 2.32 | 1.77 | 730 | 79043 | 731 | | S- |
| FISCHER-344 RATS | | 2086-10 | M | 77042 | 9WKS | | 2.32 | 1.77 | 4 | 77046 | 4 | | S-UNEXP. CONTROL |
| FISCHER-344 RATS | | 2086-11 | M | 77042 | 9WKS | | 2.32 | 1.77 | 365 | 78044 | 367 | | S- |
| FISCHER-344 RATS | | 2086-12 | M | 77042 | 9WKS | | 2.32 | 1.77 | 0 | 77042 | 0 | | S- |
| FISCHER-344 RATS | | 2086-13 | M | 77042 | 9WKS | | 2.32 | 1.77 | 0 | 77042 | 0 | | S- |
| FISCHER-344 RATS | | 2086-14 | M | 77042 | 9WKS | | 2.32 | 1.77 | 64 | 77105 | 63 | | S- |
| FISCHER-344 RATS | | 2086-15 | M | 77042 | 9WKS | | 2.32 | 1.77 | 4 | 77046 | 4 | | S- |

B-PRIMATE CAUGHT IN THE WILD. AGE ESTIMATED FROM BODY WEIGHT AT EXPOSURE
D-SPONTANEOUS DEATH
E-EUTHANIZED
S-SACRIFICED
LTR-LONG TERM RESERVE

STATUS OF INHALATION STUDIES OF AEROSOLS OF PUO2 HEAT-TREATED AT 750°C. MIXED WITH UO2 AND BALL MILLED AT HEDL IN BEAGLF DOGS, MONKEYS AND FISCHER-344 RATS (CONTINUED)

| SPECIES | NUMBER TTOO | NUMBER RADIO. | SEX | EXPOSURE DATE | EXPOSURE AGE (DAYS) | EXPOSURE WT. (KG) | EXP. AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DATE | DPE | ALIVE DPE 6-30-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FISCHER-344 RATS | | 2086-16 | M | 77042 | 9WKS | | 2.32 | 1.77 | 4 | 77046 | 4 | | S- |
| FISCHER-344 RATS | | 2086-17 | M | 77042 | 9WKS | | 2.32 | 1.77 | 4 | 77046 | 4 | | S- |
| FISCHER-344 RATS | | 2086-18 | M | 77042 | 9WKS | | 2.32 | 1.77 | 64 | 77105 | 63 | | S- |
| FISCHER-344 RATS | | 2086-19 | M | 77042 | 9WKS | | 2.32 | 1.77 | | 78304 | 627 | | D-ADENO. LUNG |
| FISCHER-344 RATS | | 2086-20 | M | 77042 | 9WKS | | 2.32 | 1.77 | 64 | 77105 | 63 | | S- |
| FISCHER-344 RATS | | 2086-21 | F | 77042 | 9WKS | | 2.32 | 1.77 | 547 | 78223 | 546 | | S- |
| FISCHER-344 RATS | | 2086-22 | F | 77042 | 9WKS | | 2.32 | 1.77 | 730 | 79043 | 731 | | S- |
| FISCHER-344 RATS | | 2086-23 | F | 77042 | 9WKS | | 2.32 | 1.77 | 0 | 77042 | 0 | | S- |
| FISCHER-344 RATS | | 2086-24 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 77326 | 284 | | D-RAD. PNEUM., PUL. FIB. |
| FISCHER-344 RATS | | 2086-25 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 77254 | 212 | | D-RAD. PNEUM., PUL. FIB. |
| FISCHER-344 RATS | | 2086-26 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 78174 | 497 | | D-SQU. CELL PAPILLOMA |
| FISCHER-344 RATS | | 2086-27 | F | 77042 | 9WKS | | 2.32 | 1.77 | 365 | 78044 | 367 | | S- |
| FISCHER-344 RATS | | 2086-28 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 78230 | 553 | | D-SQU. CELL CARC. |
| FISCHER-344 RATS | | 2086-29 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 78219 | 542 | | D-PUL. FIBROSIS |
| FISCHER-344 RATS | | 2086-30 | F | 77042 | 9WKS | | 2.32 | 1.77 | 730 | 79043 | 731 | | S- |
| FISCHER-344 RATS | | 2086-31 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 78340 | 663 | | D-SQU. CELL CARC. |
| FISCHER-344 RATS | | 2086-32 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 78176 | 499 | | D-SQU. CELL CARC. |
| FISCHER-344 RATS | | 2086-33 | F | 77042 | 9WKS | | 2.32 | 1.77 | 547 | 78223 | 546 | | S- |
| FISCHER-344 RATS | | 2086-34 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 78115 | 438 | | D-ADENO. LUNG |
| FISCHER-344 RATS | | 2086-35 | F | 77042 | 9WKS | | 2.32 | 1.77 | 0 | 77042 | 0 | | S- |
| FISCHER-344 RATS | | 2086-36 | F | 77042 | 9WKS | | 2.32 | 1.77 | 365 | 78044 | 367 | | S- |
| FISCHER-344 RATS | | 2086-37 | F | 77042 | 9WKS | | 2.32 | 1.77 | 64 | 77105 | 63 | | S- |
| FISCHER-344 RATS | | 2086-37 | F | 77042 | 9WKS | | 2.32 | 1.77 | 64 | 77105 | 63 | | S- |
| FISCHER-344 RATS | | 2086-38 | F | 77042 | 9WKS | | 2.32 | 1.77 | | 79023 | 711 | | D-SQU. CELL CARC. |
| FISCHER-344 RATS | | 2086-40 | F | 77042 | 9WKS | | 2.32 | 1.77 | 730 | 79043 | 731 | | S- |

B-PRIMATE CAUGHT IN THE WILD, AGE ESTIMATED FROM BODY WEIGHT AT EXPOSURE
D-SPONTANEOUS DEATH
E-EUTHANIZED
S-SACRIFICED
LTR-LONG TERM RESERVE

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 | NUMBER TTOO | NUMBER RADIO | SEX | EXPOSURE DATE | EXPOSURE AGE (DAYS) | EXPOSURE WT. (KG) | EXP. AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DATE | DPE | ALIVE DPE 6-30-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BEAGLE DOG | 634A | 2118-01 | M | 77083 | 1761 | 13.0 | 2.6 | 2.4 | 0 | 77083 | 0 | | S- |
| BEAGLE DOG | 643A | 2118-02 | M | 77083 | 1725 | 9.8 | 2.4 | 1.7 | 4 | 77087 | 4 | | S- |
| BEAGLE DOG | 777D | 2118-03 | M | 77083 | 1167 | 9.5 | 2.5 | 1.6 | 64 | 77147 | 64 | | S- |
| BEAGLE DOG | 640S | 2119-01 | F | 77084 | 1745 | 10.3 | 2.2 | 1.6 | 0 | 77084 | 0 | | S- |
| BEAGLE DOG | 641S | 2119-02 | F | 77084 | 1730 | 11.4 | 1.3 | 1.7 | 4 | 77088 | 4 | | S- |
| BEAGLE DOG | 796S | 2119-03 | F | 77084 | 1037 | 10.0 | 2.6 | 1.6 | 64 | 77147 | 63 | | S- |
| BEAGLE DOG | 783B | 2120-01 | M | 77088 | 1102 | 8.7 | 2.4 | 1.6 | 365 | 78088 | 365 | | S- |
| BEAGLE DOG | 789A | 2120-02 | M | 77088 | 1069 | 10.3 | 2.3 | 1.7 | 547 | 78270 | 547 | | S- |
| BEAGLE DOG | 883C | 2120-03 | M | 77088 | 763 | 9.8 | 2.4 | 1.7 | | 82167 | 1905 | | E-LTR |
| BEAGLE DOG | 961B | 2122-01 | M | 77090 | 524 | 12.0 | 3.1 | 1.8 | 730 | 79089 | 729 | | S- |
| BEAGLE DOG | 797S | 2122-02 | F | 77090 | 1035 | 8.3 | 2.7 | 1.6 | 365 | 78090 | 365 | | S- |
| BEAGLE DOG | 798T | 2122-03 | F | 77090 | 1034 | 8.6 | 2.6 | 1.6 | 547 | 78272 | 547 | | S- |
| BEAGLE DOG | 791A | 2123-01 | M | 77091 | 1063 | 9.3 | 2.4 | 1.7 | 1462 | 81092 | 1462 | | S- |
| BEAGLE DOG | 802U | 2123-02 | F | 77091 | 1020 | 9.2 | 2.9 | 1.8 | 730 | 79092 | 731 | | S- |
| BEAGLE DOG | 853T | 2124-01 | F | 77096 | 900 | 9.6 | 2.9 | 1.9 | | 78207 | 476 | | D-LTR |
| BEAGLE DOG | 863C | 2124-02 | M | 77096 | 857 | 10.2 | 2.8 | 1.7 | 2030 | 82306 | 2036 | | S- |
| BEAGLE DOG | 803S | 2124-03 | F | 77096 | 1022 | 9.4 | 2.6 | 1.8 | 1462 | 81100 | 1465 | | S- |
| BEAGLE DOG | 888S | 2124-04 | F | 77096 | 754 | 8.2 | 2.9 | 1.7 | | 79163 | 797 | | D-LTR |
| CYNOMOLGUS MONKEY | 36 | 2256-01 | M | 77236 | 3-5YRS-B | 3.3 | 2.0 | 1.6 | 365 | 78236 | 365 | | S- |
| RHESUS MONKEY | 900 | 2257-01 | M | 77237 | 5-7YRS-B | 7.5 | 2.3 | 1.7 | 0 | 77237 | 0 | | S- |
| CYNOMOLGUS MONKEY | 35 | 2257-02 | M | 77237 | 3-5YRS-B | 3.7 | 2.5 | 1.7 | 64 | 77301 | 64 | | S- |
| CYNOMOLGUS MONKEY | 39 | 2257-03 | M | 77237 | 3-5YRS-R | 3.1 | 2.4 | 1.7 | 547 | 79053 | 546 | | S- |
| CYNOMOLGUS MONKEY | 38 | 2257-04 | M | 77237 | 3-5YRS-B | 3.2 | 2.4 | 1.7 | 730 | 79239 | 732 | | S- |
| RHESUS MONKEY | 914 | 2258-01 | M | 77238 | 5-7YRS-B | 7.0 | 2.3 | 1.8 | 4 | 77242 | 4 | | S- |
| CYNOMOLGUS MONKEY | 34 | 2258-02 | M | 77238 | 3-5YRS-B | 3.8 | 2.5 | 1.7 | 1462 | 81245 | 1468 | | S- |
| CYNOMOLGUS MONKEY | 31 | 2258-03 | M | 77238 | 3-5YRS-B | 3.8 | 2.4 | 1.7 | 1952 | 82348 | 1936 | | S- |
| CYNOMOLGUS MONKEY | 44 | 2258-04 | M | 77238 | 5-7YRS-B | 4.7 | 2.8 | 1.7 | 1952 | 82350 | 1938 | | S- |
| FISCHER-344 RAT | | 2100-01 | F | 77055 | 9WKS | | 2.3 | 1.7 | 547 | 78237 | 547 | | S- |
| FISCHER-344 RAT | | 2100-02 | F | 77055 | 9WKS | | 2.3 | 1.7 | 0 | 77055 | 0 | | S- |
| FISCHER-344 RAT | | 2100-03 | F | 77055 | 9WKS | | 2.3 | 1.7 | 730 | 79058 | 733 | | S- |
| FISCHER-344 RAT | | 2100-04 | F | 77055 | 9WKS | | 2.3 | 1.7 | 64 | 77119 | 64 | | S- |
| FISCHER-344 RAT | | 2100-05 | F | 77055 | 9WKS | | 2.3 | 1.7 | 365 | 78055 | 365 | | S- |
| FISCHER-344 RAT | | 2100-06 | M | 77055 | 9WKS | | 2.3 | 1.7 | 64 | 77119 | 64 | | S- |
| FISCHER-344 RAT | | 2100-07 | F | 77055 | 9WKS | | 2.3 | 1.7 | 365 | 79055 | 365 | | S- |
| FISCHER-344 RAT | | 2100-08 | F | 77055 | 9WKS | | 2.3 | 1.7 | 64 | 77119 | 64 | | S- |
| FISCHER-344 RAT | | 2100-09 | F | 77055 | 9WKS | | 2.3 | 1.7 | 0 | 77055 | 0 | | S- |
| FISCHER-344 RAT | | 2100-10 | M | 77055 | 9WKS | | 2.3 | 1.7 | 4 | 77059 | 4 | | S- |
| FISCHER-344 RAT | | 2100-11 | F | 77055 | 9WKS | | 2.3 | 1.7 | 547 | 78237 | 547 | | S- |
| FISCHER-344 RAT | | 2100-12 | F | 77055 | 9WKS | | 2.3 | 1.7 | 730 | 79058 | 733 | | S- |
| FISCHER-344 RAT | | 2100-13 | F | 77055 | 9WKS | | 2.3 | 1.7 | | 78198 | 508 | | D- |
| FISCHER-344 RAT | | 2100-14 | F | 77055 | 9WKS | | 2.3 | 1.7 | 365 | 78055 | 365 | | S- |
| FISCHER-344 RAT | | 2100-15 | F | 77055 | 9WKS | | 2.3 | 1.7 | | 78117 | 427 | | D-ADENO. LUNG |
| FISCHER-344 RAT | | 2100-16 | F | 77055 | 9WKS | | 2.3 | 1.7 | 4 | 78059 | 4 | | S- |
| FISCHER-344 RAT | | 2100-17 | F | 77055 | 9WKS | | 2.3 | 1.7 | | 78267 | 577 | | D-SQU. CELL CARC. LUNG |

B-PRIMATE CAUGHT IN THE WILD, AGE ESTIMATED FROM BODY WEIGHT AT EXPOSURE
D-SPONTANEOUS DEATH
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LTR-LONG TERM RESERVE

STATUS OF INHALATION STUDIES OF 1750°C HEAT-TREATED (U,PU)O1.96 AEROSOLS FROM THE PELLET GRINDING OPERATION AT HEDL IN BEAGLE DOGS, MONKEYS AND FISCHER-344 RATS (CONTINUED)

| SPECIES | NUMBER TTOD | NUMBER RADIO. | SEX | DATE | EXPOSURE AGE (DAYS) | WT. (KG) | EXP. AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DA | DPE | ALIVE DPE 6-30-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FISCHER-344 RAT | | 2100-18 | F | 77055 | 9WKS | | 2.3 | 1.7 | 0 | 77055 | 0 | | S- |
| FISCHER-344 RAT | | 2100-19 | F | 77055 | 9WKS | | 2.3 | 1.7 | 730 | 79058 | 733 | | S- |
| FISCHER-344 RAT | | 2100-20 | F | 77055 | 9WKS | | 2.3 | 1.7 | | 78247 | 557 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RAT | | 2100-21 | M | 77055 | 9WKS | | 2.3 | 1.7 | 64 | 77119 | 64 | | S- |
| FISCHER-344 RAT | | 2100-22 | M | 77055 | 9WKS | | 2.3 | 1.7 | 365 | 78055 | 365 | | S- |
| FISCHER-344 RAT | | 2100-23 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 78254 | 564 | | D-LYMPH. LEUKEMIA |
| FISCHER-344 RAT | | 2100-24 | M | 77055 | 9WKS | | 2.3 | 1.7 | 0 | 77055 | 0 | | S- |
| FISCHER-344 RAT | | 2100-25 | M | 77055 | 9WKS | | 2.3 | 1.7 | 0 | 77055 | 0 | | S- |
| FISCHER-344 RAT | | 2100-26 | M | 77055 | 9WKS | | 2.3 | 1.7 | 0 | 77055 | 0 | | S- |
| FISCHER-344 RAT | | 2100-27 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 78297 | 607 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RAT | | 2100-28 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 77055 | 0 | | D-DURING EXPOSURE |
| FISCHER-344 RAT | | 2100-29 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 77055 | 0 | | D-DURING EXPOSURE |
| FISCHER-344 RAT | | 2100-30 | F | 77055 | 9WKS | | 2.3 | 1.7 | 4 | 77059 | 4 | | S- |
| FISCHER-344 RAT | | 2100-31 | M | 77055 | 9WKS | | 2.3 | 1.7 | 730 | 79058 | 733 | | S- |
| FISCHER-344 RAT | | 2100-32 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 78105 | 415 | | D-ADENO. LUNG |
| FISCHER-344 RAT | | 2100-33 | M | 77055 | 9WKS | | 2.3 | 1.7 | 547 | 78237 | 547 | | S- |
| FISCHER-344 RAT | | 2100-34 | M | 77055 | 9WKS | | 2.3 | 1.7 | 64 | 77119 | 64 | | S- |
| FISCHER-344 RAT | | 2100-35 | M | 77055 | 9WKS | | 2.3 | 1.7 | 4 | 77059 | 4 | | S- |
| FISCHER-344 RAT | | 2100-36 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 78217 | 527 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RAT | | 2100-37 | M | 77055 | 9WKS | | 2.3 | 1.7 | 4 | 77059 | 4 | | S- |
| FISCHER-344 RAT | | 2100-38 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 78207 | 517 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RAT | | 2100-39 | M | 77055 | 9WKS | | 2.3 | 1.7 | | 78210 | 520 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RAT | | 2100-40 | M | 77055 | 9WKS | | 2.3 | 1.7 | 547 | 78237 | 547 | | S- |

B-PRIMATE CAUGHT IN THE WILD, AGE ESTIMATED FROM BODY WEIGHT AT EXPOSURE
D-SPONTANEOUS DEATH
E-EUTHANIZED
S-SACRIFICED
LTR-LONG TERM RESERVE

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 | NUMBER TTOO | NUMBER RADIO. | SEX | EXPOSURE DATE | EXPOSURE AGE (DAYS) | EXPOSURE WT. (KG) | EXP. AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DATE | DPE | ALIVE DPE 6-30-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BEAGLE DOG | 791D | 2218-01 | M | 77193 | 1166 | 8.2 | 2.4 | 1.9 | 365 | 78193 | 365 | | S- |
| BEAGLE DOG | 902A | 2218-02 | M | 77193 | 806 | 8.9 | 2.3 | 1.9 | 1952 | 82320 | 1953 | | S- |
| BEAGLE DOG | 974U | 2218-03 | F | 77193 | 602 | 7.9 | 2.4 | 1.8 | 64 | 77257 | 64 | | S- |
| BEAGLE DOG | 839S | 2219-01 | F | 77194 | 1058 | 8.6 | 2.1 | 1.7 | | 77196 | 2 | | D-LTR |
| BEAGLE DOG | 837S | 2220-01 | F | 77195 | 1059 | 9.7 | 2.0 | 1.7 | 0 | 77195 | 0 | | S- |
| BEAGLE DOG | 843T | 2220-02 | F | 77195 | 1055 | 9.7 | 2.2 | 1.8 | 730 | 79194 | 729 | | S- |
| BEAGLE DOG | 789C | 2220-03 | M | 77195 | 1176 | 12.2 | 2.0 | 1.8 | 64 | 77259 | 64 | | S- |
| BEAGLE DOG | 838S | 2221-01 | F | 77196 | 1061 | 10.6 | 2.2 | 1.8 | 4 | 77200 | 4 | | S- |
| BEAGLE DOG | 800B | 2221-02 | M | 77196 | 1140 | 9.1 | 2.1 | 1.8 | 1952 | 82323 | 1953 | | S- |
| BEAGLE DOG | 912A | 2221-03 | M | 77196 | 762 | 12.4 | 2.3 | 1.6 | 1462 | 81197 | 1462 | | S- |
| BEAGLE DOG | 841U | 2222-01 | F | 77200 | 1061 | 6.1 | 2.2 | 1.8 | 547 | 79017 | 547 | | S- |
| BEAGLE DOG | 792B | 2222-02 | M | 77200 | 1168 | 13.0 | 2.2 | 1.8 | 547 | 79017 | 547 | | S- |
| BEAGLE DOG | 901T | 2222-03 | F | 77200 | 817 | 10.2 | 2.0 | 1.7 | | 80139 | 1034 | | D-LTR |
| BEAGLE DOG | 794A | 2223-01 | M | 77201 | 1163 | 9.4 | 2.2 | 1.8 | 730 | 79201 | 730 | | S- |
| BEAGLE DOG | 852S | 2223-02 | F | 77201 | 1017 | 6.9 | 2.2 | 1.8 | 365 | 78206 | 370 | | S- |
| BEAGLE DOG | 974V | 2223-03 | F | 77201 | 610 | 9.1 | 2.4 | 1.8 | 1952 | 82327 | 1952 | | S- |
| BEAGLE DOG | 695B | 2224-01 | M | 77202 | 1627 | 10.6 | 2.1 | 1.8 | 0 | 77202 | 0 | | S- |
| BEAGLE DOG | 857W | 2224-02 | F | 77202 | 985 | 10.5 | 2.3 | 1.9 | | 80290 | 1183 | | D-LTR |
| BEAGLE DOG | 897A | 2224-03 | M | 77202 | 833 | 11.4 | 2.1 | 1.8 | 4 | 77206 | 4 | | S- |
| RHESUS MONKEY | 883 | 2253-01 | M | 77234 | 5-7YRS-B | 7.2 | 2.0 | 1.7 | 547 | 79054 | 550 | | S- |
| CYNOMOLGUS MONKEY | 37 | 2253-02 | M | 77234 | 3-5YRS-B | 3.9 | 2.1 | 1.8 | 1462 | 81233 | 1460 | | S- |
| CYNOMOLGUS MONKEY | 40 | 2253-03 | M | 77234 | 3-5YRS-B | 3.8 | 2.1 | 1.7 | 730 | 79234 | 730 | | S- |
| RHESUS MONKEY | 891 | 2254-01 | M | 77235 | 5-7YRS-B | 8.3 | 2.4 | 1.8 | 0 | 77235 | 0 | | S- |
| CYNOMOLGUS MONKEY | 33 | 2254-02 | M | 77235 | 2-4YRS-B | 2.6 | 2.2 | 1.8 | 64 | 77299 | 64 | | S- |
| CYNOMOLGUS MONKEY | 41 | 2254-03 | M | 77235 | 3-5YRS-B | 3.7 | 2.6 | 1.9 | 365 | 78235 | 365 | | S- |
| CYNOMOLGUS MONKEY | 45 | 2254-04 | M | 77235 | 5-7YRS-B | 4.1 | 2.3 | 1.8 | 1952 | 82356 | 1947 | | S- |
| CYNOMOLGUS MONKEY | 30 | 2255-02 | M | 77236 | 3-5YRS-B | 3.9 | 2.2 | 1.7 | | 82257 | 1847 | | D-LTR |
| RHESUS MONKEY | 874 | 2265-01 | M | 77238 | 5-7YRS-B | 4.4 | 2.0 | 1.7 | 4 | 77242 | 4 | | S- |
| FISCHER-344 RATS | | 2217-01 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 79063 | 598 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RATS | | 2217-02 | M | 77195 | 9WKS | | 2.2 | 2.0 | 0 | 77195 | 0 | | S- |
| FISCHER-344 RATS | | 2217-03 | M | 77195 | 9WKS | | 2.2 | 2.0 | 64 | 77262 | 67 | | S- |
| FISCHER-344 RATS | | 2217-04 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 78358 | 528 | | D-SQU. CELL PAPILLOMA |
| FISCHER-344 RATS | | 2217-05 | M | 77195 | 9WKS | | 2.2 | 2.0 | 4 | 77199 | 4 | | S- |
| FISCHER-344 RATS | | 2217-06 | M | 77195 | 9WKS | | 2.2 | 2.0 | 547 | 79015 | 550 | | S- |
| FISCHER-344 RATS | | 2217-07 | M | 77195 | 9WKS | | 2.2 | 2.0 | 365 | 78195 | 365 | | S- |
| FISCHER-344 RATS | | 2217-08 | M | 77195 | 9WKS | | 2.2 | 2.0 | 547 | 79015 | 550 | | S- |
| FISCHER-344 RATS | | 2217-09 | M | 77195 | 9WKS | | 2.2 | 2.0 | 64 | 77262 | 67 | | S- |
| FISCHER-344 RATS | | 2217-10 | M | 77195 | 9WKS | | 2.2 | 2.0 | 4 | 77199 | 4 | | S- |
| FISCHER-344 RATS | | 2217-11 | M | 77195 | 9WKS | | 2.2 | 2.0 | 0 | 77195 | 0 | | S- |
| FISCHER-344 RATS | | 2217-12 | M | 77195 | 9WKS | | 2.2 | 2.0 | 365 | 78195 | 365 | | S- |
| FISCHER-344 RATS | | 2217-13 | M | 77195 | 9WKS | | 2.2 | 2.0 | 64 | 77262 | 67 | | S- |
| FISCHER-344 RATS | | 2217-14 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 79165 | 700 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RATS | | 2217-15 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 78341 | 511 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RATS | | 2217-16 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 77195 | 0 | | D-DURING EXPOSURE |
| FISCHER-344 RATS | | 2217-17 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 79157 | 692 | | D-SQU. CELL CA., ADENO. |

B-PRIMATE CAUGHT IN THE WILD. AGE ESTIMATED FROM BODY WEIGHT AT EXPOSURE
D-SPONTANEOUS DEATH
E-EUTHANIZED
S-SACRIFICED
LTR-LONG TERM RESERVE

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 (CONTINUED)

| SPECIES | NUMBER TTOO | NUMBER RADIO. | SEX | EXPOSURE DATE | EXPOSURE AGE (DAYS) | EXPOSURE WT. (KG) | EXP. AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DATE | DPE | ALIVE DPE 6-30-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FISCHER-344 RATS | | 2217-18 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 79158 | 673 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RATS | | 2217-19 | M | 77195 | 9WKS | | 2.2 | 2.0 | 547 | 79015 | 550 | | S- |
| FISCHER-344 RATS | | 2217-20 | M | 77195 | 9WKS | | 2.2 | 2.0 | | 77195 | 0 | | D-DURING EXPOSURE |
| FISCHER-344 RATS | | 2217-21 | F | 77195 | 9WKS | | 2.2 | 2.0 | 365 | 78195 | 365 | | S- |
| FISCHER-344 RATS | | 2217-22 | F | 77195 | 9WKS | | 2.2 | 2.0 | 547 | 79015 | 550 | | S- |
| FISCHER-344 RATS | | 2217-23 | F | 77195 | 9WKS | | 2.2 | 2.0 | 730 | 79197 | 732 | | S- |
| FISCHER-344 RATS | | 2217-24 | F | 77195 | 9WKS | | 2.2 | 2.0 | 64 | 77262 | 67 | | S- |
| FISCHER-344 RATS | | 2217-25 | F | 77195 | 9WKS | | 2.2 | 2.0 | 0 | 77195 | 0 | | S- |
| FISCHER-344 RATS | | 2217-26 | F | 77195 | 9WKS | | 2.2 | 2.0 | 64 | 77262 | 67 | | S- |
| FISCHER-344 RATS | | 2217-27 | F | 77195 | 9WKS | | 2.2 | 2.0 | 365 | 78195 | 365 | | S- |
| FISCHER-344 RATS | | 2217-28 | F | 77195 | 9WKS | | 2.2 | 2.0 | 4 | 77199 | 4 | | S- |
| FISCHER-344 RATS | | 2217-29 | F | 77195 | 9WKS | | 2.2 | 2.0 | | 78225 | 395 | | D-HEMANGIOSARC. LUNG |
| FISCHER-344 RATS | | 2217-30 | F | 77195 | 9WKS | | 2.2 | 2.0 | | 79054 | 589 | | D-HEMANGIOSARC. LUNG |
| FISCHER-344 RATS | | 2217-31 | F | 77195 | 9WKS | | 2.2 | 2.0 | | 78352 | 522 | | D-HEMANGIOSARC. PLEURA |
| FISCHER-344 RATS | | 2217-32 | F | 77195 | 9WKS | | 2.2 | 2.0 | 0 | 77195 | 0 | | S- |
| FISCHER-344 RATS | | 2217-33 | F | 77195 | 9WKS | | 2.2 | 2.0 | 4 | 77199 | 4 | | S- |
| FISCHER-344 RATS | | 2217-34 | F | 77195 | 9WKS | | 2.2 | 2.0 | 730 | 79197 | 732 | | S- |
| FISCHER-344 RATS | | 2217-35 | F | 77195 | 9WKS | | 2.2 | 2.0 | 730 | 79197 | 732 | | S- |
| FISCHER-344 RATS | | 2217-36 | F | 77195 | 9WKS | | 2.2 | 2.0 | 547 | 79015 | 550 | | S- |
| FISCHER-344 RATS | | 2217-37 | F | 77195 | 9WKS | | 2.2 | 2.0 | 365 | 78195 | 365 | | S- |
| FISCHER-344 RATS | | 2217-38 | F | 77195 | 9WKS | | 2.2 | 2.0 | 730 | 79197 | 732 | | S- |
| FISCHER-344 RATS | | 2217-39 | F | 77195 | 9WKS | | 2.2 | 2.0 | | 79062 | 597 | | D-SQU. CELL CARC. LUNG |
| FISCHER-344 RATS | | 2217-40 | F | 77195 | 9WKS | | 2.2 | 2.0 | 4 | 79199 | 4 | | S- |
| FISCHER-344 RATS | | 2217-46 | F | 77195 | 9WKS | | 2.2 | 2.0 | 0 | 77195 | 0 | | S- |
| FISCHER-344 RATS | | 2217-49 | F | 77195 | 9WKS | | 2.2 | 2.0 | | 78234 | 404 | | D-FIBROSARC. PLEURA |

B-PRIMATE CAUGHT IN THE WILD, AGE ESTIMATED FROM BODY WEIGHT AT EXPOSURE
D-SPONTANEOUS DEATH
E-EUTHANIZED
S-SARCIFICED
LTR-LONG TERM RESERVE

STATUS OF INHALATION STUDIES OF 850°C HEAT-TREATED $PuO_2$, MIXED WITH $UO_2$
AND ORGANIC BINDERS (PELLET PRESSING AT BABCOCK AND WILCOX) IN FISCHER-344 RATS
(PILOT STUDY)

| SPECIES | NUMBER TTOO | NUMBER RADIO. | SEX | EXPOSURE DATE | EXPOSURE AGE (DAYS) | EXPOSURE WT. (KG) | EXP AMAD (UM) | AEROSOL SIGMA | PROJ. SAC. DPE | DEATH DATE | DPE | ALIVE DATE 6-[illegible]-83 | COMMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FISCHER-344 RATS | | 1933-01 | M | 76348 | 9WKS | | 1.7 | 2.6 | 0 | 76348 | 0 | | S- |
| FISCHER-344 RATS | | 1933-02 | M | 76348 | 9WKS | | 1.7 | 2.6 | 0 | 76348 | 0 | | S- |
| FISCHER-344 RATS | | 1933-03 | M | 76348 | 9WKS | | 1.7 | 2.6 | 0 | 76348 | 0 | | S- |
| FISCHER-344 RATS | | 1933-04 | F | 76348 | 9WKS | | 1.7 | 2.6 | 0 | 76348 | 0 | | S- |
| FISCHER-344 RATS | | 1933-05 | F | 76348 | 9WKS | | 1.7 | 2.6 | 0 | 76348 | 0 | | S- |
| FISCHER-344 RATS | | 1933-06 | F | 76348 | 9WKS | | 1.7 | 2.6 | 8 | 76356 | 8 | | S- |
| FISCHER-344 RATS | | 1933-07 | F | 76348 | 9WKS | | 1.7 | 2.6 | 8 | 76356 | 8 | | S- |
| FISCHER-344 RATS | | 1933-08 | F | 76348 | 9WKS | | 1.7 | 2.6 | 8 | 76356 | 8 | | S- |
| FISCHER-344 RATS | | 1933-09 | F | 76348 | 9WKS | | 1.7 | 2.6 | 8 | 76356 | 8 | | S- |
| FISCHER-344 RATS | | 1933-10 | F | 76348 | 9WKS | | 1.7 | 2.6 | 8 | 76356 | 8 | | S- |
| FISCHER-344 RATS | | 1933-11 | M | 76348 | 9WKS | | 1.7 | 2.6 | 16 | 76364 | 16 | | S- |
| FISCHER-344 RATS | | 1933-12 | M | 76348 | 9WKS | | 1.7 | 2.6 | 16 | 76364 | 16 | | S- |
| FISCHER-344 RATS | | 1933-13 | F | 76348 | 9WKS | | 1.7 | 2.6 | 16 | 76364 | 16 | | S- |
| FISCHER-344 RATS | | 1933-14 | F | 76348 | 9WKS | | 1.7 | 2.6 | 16 | 76364 | 16 | | S- |
| FISCHER-344 RATS | | 1933-15 | F | 76348 | 9WKS | | 1.7 | 2.6 | 16 | 76364 | 16 | | S- |
| FISCHER-344 RATS | | 1933-16 | M | 76348 | 9WKS | | 1.7 | 2.6 | 64 | 77046 | 64 | | S- |
| FISCHER-344 RATS | | 1933-17 | F | 76348 | 9WKS | | 1.7 | 2.6 | 64 | 77046 | 64 | | S- |
| FISCHER-344 RATS | | 1933-18 | F | 76348 | 9WKS | | 1.7 | 2.6 | 64 | 77046 | 64 | | S- |
| FISCHER-344 RATS | | 1933-19 | F | 76348 | 9WKS | | 1.7 | 2.6 | 32 | 77014 | 32 | | S- |
| FISCHER-344 RATS | | 1933-20 | F | 76348 | 9WKS | | 1.7 | 2.6 | | 78108 | 491 | | D-SQU. CELL CA., PAPIL. LUNG |
| FISCHER-344 RATS | | 1933-21 | F | 76348 | 9WKS | | 1.7 | 2.6 | | 78070 | 453 | | D-SQU. CELL PAPILLOMA |
| FISCHER-344 RATS | | 1933-22 | M | 76348 | 9WKS | | 1.7 | 2.6 | 64 | 77046 | 64 | | S- |
| FISCHER-344 RATS | | 1933-23 | M | 76348 | 9WKS | | 1.7 | 2.6 | | 79071 | 819 | | E-ADENOCARC. LUNG |
| FISCHER-344 RATS | | 1933-24 | M | 76348 | 9WKS | | 1.7 | 2.6 | 32 | 77014 | 32 | | S- |
| FISCHER-344 RATS | | 1933-25 | M | 76348 | 9WKS | | 1.7 | 2.6 | | 78253 | 636 | | D-SQU. CELL CARC. |
| FISCHER-344 RATS | | 1933-26 | M | 76348 | 9WKS | | 1.7 | 2.6 | 32 | 77014 | 32 | | S- |
| FISCHER-344 RATS | | 1933-27 | M | 76348 | 9WKS | | 1.7 | 2.6 | 64 | 77046 | 64 | | S- |
| FISCHER-344 RATS | | 1933-28 | M | 76348 | 9WKS | | 1.7 | 2.6 | 32 | 77014 | 32 | | S- |
| FISCHER-344 RATS | | 1933-29 | M | 76348 | 9WKS | | 1.7 | 2.6 | | 77351 | 369 | | D-LARGE LUNG MASS |
| FISCHER-344 RATS | | 1933-30 | M | 76348 | 9WKS | | 1.7 | 2.6 | 32 | 77014 | 32 | | S- |
| FISCHER-344 RATS | | 1933-31 | M | 76348 | 9WKS | | 1.7 | 2.6 | | 77192 | 210 | | D-ADENOCARC. LUNG |
| FISCHER-344 RATS | | 1933-32 | F | 76348 | 9WKS | | 1.7 | 2.6 | | 78118 | 501 | | D-SQU. CELL CARC. LUNG |

D-SPONTANEOUS DEATH
S-SACRIFICED
E-EUTHANIZED

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14. ABSTRACT (200 words or less)

The objective of this project is to conduct confirmatory research on aerosol characteristics and the resulting radiation dose distribution in animals after inhalation and to provide prediction of health consequences in humans from airborne radioactivity that might be released in normal operations or under accident conditions during production of nuclear fuel composed of mixed oxides of uranium and plutonium. Two research reports summarize the progress of current research. The first paper details results from the completed radiation dose distribution studies in which dogs, monkeys, and rats were exposed to either $UO_2$ + $PuO_2$ treated at 750°C, $(U,Pu)O_2$ treated at 1750°C, or $PuO_2$ treated at 850°C. This paper focuses on analysis of the data from the last animals sacrificed in the study and updates earlier analyses of lung retention, tissue distribution, and excretion. The second paper details preliminary analyses of the lung retention in Fischer-344 rats exposed to either $(U,Pu)O_2$ or to $PuO_2$ at one of three levels of projected dose to lung for each aerosol. This paper presents the methods and the application of a rigorous statistical procedure allowing detection of similarities and differences in the lung retention of rats at different dose levels and for different aerosols.

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inhalation, exposure, dose, solubility
biological effects, health consequences
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RADIATION DOSE ESTIMATES AND HAZARD EVALUATIONS FOR INHALED AIRBORNE RADIONUCLIDES

JULY 1984