Early and Continuing Effects of Combined Alpha and Beta Irradiation of the Lung

Phase II Report

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PREVIOUS DOCUMENTS IN SERIES

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ABSTRACT

This report summarizes an inhalation exposure experiment that concerns early and continuing effects of combined alpha and beta irradiation of the lung of rats. Both morbidity at 18 months and mortality within 18 months after exposure were examined for rats exposed to the beta-emitter ^{147}Pm , the alpha-emitter ^{238}Pu , or both combined. The results were used to validate hazard-function models that were developed (1) for pulmonary functional morbidity at 18 months and (2) for lethality from radiation pneumonitis and pulmonary fibrosis within 18 months. Both models were found to adequately predict the experimental observations after combined chronic alpha and beta irradiation of the lung. A relative biological effectiveness of approximately 7 was obtained for ^{238}Pu alpha radiation compared to ^{147}Pm beta radiation for both pulmonary functional morbidity and lethality from radiation pneumonitis and pulmonary fibrosis.

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EXECUTIVE SUMMARY

Although current radiobiological research is largely focused on carcinogenic and genetic effects, the casualties caused by the recent Chernobyl nuclear power plant accident in the Soviet Union reemphasized the importance of research on acute radiobiological effects. Recognizing this need years before the Chernobyl accident occurred, the Nuclear Regulatory Commission (NRC) sponsored research on acute and continuing effects of irradiation designed to develop improved radiobiological health-effects models. This report provides experimental and theoretical results on lethality and morbidity effects caused by combined chronic alpha and beta irradiation of the lung, based on research carried out at the Inhalation Toxicology Research Institute (ITRI).

Studying effects of combined alpha and beta irradiation of the lung is important because the transport of radioactive materials associated with the nuclear fuel cycle could result in the accidental or intentional (i.e., by sabotage) release of mixtures of alpha- and beta-emitting radionuclides into the environment. If airborne, the radionuclides could be inhaled by man and could lead to large radiation doses to the lung. A large radiation dose to the lung can cause radiation pneumonitis and pulmonary fibrosis (RPPF) and could prove fatal or lead to impaired pulmonary function for a survivor.

A hazard-function (HF) model was developed at our Institute for predicting the frequency of death from RPPF after complex patterns of beta-gamma irradiation or after combined alpha and beta irradiation of the lung. Several experiments were conducted to validate the mortality model and to provide data to develop a similar model for pulmonary morbidity.

Results of four experiments using rats to test the mortality model for predicting acute effects of complex patterns of beta-gamma irradiation of the lung are in another report (NUREG/CR-5025, 1987). The experiment described in this report was carried out to validate the model for predicting death from RPPF after combined alpha and beta irradiation of the lung and to provide data for developing and validating a similar model for pulmonary morbidity.

Prediction of death from RPPF after combined alpha and beta irradiation of the lung is based on a hazard-function model expressed by the Weibull-type function

$$\text{LETHALITY HAZARD} = \ln(2) \cdot X^V,$$

where V is a positive parameter that determines the shape of the dose-effect relationship. X is the total alpha plus beta dose in ILB_{50} units. It is calculated by dividing the initial lung burden for the alpha emitter by the median lethal initial lung burden (ILB_{50}) for the alpha emitter resulting in the alpha dose, X_a , in ILB_{50} units for the alpha emitter. A similar procedure is used to derive a similar dose for the beta emitter, X_b . X is then equal to $X_a + X_b$.

Doses X_a , X_b , and X can also be defined in terms of the cumulative radiation dose to the lung evaluated to a fixed time (e.g., 1.5 year dose). To do so, the median lethal radiation dose (D_{50}) must be known for both the alpha and the beta emitter, evaluated to the same fixed time as the cumulative radiation dose.

The lethality risk is related to the lethality hazard by the expression

$$\text{RISK} = 1 - \exp[-\text{HAZARD}].$$

The risk for pulmonary morbidity was estimated in a similar way.

To validate the HF model for lethality and to develop and validate a similar model for morbidity, 395 F344/Crl rats, approximately 15 weeks of age were exposed via inhalation to ^{238}Pu only, ^{147}Pm only, or mixtures of both, in insoluble fused aluminosilicate particles (FAP). Control animals were exposed to fused aluminosilicate particles only.

The alpha emitter selected for the study was ^{238}Pu because of its high specific activity. This made it possible to use the same FAP aerosol for both ^{238}Pu and ^{147}Pm , as well as permitting the use of a single radioactive tag, in a single inhalation exposure, thus minimizing the variability in lung deposition of the radionuclides.

Lung tissue content of ^{238}Pu and ^{147}Pm was determined using both whole-body counting of a ^{169}Yb gamma-emitting tag and radiochemical analyses of tissues from sacrificed rats and those dying during the study. The radiochemical procedures included ashing, dissolution, and counting by liquid scintillation methods.

Biological endpoints monitored on all rats during the study were body weights, histological changes, and survival time. The probable cause of death was determined for each rat that died during the 1.5 year followup period. Respiratory function tests were performed on 117 survivors at 1.5 years after inhalation exposure.

For the ^{238}Pu -alpha irradiation of the lung, the ILB_{50} for death within 1.5 years from RPPF was 123 nCi/g-lung, which corresponds to a cumulative 1.5 year radiation dose of 4500 rad (45 Gy) to the lung. For ^{147}Pm -beta irradiation of the lung, the ILB_{50} was 160 $\mu\text{Ci/g-lung}$, which corresponded to a cumulative 1.5 year radiation dose of about 30,000 rad (300 Gy) to the lung. The shape parameter, V , for lethality from RPPF was similar for alpha and beta irradiation of the lung with an average value of approximately 5.

After review of several respiratory parameters, four were selected and used to determine the prevalence of pulmonary functional morbidity. These parameters were vital capacity, quasistatic compliance, CO-diffusing capacity per kg body weight, and slope of phase 3 of the single-breath N_2 washout curve. Vital capacity reflected changes in lung volume; quasistatic lung compliance reflected changes in lung elasticity; the slope of phase 3 of the single-breath N_2 washout reflected the uniformity of gas distribution; and carbon monoxide diffusing capacity per kg body weight reflected alveolar-capillary gas exchange efficiency. Individuals having abnormal values for 3 or more of these 4 functional parameters were judged to have pulmonary morbidity.

For the ^{238}Pu -alpha irradiation of the lung, the ILB_{50} for pulmonary morbidity was 30 nCi/g-lung, which corresponded to a 1.5 year cumulative radiation dose of about 1,100 rad (11 Gy) to the lung. For the ^{147}Pm -beta irradiation of the lung, the ILB_{50} was 40 $\mu\text{Ci/g-lung}$, which corresponded to a 1.5 year cumulative radiation dose of about 7,500 rad (75 Gy) to the lung. The shape parameter, V , was assumed to be the same for both morbidity and lethality. A value of 5 was therefore also used for morbidity.

The results indicate that the same shape parameter can be used for alpha and beta irradiation of the lung and for mortality and morbidity. However, about four times as much dose is required for 1.5-year lethality from RPPF as is required for morbidity.

After adjusting for competing modes of death, 80 rats were judged at risk for death from RPPF after combined alpha and beta irradiation of the lung. Of these, 43 deaths were expected and 54 were observed. Also, for rats receiving combined alpha and beta irradiation of the lung, 21 out of 24 surviving rats were expected to have pulmonary functional morbidity while 22 cases were observed. The results indicate that the hazard-function mortality and hazard-function morbidity models for combined alpha and beta irradiation of the lung should be adequate for reactor accident risk assessment.

CHAPTER 1

INTRODUCTION

The transport of radioactive materials associated with the nuclear fuel cycle could result in accidental or intentional (i.e., by sabotage) release of mixtures of alpha- and beta-emitting radionuclides into the environment. If released, the radioactive substances could become airborne and be inhaled by people leading to irradiation of critical body organs. When radionuclides are inhaled in an insoluble form, the lung is the main organ at risk. Small doses (hundreds of rad) to the lung may result in lung cancer, while large doses (thousands of rad) may result in other morbidity as well as death from radiation pneumonitis and pulmonary fibrosis (RPPF).

The experiment described in this report is the last of a series of inhalation-exposure experiments carried out at the Inhalation Toxicology Research Institute (ITRI) for the Nuclear Regulatory Commission (NRC) to validate an acute mortality model (Scott *et al.*, 1984, 1986). The model was developed for predicting death from RPPF after inhalation exposure of a population to mixtures of beta emitting or mixtures of alpha- and beta-emitting radionuclides. The series of experiments was to also provide morbidity data for developing a similar model to predict morbidity from similar exposures.

The experiment described in this report was carried out to determine if the mortality model adequately predicts lethality from RPPF after combined alpha and beta irradiation of the lung from radionuclides deposited via inhalation. The experiment also provided pulmonary function, body weight, and hematology data to use in an exploratory analysis for morbidity.

Another report (NUREG/CR-5025, 1987) describes results of inhalation exposure experiments carried out to (1) determine the affect of beta energy on the risk of death from RPPF and (2) to validate model predictions of acute lethality from RPPF after internal exposure of the lung to complex patterns of low linear energy transfer (LET) radiation from beta-emitting radionuclides deposited in the lung.

CHAPTER 2 METHODS

2.1 Animals

Male and female F344/Cr1 rats were obtained from the Lovelace ITRI breeding colony for use in the study. The colony is free of known rat respiratory pathogens and is tested serologically every three months. The rats were 15 ± 2 weeks of age at exposure.

2.2. Housing of Animals

Before the rats were exposed, each was given a unique ear tag for identification. Rats of each gender were weighed and housed separately (two per polycarbonate cage). The room housing the rats was maintained at 20 to 22°F. The relative humidity was maintained at 20 to 50%. A 12-hour-on 12-hour-off light cycle was used. Rats were fed Lab Blox (Allied Mills, Chicago, IL) and given water ad libitum.

2.3 Experimental Design

Equal numbers of both genders were randomized by body weight into exposure groups as indicated in Table 2.1. Randomization into mortality and hematology groups was constrained such that average body weights were similar over all exposure concentrations and groups for a given gender. Exposure levels L₀₁ and L₅₀ were based on concentrations intended to produce about 1% and 50% lethality, respectively, from RPPF, for exposure to the alpha-emitter ²³⁸Pu or beta-emitter ¹⁴⁷Pm only. A gamma-emitting label, ¹⁶⁹Yb, was incorporated into each of the FAP aerosols containing ¹⁴⁷Pm and for ²³⁸Pu to make it possible to estimate the initial lung burdens of these latter two radionuclides by whole-body counting. A uniform distribution of the initial lung burden (ILB) was assumed for each exposure group. Thirty-six rats were included in each of 9 exposure categories (L₀₁, L₅₀, for ²³⁸Pu or ¹⁴⁷Pm, and combinations of both in the same particle) as indicated in Table 2.1. For example, 36 rats were exposed to the L₀₁ (alpha) + L₀₁ (beta) combination.

Table 2.1
²³⁸Pu-Alpha + ¹⁴⁷Pm-Beta Study Design and 1.5-Year
Survivors Among F344/Cr1 Rats Exposed by Exposure Level

Betas (¹⁴⁷ Pm)	Alphas (²³⁸ Pu)				
	L ₀₀		L ₀₁		L ₅₀
L ₀₀	Mortality (C)*	Hematology (C1)	Mortality (A2)		Mortality (A1)
	3/36	0/8	12/36		28/36
L ₀₁	Mortality (B2)		Mortality (AB4)	Sacrifice (AB5)	Hematology (AB5)
	3/36		21/36	50/50	9/22
L ₅₀	Mortality (B1)		Mortality (AB2)		Mortality (AB1)
	18/36		19/36		35/35

*Items within parentheses represent experimental group designation. Ratios represent number dead at 1.5 years over number exposed. A hematology group (C1) of size 8 at L₀₀ + L₀₀ level was added after initiation of the study. The hematology group at L₀₁ + L₀₁ level was taken from animals initially assigned to the sacrifice study. One rat at L₅₀ + L₅₀ level died at time of exposure. L₀₁ was intended to be a 1% affected level. L₅₀ was intended to be a 50% affected level. L₀₀ represents control exposure to nonradioactive fused aluminosilicate particles.

Fifty additional rats were assigned to the L₀₁ (alpha) + L₀₁ (beta) exposure level to be sacrificed 6 at a time (3 of each gender) at 0, 4, 14, 30, 60, 90, 120 and 150 days after inhalation exposure to provide needed dosimetry information. The remaining two were used as backups.

Eight rats were added to the L₀₀ (control) level and 22 to the L₀₁ (alpha) + L₀₁ (beta) level to provide hematological data at 7, 14, 30, 60, 90, 180, 365 and 540 days after exposure. The eight control rats were not sham exposed.

2.4 Biological Measurements

Biological endpoints monitored on all rats during the study were body weight, histologic changes and survival time. Body weights were measured before exposure and at monthly intervals to 1.5 years after exposure. Surviving animals were observed twice per day for the 1.5-year observation period. Those moribund or critically ill were euthanized. After death, all animals were examined for gross lesions. The lungs were weighed and fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 5 microns and stained with hematoxylin and eosin for histologic evaluation. The probable cause of death was determined for each animal that died during the study.

Respiratory-function tests were performed on 117 (60 males and 57 females) survivors at 1.5 years after inhalation exposure using previously reported techniques (Harkema *et al.*, 1982). The distribution of these survivors among exposure concentrations is shown in Table 2.2. Measurements by plethysmography during halothane anesthesia included 35 parameters for breathing patterns, lung volumes, lung mechanics, gas distribution, CO diffusing capacity and forced exhalation. Data for all respiratory function parameters were reviewed, then a limited number of parameters reflecting key facets of function were selected for detailed analysis. Vital capacity reflected changes in lung volume, quasistatic lung compliance reflected changes in lung elasticity, the slope of phase 3 of the single-breath N₂ washout reflected the uniformity of gas distribution, and carbon

Table 2.2
Survivors That Were Subjected to Pulmonary Function Testing at 1.5 Years
After Inhalation Exposure

Beta Exposure Level	Alpha Exposure Level					
	L ₀₀		L ₀₁		L ₅₀	
	Male	Female	Male	Female	Male	Female
L ₀₀	10	10	10	10	10	5
L ₀₁	6	10	10	4	--	--
L ₅₀	8	5	6	13	--	--

Total males = 60

Total females = 57

Grand total = 117

monoxide diffusing capacity per kg body weight reflected alveolar-capillary gas exchange efficiency.

Hematology was performed only on rats assigned to the hematology group (Table 2.1). Measurements were taken at 7, 14, 30, 60, 90, 180, 360 and 540 days after inhalation exposure. Blood was collected from the retrobulbar sinus in a capillary tube. Blood smears were made and the blood diluted in Unopettes®. Hematocrit, total red and white blood cells and white blood cell differential counts were determined.

2.5 Aerosol Preparation and Generation

Suspensions for aerosol generation were prepared by cation exchange of ^{147}Pm , ^{238}Pu , or ^{169}Yb into montmorillonite clay. The ^{238}Pu and ^{147}Pm were incorporated into separate batches of montmorillonite clay suspended in water. Appropriate aliquots of each batch were mixed together to achieve the desired initial ratios of alpha to beta activity in the exposure aerosol. With this approach, the initial ratio of alpha to beta activity was fixed for each exposure aerosol but differed among them. Polydisperse aerosols were generated with a Lovelace nebulizer and heat treated by passing through a heating column at 1150°C with a flow rate of 2 lpm. The ^{169}Yb gamma-emitting tag was incorporated into the particles in small amounts (Table 2.3) to allow determination of particle retention in the lung through total-body counting.

The ^{238}Pu was selected for this study because of its high specific activity. This made it possible to use the same fused aluminosilicate particle (FAP) aerosols for both ^{238}Pu and ^{147}Pm , as well as permitting the use of a single radioactive tag in a single inhalation exposure, thus minimizing the variability in the lung deposition of the radionuclides. Two separate aerosols would have required two exposures (one for the alpha emitter and one for the beta-emitter) and would have led to larger variability in the initial lung deposition and in the initial alpha to beta activity ratio.

2.6 Total-Body Counting

Shielded NaI(Tl) crystal counters were used to detect gamma radiation from the ^{169}Yb radioactive tag. Each counting unit consisted of three 5 cm by 3 cm sodium iodide crystals with built-in photomultiplier tubes spaced 120° apart around a centrally located sample holder. Detectors were shielded by 10 cm of lead.

2.7 Determination of Lung Radioactivity Content

Rat lung specimens were analyzed for ^{238}Pu and for ^{147}Pm , as detailed below, after the ^{169}Yb had decayed to nondetectable levels. The procedures used included ashing, dissolution, and counting by liquid scintillation methods (Keough and Powers, 1970). This was a double label procedure that required mathematical resolution of the sample content of ^{238}Pu and ^{147}Pm . Quench correction was by the external standard, channels-ratio method.

Tissue samples awaiting analysis were stored in 10% neutral buffered formalin solution in glass vials. For analysis, each sample was transferred to a Pyrex beaker, dried in an oven, dry ashed in a muffle furnace, and wet ashed with HNO_3 and H_2O_2 to destroy the organic matrix. The resulting sample was redissolved in 100 ml of 2 M HNO_3 . A 5 ml aliquot of the clear, colorless solution was transferred to a liquid scintillation counting vial. Fifteen ml of Ready-Solv EP liquid scintillation cocktail (Beckman Instruments) was added to the vial. A one-day period was allowed between preparation of a sample and actual counting to allow the sample to stabilize chemically.

Quench correction standards were prepared for ^{238}Pu and ^{147}Pm . These standards were necessary for quench correction and mathematical resolution of the ^{238}Pu and ^{147}Pm activity content in the rat tissues. There were 5 quench correction standards for ^{147}Pm , 5 for ^{238}Pu , and 5 for standards that contained both ^{238}Pu and ^{147}Pm . Five standards were used to provide a range of quenching that covered the anticipated range for the lung tissue samples. The degree of

Table 2.3

Aerosol Concentrations, Aerosol Size, Exposure Run Time and
Initial Radionuclide to ^{169}Yb Activity Ratios by Experiment Number

Experiment Group	Aerosol Concentration			Aerosol Size*		^{169}Yb to Nuclide Ratio		Predicted ILB's			Run Time (min)
	^{169}Yb (nCi/l)	^{238}Pu (nCi/l)	^{147}Pm ($\mu\text{Ci/l}$)	AMAD (μm)	σ_g	^{238}Pu	^{147}Pm	^{169}Yb (nCi)	^{238}Pu (nCi)	^{147}Pm (μCi)	
A1	772	550	0	1.60	1.50	2.59	NA	320	230	0	35
A2	775	71.4	0	1.70	1.59	9.56	NA	420	40	0	60
B1	621	NA	132	1.42	1.77	NA	0.0047	447	NA	100	60
B2	943	NA	73	1.44	2.2	NA	0.013	475	NA	40	42
AB1	661	248	107	1.40	1.50	2.67	0.0062	560	210	90	70
AB2	622	72	114	1.27	1.6	12.3	0.0245	450	50	90	60
AB3	541	294	29	1.42	1.56	1.93	0.019	380	210	20	59
AB4	429	45.4	18.1	1.45	1.61	11.2	0.0237	360	40	15	70
AB5	387	44	23.1	1.49	1.58	9.33	0.0167	380	50	20	60

*AMAD represents activity median aerodynamic diameter, σ_g represents the geometric standard deviation.

NA = not applicable.

quenching was controlled by the amount of HNO_3 in the vials. Techniques used for preparation of quenching correction standards were identical to those for preparation of samples. A new series of standards was prepared for each batch of rat tissue.

Samples were counted by liquid scintillation for 20 minutes. The ^{238}Pu and ^{147}Pm activities were counted in two channels (indicated here as A and B) of the liquid scintillation counter. The efficiencies of counting ^{147}Pm and ^{238}Pu in Channel A were indicated by E_{11} and E_{21} , respectively. For Channel B they were indicated by E_{12} and E_{22} , respectively. Sample gross counts in Channels A and B were corrected for background by counting blanks and obtaining net counts per minute (cpm). Net cpm in Channels A and B were represented by CPM_1 and CPM_2 , respectively. The counting efficiencies were functions of the external standard channels ratio. Curves were prepared relating counting efficiency to the external standard channels ratio for each radionuclide. Total disintegrations per minute (DPM) for ^{147}Pm and ^{238}Pu , represented by DPM_1 and DPM_2 , respectively, were calculated using

$$\text{DPM}_1 = [\text{CPM}_1 * E_{22} - \text{CPM}_2 * E_{21}] / [E_{11} * E_{22} - E_{12} * E_{21}] \quad (1)$$

$$\text{DPM}_2 = [\text{CPM}_2 * E_{11} - \text{CPM}_1 * E_{12}] / [E_{11} * E_{22} - E_{12} * E_{21}] \quad (2)$$

After calculating DPM_1 and DPM_2 , the total DPM for ^{238}Pu and ^{147}Pm in lung was calculated by multiplying the results by 20, since only 1/20 of each sample was counted.

2.8 Estimation of Initial Lung Burdens

Initial lung burdens for ^{238}Pu and ^{147}Pm were estimated indirectly. First, the initial lung burden of ^{169}Yb was estimated from total-body counts of ^{169}Yb at early times (from 14 to 104 days after exposure). Most of the total-body activity from 14 to 104 days was assumed to be in the lung. A single-component exponential retention function was used to estimate the day 0 intercept for ^{169}Yb , the estimated initial lung burden. Additional total-body activity cleared at early times was excluded. The initial lung burdens of ^{238}Pu and ^{147}Pm were estimated for each animal indirectly by multiplying the initial lung burden of ^{169}Yb by the respective initial activity ratios (^{238}Pu to ^{169}Yb and ^{147}Pm to ^{169}Yb activity ratios).

The aerosol concentrations of ^{238}Pu , ^{147}Pm , and ^{169}Yb were determined by analyzing filters taken during exposure and are given in Table 2.3. Radioactivity counts for ^{238}Pu were obtained using a ZnS scintillation technique; for ^{147}Pm they were achieved using a P-10 gas proportional counter technique; and for ^{169}Yb they were obtained using a NaI(Tl) detector.

2.9 Estimation of Doses to Lung

Separate curves were developed for retention of ^{238}Pu and ^{147}Pm in the lung using initial lung burden estimates and results of radiochemical analysis on specific rats assigned to the study for dosimetry purposes (sacrifice group) and those that died or were euthanized when critically ill. Retention curves for lung were obtained by fitting two-component exponential functions to the radiochemistry data using SAS nonlinear regression software (SAS, 1982).

The cumulative radiation dose to the lung at death and the cumulative dose to a specified time (e.g., 1 year after inhalation exposure) were evaluated by numerical integration over the dose rate pattern for each exposed individual. Numerical evaluation of dose was required because the lung weight changed with time as the animals grew. Instantaneous dose rates $\text{DR}(t)$ at any given time t after inhalation exposure were given by

$$\text{DR}(t) = 51.2 * E * A(t) * f / W(t), \text{ rad/day} \quad (3)$$

where

$$E = 0.062 \text{ MeV for } ^{147}\text{Pm}$$

$$E = 5.5 \text{ MeV for } ^{238}\text{Pu}$$

$A(t)$ = the activity retained at time t which equals the product of the initial lung burden in μCi and the radionuclide-specific lung retention function

f = fractional energy absorption in the lung; 0.97 for ^{147}Pm betas and 1 for ^{238}Pu alphas (Snipes, 1980)

$W(t)$ = lung weight in g at t days after inhalation exposure

$$= 0.0050 * [\text{Initial body weight in g} + 124 * GF(t)], \text{ females}$$

$$= 0.0041 * [\text{Initial body weight in g} + 166 * GM(t)], \text{ males}$$

where the empirical function $GF(t)$ and $GM(t)$ obtained from an earlier publication (NUREG/CR-5025, 1987) are given by

$$GF(t) = 1 - \exp(-0.0169 * t^{0.822}) \quad (4)$$

and

$$GM(t) = 1 - \exp(-0.0133 * t^{0.938}). \quad (5)$$

This method of evaluating doses was based on the assumption that the lungs continue to grow in irradiated rats as they do in unirradiated controls. Cumulative radiation doses to the lung for ^{147}Pm betas and ^{238}Pu alphas were evaluated separately at 1, 14, 30, 90, 180, 200, 360, 540, 730 and 1096 days after exposure, for an initial lung burden of 1 $\mu\text{Ci/g-lung}$ for ^{147}Pm and 1 nCi/g-lung for ^{238}Pu , using numerical integration with a FORTRAN program. The data obtained for the cumulative dose in rad were then fitted with a two-component exponential function of the form

Cumulative dose/unit activity/g-lung =

$$C1 * [1 - \exp(-B1 * t)] + C2 * [1 - \exp(-B2 * t)], \quad (6)$$

where the parameters $C1$, $C2$, $B1$ and $B2$ were positive and depended on the type of radiation. A single set of parameters were determined from the data for exposure to ^{147}Pm only; a single set was obtained for exposure to ^{238}Pu only, and a single set was obtained for exposure to mixtures of ^{147}Pm and ^{238}Pu . The fitted curves for the cumulative dose per $\mu\text{Ci } ^{147}\text{Pm}$ per g-lung or per $\text{nCi } ^{238}\text{Pu}$ per g-lung were used to evaluate cumulative rads to the lung at any desired time including the dose to death. To make this evaluation, the cumulative rads per unit initial lung burden (in $\mu\text{Ci } ^{147}\text{Pm}$ per g-lung or $\text{nCi } ^{238}\text{Pu}$ per g-lung) at the time of interest were multiplied by the initial lung burden expressed in activity per gram of lung.

CHAPTER 3

RESULTS

3.1 Initial Activity, Biological Clearance and Retention of Radioactive Material in the Lung

Aerosols were polydisperse in their size distribution. Activity median aerodynamic diameters (AMAD) and geometric standard deviations are given in Table 3.1 along with aerosol concentrations and exposure durations. The activity ratios of ^{147}Pm to ^{169}Yb and ^{238}Pu to ^{169}Yb in Table 2.3 were used to estimate actual initial lung burdens from total body ^{169}Yb counts. The desired and actual initial lung burdens (averages) are given, by exposure level, in Table 3.1.

Table 3.1
Desired and Observed Average Initial Lung Burdens of ^{147}Pm and/or ^{238}Pu
Inhaled in Fused Aluminosilicate Particles by Rats

^{147}Pm Exposure	Category	^{238}Pu Exposure Level					
		L ₀₀		L ₀₁		L ₅₀	
		Pm (μCi)	Pu (nCi)	Pm (μCi)	Pu (nCi)	Pm (μCi)	Pu (nCi)
L ₀₀	Desired	0	0	0	40	0	180
	Observed	0	0	0	24 ± 6	0	130 ± 40
L ₀₁	Desired	20	0	20	40	20	180
	Observed	21 ± 12	0	14 ± 5	26 ± 10	13 ± 4	130 ± 44
L ₅₀	Desired	100	0	100	40	100	180
	Observed	57 ± 20	0	42 ± 15	26 ± 10	51 ± 20	120 ± 40

Curves for retention of radioactivity in lung (lung-retention functions) that were obtained using two-component exponential functions are plotted in Figures 3.1 and 3.2. Separate lung-retention functions for ^{147}Pm retention were obtained for exposure to ^{147}Pm alone and for exposure to ^{147}Pm in combination with ^{238}Pu (mixture). The lung-retention functions are given in Table 3.2. Separate lung-retention functions were also obtained for ^{238}Pu retention for exposure to ^{238}Pu alone and for exposure to ^{238}Pu in combination with ^{147}Pm .

Table 3.2
Lung Retention Functions for Retention of ^{238}Pu or ^{147}Pm in the Lung
of F344/Cr1 Rats*

Radionuclide	Type of Exposure	Retention Function Parameter		
		A1	B1	B2
^{238}Pu	^{238}Pu only	0.41 ± 0.11	0.028 ± 0.022	0.0027 ± 0.00036
^{238}Pu	$^{238}\text{Pu} + ^{147}\text{Pm}$	0.69 ± 0.074	0.015 ± 0.0033	0.00094 ± 0.00045
^{147}Pm	^{147}Pm only	0.67 ± 0.10	0.15 ± 0.033	0.0036 ± 0.00059
^{147}Pm	$^{238}\text{Pu} + ^{147}\text{Pm}$	0.54 ± 0.023	0.091 ± 0.044	0.0033 ± 0.00016

*Retention function = $A1 \cdot \exp[-B1 \cdot t] + (1 - A1) \exp[-B2 \cdot t]$, where t is in days.

Figure 3.1 Pulmonary retention of ^{238}Pu in F344/Cr1 rats after (a) inhalation exposure to ^{238}Pu only, in fused aluminosilicate particles and after (b) inhalation exposure to mixtures of $^{238}\text{Pu} + ^{147}\text{Pm}$ in the same fused aluminosilicate particle matrix.

Figure 3.2 Pulmonary retention of ^{147}Pm in F344/Cr1 rats after (a) inhalation exposure to ^{147}Pm only, in fused aluminosilicate particles and after (b) inhalation exposure to mixtures of $^{238}\text{Pu} + ^{147}\text{Pm}$ in the same fused aluminosilicate particle matrix.

Dose accumulation expressed as rads per nCi ^{238}Pu per g-lung or rads per $\mu\text{Ci } ^{147}\text{Pm}$ per g-lung were first evaluated numerically by gender. Results obtained were essentially the same for both genders so that an average of both was obtained and fitted with a two-component exponential function. The fitted functions obtained are plotted in Figures 3.3 and 3.4 and are given in Table 3.3. These functions were used to calculate radiation doses to the lung to the desired times as described above.

Figure 3.3 Fitted two-component exponential curves for calculating, as a function of time after inhalation exposure, rads per nCi/g-lung due to ^{238}Pu initially deposited in the lung (ILB). Separate curves are provided for exposure to " ^{238}Pu only" and for exposure to " $^{238}\text{Pu} + ^{147}\text{Pm}$." To get cumulative rads to the lung at a specified time, multiply the value of the curve at that time by the initial lung burden for ^{238}Pu in nCi/g-lung.

Figure 3.4 Fitted two-component exponential curves for calculating, as a function of time after inhalation exposure, rads per $\mu\text{Ci/g-lung}$ due to ^{147}Pm initially deposited in the lung (ILB). Separate curves are provided for exposure to " ^{147}Pm only" and for exposure to " $^{238}\text{Pu} + ^{147}\text{Pm}$." To get cumulative rads to the lung at a specified time, multiply the value of the curve at that time by the initial lung burden for ^{147}Pm in $\mu\text{Ci/g-lung}$.

Table 3.3

Dose Accumulation Functions for Calculating Cumulative Rads per nCi/g-Lung of ^{238}Pu or per $\mu\text{Ci/g-Lung}$ of ^{147}Pm Initially Deposited in the Lung (ILB) as a Function of the Time (t) in Days After Inhalation Exposure of F344/Cr1 Rats*

Radionuclide	Type of Exposure	Dose Accumulation Function Parameter			
		C1	B1	C2	B2
^{238}Pu	^{238}Pu only	6.10	0.0268	39.2	0.00285
^{238}Pu	$^{238}\text{Pu} + ^{147}\text{Pm}$	12.0	0.0176	53.3	0.00109
^{147}Pm	^{147}Pm only	20.7	0.0831	186	0.00411
^{147}Pm	$^{238}\text{Pu} + ^{147}\text{Pm}$	30.9	0.0540	283	0.00360

Dose in rad = $C1(1-\exp[-B1*t]) + C2*(1-\exp[-B2*t])$.

3.2 Mortality Distribution

The fraction dying from all causes to about 1.5 years after inhalation exposure is shown in Figure 3.5 as a function of exposure level. After adjusting for spontaneous deaths, the results indicate synergistic effects of the alpha and beta radiations for mortality from all causes for three of the four combinations. Adjustments were made by assuming that radiation induced and spontaneous effects were independent. A pronounced synergistic effect was observed for the L_{01} (alpha) + L_{01} (beta) combination. While the L_{01} level beta exposure caused no radiation induced early deaths and the L_{01} alpha level caused 27% lethality, a combination of these two levels caused 54% lethality (all based on adjusted results).

Figure 3.5 Unadjusted (UNADJ) distribution of 1.5 year mortality from all causes of death (except sacrifices) as a function of exposure level. Adjusted values (ADJ) to correct for spontaneous effects are also given and were calculated assuming independence of radiation-induced and nonradiation-induced effects.

Histological examination of the rats that died revealed several causes of death, including RPPF and lung tumors. The major cause of death before 1.5 years was RPPF. It was characterized histologically by increased numbers of vacuolated alveolar macrophages and occasional neutrophils, alveolar hemosiderin, vasculitis and fine alveolar septal fibrosis. Thrombosis was also occasionally present. The cause of death was considered RPPF when these characteristics were found and there was no other obvious cause.

Survival times for death from all causes (except RPPF) vs the initial lung burdens of ^{238}Pu and ^{147}Pm are given in Figure 3.6. Survival times for rats dying from RPPF are given in Figure 3.7 as a function of the initial lung burdens of ^{238}Pu and ^{147}Pm . Note that survival time was inversely related to the total radionuclide activity deposited in the lung.

Figure 3.6 Survival time for death from all causes except radiation pneumonitis and pulmonary fibrosis as a function of the initial lung burden of ^{238}Pu in nCi/g-lung and ^{147}Pm in $\mu\text{Ci/g-lung}$. Time to euthanasia of morbid rats was used as estimates of time to death from radiation-induced and natural causes.

Figure 3.7 Survival time for death from radiation pneumonitis and pulmonary fibrosis. Time to euthanasia of morbid rats was used as an estimate of time to death from radiation induced causes.

Risk estimators were developed for 1.5-year lethality from RPPF after inhalation exposure to only ^{238}Pu and to only ^{147}Pm when inhaled in fused aluminosilicate particles. Use of the maximum likelihood procedure allowed the analysis of individual data without having to form dose groups. This eliminated the systematic error associated with grouping of individuals that had different initial lung burdens. We have used a Weibull type risk function for lethality that depends on the median lethal dose D_{50} and shape parameter V (Scott *et al.*, 1987). With this risk function model, the lethality hazard H is related to the lethality risk R by

$$R = 1 - \exp(-H) \quad (7)$$

where

$$H = \ln(2) * [ILB/ILB_{50}]^V. \quad (8)$$

The variable named ILB is the initial lung burden in $\mu\text{Ci/g-lung}$ of ^{147}Pm or nCi/g-lung of ^{238}Pu , and ILB_{50} is the median lethal initial lung burden. Once the ILB_{50} is known for ^{238}Pu only or ^{147}Pm only, it can be used to calculate the median lethal dose D_{50} in rads to any specified time (e.g., 1 year). In this case, the ratio ILB/ILB_{50} in the above equation can be replaced by D/D_{50} where D is the dose in rads to the time at which the D_{50} dose is evaluated.

For ^{238}Pu , the median lethal initial lung burden and shape parameter obtained for death from RPPF within 1.5 years, were $123 \pm 7.5 \text{ nCi/g-lung}$ and 4.1 ± 1.6 , respectively. For ^{147}Pm , the corresponding median lethal lung burden and shape parameter estimates were $160 \pm 190 \mu\text{Ci/g-lung}$ and 5.4 ± 0.9 , respectively. The large uncertainty in the median lethal initial lung burden for ^{147}Pm arises because intended initial lung burdens were not achieved. The rats were underexposed, leading to only one death attributed to RPPF after exposure to ^{147}Pm only. Twenty-five deaths were attributed to other causes, primarily pulmonary tumors. The estimate of $160 \mu\text{Ci/g-lung}$ for the median lethal initial lung burden was identical to that obtained in an earlier experiment where there were many deaths attributed to RPPF (NUREG/CR-5025, 1987).

An attempt was made to use the unimodal Weibull model to characterize dose-effect curves for 1-year lethality from all causes. However, because deaths from causes other than RPPF occurred at doses below the effective threshold for death from RPPF, satisfactory fits to the multimodal data could not be obtained using the unimodal model.

3.3 Expected and Observed Deaths

Based on the hazard function model for predicting the combined effects of high-LET alpha and low-LET beta irradiation of the lung, the lethality hazard for death from RPPF can be predicted in the following way. Divide the ^{147}Pm initial lung burden by the ILB_{50} for ^{147}Pm to obtain the beta dose X_b in units of the ILB_{50} . Also divide the ^{238}Pu initial lung burden by the ILB_{50} for ^{238}Pu to obtain the alpha dose X_a in units of the ILB_{50} . Add X_a and X_b to obtain the total dose X in units of the D_{50} . Next calculate the fraction F_a of the dose X that is due to X_a , where

$$F_a = X_a/X.$$

Also calculate the fraction F_b of the dose X that is due to X_b , where

$$F_b = X_b/X.$$

For exposure to the mixture, the shape parameter V can be obtained using the weighted reciprocal relationship (Scott, 1987; Scott et al., 1986)

$$1/V = F_a/V_a + F_b/V_b \quad (9)$$

where V_a and V_b are the shape parameters for exposure to alphas only and betas only, respectively. The reciprocal relationship is needed only when V_a and V_b differ significantly. When V_a and V_b are approximately equal, V can be calculated as the average of V_a and V_b . This latter averaging procedure has been used here because V_a and V_b were found to be approximately the same. The reciprocal relationship is included for completeness.

Based on the hazard function model of predicting the combined effects of alpha and beta irradiation of the lung, the lethality hazard is given by

$$H = \ln(2) * xV. \quad (10)$$

Knowing the lethality hazard H , one can then calculate the individual risk of dying from RPPF using the relationship

$$\text{Individual Risk} = 1 - \exp(-H). \quad (11)$$

Adding the individual risks over the dose distribution for the exposed sample of rats leads to the expected cases of deaths when all other competing risks are eliminated. We have used this method to predict the number of deaths from RPPF occurring within 1.5 years after inhalation exposure of F344 rats to mixtures of ^{238}Pu and ^{147}Pm . All rats dying of other competing risks during the 1.5-year interval were excluded from the analysis. Only rats that died from RPPF or survived to 1.5 years were included. The expected and observed numbers of deaths are shown in Table 3.4 and are in good agreement. This indicates that the hazard-function method of predicting the combined lethal effects of alpha and beta irradiation of the lung should be adequate for use in reactor accident consequence modeling.

3.4 Morbidity

3.4.1 Body Weight Changes

A reduced body weight was observed only in rats that died from radiation-induced injury. Average body weights by exposure level are given in Figures 3.8-3.10 for 3, 6 and 12 months after the inhalation exposure. Similar results were obtained at all other times that body weights were recorded. An exploratory analysis of the data revealed that a reduction in body weight mainly occurred in rats that accumulated lethal radiation doses.

3.4.2 Hematology

Hematological measurements were made repeatedly on the same males and females from the L_{01} (alpha) + L_{01} (beta) level and on preselected controls assigned to the hematology group. No significant effects on the peripheral blood were observed. Data for the radiosensitive lymphocytes are given in Table 3.5 where L_c and L_t represent the average control and average test group [L_{01} (alpha) + L_{01} (beta) level] counts at various times after exposure; SL_c and SL_t represent standard deviations for L_c and L_t , respectively. The expression $100L_t/L_c$ with standard deviation SD represents the average test counts expressed as a percentage of the average control value at the specified time. Based on an assumed normal distribution, no significant departure from control values could be demonstrated. None of the other hematological parameters was significantly different from control values.

Table 3.4

Expected and Observed Deaths from Radiation Pneumonitis and Pulmonary Fibrosis
 Within 1.5 Years After Inhalation Exposure of F344/Cr1 Rats to
 Mixtures of ^{238}Pu and ^{147}Pm Inhaled in Fused Aluminosilicate Particles

Experiment Group	Average Initial Lung Burden		Risk Set Size N*	Expected Deaths**	Observed Deaths
	^{238}Pu (nCi/g)	^{147}Pm ($\mu\text{Ci/g}$)			
AB1	120 $\pm$ 40	51 $\pm$ 20	32	25 $\pm$ 2.4	32
AB2	26 $\pm$ 10	42 $\pm$ 15	18	1 $\pm$ 1	1
AB3	130 $\pm$ 44	13 $\pm$ 4	22	17 $\pm$ 2	21
AB4	26 $\pm$ 10	14 $\pm$ 5	8	0	0

*After elimination of animals dying within 1.5 years from all causes other than radiation pneumonitis.

**Individual risk = $1 - \text{EXP}(-0.693 \times X^5)$

$$X = X_{\text{Pm}} + X_{\text{Pu}}$$

$$X_{\text{Pm}} = \text{ILB}_{\text{Pm}}(\mu\text{Ci/g-LUNG})/160$$

$$X_{\text{Pu}} = \text{ILB}_{\text{Pu}}(\text{nCi/g-LUNG})/123$$

$$\text{Average risk} = (\text{Sum of individual risks})/N$$

$$\text{Variance} = N \times (\text{Average risk}) \times (1 - \text{Average risk})$$

$$\text{Expected deaths} = (\text{Risk set size}) \times (\text{Average risk})$$

AVERAGE BODY WEIGHT: 3 MONTHS

Figure 3.8. Average body weight in grams, as a function of the exposure level, evaluated at 3 months after inhalation exposure; (a) males, (b) females.

AVERAGE BODY WEIGHT: 6 MONTHS

Figure 3.9. Average body weight in grams, as a function of exposure level, evaluated at 6 months after inhalation exposure; (a) males, (b) females.

AVERAGE BODY WEIGHT: 12 MONTHS

Figure 3.10 Average body weight in grams, as a function of exposure level, evaluated at 12 months after inhalation exposure; (a) males, (b) females.

Table 3.5
Blood Lymphocyte Counts After Inhalation Exposure of Rats to $^{238}\text{Pu} + ^{147}\text{Pm}$
Inhaled in Fused Aluminosilicate Particles*

DPE	Controls		L_{01} alpha + L_{01} beta		Average as Percent of Controls	
	Average (L_c)	Standard Deviation (SL_c)	Average (L_t)	Standard Deviation (SL_t)	Average ($100L_t/L_c$)	Standard Deviation (SD)
0	---	--	--	--	100	--
30	7009	1552	7088	2058	101	37
60	7796	1516	9463	4322	121	60
90	7485	2937	6850	1845	92	44
120	7350	2462	7497	3601	102	60
150	8800	4029	8328	3337	95	58
180	5044	2451	5667	4913	112	112
270	5203	1634	5618	3042	108	68
360**	3002	812	3272	974	109	44

* L_c = control group average lymphocyte count (cells/cmm)
 L_t = test group (D01 alpha + D01 beta level) average lymphocyte counts (cells/cmm)
 $100L_t/L_c$ = average lymphocyte count for test group expressed as percent of average control value at specified time
 SL_c = standard deviation of L_c
 SL_t = standard deviation of L_t
SD = standard deviation of $100L_t/L_c$
DPE = days after exposure

**Lymphocyte counts as well as other hematological data had systematic error at 360 days. Data were multiplied by correction factor of 2 for sampling volume error correction to reduce systematic error. Systematic error was eliminated by taking ratio L_t/L_c .

3.4.3 Respiratory Function

It is shown in Figures 3.11-3.14 that survivors 1.5 years after inhalation exposure had a reduction in vital capacity (Fig. 3.11), CO diffusing capacity (Fig. 3.12), and quasistatic compliance (Fig. 3.13), and an increase in the slope of phase 3 of the single-breath nitrogen washout curve (Fig. 3.14). These changes reflected the presence of a restrictive lung disorder (smaller, stiffer lungs) with an uneven distribution of lesions (nonuniform gas distribution) and an impairment of gas exchange. The alterations are characteristic of RPPF from internally deposited alpha and beta-gamma emitters (Mauderly *et al.*, 1980A, 1980B).

Pulmonary function data were quantified in the following way to develop risk parameters for estimating the prevalence of respiratory dysfunction resulting from irradiation of the lung. Each irradiated rat having a vital capacity measurement less than the lower 95% confidence interval for control values was judged to have a reduced lung volume. Each irradiated rat having a CO diffusing capacity (normalized to kg body weight) less than the lower 95% confidence interval for controls was judged to have abnormal gas exchange in the lung. Each irradiated rat having a quasistatic compliance less than the lower 95% confidence interval for control values was judged to have stiffer than normal lungs. Each rat having a slope of phase 3 of the N_2 washout curve greater than the upper 95% confidence interval for controls was judged to have an abnormal ventilation distribution in the lung.

Figure 3.11. Average value for vital capacity in ml, as a function of the exposure level, evaluated at 1.5 years after inhalation exposure; (a) males, (b) females.

Figure 3.12. Average value for CO diffusing capacity per kg body weight, as a function of the exposure level, at 1.5 years after inhalation exposure, and expressed in ml/min/mmHg/kg; (a) males, (b) females.

Figure 3.13. Average value for quasistatic compliance (CQ10), in ml/cmH₂O, as a function of the exposure level, at 1.5 years after inhalation exposure; (a) males, (b) females.

Figure 3.14. Average value for slope of phase III of the single breath nitrogen washout curve expressed in % N₂/ml, as a function of the exposure level, at 1.5 years after inhalation exposure; (a) males, (b) females.

Rats having one or more of these abnormalities were assigned a risk parameter $R_1=1$; otherwise, $R_1=0$; rats having two or more abnormalities were assigned a risk parameter $R_2=1$; otherwise, $R_2=0$. Rats having three or more abnormalities were assigned a risk parameter $R_3=1$; otherwise $R_3=0$. Risk parameters R_1 , R_2 , and R_3 were examined theoretically to see which would best represent radiation-induced effects.

It is reasonable to assume, for a given gender, that values for the vital capacity, CO diffusing capacity per kg body weight, quasistatic compliance, and slope of phase III of the single breath N_2 washout curve each are normally distributed. If so, R_1 would be expected to lead to the wrong conclusion about radiation induced effects about 20% of the time when there are no radiation induced effects; similarly, the use of R_2 would be expected to lead to the wrong conclusion 1.5% of the time; however, the use of R_3 would be expected to lead to the wrong conclusion only 0.05% of the time. Thus, we selected R_3 as the risk parameter to use in defining the presence or absence of pulmonary functional morbidity after irradiation of the lung. A value of $R_3=1$ was taken to indicate pulmonary functional morbidity due to injury to the lung. A value of $R_3=0$ was taken to indicate the absence of pulmonary functional morbidity.

A modified version of the Weibull model was then used to fit the data for the prevalence of pulmonary functional morbidity at 1.5 years after inhalation exposure to ^{238}Pu or ^{147}Pm . Data for combined exposure to both radionuclides were not fitted but were reserved for model validation. The modified model is given by

$$\text{Prevalence} = R_0 + (1-R_0)R \quad (12)$$

where R is the same type of Weibull function as in Equation 7, and R_0 accounts for effects not due to irradiation. Use of this form of the Weibull model allows the determination of a shape parameter V and ILB_{50} for morbidity even though some rats may have pulmonary morbidity unrelated to irradiation. Using a maximum likelihood approach so that individual datum points could be used, the ILB_{50} was estimated for the prevalence of pulmonary morbidity among rats exposed to ^{238}Pu only or ^{147}Pm only. Because of the small sample sizes used, the shape parameter could not be adequately determined and was therefore assumed to be the same as for lethality from RPPF. For ^{238}Pu , the ILB_{50} for pulmonary morbidity was 30 ± 3 nCi/g-lung. For ^{147}Pm , it was 40 ± 4 $\mu\text{Ci/g-lung}$. Corresponding D_{50} values for ^{238}Pu alphas and ^{147}Pm betas, based on cumulative radiation doses to the lung at 1.5 years after inhalation exposure, were $1,100 \pm 110$ rad (11 Gy) and $7,500 \pm 750$ rad (75 Gy), respectively. The parameter R_0 was found to be zero for these data. However, we have retained the modified model so that results can be compared with those obtained at Pacific Northwest Laboratory (PNL) by Dr. R. Filipy and coworkers who are using the same model.

Because the shape parameters for morbidity could not be adequately determined, a value of 5 was assumed and used. With the ILB_{50} 's and shape parameter given, doses in units of the ILB_{50} could be calculated for those rats exposed to both alpha and beta radiation; this was achieved by dividing the initial lung burden of ^{238}Pu in nCi/g-lung by 30 and dividing the initial lung burden of ^{147}Pm by 40 and adding the results to obtain the total dose X in units of the ILB_{50} or D_{50} . The individual risk for the prevalence of morbidity at 1.5 years was then calculated using

$$\text{Individual risk} = 1 - \exp[-H_m], \quad (13)$$

where the morbidity hazard H_m is given by

$$H_m = \ln(2) * X^5, \quad (14)$$

for radiation-induced pulmonary functional morbidity.

Adding the individual risk for a given ILB distribution over a given exposure level and dividing by the number of rats in the level gave the average risk for that level and for that ILB distribution. This average risk can only be used for the specific ILB distribution used to derive it because of the nonlinear shape of the curves for morbidity. The expected number of morbidity cases at a given exposure level is equal to the product of the average risk times the number of rats in the exposure level. Using the same hazard-function approach as was used for mortality from RPPF, the number of morbid rats at 1.5 years after combined alpha and beta irradiation of the lung was predicted for experimental groups AB2 and AB4. Predicted and observed values are given in Table 3.6 and are in good agreement.

Table 3.6
Predicted and Observed Cases of Respiratory Functional Morbidity Among F344/Cr1 Rats
After Combined Alpha and Beta Irradiation of the Lung from Inhaled ^{147}Pm and ^{238}Pu in
Fused Aluminosilicate Particles*

Experiment Group	Number Surviving Rats	Dose (Rads)**		Predicted Average Risk	Predicted Cases of Morbidity Rats	Observed Cases of Morbidity Rats
		Alpha	Beta			
AB2	19	840	10400	0.97	18.5 ± 0.7	18
AB4	5	840	2640	0.54	2.7 ± 1.1	4
C	20	0	0	0	0	0
A1	6	4350	0	1	6	6
A2	19	930	0	0.29	5.5 ± 2.0	5
B1	13	0	8780	0.65	8.5 ± 1.7	10
B2	16	0	2910	0.04	0.7 ± 0.8	1

*Predictions were only made for Groups AB2 and AB4 where rats were exposed to both alpha and beta radiations. There were no survivors in Group AB1 and only one survivor in Group AB3 at 1.5 years. Values listed for Groups C, A1, A2, B1 and B2 are not predictions; data from these groups were fitted with the Weibull dose-response model to obtain model parameters to use to predict the results for Groups AB2 and AB4.

**Group average cumulative 1.5 year radiation dose to lung.

In earlier mortality experiments, in which rats were exposed via inhalation to one or more beta-emitting radionuclides (NUREG/CR-5025, 1987), the shape parameter for lethality from RPPF was also found to be about 5, and seemed to be independent of beta dose rate. It is shown in Table 3.7 that the ILB_{50} for acute lethality is about 4 times larger than that for morbidity. Corresponding doses to 1.5 years after inhalation exposure are given in Table 3.8. These results suggest that the same model used for acute mortality from beta irradiation to the lung could be used for morbidity if the D_{50} parameters for mortality are reduced by a factor of 4 for low energy betas.

A similar analysis of data from previous experiments in which F344/Cr1 rats inhaled mainly ^{90}Y or an equilibrium mixture of $^{90}\text{Sr} + ^{90}\text{Y}$ in fused aluminosilicate particles (NUREG/CR-5025, 1987) did not reveal any significant difference between the median-lethal and median-effective doses for morbidity. Both ^{90}Y and ^{90}Sr are high-energy beta emitters with average energies of 0.935 and 0.196 MeV, respectively; while for ^{147}Pm , the average energy is only 0.062 MeV. The

Table 3.7

Median Lethal Lung Burdens for Death* from Radiation Pneumonitis and Pulmonary Fibrosis and Median Effective Lung Burdens for Respiratory Morbidity After Inhalation Exposure of F344/Cr1 Rats to ^{238}Pu or ^{147}Pm Inhaled in Fused Aluminosilicate Particles

Type of Radiation	Median Lethal	Median Effective	Ratio**
^{238}Pu alphas	123 ± 7.5 nCi/g-lung	30 ± 3 nCi/g-lung	4.1
^{147}Pm betas	160 ± 190 $\mu\text{Ci/g-lung}$	40 ± 4 $\mu\text{Ci/g-lung}$	4.0
Average Ratio = 4.0			

*Death within 1.5 years.

**Median lethal divided by median effective burden.

Table 3.8

Median Lethal 1.5 Year Radiation Doses to the Lung for Death Within 1.5 Years From Radiation Pneumonitis and Pulmonary Fibrosis and Median Effective Doses for Respiratory Morbidity at 1.5 Years After Inhalation Exposure of F344/Cr1 Rats to ^{238}Pu or ^{147}Pm Inhaled in Fused Aluminosilicate Particles

Type of Radiation	Median Lethal (rads)*	Median Effective (rads)*	Ratio**
^{238}Pu alphas	4,500	1,100	4.1
^{147}Pm betas	30,000	7,500	4.0
RBE***	6.7	6.8	

*1.5 year dose. Multiply beta dose by 0.88 to get 1-year dose. Multiply alpha dose by 0.85 to get 1-year dose.

**Median lethal divided by median effective dose.

***For 1.5 year followup.

results therefore suggest that the factor of 4 derived for comparing lethality and morbidity (respiratory dysfunction) may be applicable to alpha and low-energy beta radiations only.

Data in Table 3.8 were used to estimate the relative biological effectiveness of ^{238}Pu alphas relative to ^{147}Pm betas. An RBE of approximately 7 was obtained for both lethality and morbidity.

Dose-effect surfaces are given in Figures 3.15 and 3.16 for 1.5-year lethality from RPPF and for the prevalence of pulmonary morbidity at 1.5 years after inhalation exposure to a mixture of ^{238}Pu + ^{147}Pm inhaled in an insoluble form. Although the results are based on studies with F344/Cr1 rats, it is assumed that they are also applicable to man.

Figure 3.15 Dose-effect surface for F344/Cr1 rats for estimating the 1.5-year lethality risk for death from radiation pneumonitis and pulmonary fibrosis after inhalation exposure to mixtures of ^{238}Pu + ^{147}Pm inhaled in an insoluble form. Results are based on the hazard-function model. Doses represent 1.5-year doses to the lung.

Figure 3.16 Dose-effect surface for F344/Cr1 rats for estimating the prevalence of respiratory morbidity at 1.5 years after inhalation exposure to mixtures of ^{238}Pu + ^{147}Pm inhaled in an insoluble form. Doses represent 1.5-year doses to the lung.

CHAPTER 4

CONCLUSIONS

The experiment described in this document was part of a series of inhalation exposure experiments carried out at the Inhalation Toxicology Research Institute to validate a mortality model (Scott *et al.*, 1986) developed for predicting deaths from RPPF after inhalation exposure to mixtures of alpha- and beta-emitting radionuclides. Results of the experiment demonstrated that the hazard-function model adequately predicted the observed deaths from RPPF that occurred throughout the 1.5-year observation period.

Hematological evaluations were carried out on rats assigned to the hematology group at various times after inhalation exposure. However, no significant effects on the peripheral blood could be demonstrated. The implications are that low energy betas from ^{147}Pm and alphas from ^{238}Pu deposited in the lung do not deliver significant doses to the radiosensitive bone marrow because of their short range in tissue. In addition, combined alpha and beta irradiation of the blood traversing the lung does not lead to any significant alterations in the cellularity of the peripheral blood of rats.

Body weights of all rats were recorded at various times after inhalation exposure. Significant alterations in body weights were observed mainly in rats with lethal doses to the lung. The results indicate that body weight change is not a good indicator of morbidity among survivors.

Pulmonary function was evaluated in survivors at 1.5 years after inhalation exposure. It was demonstrated using pulmonary function measurements for the vital capacity, CO diffusing capacity, quasistatic compliance, and slope of phase 3 of the N_2 washout curve that irradiation of the lung leads to a reduction in lung volume, a decreased efficiency in gas exchange, a stiffer lung and an altered intrapulmonary gas distribution in some rats. These changes are all characteristic of RPPF and occurred at doses approximately one fourth of that required for acute lethality. A hazard-function model was developed for predicting the prevalence of pulmonary functional morbidity among rats exposed to both alpha and beta radiation. Model predictions were demonstrated to be in good agreement with experimental observations.

Assuming that these results are applicable to man, the implication is that a ^{239}Pu -alpha dose to the lung of approximately 1,100 rad (11 Gy) or a ^{147}Pm -beta dose of approximately 7,500 rad (75 Gy) could cause pulmonary functional morbidity in one-half of those exposed. In a recent report by Muggenburg *et al.* (1986), it was demonstrated that ^{239}Pu -alpha doses from 240 to 730 rad (2.4 to 7.3 Gy) to the lung of dogs caused clinical signs and pulmonary function values indicating RPPF at 7.1 years after inhalation exposure.

Among 19 rats exposed to ^{238}Pu -alpha doses (1.5 year doses) from 670 to 1,500 rad (6.7 to 15 Gy) to the lung, five had pulmonary functional morbidity, based on the risk parameter R_3 . All of these five also had septal fibrosis, suggesting that the fibrosis may have been a cause of the functional morbidity.

Among 29 rats that had 1.5 year ^{147}Pm -beta doses to the lung from 1,100 to 13,000 rad (11 to 130 Gy), 11 had pulmonary functional morbidity, based on the risk parameter R_3 . All except one of these 11 rats had septal fibrosis, suggesting that the fibrosis may have been a cause of the functional morbidity.

Together, the results presented imply that doses required for causing acute lethality from RPPF after alpha or low-energy-beta irradiation of the lung are considerably higher than those required for causing pulmonary functional morbidity. The results also indicate that pulmonary functional morbidity can be prevalent after more than a year of prolonged alpha or low-energy-beta irradiation of the lung.

After adjusting for competing modes of death, 80 rats were judged at risk for death from RPPF. Of these, 43 deaths were expected and 54 were observed. Also, for rats receiving combined alpha and beta irradiation of the lung, 21 out of 24 surviving rats were expected to have pulmonary functional morbidity while 22 cases were observed. The results indicate that the hazard-function mortality and hazard-function morbidity models for combined alpha and beta irradiation of the lung should be adequate for reactor accident risk assessment.

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APPENDIX: DATA BASES

Listing of rats exposed to aerosols of alpha- or beta-emitting radionuclides or both in fused aluminosilicate particles (FAP).

1. Rats exposed to aerosols of ^{238}Pu FAP, ^{147}Pm FAP, or $^{238}\text{Pu} + ^{147}\text{Pm}$ in FAP.
2. Pulmonary function measurements in rats exposed to aerosols of ^{238}Pu FAP, ^{147}Pm FAP, or $^{238}\text{Pu} + ^{147}\text{Pm}$ in FAP.

3
1A. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING IN LUNG	OTHER FINDINGS AT DEATH
91	3941A	F	HEMATOLOGY	153	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
92	3941A	F	HEMATOLOGY	154	0	0	562	0	0	0	0	0	0	DIED	NO LESION	
93	3941A	F	HEMATOLOGY	185	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
94	3941A	F	HEMATOLOGY	168	0	0	586	0	0	0	0	0	0	SAC	ALVEOLAR_HISTEO	
95	3941A	M	HEMATOLOGY	273	0	0	586	0	0	0	0	0	0	SAC	INTERSTIT_PNEUMONIA	
96	3941A	M	HEMATOLOGY	279	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
97	3941A	M	HEMATOLOGY	247	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
98	3941A	M	HEMATOLOGY	271	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
892	3950	M	HEMATOLOGY	278	13	7	124	90	380	600	2100	200	900	SAC	NO LESION	
897	3950	M	HEMATOLOGY	295	26	14	523	170	750	1200	4300	900	3800	EUTHANIZED	NOT SUBMITTED	
937	3950	F	HEMATOLOGY	144	15	8	487	100	450	700	2500	500	2200	DIED	SQUAM_CELL_CA	
941	3950	F	HEMATOLOGY	157	64	33	317	420	1780	2900	10000	1800	7400	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,HEMORRHAGE,BA_HYPERPLASIA
943	3950	F	HEMATOLOGY	160	26	14	582	170	740	1200	4200	1000	3800	SAC	SQUAM_CELL_CA	PULMONARY_THROMBOSIS,HEMORRHAGE,SEPT_FIBROSIS
950	3950	F	HEMATOLOGY	169	36	19	581	230	1020	1600	5700	1300	5300	SAC	SQUAM_CELL_CA	BA CARCINOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
953	3950	F	HEMATOLOGY	183	27	14	581	180	760	1200	4300	1000	4000	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
958	3950	F	HEMATOLOGY	153	17	9	565	110	490	800	2800	600	2500	DIED	SQUAM_CELL_CA	
959	3950	F	HEMATOLOGY	157	19	10	258	130	550	900	3100	500	2100	EUTHANIZED	ALVEOLAR_HISTEO	
960	3950	F	HEMATOLOGY	158	43	23	547	280	1220	2000	6900	1600	6300	DIED	SQUAM_CELL_CA	RAD_PNEUMONITIS,SEPT_FIBROSIS,BA_HYPERPLASIA
961	3950	F	HEMATOLOGY	159	16	9	341	110	470	700	2700	500	2000	EUTHANIZED	SEPT_FIBROSIS	ALVEOLAR_HISTEO,BA_HYPERPLASIA
968	3950	F	HEMATOLOGY	171	26	14	581	170	750	1200	4300	1000	3900	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS
974	3950	M	HEMATOLOGY	242	43	23	581	290	1240	2000	7000	1600	6500	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
977	3950	M	HEMATOLOGY	260	17	8	581	110	450	800	2600	600	2400	SAC	BA CARCINOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
979	3950	M	HEMATOLOGY	266	14	7	581	90	390	600	2200	500	2100	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS
985	3950	M	HEMATOLOGY	284	25	13	581	160	690	1100	3900	900	3600	SAC	SQUAM_CELL_CA	ADENOCARCINOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
986	3950	M	HEMATOLOGY	288	44	24	581	290	1270	2000	7200	1600	6600	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
987	3950	M	HEMATOLOGY	292	37	19	581	240	1030	1700	5800	1400	5400	SAC	ADENOSQUAM CARCINOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
991	3950	M	HEMATOLOGY	238	32	16	124	210	880	1400	5000	600	2200	SAC	BA_HYPERPLASIA	
993	3950	M	HEMATOLOGY	247	29	15	187	190	800	1300	4500	600	2500	EUTHANIZED	SEPT_FIBROSIS	ALVEOLAR_HISTEO
994	3950	M	HEMATOLOGY	254	29	15	581	190	830	1300	4700	1100	4300	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS,ALVEOLAR_HISTEO
997	3950	M	HEMATOLOGY	266	41	22	562	270	1180	1900	6700	1500	6100	EUTHANIZED	BA CARCINOMA	SQUAM_CELL_CA,SEPT_FIBROSIS,BA_HYPERPLASIA
327	3743	M	MORTALITY	270	31	0	579	200	0	1400	0	1200	0	DIED	LEUKEMIA	SEPT_FIBROSIS,BA_HYPERPLASIA
824	3848	M	MORTALITY	260	67	7	525	450	360	3100	2000	2300	2700	EUTHANIZED	SQUAM_CELL_CA	RAD_PNEUMONITIS,SEPT_FIBROSIS,BA_HYPERPLASIA
101	3941	F	MORTALITY	140	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
102	3941	F	MORTALITY	149	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
103	3941	F	MORTALITY	151	0	0	586	0	0	0	0	0	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO
104	3941	F	MORTALITY	154	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
105	3941	F	MORTALITY	155	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
106	3941	F	MORTALITY	158	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
107	3941	F	MORTALITY	160	0	0	586	0	0	0	0	0	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO
108	3941	F	MORTALITY	162	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
109	3941	F	MORTALITY	163	0	0	586	0	0	0	0	0	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO
110	3941	F	MORTALITY	164	0	0	586	0	0	0	0	0	0	SAC	ALVEOLAR_HISTEO	
111	3941	F	MORTALITY	165	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
112	3941	F	MORTALITY	167	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
113	3941	F	MORTALITY	168	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
114	3941	F	MORTALITY	169	0	0	476	0	0	0	0	0	0	EUTHANIZED	ALVEOLAR_HISTEO	
115	3941	F	MORTALITY	173	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
116	3941	F	MORTALITY	176	0	0	586	0	0	0	0	0	0	SAC	NO LESION	

1B. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING IN LUNG	OTHER FINDINGS AT DEATH
117	3941	F	MORTALITY	179	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
118	3941	F	MORTALITY	186	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
119	3941	M	MORTALITY	205	0	0	586	0	0	0	0	0	0	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
120	3941	M	MORTALITY	232	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
121	3941	M	MORTALITY	242	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
122	3941	M	MORTALITY	251	0	0	586	0	0	0	0	0	0	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
123	3941	M	MORTALITY	256	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
124	3941	M	MORTALITY	258	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
125	3941	M	MORTALITY	262	0	0	515	0	0	0	0	0	0	DIED	NOT SUBMITTED	
126	3941	M	MORTALITY	267	0	0	586	0	0	0	0	0	0	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
127	3941	M	MORTALITY	271	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
128	3941	M	MORTALITY	272	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
129	3941	M	MORTALITY	276	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
130	3941	M	MORTALITY	279	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
131	3941	M	MORTALITY	283	0	0	586	0	0	0	0	0	0	SAC	NO LESION	
132	3941	M	MORTALITY	286	0	0	582	0	0	0	0	0	0	EUTHANIZED	NO LESION	
134	3941	M	MORTALITY	291	0	0	586	0	0	0	0	0	0	SAC	NO LESIONS	
135	3941	M	MORTALITY	298	0	0	572	0	0	0	0	0	0	DIED	NO LESIONS	AUTOLYTIC
136	3941	M	MORTALITY	315	0	0	586	0	0	0	0	0	0	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
201	3942	F	MORTALITY	141	115	0	586	760	0	4900	0	4400	0	SAC	SQUAM CELL CA	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA
202	3942	F	MORTALITY	150	143	0	506	940	0	6000	0	5100	0	DIED	RAD_PNEUMONITIS	HEMORRHAGE, SEPT_FIBROSIS, BA_HYPERPLASIA
203	3942	F	MORTALITY	150	141	0	586	930	0	6000	0	5400	0	SAC	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA
204	3942	F	MORTALITY	154	188	0	285	1240	0	8000	0	5300	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
205	3942	F	MORTALITY	155	139	0	586	920	0	5900	0	5300	0	SAC	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, VASCULITIS, SQUA_METAPLAS
206	3942	F	MORTALITY	157	124	0	450	820	0	5200	0	4300	0	DIED	HEMANGIOSARCOMA	SEPT_FIBROSIS, SQUAMOUS METAPLAS
207	3942	F	MORTALITY	160	204	0	341	1340	0	8600	0	6200	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA
208	3942	F	MORTALITY	161	176	0	373	1160	0	7500	0	5600	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, SQUAM_CELL_CA
209	3942	F	MORTALITY	163	114	0	586	750	0	4800	0	4300	0	SAC	SQUAM_CELL_CA	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA
210	3942	F	MORTALITY	164	133	0	497	880	0	5600	0	4800	0	EUTHANIZED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, SQUA_METAPLAS
211	3942	F	MORTALITY	165	107	0	407	700	0	4500	0	3500	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, SQUAM_CELL_CA
212	3942	F	MORTALITY	166	106	0	312	700	0	4500	0	3100	0	DIED	SQUAM_CELL_CA	RAD_PNEUMONITIS, SEPT_FIBROSIS
213	3942	F	MORTALITY	167	115	0	586	760	0	4900	0	4400	0	SAC	SQUAM_CELL_CA	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA
214	3942	F	MORTALITY	171	144	0	477	950	0	6100	0	5100	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, SQUAM_CELL_CA
215	3942	F	MORTALITY	173	102	0	586	670	0	4300	0	3900	0	SAC	SQUAM_CELL_CA	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA
216	3942	F	MORTALITY	176	141	0	421	930	0	6000	0	4700	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, SQUA_METAPLAS, VASCULITIS
218	3942	F	MORTALITY	184	221	0	74	1460	0	9300	0	2800	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, SQUA_METAPLAS, VASCULITIS
219	3942	M	MORTALITY	161	282	0	85	1860	0	11900	0	3900	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
220	3942	M	MORTALITY	232	161	0	497	1060	0	6800	0	5800	0	EUTHANIZED	SQUAM_CELL_CA	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA, VASCULITIS
221	3942	M	MORTALITY	244	109	0	366	720	0	4600	0	3400	0	DIED	HEMANGIOSARCOMA	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA
222	3942	M	MORTALITY	251	119	0	405	780	0	5000	0	3900	0	DIED	SQUAM_CELL_PAP	RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA
223	3942	M	MORTALITY	256	193	0	262	1280	0	8200	0	5200	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
224	3942	M	MORTALITY	259	113	0	455	750	0	4800	0	3900	0	EUTHANIZED	PAP_ADENOCARCINOMA	RAD_PNEUMONITIS, SEPT_FIBROSIS
226	3942	M	MORTALITY	266	162	0	68	1070	0	6900	0	2000	0	DIED	SEPT_FIBROSIS	ALVEOLAR HISTEO
227	3942	M	MORTALITY	271	136	0	79	900	0	5700	0	1800	0	DIED	RAD_PNEUMONITIS	VASCULITIS
228	3942	M	MORTALITY	274	143	0	497	950	0	6100	0	5100	0	EUTHANIZED	SQUAM_CELL_CA	SEPT_FIBROSIS, BA_HYPERPLASIA
229	3942	M	MORTALITY	276	87	0	121	570	0	3700	0	1500	0	DIED	METASTAT_LUNG-TUMOR	
230	3942	M	MORTALITY	278	77	0	586	510	0	3300	0	2900	0	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA, SQUAM_CELL_PAP
231	3942	M	MORTALITY	283	129	0	472	850	0	5500	0	4500	0	DIED	SQUAM_CELL_CA	RAD_PNEUMONITIS, SEPT_FIBROSIS

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1C. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ^{238}Pu , ^{147}Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 ($\mu\text{Ci/g-LUNG}$)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING IN LUNG	OTHER FINDINGS AT DEATH
232	3942	M	MORTALITY	285	98	0	575	640	0	4100	0	3700	0	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA, SQUA_METAPLAS
233	3942	M	MORTALITY	288	167	0	74	1100	0	7100	0	2100	0	DIED	RAD_PNEUMONITIS	VASCULITIS
234	3942	M	MORTALITY	292	134	0	451	880	0	5700	0	4600	0	EUTHANIZED	RAD_PNEUMONITIS	SEPT_FIBROSIS, BA_HYPERPLASIA
235	3942	M	MORTALITY	297	166	0	289	1090	0	7000	0	4700	0	EUTHANIZED	RAD_PNEUMONITIS	SEPT_FIBROSIS
236	3942	M	MORTALITY	316	147	0	70	970	0	6200	0	1800	0	DIED	RAD_PNEUMONITIS	VASCULITIS, HEMORRHAGE
301	3943	F	MORTALITY	143	25	0	583	170	0	1100	0	1000	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO, BA_HYPERPLASIA
302	3943	F	MORTALITY	148	34	0	583	220	0	1400	0	1300	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO, BA_HYPERPLASIA
303	3943	F	MORTALITY	151	19	0	583	120	0	800	0	700	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO, BA_HYPERPLASIA, SQUAM_CELL_CA
304	3943	F	MORTALITY	153	39	0	583	260	0	1700	0	1500	0	SAC	SQUAM_CELL_CA	ADENOCARCINOMA, SEPT_FIBROSIS, ALVEOLAR_HISTEO, BA_HYPERPLASIA
305	3943	F	MORTALITY	156	26	0	583	170	0	1100	0	1000	0	SAC	SQUAM_CELL_CA	BA_HYPERPLASIA
306	3943	F	MORTALITY	159	26	0	424	170	0	1100	0	900	0	EUTHANIZED	SEPT_FIBROSIS	ALVEOLAR_HISTEO
307	3943	F	MORTALITY	160	30	0	584	200	0	1300	0	1100	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO
308	3943	F	MORTALITY	162	36	0	530	240	0	1500	0	1300	0	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS, BA_HYPERPLASIA
309	3943	F	MORTALITY	162	22	0	584	150	0	900	0	800	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO, BA_HYPERPLASIA
310	3943	F	MORTALITY	164	22	0	469	140	0	900	0	800	0	DIED	BA_CARCINOMA	
311	3943	F	MORTALITY	165	36	0	533	240	0	1500	0	1300	0	DIED	UNDIF_CARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA, AUTOLYTIC
312	3943	F	MORTALITY	166	24	0	583	160	0	1000	0	900	0	SAC	PAP_ADENOCARCINOMA	BA_HYPERPLASIA,
313	3943	F	MORTALITY	169	22	0	584	150	0	1000	0	900	0	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS, ALVEOLAR_HISTEO
314	3943	F	MORTALITY	169	18	0	584	120	0	800	0	700	0	SAC	NO_LESION	
315	3943	F	MORTALITY	174	26	0	516	170	0	1100	0	1000	0	DIED	NO_LESION	
316	3943	F	MORTALITY	176	15	0	584	100	0	600	0	600	0	SAC	ADENOSQUAM_CARINOMA	SEPT_FIBROSIS, ALVEOLAR_HISTEO, BA_HYPERPLASIA
317	3943	F	MORTALITY	180	16	0	584	100	0	700	0	600	0	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO, BA_HYPERPLASIA
318	3943	F	MORTALITY	183	33	0	584	220	0	1400	0	1200	0	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS, ALVEOLAR_HISTEO
319	3943	M	MORTALITY	224	27	0	574	180	0	1200	0	1000	0	DIED	PAP_ADENOCARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
320	3943	M	MORTALITY	241	30	0	584	200	0	1300	0	1200	0	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA
321	3943	M	MORTALITY	243	34	0	584	230	0	1400	0	1300	0	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS
322	3943	M	MORTALITY	249	32	0	479	210	0	1400	0	1100	0	DIED	PAP_ADENOCARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA, AUTOLYTIC
323	3943	M	MORTALITY	353	21	0	584	140	0	900	0	800	0	SAC	ADENOCARCINOMA	SQUAM_CELL_CA, SEPT_FIBROSIS, BA_HYPERPLASIA
324	3943	M	MORTALITY	261	25	0	584	170	0	1100	0	1000	0	SAC	ADENOCARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
325	3943	M	MORTALITY	261	18	0	584	120	0	800	0	700	0	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA
326	3943	M	MORTALITY	267	29	0	584	190	0	1200	0	1100	0	SAC	PAP_ADENOCARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
328	3943	M	MORTALITY	272	20	0	584	130	0	800	0	800	0	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS
329	3943	M	MORTALITY	277	17	0	554	110	0	700	0	600	0	EUTHANIZED	UNDIF_CARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
330	3943	M	MORTALITY	278	21	0	579	140	0	900	0	800	0	DIED	SQUAM_CELL_CA	
331	3943	M	MORTALITY	283	26	0	583	170	0	1100	0	1000	0	SAC	BA_HYPERPLASIA	SEPT_FIBROSIS
332	3943	M	MORTALITY	285	19	0	584	120	0	800	0	700	0	SAC	PAP_ADENOCARCINOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
333	3943	M	MORTALITY	288	20	0	566	130	0	900	0	800	0	EUTHANIZED	SEPT_FIBROSIS	BA_HYPERPLASIA
334	3943	M	MORTALITY	294	28	0	521	190	0	1200	0	1000	0	DIED	LEUKEMIA	BA_CARCINOMA
335	3943	M	MORTALITY	300	18	0	579	120	0	800	0	700	0	EUTHANIZED	BA_CARCINOMA	SEPT_FIBROSIS
336	3943	M	MORTALITY	310	17	0	584	110	0	700	0	700	0	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA
337	3943	M	MORTALITY	268	23	0	584	150	0	1000	0	900	0	SAC	ADENOCARCINOMA	
401	3944	F	MORTALITY	142	0	87	581	0	3540	0	17600	0	16600	DIED	HEMANGIOSARCOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
402	3944	F	MORTALITY	147	0	87	533	0	3530	0	17600	0	16200	DIED	HEMANGIOSARCOMA	
403	3944	F	MORTALITY	152	0	68	467	0	2770	0	13800	0	12300	DIED	HEMANGIOSARCOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
404	3944	F	MORTALITY	153	0	64	317	0	2590	0	12900	0	10000	DIED	HEMANGIOSARCOMA	SEPT_FIBROSIS, BA_HYPERPLASIA
405	3944	F	MORTALITY	155	0	95	420	0	3870	0	19300	0	16600	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
407	3944	F	MORTALITY	160	0	59	583	0	2380	0	11900	0	11200	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS, BA_HYPERPLASIA
408	3944	F	MORTALITY	162	0	56	583	0	2250	0	11200	0	10500	SAC	BA_CARCINOMA	SQUAM_CELL_CA, SEPT_FIBROSIS, BA_HYPERPLASIA

1D. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING IN LUNG	OTHER FINDINGS AT DEATH
409	3944	F	MORTALITY	163	0	43	309	0	1740	0	8700	0	6600	DIED	METASTAT LUNG-TUMOR	
410	3944	F	MORTALITY	164	0	35	583	0	1430	0	7100	0	6700	SAC	SQUAM CELL CA	SEPT FIBROSIS, BA HYPERPLASIA
411	3944	F	MORTALITY	166	0	57	447	0	2290	0	11400	0	10000	DIED	HEMANGIOSARCOMA	SQUAM CELL CA, SEPT FIBROSIS
412	3944	F	MORTALITY	166	0	67	513	0	2730	0	13600	0	12400	DIED	HEMANGIOSARCOMA	SQUAM CELL CA, SEPT FIBROSIS, BA HYPERPLASIA
413	3944	F	MORTALITY	167	0	96	482	0	3880	0	19400	0	17400	DIED	HEMANGIOSARCOMA	RAD PNEUMONITIS, SEPT FIBROSIS, BA HYPERPLASIA
414	3944	F	MORTALITY	171	0	50	268	0	2040	0	10200	0	7300	DIED	RAD PNEUMONITIS	SEPT FIBROSIS, SQUAM CELL CA
415	3944	F	MORTALITY	173	0	61	500	0	2480	0	12400	0	11200	DIED	HEMANGIOSARCOMA	SEPT FIBROSIS, BA HYPERPLASIA
416	3944	F	MORTALITY	175	0	53	583	0	2130	0	10600	0	10000	SAC	SEPT FIBROSIS	BA HYPERPLASIA, BA CARCINOMA
417	3944	F	MORTALITY	178	0	38	465	0	1550	0	7700	0	6900	DIED	HEMANGIOSARCOMA	
418	3944	F	MORTALITY	185	0	38	583	0	1530	0	7600	0	7200	SAC	SQUAM CELL CA	LEUKEMIA, SEPT FIBROSIS, ALVEOLAR HISTEO
419	3944	M	MORTALITY	164	0	67	583	0	2710	0	13500	0	12700	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
420	3944	M	MORTALITY	241	0	87	476	0	3520	0	17600	0	15700	DIED	SQUAM CELL CA	SEPT FIBROSIS
421	3944	M	MORTALITY	243	0	91	364	0	3700	0	18500	0	15100	DIED	HEMANGIOSARCOMA	SEPT FIBROSIS, AUTOLYTIC
422	3944	M	MORTALITY	249	0	64	583	0	2580	0	12900	0	12100	SAC	SQUAM CELL CA	HEMANGIOSARCOMA, SEPT FIBROSIS, BA HYPERPLASIA
423	3944	M	MORTALITY	254	0	66	568	0	2680	0	13400	0	12500	DIED	HEMANGIOSARCOMA	SQUAM CELL CA, SEPT FIBROSIS
424	3944	M	MORTALITY	258	0	55	398	0	2220	0	11100	0	9400	DIED	HEMANGIOSARCOMA	SQUAM CELL CA
425	3944	M	MORTALITY	263	0	67	504	0	2700	0	13500	0	12200	DIED	SQUAM CELL CA	SEPT FIBROSIS, SQUA METAPLAS
426	3944	M	MORTALITY	265	0	77	537	0	3130	0	15600	0	14400	DIED	SQUAM CELL CA	SEPT FIBROSIS, BA HYPERPLASIA
427	3944	M	MORTALITY	271	0	85	414	0	3430	0	17100	0	14600	DIED	HEMANGIOSARCOMA	SEPT FIBROSIS
428	3944	M	MORTALITY	273	0	59	538	0	2390	0	11900	0	11000	DIED	SQUAM CELL CA	
429	3944	M	MORTALITY	275	0	49	583	0	1980	0	9900	0	9300	SAC	ADENOCARCINOMA	SEPT FIBROSIS, BA HYPERPLASIA
430	3944	M	MORTALITY	278	0	28	583	0	1140	0	5700	0	5300	SAC	BA HYPERPLASIA	SEPT FIBROSIS, ALVEOLAR HISTEO
431	3944	M	MORTALITY	281	0	27	583	0	1090	0	5400	0	5100	SAC	SQUAM CELL CA	SEPT FIBROSIS
432	3944	M	MORTALITY	286	0	38	583	0	1550	0	7800	0	7300	SAC	SQUAM CELL CA	SEPT FIBROSIS, BA HYPERPLASIA
433	3944	M	MORTALITY	289	0	52	583	0	2120	0	10600	0	9900	SAC	SQUAM CELL CA	HEMANGIOSARCOMA, SEPT FIBROSIS, BA HYPERPLASIA
434	3944	M	MORTALITY	289	0	52	540	0	2120	0	10600	0	9800	DIED	HEMANGIOSARCOMA	SQUAM CELL CA, SEPT FIBROSIS, BA HYPERPLASIA
435	3944	M	MORTALITY	294	0	50	463	0	2020	0	10100	0	8900	DIED	HEMANGIOSARCOMA	SEPT FIBROSIS, HEMORRHAGE
436	3944	M	MORTALITY	322	0	39	583	0	1560	0	7800	0	7300	SAC	SEPT FIBROSIS	BA HYPERPLASIA, BA CARCINOMA
501	3945	F	MORTALITY	130	0	22	583	0	870	0	4400	0	4100	SAC	SQUAM CELL CA	SEPT FIBROSIS, ALVEOLAR HISTEO
502	3945	F	MORTALITY	149	0	20	583	0	820	0	4100	0	3800	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
503	3945	F	MORTALITY	152	0	17	315	0	690	0	3500	0	2700	DIED	SEPT FIBROSIS	ALVEOLAR HISTEO
504	3945	F	MORTALITY	154	0	19	583	0	790	0	3900	0	3700	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
505	3945	F	MORTALITY	156	0	31	583	0	1250	0	6200	0	5800	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
506	3945	F	MORTALITY	158	0	15	583	0	620	0	3100	0	2900	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
507	3945	F	MORTALITY	160	0	6	583	0	250	0	1300	0	1200	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
508	3945	F	MORTALITY	162	0	7	583	0	300	0	1500	0	1400	SAC	NO LESION	
509	3945	F	MORTALITY	163	0	9	583	0	350	0	1700	0	1600	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO
510	3945	F	MORTALITY	164	0	7	583	0	300	0	1500	0	1400	SAC	ALVEOLAR HISTEO	
511	3945	F	MORTALITY	164	0	12	583	0	490	0	2500	0	2300	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
512	3945	F	MORTALITY	167	0	55	533	0	2230	0	11100	0	10200	DIED	HEMANGIOSARCOMA	SQUAM CELL CA
513	3945	F	MORTALITY	168	0	31	583	0	1250	0	6300	0	5900	SAC	ADENOSQUAM CARINOMA	LEUKEMIA
514	3945	F	MORTALITY	172	0	29	583	0	1180	0	5900	0	5500	SAC	PAP ADENOCARCINOMA	BA HYPERPLASIA, SEPT FIBROSIS, ALVEOLAR HISTEO
515	3945	F	MORTALITY	172	0	27	583	0	1080	0	5400	0	5100	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA, HEMORRHAGE
516	3945	F	MORTALITY	178	0	21	583	0	860	0	4300	0	4100	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
517	3945	F	MORTALITY	181	0	19	583	0	760	0	3800	0	3600	SAC	SEPT FIBROSIS	BA HYPERPLASIA
518	3945	F	MORTALITY	189	0	17	583	0	690	0	3400	0	3200	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
519	3945	M	MORTALITY	217	0	10	583	0	410	0	2000	0	1900	SAC	SEPT FIBROSIS	ALVEOLAR HISTEO, BA HYPERPLASIA
520	3945	M	MORTALITY	227	0	4	520	0	170	0	900	0	800	DIED	NO LESION	

3 1E. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING	IN LUNG	OTHER FINDINGS AT DEATH
521	3945	M	MORTALITY	246	0	6	583	0	240	0	1200	0	1100	SAC	LEUKEMIA		
522	3945	M	MORTALITY	246	0	9	583	0	360	0	1800	0	1700	SAC	NO LESION		
523	3945	M	MORTALITY	254	0	14	583	0	580	0	2900	0	2700	SAC	BA_HYPERPLASIA		
524	3945	M	MORTALITY	260	0	13	583	0	530	0	2700	0	2500	SAC	BA_HYPERPLASIA		
525	3945	M	MORTALITY	263	0	35	583	0	1430	0	7100	0	6700	SAC	SEPT_FIBROSIS		BA_HYPERPLASIA
526	3945	M	MORTALITY	269	0	42	583	0	1690	0	8400	0	7900	SAC	HEMANGIOSARCOMA		BA_CARCINOMA, SEPT_FIBROSIS, BA_HYPERPLASIA
527	3945	M	MORTALITY	269	0	26	582	0	1060	0	5300	0	5000	SAC	SQUAM_CELL_CA		BA_HYPERPLASIA
528	3945	M	MORTALITY	273	0	28	584	0	1120	0	5600	0	5300	SAC	SEPT_FIBROSIS		BA_HYPERPLASIA
529	3945	M	MORTALITY	276	0	27	584	0	1110	0	5500	0	5200	SAC	SEPT_FIBROSIS		BA_HYPERPLASIA, HEMORRHAGE
530	3945	M	MORTALITY	279	0	24	584	0	960	0	4800	0	4500	SAC	SEPT_FIBROSIS		BA_HYPERPLASIA
531	3945	M	MORTALITY	281	0	36	584	0	1480	0	7400	0	6900	SAC	SQUAM_CELL_CA		BA_CARCINOMA, BA_HYPERPLASIA, SEPT_FIBROSIS
532	3945	M	MORTALITY	284	0	32	584	0	1290	0	6400	0	6000	SAC	SEPT_FIBROSIS		BA_HYPERPLASIA
533	3945	M	MORTALITY	287	0	29	584	0	1170	0	5800	0	5500	SAC	BA_HYPERPLASIA		
534	3945	M	MORTALITY	293	0	25	584	0	1010	0	5000	0	4700	SAC	BA_HYPERPLASIA		SEPT_FIBROSIS
535	3945	M	MORTALITY	299	0	19	584	0	760	0	3800	0	3600	SAC	BA_HYPERPLASIA		SEPT_FIBROSIS
602	3946	F	MORTALITY	150	89	39	179	590	2080	4100	11700	1900	6400	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
603	3946	F	MORTALITY	152	91	39	376	600	2120	4100	12000	2700	9500	EUTHANIZED	SQUAM_CELL_CA		SEPT_FIBROSIS, BA_HYPERPLASIA
604	3946	F	MORTALITY	153	139	60	120	910	3230	6300	18200	2400	7800	DIED	SQUAM_CELL_CA		SEPT_FIBROSIS
605	3946	F	MORTALITY	154	138	60	276	910	3210	6300	18100	3600	12500	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
606	3946	F	MORTALITY	158	162	70	195	1070	3740	7400	21100	3500	12100	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, AUTOLYTIC
607	3946	F	MORTALITY	160	215	93	104	1420	4970	9800	28000	3400	11000	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
608	3946	F	MORTALITY	161	181	78	145	1200	4200	8300	23700	3400	11400	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
609	3946	F	MORTALITY	162	121	52	186	800	2780	5500	15700	2600	8800	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS, HEMORRHAGE
610	3946	F	MORTALITY	163	194	83	108	1280	4480	8800	25300	3100	10200	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
611	3946	F	MORTALITY	165	125	53	160	820	2860	5700	16200	2500	8300	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, AUTOLYTIC
612	3946	F	MORTALITY	166	129	55	193	850	2980	5900	16800	2800	9600	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS
613	3946	F	MORTALITY	168	133	57	191	880	3070	6100	17300	2900	9800	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS
614	3946	F	MORTALITY	171	90	39	317	590	2070	4100	11700	2500	8600	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, SQUA_METAPLAS
615	3946	F	MORTALITY	174	79	34	433	520	1850	3600	10400	2500	8800	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, HEMORRHAGE, BA_CARCINOMA
616	3946	F	MORTALITY	177	120	52	198	790	2790	5400	15700	2600	9100	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
617	3946	F	MORTALITY	180	86	37	379	560	1970	3900	11100	2600	8900	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
618	3946	F	MORTALITY	183	89	38	320	580	2050	4000	11600	2500	8600	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, SQUA_METAPLAS
619	3946	M	MORTALITY	217	84	36	491	560	1930	3800	10900	2900	9600	EUTHANIZED	SQUAM_CELL_CA		HEMANGIOSARCOMA, RAD_PNEUMONITIS, SEPT_FIBROSIS, BA_HYPERPLASIA, HEMORRHAGE
620	3946	M	MORTALITY	240	118	51	104	780	2730	5400	15400	1900	6100	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, AUTOLYTIC
621	3946	M	MORTALITY	244	99	43	236	650	2310	4500	13000	2400	8300	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
622	3946	M	MORTALITY	250	179	77	119	1180	4140	8100	23400	3000	10000	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS
623	3946	M	MORTALITY	257	184	79	111	1220	4230	8400	23900	3000	9800	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
624	3946	M	MORTALITY	259	115	49	94	760	2630	5200	14800	1700	5500	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
625	3946	M	MORTALITY	263	128	56	142	840	2990	5800	16900	2400	8000	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, HEMORRHAGE
626	3946	M	MORTALITY	267	77	33	93	510	1770	3500	10000	1100	3700	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS
627	3946	M	MORTALITY	270	105	45	110	690	2430	4800	13700	1700	5600	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
628	3946	M	MORTALITY	273	92	39	160	610	2110	4200	11900	1800	6100	EUTHANIZED	RAD_PNEUMONITIS		SEPT_FIBROSIS, HEMORRHAGE
629	3946	M	MORTALITY	276	138	59	104	910	3180	6300	17900	2200	7100	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS, AUTOLYTIC
630	3946	M	MORTALITY	280	170	73	121	1120	3930	7700	22200	2900	9600	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS, HEMORRHAGE
631	3946	M	MORTALITY	283	113	48	215	750	2590	5100	14600	2600	8900	EUTHANIZED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS
632	3946	M	MORTALITY	285	84	36	243	550	1930	3800	10900	2000	7000	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS
633	3946	M	MORTALITY	287	142	61	139	940	3290	6500	18500	2600	8700	DIED	RAD_PNEUMONITIS		VASCULITIS, SEPT_FIBROSIS, HEMORRHAGE
634	3946	M	MORTALITY	291	127	54	135	840	2930	5800	16500	2300	7600	DIED	RAD_PNEUMONITIS		SEPT_FIBROSIS

1F. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (µCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING	OTHER FINDINGS AT DEATH
635	3946	M	MORTALITY	298	70	30	252	460	1630	3200	9200	1700	6100	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
636	3946	M	MORTALITY	315	122	53	116	810	2830	5600	16000	2100	6700	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS
701	3947	F	MORTALITY	140	26	40	540	170	2150	1200	12100	900	10900	DIED	HEMANGIOSARCOMA	SQUAM_CELL_CA,SEPT_FIBROSIS,BA_HYPERPLASIA
702	3947	F	MORTALITY	146	34	53	583	230	2870	1600	16200	1300	14900	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,INTERSTIT_PNEUMONIA
703	3947	F	MORTALITY	153	22	34	574	150	1830	1000	10300	800	9500	DIED	SQUAM_CELL_CA	BA_CARCIOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
704	3947	F	MORTALITY	154	18	30	583	120	1600	800	9100	700	8300	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA,SQUAM_CELL_CA,SQUA_METAPLAS
705	3947	F	MORTALITY	156	15	24	583	100	1310	700	7400	600	6800	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA,SQUAM_CELL_CA,SQUA_METAPLAS
706	3947	F	MORTALITY	157	25	41	583	170	2190	1200	12400	900	11400	SAC	SEPT_FIBROSIS	BA_HYPERPLASIA
707	3947	F	MORTALITY	159	21	34	583	140	1820	1000	10300	800	9500	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
708	3947	F	MORTALITY	162	23	37	583	150	1990	1100	11200	900	10300	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,HEMANGIOSARCOMA
709	3947	F	MORTALITY	163	47	74	435	310	3950	2100	22300	1500	18800	DIED	ADENOCARCINOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
710	3947	F	MORTALITY	163	29	47	557	190	2500	1300	14100	1100	12900	DIED	SQUAM_CELL_CA	HEMANGIOSARCOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
711	3947	F	MORTALITY	165	34	53	567	220	2860	1500	16200	1200	14800	DIED	SQUAM_CELL_CA	HEMORRHAGE,SEPT_FIBROSIS,BA_HYPERPLASIA
712	3947	F	MORTALITY	166	20	33	583	140	1750	900	9900	800	9100	SAC	SQUAM_CELL_CA	PAP_ADENOCARCINOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
713	3947	F	MORTALITY	168	19	31	583	130	1660	900	9400	700	8600	SAC	SQUAM_CELL_CA	BA_CARCIOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
714	3947	F	MORTALITY	171	62	98	390	410	5280	2800	29800	1900	24000	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,SQUA_METAPLAS
715	3947	F	MORTALITY	174	29	46	580	190	2470	1300	13900	1100	12800	SAC	HEMANGIOSARCOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
716	3947	F	MORTALITY	176	19	31	583	130	1650	900	9300	700	8600	SAC	SQUAM_CELL_CA	HEMORRHAGE,SEPT_FIBROSIS,BA_HYPERPLASIA
717	3947	F	MORTALITY	180	21	32	583	140	1730	1000	9800	800	9000	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
718	3947	F	MORTALITY	183	20	32	583	130	1700	900	9600	700	8900	SAC	PAP_ADENOCARCINOMA	SQUAM_CELL_CA,SEPT_FIBROSIS,BA_HYPERPLASIA,SQUA_METAPLAS
719	3947	M	MORTALITY	225	33	51	570	210	2740	1500	15400	1200	14100	DIED	SQUAM_CELL_CA	HEMORRHAGE,SEPT_FIBROSIS
720	3947	M	MORTALITY	240	38	60	500	250	3220	1700	18200	1300	16000	DIED	HEMANGIOSARCOMA	SQUAM_CELL_CA,BA_CARCIOMA,SEPT_FIBROSIS
721	3947	M	MORTALITY	246	35	55	574	230	2930	1600	16500	1300	15200	DIED	HEMANGIOSARCOMA	SQUAM_CELL_CA,MESOTHELIOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
722	3947	M	MORTALITY	250	42	66	479	280	3560	1900	20100	1400	17500	DIED	FIBROSARCOMA_LUNG	SEPT_FIBROSIS,BA_HYPERPLASIA,AUTOLYTIC
723	3947	M	MORTALITY	255	34	55	490	230	2930	1600	16500	1200	14500	DIED	HEMANGIOSARCOMA	SQUAM_CELL_CA,SEPT_FIBROSIS
724	3947	M	MORTALITY	260	25	40	336	170	2170	1200	12200	700	9300	DIED	ADENOCARCINOMA	SEPT_FIBROSIS
725	3947	M	MORTALITY	262	25	39	583	170	2100	1100	11800	900	10900	SAC	SQUAM_CELL_CA	BA_CARCIOMA,ADENOCARCINOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
726	3947	M	MORTALITY	264	29	46	583	190	2480	1300	14000	1100	12900	SAC	SQUAM_CELL_CA	HEMANGIOSARCOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
727	3947	M	MORTALITY	271	23	37	445	150	1980	1100	11200	800	9500	EUTHANIZED	SQUAM_CELL_CA	SEPT_FIBROSIS
728	3947	M	MORTALITY	273	19	29	494	120	1580	900	8900	600	7900	DIED	BA_CARCIOMA	SQUAM_CELL_CA,SEPT_FIBROSIS,BA_HYPERPLASIA
729	3947	M	MORTALITY	278	18	28	583	120	1510	800	8500	700	7800	SAC	UNDIFF_CARCIOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
730	3947	M	MORTALITY	278	31	48	467	200	2590	1400	14600	1000	12600	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
731	3947	M	MORTALITY	281	19	30	583	130	1630	900	9200	700	8500	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
732	3947	M	MORTALITY	285	27	43	583	180	2300	1200	13000	1000	12000	SAC	SQUAM_CELL_CA	HEMANGIOSARCOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
733	3947	M	MORTALITY	288	35	54	509	230	2910	1600	16400	1200	14600	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
734	3947	M	MORTALITY	289	24	39	560	160	2080	1100	11800	900	10700	DIED	LEUKEMIA	SEPT_FIBROSIS
735	3947	M	MORTALITY	300	25	40	457	170	2140	1100	12100	800	10300	DIED	UNDIFF_CARCIOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
736	3947	F	MORTALITY	331	19	31	518	130	1650	900	9300	700	8300	EUTHANIZED	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,SQUA_METAPLAS
801	3948	F	MORTALITY	136	274	26	95	1810	1420	12400	8000	4100	3000	EUTHANIZED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE
802	3948	F	MORTALITY	149	236	23	80	1560	1230	10700	6900	3200	2300	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE
803	3948	F	MORTALITY	151	94	9	582	620	500	4300	2800	3500	2600	SAC	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,BA_HYPERPLASIA
804	3948	F	MORTALITY	153	128	13	467	850	700	5800	4000	4300	3400	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
805	3948	F	MORTALITY	156	218	22	178	1440	1170	9900	6600	4600	3600	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS
806	3948	F	MORTALITY	158	110	11	190	730	610	5000	3500	2400	2000	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,AUTOLYTIC
807	3948	F	MORTALITY	159	125	13	526	820	680	5700	3800	4400	3400	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,SQUAM_CELL_CA
808	3948	F	MORTALITY	161	143	14	329	940	730	6500	4100	4000	3100	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,SQUA_METAPLAS
809	3948	F	MORTALITY	163	115	11	440	760	590	5200	3300	3700	2800	DIED	HEMANGIOSARCOMA	RAD_PNEUMONITIS,SEPT_FIBROSIS,SQUA_METAPLAS
810	3948	F	MORTALITY	164	102	10	446	680	520	4700	3000	3300	2500	DIED	UNDIFF_CARCIOMA	HEMORRHAGE,SEPT_FIBROSIS

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1G. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING IN LUNG	OTHER FINDINGS AT DEATH
811	3948	F	MORTALITY	164	87	9	506	570	460	3900	2600	3000	2300	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
812	3948	F	MORTALITY	166	125	12	299	830	650	5700	3700	3400	2600	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,BA_HYPERPLASIA
813	3948	F	MORTALITY	169	205	20	182	1350	1080	9300	6100	4300	3400	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS
814	3948	F	MORTALITY	170	120	12	491	790	630	5500	3600	4100	3100	EUTHANIZED	RAD_PNEUMONITIS	SEPT_FIBROSIS,SQUA_METAPLAS
815	3948	F	MORTALITY	175	143	14	300	940	740	6500	4200	3800	3000	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,BA_HYPERPLASIA
816	3948	F	MORTALITY	175	105	10	491	690	550	4800	3100	3600	2700	EUTHANIZED	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,RAD_PNEUMONITIS
817	3948	F	MORTALITY	180	68	7	495	450	360	3100	2000	2300	1800	DIED	SQUAM_CELL_CA	RAD_PNEUMONITIS,SEPT_FIBROSIS
818	3948	F	MORTALITY	193	86	8	512	570	450	3900	2500	3000	2200	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
819	3948	M	MORTALITY	199	191	18	67	1260	990	8700	5600	2300	1700	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
820	3948	M	MORTALITY	233	131	13	93	860	670	6000	3800	1900	1400	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS
821	3948	M	MORTALITY	244	110	11	463	730	590	5000	3300	3600	2900	DIED	SEPT_FIBROSIS	
822	3948	M	MORTALITY	252	99	10	251	650	510	4500	2900	2400	1900	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS,SQUAM_CELL_PAP
825	3948	M	MORTALITY	264	141	14	69	930	740	6400	4200	1700	1300	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE
826	3948	M	MORTALITY	266	152	15	100	1000	790	6900	4400	2400	1700	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE,AUTOLYTIC
827	3948	M	MORTALITY	269	190	18	105	1250	970	8600	5500	3000	2200	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
828	3948	M	MORTALITY	273	78	7	497	510	380	3500	2200	2700	1900	EUTHANIZED	SQUAM_CELL_CA	SEPT_FIBROSIS
829	3948	M	MORTALITY	275	141	13	94	930	710	6400	4000	2100	1500	DIED	UNDIF CARCINOMA	SEPT_FIBROSIS,AUTOLYTIC
830	3948	M	MORTALITY	280	107	10	260	710	560	4900	3200	2700	2100	DIED	RAD_PNEUMONITIS	SEPT_FIBROSIS
831	3948	M	MORTALITY	282	92	9	563	610	460	4200	2600	3300	2400	DIED	SQUAM_CELL_CA	ADENOCARCINOMA,SEPT_FIBROSIS
832	3948	M	MORTALITY	284	196	19	74	1290	1010	8900	5700	2500	1800	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE
833	3948	M	MORTALITY	289	159	15	72	1050	820	7200	4600	2000	1400	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE
834	3948	M	MORTALITY	294	158	16	73	1040	850	7200	4800	2000	1500	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,EDEMA,HEMORRHAGE
835	3948	M	MORTALITY	301	143	14	69	940	740	6500	4200	1800	1300	DIED	RAD_PNEUMONITIS	VASCULITIS,SEPT_FIBROSIS,HEMORRHAGE
836	3948	M	MORTALITY	306	88	9	439	580	470	4000	2700	2900	2200	EUTHANIZED	SEPT_FIBROSIS	BA_HYPERPLASIA,SQUA_METAPLAS
901	3949	F	MORTALITY	139	20	7	582	130	390	900	2200	800	2000	SAC	ADENOCARCINOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
902	3949	F	MORTALITY	149	27	12	547	180	650	1200	3700	1000	3300	DIED	SQUAM_CELL_CA	HEMANGIOSARCOMA,SEPT_FIBROSIS
903	3949	F	MORTALITY	152	41	16	448	270	850	1900	4800	1300	4100	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
904	3949	F	MORTALITY	153	21	8	582	140	420	1000	2400	800	2200	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,ALVEOLAR_HISTEO,BA_HYPERPLASIA
905	3949	F	MORTALITY	157	27	10	544	180	550	1200	3100	1000	2800	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
906	3949	F	MORTALITY	157	23	9	497	150	480	1000	2700	800	2400	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,AUTOLYTIC
907	3949	F	MORTALITY	159	29	11	555	190	610	1300	3400	1100	3100	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
908	3949	F	MORTALITY	161	17	7	582	110	400	800	2300	600	2100	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO,BA_HYPERPLASIA,SQUA_METAPLAS
909	3949	F	MORTALITY	163	27	11	582	180	590	1200	3300	1000	3100	SAC	SQUAM_CELL_CA	ADENOCARCINOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
910	3949	F	MORTALITY	164	21	7	509	140	390	900	2200	700	2000	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
911	3949	F	MORTALITY	165	23	10	582	150	520	1000	2900	900	2700	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,ALVEOLAR_HISTEO,BA_HYPERPLASIA
912	3949	F	MORTALITY	166	20	8	582	140	450	900	2600	800	2400	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA
913	3949	F	MORTALITY	168	30	12	582	200	640	1400	3600	1100	3300	SAC	UNDIF CARCINOMA	SEPT_FIBROSIS,ALVEOLAR_HISTEO,BA_HYPERPLASIA
914	3949	F	MORTALITY	170	15	6	582	100	320	700	1800	600	1600	SAC	SQUAM_CELL_CA	BA_CARCINOMA,SEPT_FIBROSIS,ALVEOLAR_HISTEO,BA_HYPERPLASIA
915	3949	F	MORTALITY	175	23	9	582	150	490	1000	2800	900	2600	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,HEMORRHAGE,BA_HYPERPLASIA
916	3949	F	MORTALITY	175	33	13	517	220	680	1500	3800	1200	3400	EUTHANIZED	SQUAM_CELL_CA	SEPT_FIBROSIS,SQUA_METAPLAS
917	3949	F	MORTALITY	181	28	11	582	180	590	1300	3300	1000	3100	SAC	SEPT_FIBROSIS	ALVEOLAR_HISTEO,BA_HYPERPLASIA
918	3949	F	MORTALITY	188	13	5	480	80	290	600	1600	400	1400	DIED	AUTOLYTIC	
919	3949	F	MORTALITY	163	13	5	560	90	260	600	1500	500	1400	EUTHANIZED	LEUKEMIA	SEPT_FIBROSIS,ALVEOLAR_HISTEO
920	3949	M	MORTALITY	239	21	8	582	140	440	1000	2500	800	2300	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS
921	3949	M	MORTALITY	244	16	6	446	110	320	700	1800	500	1500	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS
922	3949	M	MORTALITY	249	19	8	582	120	420	800	2400	700	2200	SAC	SQUAM_CELL_CA	BA_HYPERPLASIA
923	3949	M	MORTALITY	254	17	7	475	110	360	800	2000	600	1800	DIED	SQUAM_CELL_CA	BA_CARCINOMA,SEPT_FIBROSIS
924	3949	M	MORTALITY	258	16	7	582	110	360	700	2000	600	1900	SAC	RAD_PNEUMONITIS	PAP_ADENOCARCINOMA

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1H. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING	OTHER FINDINGS AT DEATH
925	3949	M	MORTALITY	261	21	8	582	140	450	1000	2500	800	2400	SAC	SQUAM_CELL_CA	HEMANGIOSARCOMA,RAD_PNEUMONITIS,SEPT_FIBROSIS,BA_HYPERPLASIA,ALVEOLAR_HISTEO
926	3949	M	MORTALITY	268	25	10	571	170	540	1200	3000	900	2800	DIED	HEMANGIOSARCOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
927	3949	M	MORTALITY	270	115	44	582	760	2380	5200	13400	4300	12400	DIED	ADENOSQUAM_CARINOMA	SEPT_FIBROSIS,BA_HYPERPLASIA,SQUA_METAPLAS
928	3949	M	MORTALITY	272	27	11	582	180	580	1200	3300	1000	3000	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,ADENOCARCINOMA
929	3949	M	MORTALITY	275	13	5	502	90	290	600	1600	500	1400	DIED	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,AUTOLYTIC
930	3949	M	MORTALITY	280	23	10	582	150	510	1000	2900	800	2700	SAC	SQUAM_CELL_CA	SEPT_FIBROSIS,BA_HYPERPLASIA,HEMORRHAGE
931	3949	M	MORTALITY	282	14	5	507	90	280	600	1600	500	1400	DIED	SEPT_FIBROSIS	ALVEOLAR_HISTEO,BA_HYPERPLASIA,HEMORRHAGE
932	3949	M	MORTALITY	284	22	9	381	150	460	1000	2600	700	2100	DIED	ADENOCARCINOMA	SEPT_FIBROSIS,BA_HYPERPLASIA
933	3949	M	MORTALITY	287	28	11	582	190	590	1300	3300	1000	3100	SAC	SQUAM_CELL_CA	ADENOCARCINOMA,SEPT_FIBROSIS,BA_HYPERPLASIA
934	3949	M	MORTALITY	293	12	5	567	80	270	600	1500	500	1400	EUTHANIZED	SEPT_FIBROSIS	ALVEOLAR_HISTEO,BA_HYPERPLASIA
936	3949	M	MORTALITY	308	27	11	540	180	600	1200	3400	1000	3000	DIED	SQUAM_CELL_CA	PULMONARY_THROMBOSIS,SEPT_FIBROSIS,BA_HYPERPLASIA,HEMORRHAGE
891	3950	M	MORTALITY	276	13	7	5	90	380	600	2100	0	100	SAC	NOT SUBMITTED	
893	3950	M	MORTALITY	284	18	9	15	120	510	800	2900	100	300	SAC	NO LESION	
894	3950	M	MORTALITY	285	22	12	124	150	640	1000	3600	400	1600	SAC	ALVEOLAR_HISTEO	
895	3950	M	MORTALITY	287			1							SAC	NOT SUBMITTED	
896	3950	M	MORTALITY	293	17	8	91	110	450	800	2500	200	900	SAC	NO LESION	
898	3950	M	MORTALITY	309	21	11	32	140	590	900	3300	100	600	SAC	NO LESION	
899	3950	M	MORTALITY	198			1							SAC	NOT SUBMITTED	
938	3950	F	MORTALITY	144	26	14	124	170	750	1200	4200	500	1800	SAC	RAD_PNEUMONITIS	
939	3950	F	MORTALITY	152	41	21	32	270	1130	1900	6400	300	1200	SAC	RAD_PNEUMONITIS	
940	3950	F	MORTALITY	154	36	19	151	240	1050	1700	5900	700	2900	SAC	RAD_PNEUMONITIS	
942	3950	F	MORTALITY	157	62	32	5	410	1710	2800	9600	100	400	SAC	NOT SUBMITTED	
944	3950	F	MORTALITY	161			1							SAC	NOT SUBMITTED	
945	3950	F	MORTALITY	163	21	11	32	140	590	900	3300	200	600	SAC	ALVEOLAR_HISTEO	
946	3950	F	MORTALITY	164			1							SAC	NOT SUBMITTED	
947	3950	F	MORTALITY	164	35	18	5	230	980	1600	5500	100	200	SAC	NOT SUBMITTED	
948	3950	F	MORTALITY	167	0	0	418	0	0	0	0	0	0	DIED	CONGESTION	
949	3950	F	MORTALITY	168			1							SAC	NOT SUBMITTED	
951	3950	F	MORTALITY	174	30	16	61	200	860	1400	4900	300	1400	SAC	ALVEOLAR_HISTEO	
952	3950	F	MORTALITY	176	24	13	32	160	670	1100	3800	200	700	SAC	ALVEOLAR_HISTEO	
954	3950	F	MORTALITY	186	17	9	91	110	460	800	2600	300	900	SAC	ALVEOLAR_HISTEO	
955	3950	F	MORTALITY	137	28	15	124	180	780	1300	4400	500	1900	SAC	ALVEOLAR_HISTEO	
957	3950	F	MORTALITY	150	53	29	5	350	1560	2400	8800	100	200	SAC	NOT SUBMITTED	
962	3950	F	MORTALITY	161	21	11	151	140	600	1000	3400	400	1700	SAC	ALVEOLAR_HISTEO	
963	3950	F	MORTALITY	162	22	11	91	150	600	1000	3400	300	1200	SAC	ALVEOLAR_HISTEO	
964	3950	F	MORTALITY	164	22	11	61	140	590	1000	3300	300	900	SAC	ALVEOLAR_HISTEO	
965	3950	F	MORTALITY	165	38	19	124	250	1040	1700	5900	700	2600	SAC	NO LESION,AUTOLYTIC	
966	3950	F	MORTALITY	166	47	25	15	310	1360	2100	7700	200	800	SAC	NOT SUBMITTED	
967	3950	F	MORTALITY	168	32	17	91	210	900	1500	5100	500	1800	SAC	NO LESION	
969	3950	F	MORTALITY	173	29	15	15	190	810	1300	4600	100	500	SAC	NOT SUBMITTED	
970	3950	F	MORTALITY	177	9	5	93	60	240	400	1400	100	500	DIED	NO LESION	AUTOLYTIC
971	3950	F	MORTALITY	180	22	12	15	150	660	1000	3700	100	400	SAC	NOT SUBMITTED	
972	3950	F	MORTALITY	183	22	11	61	140	590	1000	3300	300	900	SAC	ALVEOLAR_HISTEO	
973	3950	M	MORTALITY	231	19	10	32	130	510	900	2900	100	500	SAC	NO LESION	
975	3950	M	MORTALITY	252	30	15	91	200	830	1400	4700	400	1700	SAC	NO LESION	
976	3950	M	MORTALITY	253	16	9	151	110	470	700	2600	300	1300	SAC	NO LESION	
978	3950	M	MORTALITY	263	18	9	151	120	500	800	2800	300	1400	SAC	NO LESION	
980	3950	M	MORTALITY	269	22	12	32	140	630	1000	3600	200	700	SAC	NO LESION	

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11. PATHOLOGICAL OBSERVATIONS AND OTHER COMMENTS FOR RATS THAT DIED, WERE SACRIFICED OR EUTHANIZED AFTER INHALATION EXPOSURE TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	GROUP	INITIAL WEIGHT (g)	ILB Pu238 (nCi/g-LUNG)	ILB Pm147 (μCi/g-LUNG)	DPE	30-DAY ALPHA RADS	30-DAY BETA RADS	900-DAY ALPHA RADS	900-DAY BETA RADS	ALPHA RADS AT DEATH	BETA RADS AT DEATH	MODE OF DEATH	MAJOR FINDING IN LUNG	OTHER FINDINGS AT DEATH
981	3950	M	MORTALITY	272	17	9	91	110	480	800	2700	300	1000	SAC	NO LESION	
982	3950	M	MORTALITY	274	25	13	15	160	720	1100	4000	100	400	SAC	NO LESION	
983	3950	M	MORTALITY	278			1							SAC	NOT SUBMITTED	
984	3950	M	MORTALITY	282	16	9	61	110	460	700	2600	200	700	SAC	ALVEOLAR_HISTEO	
988	3950	M	MORTALITY	300	23	11	5	150	610	1000	3400	0	100	SAC	NOT SUBMITTED	
989	3950	M	MORTALITY	304	23	12	61	150	650	1100	3600	300	1000	SAC	NO LESION	
990	3950	M	MORTALITY	154	54	29	15	360	1530	2500	8600	200	900	SAC	NO LESION	
992	3950	M	MORTALITY	242	22	12	61	150	650	1000	3700	300	1000	SAC	ALVEOLAR_HISTEO	
995	3950	M	MORTALITY	259	24	13	527	160	710	1100	4000	900	3600	DIED	SEPT_FIBROSIS	ALVEOLAR_HISTEO,AUTOLYTIC
996	3950	M	MORTALITY	262	33	18	151	220	950	1500	5400	600	2700	SAC	ALVEOLAR_HISTEO	
998	3950	M	MORTALITY	271	20	11	5	130	580	900	3300	0	100	SAC	NOT SUBMITTED	
999	3950	M	MORTALITY	272	17	9	581	110	480	800	2700	600	2500	SAC	BA_CARCIOMA	BA_HYPERPLASIA,SEPT_FIBROSIS

2A. PULMONARY FUNCTION MEASUREMENTS FOR RATS EXPOSED VIA INHALATION TO ²³⁸Pu, ¹⁴⁷Pm OR BOTH IN FAP

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ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	MONTHS AFTER EXPOSURE	ILB Pu-238 (nCi/g-LUNG)	ILB Pm-147 (μCi/g-LUNG)	ALPHA RADS	BETA RADS	VITAL CAPAC. (ml)	CO DIF- FUSING CAPAC. (ml/min/ mm Hg)	DIFFUSING CAPACITY PER Kg BODY WT	QUASISTATIC COMPLIANCE (ml/cm-H ₂ O)	SLOPE PHASE 3
101	3941	F	18	0	0	0	0	10.8	0.19	0.87	0.81	0.60
103	3941	F	18	0	0	0	0	10.6	0.19	0.80	0.79	0.42
105	3941	F	18	0	0	0	0	11.7	0.22	0.87	0.92	0.69
107	3941	F	18	0	0	0	0	12.0	0.23	0.90	0.93	0.35
109	3941	F	18	0	0	0	0	11.4	0.23	0.81	0.86	0.68
111	3941	F	18	0	0	0	0	9.6	0.16	0.70	0.73	0.51
113	3941	F	18	0	0	0	0	11.2	0.22	0.92	0.85	0.47
115	3941	F	18	0	0	0	0	11.9	0.23	0.79	0.69	0.49
117	3941	F	18	0	0	0	0	12.5	0.22	0.67	1.00	0.52
118	3941	F	18	0	0	0	0	13.7	0.25	0.79	1.10	0.27
119	3941	M	18	0	0	0	0	14.3	0.25	0.77	1.03	0.48
121	3941	M	18	0	0	0	0	14.8	0.31	0.84	1.06	0.51
123	3941	M	18	0	0	0	0	17.1	0.35	0.79	1.30	0.48
126	3941	M	18	0	0	0	0	16.9	0.33	0.95	1.22	0.44
127	3941	M	18	0	0	0	0	16.1	0.30	0.74	1.21	0.45
129	3941	M	18	0	0	0	0	17.1	0.38	0.66	1.29	0.38
131	3941	M	18	0	0	0	0	16.4	0.27	0.65	1.27	0.28
133	3941	M	18	.	.	0	0	15.6	0.18	0.44	1.17	0.40
135	3941	M	18	0	0	0	0	16.5	0.35	0.74	1.26	0.42
136	3941	M	18	0	0	0	0	15.1	0.36	0.74	1.13	0.56
201	3942	F	18	115	0	4300	0	4.9	0.06	0.27	0.28	9.01
203	3942	F	18	141	0	5200	0	4.9	0.04	0.23	0.30	8.66
205	3942	F	18	139	0	5200	0	5.2	0.06	0.24	0.32	7.65
209	3942	F	18	114	0	4200	0	4.6	0.05	0.21	0.27	8.82
213	3942	F	18	115	0	4300	0	6.5	0.08	0.34	0.46	3.20
230	3942	M	18	77	0	2900	0	11.1	0.19	0.48	0.84	0.86
301	3943	F	18	25	0	930	0	9.2	0.14	0.65	0.67	0.78
302	3943	F	18	34	0	1300	0	9.9	0.17	0.67	0.69	0.58
303	3943	F	18	19	0	700	0	10.6	0.19	0.73	0.80	0.77
304	3943	F	18	39	0	1500	0	7.2	0.12	0.48	0.50	1.37
305	3943	F	18	26	0	960	0	9.8	0.17	0.69	0.75	0.57
307	3943	F	18	30	0	1100	0	10.0	0.18	0.69	0.74	0.47
309	3943	F	18	22	0	820	0	10.7	0.18	0.70	0.81	0.48
312	3943	F	18	24	0	890	0	10.5	0.15	0.60	0.77	0.45
313	3943	F	18	22	0	820	0	11.1	0.21	0.85	0.84	0.73
314	3943	F	18	18	0	670	0	11.1	0.22	0.83	0.85	0.39
319	3943	M	18	27	0	1000	0	9.1	0.15	0.48	0.72	0.77
320	3943	M	18	30	0	1100	0	15.0	0.31	0.83	1.13	0.46
321	3943	M	18	34	0	1300	0	12.2	0.26	0.72	0.84	0.64
325	3943	M	18	18	0	670	0	11.8	0.23	0.62	0.95	0.30
328	3943	M	18	20	0	740	0	13.8	0.27	0.61	1.08	0.50
330	3943	M	18	21	0	780	0	14.4	0.35	0.87	1.10	0.54
331	3943	M	18	26	0	960	0	15.7	0.27	0.62	1.24	0.36
332	3943	M	18	19	0	700	0	11.9	0.21	0.53	0.84	0.72
333	3943	M	18	20	0	740	0	15.6	0.30	0.68	1.19	0.48
407	3944	F	18	0	59	0	11000	7.2	0.12	0.47	0.46	2.22
408	3944	F	18	0	56	0	11000	7.6	0.14	0.56	0.49	0.82
410	3944	F	18	0	35	0	6600	5.1	0.10	0.39	0.37	8.22
416	3944	F	18	0	53	0	9900	8.5	0.15	0.53	0.59	1.04
418	3944	F	18	0	38	0	7100	10.0	0.18	0.69	0.78	0.56
419	3944	M	18	0	67	0	13000	12.2	0.26	0.67	0.83	0.72
422	3944	M	18	0	64	0	12000	8.0	0.15	0.42	0.54	1.66
429	3944	M	18	0	49	0	9200	15.4	0.27	0.61	1.17	0.36
430	3944	M	18	0	28	0	5200	12.7	0.25	0.58	0.97	0.69
431	3944	M	18	0	27	0	5100	13.0	0.31	0.74	0.94	0.70

2B. PULMONARY FUNCTION MEASUREMENTS FOR RATS EXPOSED VIA INHALATION TO ^{238}Pu , ^{147}Pm OR BOTH IN FAP

ANIMAL NUMBER	EXPERI- MENT NUMBER	SEX	MONTHS AFTER EXPOSURE	ILB Pu-238 (nCi/g-LUNG)	ILB Pm-147 ($\mu\text{Ci/g-LUNG}$)	ALPHA RADS	BETA RADS	VITAL CAPAC. (ml)	CO DIF- FUSING CAPAC. (ml/min/ mm Hg)	DIFFUSING CAPACITY PER Kg BODY WT	QUASISTATIC COMPLIANCE (ml/cm-H ₂ O)	SLOPE PHASE 3
432	3944	M	18	0	38	0	7100	12.3	0.21	0.53	0.93	0.59
433	3944	M	18	0	52	0	9700	12.2	0.22	0.57	0.89	0.75
436	3944	M	18	0	39	0	7300	14.1	0.24	0.54	1.08	0.42
501	3945	F	18	0	22	0	4100	8.6	0.14	0.63	0.67	0.68
502	3945	F	18	0	20	0	3700	11.5	0.21	0.85	0.87	0.76
504	3945	F	18	0	19	0	3600	11.3	0.19	0.71	0.87	0.44
507	3945	F	18	0	6	0	1100	11.2	0.20	0.76	0.80	0.63
508	3945	F	18	0	7	0	1300	10.5	0.19	0.77	0.75	0.88
509	3945	F	18	0	9	0	1700	12.6	0.23	0.97	0.94	0.65
510	3945	F	18	0	7	0	1300	10.9	0.21	0.85	0.83	0.74
511	3945	F	18	0	12	0	2200	12.7	0.21	0.77	0.99	0.52
513	3945	F	18	0	31	0	5800	11.8	0.10	0.39	0.88	0.51
514	3945	F	18	0	29	0	5400	12.3	0.19	0.71	0.87	0.42
519	3945	M	18	0	10	0	1900	15.4	0.31	0.86	1.13	0.50
521	3945	M	18	0	6	0	1100	14.6	0.17	0.45	1.03	0.52
522	3945	M	18	0	9	0	1700	16.5	0.28	0.74	1.28	0.32
523	3945	M	18	0	14	0	2600	16.2	0.32	0.77	1.17	0.47
524	3945	M	18	0	13	0	2400	15.3	0.31	0.75	1.09	0.34
525	3945	M	18	0	35	0	6600	14.6	0.31	0.77	1.10	0.54
702	3947	F	18	34	53	1200	15000	4.4	0.05	0.24	0.28	12.06
704	3947	F	18	18	30	650	8300	9.3	0.16	0.68	0.67	0.73
705	3947	F	18	15	24	540	6600	9.4	0.15	0.60	0.65	0.67
706	3947	F	18	25	41	900	11000	9.2	0.13	0.48	0.69	0.58
707	3947	F	18	21	34	760	9400	5.2	0.07	0.29	0.33	5.62
708	3947	F	18	23	37	830	10000	6.3	0.09	0.35	0.38	2.47
711	3947	F	18	34	53	1200	15000	5.3	0.07	0.31	0.41	5.09
712	3947	F	18	20	33	720	9100	7.9	0.15	0.59	0.55	1.13
713	3947	F	18	19	31	680	8500	7.8	0.15	0.52	0.57	1.35
715	3947	F	18	29	46	1000	13000	6.2	0.10	0.33	0.43	3.49
716	3947	F	18	19	31	680	8500	8.6	0.12	0.49	0.57	0.68
717	3947	F	18	21	32	760	8800	9.5	0.15	0.54	0.66	0.80
718	3947	F	18	20	32	720	8800	7.5	0.10	0.40	0.49	1.24
719	3947	M	18	33	51	1200	14000	8.2	0.12	0.32	0.60	1.55
725	3947	M	18	25	39	900	11000	9.9	0.21	0.55	0.67	1.39
726	3947	M	18	29	46	1000	13000	7.3	0.14	0.38	0.52	1.92
729	3947	M	18	18	28	650	7700	13.8	0.24	0.55	1.03	0.52
731	3947	M	18	19	30	680	8300	10.4	0.21	0.56	0.78	0.78
732	3947	M	18	27	43	970	12000	8.1	0.13	0.33	0.53	1.51
909	3949	F	18	27	11	970	3000	6.8	0.12	0.48	0.45	1.64
920	3949	M	18	21	8	760	2200	14.7	0.25	0.68	1.14	0.39
922	3949	M	18	19	8	680	2200	10.8	0.13	0.38	0.88	0.67
928	3949	M	18	27	11	970	3000	10.4	0.21	0.50	0.76	0.86
930	3949	M	18	23	10	830	2800	9.5	0.14	0.38	0.70	1.26