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Inhaled ^{147}Pm and/or Total-Body Gamma Radiation: Early Mortality and Morbidity in Rats

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Pacific Northwest Laboratory
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Prepared for
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ABSTRACT

Rats were given doses of ^{60}Co gamma radiation and/or lung burdens of ^{147}Pm (in fused aluminosilicate particles) within lethal ranges in an experiment to determine and compare morbidity and mortality responses for the radiation insults within 1 year after exposure. Radiation-induced morbidity was assessed by measuring changes in body weights, hematologic parameters, and pulmonary-function parameters.

Acute mortality and morbidity from inhaled promethium were caused primarily by radiation pneumonitis and pulmonary fibrosis that occurred more than 53 days after exposure. Acute mortality and morbidity from total-body gamma irradiation occurred within 30 days of exposure and resulted from the bone-marrow radiation syndrome.

Gamma radiation caused transient morbidity, reflected by immediately depressed blood cell levels and by reduced body weight gain in animals that survived the acute gamma radiation syndrome. Inhaled promethium caused a loss of body weight and diminished pulmonary function, but its only effect on blood cell levels was lymphocytopenia. Combined gamma irradiation and promethium lung burdens were synergistic, in that animals receiving both radiation insults had higher morbidity and mortality rates than would be predicted based on the effect of either kind of radiation alone. Promethium lung burdens enhanced the effect of gamma radiation in rats within the first 30 days of exposure, and gamma radiation enhanced the later effect of promethium lung burdens.

A model, based on a statistical tool called the hazard function, was applied to the data from rats exposed to either promethium aerosols or total-body gamma radiation and accurately predicted the $\text{LD}_{50/365}$ lung doses for rats exposed to combined radiation insults.

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EXECUTIVE SUMMARY

A review of pertinent literature, including the Nuclear Reactor Safety Study (U.S. Nuclear Regulatory Commission, 1975), suggested that improved methods were needed to predict the combined effects of high doses of external and internal irradiation on laboratory animals and humans. Additional research was required to address methods for predicting dose/mortality and dose/morbidity relationships of combined radiation insults.

This research was designed to determine the effect of total-body gamma radiation and an inhaled beta-emitting radionuclide in an insoluble form. It was part of a larger research program involving exposure of animals to high levels of alpha-emitting radionuclides, beta-emitting radionuclides, and total-body gamma radiation, alone or in combinations.

Rats were exposed to near-lethal total-body doses of ^{60}Co gamma radiation and/or an aerosol of ^{147}Pm in fused aluminosilicate particles (FAP) that resulted in lung burdens in the lethal range. Mortality fractions within 1 year of exposure were derived, respectively, for groups exposed only to gamma radiation, to a promethium aerosol, or to gamma radiation followed, within 1 hour, by exposure to a promethium aerosol. Radiation-induced morbidity was monitored for 1 year after exposure by measuring changes in body weights, hematologic parameters, and pulmonary-function parameters.

Acute mortality and morbidity from inhaled promethium were caused primarily by radiation pneumonitis and pulmonary fibrosis that occurred more than 53 days after exposure. Acute mortality and morbidity from total-body gamma irradiation occurred within 30 days of exposure and resulted from the bone-marrow radiation syndrome.

Inhaled promethium and total-body gamma exposure were synergistic in their lethal effects. Promethium lung burdens significantly enhanced mortality from gamma irradiation within 30 days of exposure compared to mortality from gamma radiation alone. Sublethal doses of gamma radiation increased the lethal effect of promethium in the lungs within 1 year of exposure.

A 365-day lung dose of approximately 290 Gy (29,000 rad) from inhaled promethium caused 50% mortality in rats within a year of exposure ($\text{LD}_{50/365}$). When rats received total-body gamma doses between 8.2 and 9.2 Gy (850 and 915 rad) with the promethium aerosol, the $\text{LD}_{50/365}$ was reduced to 160 Gy (16,000 rad). These results indicated that the lethal effect of combined exposures was greater than that which would be predicted by models that sum mortality rates of given doses of each kind of radiation.

There was a transient reduction of body-weight gain in survivors of total-body gamma irradiation but in rats that were exposed to promethium, weight loss was an indicator of imminent death. Likewise, animals that had depressed hematologic parameters induced by gamma irradiation either died within 30 days of exposure, or they survived and their hematologic parameters returned to control ranges. Lymphocytopenia resulted from lung burdens of promethium in rats although lymphocyte concentrations in circulating blood gradually returned toward control levels. A full year passed before the control range was reached for this parameter in rats that were exposed to promethium plus gamma radiation.

Pulmonary-function test results were determined to be reliable indicators of respiratory-function impairment from radiation pneumonitis. The most consistent indicators were reduction of vital capacity, increased slope of Phase III of the single-breath nitrogen washout curve, decreased quasistatic compliance, and diminished carbon-monoxide diffusing capacity. Of those indicators, the slope of Phase III and the vital capacity provided the earliest indications; quasistatic lung compliance and carbon-monoxide diffusing capacity indicated the later, fibrotic stages of radiation pneumonitis.

Morbidity as a response to promethium lung burdens was aggravated by total-body gamma doses to the same extent as mortality. Pulmonary function was impaired in 50% of rats by cumulative lung doses from promethium of approximately 300 Gy (30,000 rad). Gamma exposure reduced those doses to 180 Gy (18,000 rad; the difference was nearly 14 times the total-body gamma dose of 8.5 Gy (8500 rad).

The hazard function model, proposed by Scott et al. (1989), applied to the data from rats exposed either to promethium aerosols or total-body gamma radiation predicted the LD_{50/365} lung doses for rats exposed to combined radiation insults.

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ABBREVIATIONS

AMAD	= Activity mass median aerodynamic diameter
ANOVA	= Analysis of variance
C_L	= Lung compliance
C_{QS}	= Quasistatic compliance
DL_{CO}	= Carbon-monoxide diffusing capacity
F-344	= Fischer-344
FAP	= Fused aluminosilicate particles
FRC	= Functional residual capacity
FVC	= Forced vital capacity
GLM	= General linear model
GSD	= Geometric standard deviation
Gy	= Gray
IAD	= Initial alveolar deposition
IC	= Inspiratory capacity
ID	= Inside diameter
ILB	= Initial lung burden(s)
IP	= Intraperitoneal
ITRI	= Inhalation Toxicology Research Institute
IV	= Intravenous
kBq	= Kilobecquerel(s)
kVp	= Kilovolt potential
LCI	= Lung clearance index
LCL	= Lower confidence limit
$LD_{50/30}$	= Dose sufficient to cause 50% lethality within 30 days of exposure
MBN_2	= Multiple-breath nitrogen washout
MBq	= Megabecquerel(s)
MCH	= Mean corpuscular hemoglobin
MCHC	= Mean corpuscular hemoglobin concentration
MCV	= Mean corpuscular volume
MMD	= Mass median diameter
μCi	= Microcurie(s)
N_2	= Nitrogen
NBS	= U.S. National Bureau of Standards
O_2	= Oxygen
OD	= Outside diameter
P_aCO_2	= Partial pressure of arterial CO_2
PNL	= Pacific Northwest Laboratory
Ptp	= Transpulmonary pressure
P-V	= Pressure-volume

R	= Roentgens
rad	= Absorbed dose
RR	= Respiratory rate(s)
RV	= Residual volume
SAS	= Statistical Analysis System
SBN ₂	= Single-breath nitrogen washout
SD	= Standard deviation
TLC	= Total lung capacity
TLD	= Thermoluminescent dosimeter(s)
UCL	= Upper confidence limit
U.S. NRC	= U.S. Nuclear Regulatory Commission
VC	= Vital capacity
V _m	= Minute volume(s)
VPRC	= Volume of packed red cells
V _T	= Tidal volume(s)

INTRODUCTION

The Nuclear Reactor Safety Study (U.S. Nuclear Regulatory Commission; U.S. NRC, 1975) was used to define the health consequences resulting from exposure of a human population to external radiation and internally deposited radionuclides released during a hypothetical accident at a nuclear power plant. Several potential health consequences were addressed, including acute morbidity and mortality, genetic mutation, teratogenesis and carcinogenesis. Because the study was limited in scope, a revision is currently underway; where certain kinds of data were not available for the earlier report, research was performed to provide some of those data. This report describes one of those research projects.

One area of concern was how to estimate the health effects on one or more organ systems from the combination of different kinds (internal, external, alpha, beta, gamma) of radiation insults that potentially will occur from a reactor accident. Virtually all laboratory animal research performed in the past dealt with exposure to total-body X- or gamma radiation or to individual radionuclides, either by feeding or inhalation. This research permitted strict control of exposures and well-defined end points, but only rarely would a human population be accidentally exposed in such a manner. Also, previous research provided little information regarding the interaction between organ systems, or on the effects of two kinds (external and internal) of irradiation on the same organ system.

A series of experiments were planned by scientists of NRC, the Inhalation Toxicology Research Institute (ITRI), and Pacific Northwest Laboratory (PNL) to broaden the data base from which mathematical models could be constructed for predicting acute mortality and morbidity from combined radiation exposures. The experiments were limited to inhalation exposure of relatively insoluble forms of radionuclides and/or total-body ^{60}Co gamma irradiation of laboratory animals; thus, the lung and bone marrow were the primary target organs. "Acute" was defined as "within a year of exposure," and the end points included radiation-induced mortality as well as morbidity. Morbidity included hematologic parameters, body weight changes, and pulmonary function impairment. The experiments were conducted to determine:

- Influence of beta energy and dose-rate patterns of inhaled beta-emitting radionuclides on acute mortality and morbidity in rats (Scott et al., 1987b)
- Influence of total-body gamma irradiation and/or an inhaled alpha-emitting radionuclide on acute mortality and morbidity in rats and beagle dogs (Filipy et al., 1988)
- Influence of inhaled beta-emitting and/or alpha-emitting radionuclides on acute mortality and morbidity in rats (Scott et al., 1988)
- Influence of total-body gamma irradiation and/or inhaled beta-emitting radionuclides on acute mortality and morbidity in rats (subject of this report).

Data from those experiments were used to derive and verify a proposed mathematical model for predicting acute mortality and morbidity from combined radiation exposures. The model was initially proposed by Hahn (1979) and was based on a

statistical tool called the hazard function. Application of the data from the experiments listed above to validate the model for combined radiation insults was discussed in the publication by Scott et al. (1989).

BACKGROUND

TOTAL-BODY X- AND GAMMA IRRADIATION

A large number of experiments have been performed in which laboratory animals were exposed to lethal doses of total-body gamma- or X-radiation. Reports of these experiments frequently listed midline radiation exposures in roentgens (R), and not enough information was given for an accurate estimate of absorbed dose (rad). For comparisons of data, conversion factors of 0.95, 0.9, and 0.8 rad/R for mice, rats, and dogs would be reasonable approximations. Absorbed doses to rats from 200- to 300-kVp X-rays would be slightly higher and those from ^{60}Co gamma irradiation would be slightly lower than the conversion factors would indicate (Sinclair, 1962, 1963).

The hematologic response of animals from total-body X- or gamma-ray exposures was quite thoroughly described by Bond et al. (1965); they also characterized the bone-marrow radiation syndrome as it occurred in selected instances of human total-body gamma exposure. Radiation doses resulting in lethal bone-marrow responses are frequently expressed as LD_{50/30}, a dose sufficient to cause 50% lethality within 30 days of exposure. These values vary with dose rate, portion of the body irradiated, and within species. For brief exposures, they are generally listed as between 6 and 7.5 Gy (600 and 750 rad) for mice, 7 and 8 Gy (700 and 800 rad) for rats and between 2 and 3 Gy (200 and 300 rad) for dogs (Jones, 1981). The value for humans that was used in the Nuclear Reactor Safety Study (U.S. NRC, 1975) was 3.4 Gy (340 rad) $\pm$ 10% with a single exposure at a dose rate of less than 1 Gy (100 rad)/minute, and minimal postexposure supportive treatment.

THORACIC X- AND GAMMA IRRADIATION

Radiation pneumonitis may also result from X- or gamma irradiation from external sources, although the disease is not generally considered a primary effect of total-body exposure because death results from the hematologic syndrome before pneumonitis develops. In instances where exposure is only to the thoracic region of the body, as in tumor therapy, radiation pneumonitis is a major concern.

The relationship between incidence of radiation pneumonitis and dose in humans who received thoracic exposures was investigated by Van Dyk et al. (1981). They concluded that the disease could be expected to occur with a 7.5-Gy (750-rad) dose, and a 5% incidence could be expected with 8.2 Gy (820 rad). Their dose-response curves indicate 50% incidence at between 9 and 9.5 Gy (900 and 950 rad) and essentially 100% incidence above 11 Gy (1100 rad). They indicated a peak time of onset between 2 and 3 months but reported that there was no correlation between time of onset and dose. The data they used were based on 150 patients with no previous lung disease; exposures were to radiation from various sources, but doses were calculated for radiation equivalent to that of ^{60}Co gamma rays.

A number of experiments have been performed in which the thoracic areas of laboratory animals were exposed to X- or gamma radiation. The time course of radiation pneumonitis in mice, as manifested in histologic changes and changes in breathing patterns, was characterized by Travis (1980) and Travis et al. (1977, 1980). An acute phase, with peak response at 18 weeks after exposure, consisted of increased numbers of alveolar macrophages, interstitial edema and fibrinous exudate within alveoli. An intermediate phase, peaking at 36 weeks after exposure, was described

as increased alveolar septal cellularity and the presence of large foamy cells in alveoli. The late phase, characterized by collagen deposition (fibrosis) and detectable at 36 weeks after exposure, either became more severe, eventually causing death, or remained at a plateau in surviving mice. The peak response times of the first two phases were not dose-dependent, but the degree of severity of each response was greater at higher doses. No pneumonitis was present in lungs of mice that received 8 Gy (800 rad). The threshold dose was 11 Gy (1100 rad), although it was not usually lethal, and 15 Gy (1500 rad) caused 100% mortality within 22 weeks.

Siemann et al. (1982) constructed sigmoid dose-response curves using groups of mice in which the lungs were gamma-irradiated. They determined an LD_{50/180} of between 13 and 16 Gy (1300 and 1600 rad) and an LD_{50/420} of between 9.8 and 12.5 Gy (980 and 1250 rad); they irradiated two different strains at different dose rates, hence the wide range of doses. Death within 180 days was reportedly caused by acute radiation pneumonitis (presumed to correspond to the acute phase described by Travis et al. [1980]), and the later deaths were ascribed to pulmonary fibrosis.

Reports concerning thoracic irradiation of rats indicate a dose-response similar to that of mice. The data of Dunjic et al. (1960) indicate an LD_{50/90} between 1000 and 1100 R from 250-kVp X-rays; 1000 R killed nearly 50% of a group of rats between 30 and 150 days after exposure. In another study (Kurohara and Casarett, 1972), it was concluded that mortality resulting from thoracic exposure of rats to X-rays at doses of 6 and 12 Gy (600 and 1200 rad) did not differ significantly from that of unexposed controls, however; there was an unusually high mortality rate for control rats in that study.

The long-term response of beagle dogs that received upper-body, 1000-kVp X-irradiation was described by Michaelson and Schreiner (1971). Most dogs exposed to 2100 R died within a year as a result of acute respiratory difficulty associated with radiation pneumonitis. Dogs that survived exposure to 2100 R and those that received 1800-R exposures were able to accommodate the cardiopulmonary dysfunction but exhibited clinical symptoms of pneumonitis. Histological examination of lungs from sacrificed dogs and those that died indicated that they were in the late stages of radiation pneumonitis that involve fibrosis and hypercellularity.

INHALED AEROSOLS OF BETA-EMITTING RADIONUCLIDES

Much of the dosimetric data presented in reports of inhaled radionuclides consist of total initial lung burdens (ILB). For purposes of comparison, the values have been converted to activity/gram lung whenever possible. Factors used in those conversions were: lung weight of 2 g for rats, lung weight of 100 g for beagle dogs, or 11 g of lung/kg body weight (Hahn et al., 1987) if lung burdens were expressed as activity/kilogram body weight.

In the following discussions, the terms ⁹⁰Sr and ¹⁴⁴Ce will be used for the equilibrium states between ⁹⁰Sr-⁹⁰Y and ¹⁴⁴Ce-¹⁴⁴Pr, respectively.

One of the relatively short-term effects of inhaled beta-radiation-emitting radionuclides in early studies with rats and dogs was radiation pneumonitis. Stuart et al. (1964) exposed 12 beagle dogs to an aerosol of ¹⁴⁴Ce to achieve an initial alveolar deposition (IAD) between 18.5 and 81.5 MBq (0.5 and 22 mCi). One dog with an IAD of approximately 0.7 MBq (20 μ Ci)/g lung died 8 months after exposure. It was noted that the dog had respiratory difficulty by 5 months after exposure, and it grew progressively worse until death. Thoracic radiographs indicated opacity of the

lung with dilatation of the trachea and bronchi. Histologically, radiation pneumonitis was present in the form of fibrinous exudate, necrotic debris, and hemorrhage in alveolar lumina. The lung dose of the dog was estimated to be between 500 and 1300 Gy (50 and 130 krad).

Thomas et al. (1972) exposed rats to a $^{144}\text{CeOH}$ aerosol, with a resultant estimated ILB between 0.07 and 0.47 MBq (1.8 and 12.6 μCi). Based on the data presented, the average ILB of rats that died within a year of exposure was estimated to be approximately 0.14 MBq (3.7 μCi)/g lung. The average cumulative lung dose of animals that died from radiation pneumonitis was 57 Gy (5700 rad). Five rats lived for more than a year after exposure (up to 607 days), and histological examination of their lungs indicated radiation pneumonitis, although two of them also had lung carcinomas. The average lung dose to death of those five rats was 36.6 Gy (3660 rad).

A group of 55 dogs were exposed to $^{144}\text{CeCl}_3$ by Benjamin et al. (1973); lung burdens ranged between 0.7 and 10.7 MBq (2 and 290 μCi)/g lung. This was considered a relatively soluble form of cerium. Eight of the dogs with lung burdens between 0.4 and 1.2 MBq (11 and 33 μCi)/g lung died within 2 months of exposure as a result of severe bone-marrow aplasia. Pulmonary injury was noted in three other dogs that died between 100 and 400 days after exposure. Their ILB were also between 0.4 and 1.2 MBq (11 and 33 μCi)/g lung with lung doses of 80 to 95 Gy (8000 to 9500 rad) as indicated by their data.

The differences in the tissue solubility of the oxide, hydroxide, and chloride forms of cerium preclude comparisons of the data in the three studies discussed above. However, the ILB that caused radiation pneumonitis in the single dog in the study of Stuart et al. (1964) was within the range of that which caused radiation pneumonitis in the three dogs studied by Benjamin et al. (1973). The effective half-lives of the chemical forms of cerium used in the two studies also appeared similar.

Exposure of animals to an aerosol of radionuclides incorporated into fused aluminosilicate (clay) particles (FAP) is a means of circumventing the problems of solubility difference. There have been a number of these experiments with beagle dogs, and the results were summarized in *Publication 31* of the International Commission on Radiological Protection (ICRP, 1980).

Yttrium-90 (FAP) caused death by radiation pneumonitis and pulmonary fibrosis in 38 of 89 exposed dogs within 7 to 463 days of exposure. The ILB of those 38 dogs were between 22 and 193 MBq (590 and 5200 μCi)/kg body weight. With the lung:body weight ratio used by Hahn et al. (1987), this translates to approximately 2 to 18 MBq (54 to 473 μCi)/g lung. Lung doses to death were between 93 and 700 Gy (9,300 and 70,000 rad). Because of the short physical half-life of ^{90}Y , the doses were delivered to the lungs within 9 days of exposure (ICRP, 1980).

Radiation pneumonitis and pulmonary fibrosis affected 40 of 96 dogs exposed to ^{91}Y (FAP) between 113 and 1011 days after exposure. Lung doses between 83 and 600 Gy (8,300 and 60,000 rad) were listed for those 40 animals, resulting from ILB between 0.15 and 1.2 MBq (4 and 33 μCi)/g lung. Most of the dose from ^{91}Y was delivered to the lungs within 6 months of exposure (ICRP, 1980).

Cerium-144 (FAP) caused radiation pneumonitis in 17 of 111 exposed dogs within 143 to 410 days of exposure. The 17 dogs had ILB of 0.14 to 0.7 MBq (3.7 to 19 μCi)/g lung with resultant cumulative lung doses to death between 280 and 1400 Gy (28,000 and 140,000 rad) delivered within 18 months of exposure (ICRP, 1980).

Thirty-three of 106 exposed dogs had radiation pneumonitis as a result of inhaled ^{90}Sr (FAP). The 33 dogs died between 159 and 2373 days after exposure with cumulative lung doses of 400 to 960 Gy (40,000 to 96,000 rad). Their ILB were 0.05 to 0.3 MBq (1.5 to 8.5 μCi)/g lung, delivered within 48 months of exposure (ICRP, 1980).

Data from the experiment with dogs exposed to the FAP aerosols were analyzed by Scott (1980), who derived values for cumulative lung doses necessary to cause radiation pneumonitis in 50% of exposed dogs (D_{50}). Resultant D_{50} values, based on his analyses, were approximately 100 Gy (10 krad) for ^{90}Y , 230 Gy (23 krad) for ^{91}Y , 520 Gy (52 krad) for ^{144}Ce , and 570 Gy (57 krad) for ^{90}Sr . The differences were attributed to the temporal distribution of dose in the lung from the four radionuclides.

Studies of mortality and morbidity caused by beta-emitting radionuclides (FAP) were performed with rats (Scott et al., 1987a). In one study, 200 rats were exposed to an aerosol of ^{147}Pm (FAP) with ILB ranging between 0.07 and 18.5 MBq (2.6 and 685 μCi)/g lung. Approximately 55 of 75 rats with ^{147}Pm (FAP) ILB greater than 7 MBq (189 μCi)/g lung died within a year of exposure. Of the approximately 20 rats with similar ILB that lived longer than a year, approximately half died with radiation pneumonitis; most of the others died with lung tumors. There were very few rats (three) with radiation pneumonitis within a year among those with ILB less than 7 MBq (189 μCi); most of the rats with lesser ILB died with lung tumors. Cumulative lung doses to death were not considered pertinent in that study; instead, cumulative doses to specified times were used. A 365-day lung dose, equivalent to an ILB of 6 MBq (160 μCi)/g lung, was approximately 275 Gy (27,500 rad) based on information the authors provided. This was the ILB shown to cause radiation pneumonitis in 50% of their rats within a year of exposure.

In another series of experiments, Scott et al. (1987b) investigated the effect of temporal distribution of lung dose on radiation-induced pneumonitis in rats. They used ^{90}Sr (FAP), ^{90}Y (FAP), and a mixture of the radionuclides, also FAP, to vary the rate at which the dose was delivered to the lungs.

The ILB of ^{90}Sr that caused radiation pneumonitis within a year of exposure appeared, from their data, to be approximately 1.3 MBq (35 μCi)/g lung. Of the 35 rats with ILB greater than that, 20 died within a year, 1 with a lung tumor and the remainder with radiation pneumonitis. There were 15 rats with ILB greater than 1.3 MBq, which survived more than a year, and 5 of those had radiation pneumonitis; the rest had lung tumors. The D_{50} , in terms of cumulative 365-day dose that resulted in death from radiation pneumonitis within 1.5 years, was listed as 320 Gy (32,000 rad), resulting from an ILB of 1.2 MBq (32 μCi)/g lung.

Radiation pneumonitis within a year of exposure was caused by ILB of ^{90}Y (FAP) of approximately 7.5 MBq (203 μCi)/g lung. Most of the rats with greater ILB died less than 100 days after exposure, all with radiation pneumonitis. They had 11 rats with ILB of approximately 7.5 MBq (203 μCi)/g lung that died between 365 and 540 days after exposure; 5 of those had radiation pneumonitis, 5 had lung tumors, and 1 was euthanized for unstated reasons. A D_{50} 365-day lung dose was given as 190 Gy (19,000 rad), corresponding to an ILB of 10 MBq (270 μCi)/g lung. The aerosol contained primarily ^{90}Y , with 2.3% ^{90}Sr residual from the separation process, therefore the major part of the lung dose was delivered within the first few days of exposure.

The mixture of ^{90}Sr and 25% ^{90}Y (FAP) generally caused death by radiation pneumonitis within a year of exposure if the ILB was greater than 4 MBq (108 μCi)/g lung.

There were, however, a large number of rats (approximately 50) that survived beyond a year of exposure. Fifteen of those had radiation pneumonitis, and 10 had ILB less than 2 MBq (54 μ Ci)/g lung; 7 of the 10 lived past 600 days of exposure. Twenty-nine rats of those that survived more than a year had lung tumors. No lung tumors appeared sooner than 450 days after exposure. The D₅₀ for radiation pneumonitis caused by the inhaled mixture was 290 Gy (29,000 rad; 365-day dose), resulting from the ILB of 4 MBq (108 μ Ci)/g lung.

The most direct comparison of species response to inhaled beta-emitting radionuclides can be made with two of the radionuclides, ⁹⁰Y and ⁹⁰Sr. On the basis of those comparisons, it appears that the lungs of beagle dogs are more sensitive to pneumonitis induced by beta radiation than are the lungs of rats. A report by Hobbs et al. (1972) indicated that lung doses greater than 80 Gy (8000 rad) from ⁹⁰Y (FAP) killed beagle dogs within 200 days of exposure. Other dogs with lung doses up to 60 Gy (6000 rad) were alive up to 450 days after exposure. Scott (1980) calculated an LD₅₀ of 100 Gy (10,000 rad) for dogs of that experiment; however, he included dogs that died later than 400 days after exposure and had radiation pneumonitis. A corresponding LD₅₀ for rats was 190 Gy (19,000 rad; Scott et al; 1987b). The LD₅₀ for rats corresponded to an ILB of 10 MBq (270 μ Ci)/g lung, and the ILB of dogs corresponding to a 100-Gy (10,000-rad) infinite dose to lungs was approximately 0.8 MBq (10 μ Ci)/g lung.

For ⁹⁰Sr (FAP), an ILB in rats that would be expected to cause death within a year is 1.2 MBq (32 μ Ci)/g lung. Corresponding values for beagle dogs were between 0.06 and 0.3 MBq (1.5 and 8.5 μ Ci)/g lung. An average ILB that caused the death of beagle dogs within a year of exposure was 0.2 MBq (5.6 μ Ci)/g lung (Hahn, 1979).

DOSE/MORTALITY MODELS

There is at present no empirically confirmed model dealing with acute mortality resulting from two or more kinds of radiation exposure. When a specific target organ is considered, doses to that organ are added in current models, using appropriate quality (Q) factors, and the total dose is related to the response. When more than one organ is irradiated, the most commonly used model is the independent-effects model, assuming no interaction between organs; for example:

$$\text{Total mortality} = F_1 + (1 - F_1)F_2$$

where

- F₁ = fraction of population with lethal injury to the lung
- F₂ = fraction of population with lethal injury to the bone-marrow.

In this equation, with an expected mortality rate of 20% from either exposure, the total mortality from both competing causes would be 36%. This approach was used in the Nuclear Reactor Safety Study (U.S. NRC, 1975).

RADIATION-INDUCED MORBIDITY

Several forms of radiation-induced acute morbidity have been cited in studies of total-body gamma irradiation, upper-body gamma irradiation, and inhalation of beta-emitting radionuclides. They include: loss of body weight, decreased concentration of circulating blood elements, and radiation pneumonitis.

Body-Weight Changes

Loss of body weight resulting from whole-body exposure to penetrating radiation was reported in rats by Smith and Tyree (1954). Rats that survived 28 days after 800-R (200-kVp) X-ray exposure lost approximately 20% of their weight at exposure during the first 5 days afterward. Thereafter, they gained weight steadily, reaching their initial weight at 10 to 12 days after exposure; by 25 days after exposure, they weighed approximately 25% more than at exposure. Carsten and Noonan (1964) related weight loss in rats to intake of food, which dropped sharply immediately after exposure and returned to normal by the seventh day afterward.

Mongrel dogs that died following exposure to total-body ^{60}Co gamma irradiation (292 to 436 R) lost a mean of 18.2% of their pre-exposure weight. Generally, the dogs with lower exposures survived longer and lost more weight before they died (Shively et al., 1958). Survivors in the same dose ranges did not lose a significant amount of weight, although dogs exposed to 320 to 420 R had lost approximately 4% of their pre-exposure weight by the third and fourth weeks after exposure (Shively et al., 1961). In another study with beagle dogs exposed to ^{60}Co gamma irradiation (213 to 300 rad), maximum weight loss among survivors occurred between 15 and 43 days after exposure, with a mean loss of 8.8%; their weight returned to normal between 40 and 80 days after exposure. The maximum loss in survivors was reportedly 25% (Norris et al., 1968).

Thoracic X-irradiation of rats did not cause a loss of body weight; however, rats exposed to 600 or 1200 R (280-kVp X-rays) gained weight at a slower rate than did the control (unexposed) rats. The differences between exposed and control rats were most pronounced during the first 5 days after exposure and from 2 weeks after exposure, even though the exposed animals generally consumed more food than controls during these times (Kurohara and Casarett, 1972). Beagle dogs exposed to between 1700- and 2125-R (1000-kVp) thoracic X-irradiation also lost weight. Maximum weight loss occurred at 14 days after exposure, with recovery to normal values by 60 days. Although these dogs were observed longer than 60 days, and many subsequently developed radiation pneumonitis, no further mention was made of body weight gain or loss (Michaelson and Schreiner, 1971).

Some of the early studies of animals exposed to aerosols of beta-emitting radio-nuclides indicated loss of body weight after exposure. A dog reported by Stuart et al. (1964) to have died 8 months after inhaling 0.7 MBq (20 μCi)/g lung of ^{144}Ce had lost 40% of its pre-exposure body weight at death. Hobbs et al. (1972) also reported a progressive weight loss in dogs exposed to ^{90}Y (FAP). In their studies with rats, Scott et al. (1987b, 1988) indicated reduced weight gain as a result of inhaled ^{90}Y (FAP), ^{90}Sr (FAP), and ^{147}Pm (FAP). Even though their data indicated a weight loss in rats with high ILB of ^{90}Y (FAP), they stated that the loss, or reduced gain, was associated with the induction of pulmonary injury (Scott et al, 1987b). One of their studies (Scott et al, 1988) indicated that ^{238}Pu (FAP), an alpha-emitter, slightly inhibited weight gain, while ^{147}Pm (FAP) did not have a similar effect.

Hematologic Changes

The major morbid effect of total-body gamma- or X-irradiation is depletion of circulating blood elements, such as erythrocytes, lymphocytes, granulocytes, and thrombocytes (platelets), caused by loss of stem-cell reproductive capability in bone marrow and lymph nodes. This effect is generally not lethal unless an infection (result-

ing from depression of leukocyte concentrations) is allowed to progress and/or internal bleeding results from reduced numbers of platelets. In the absence of infections, the subject (human or animal) recovers, with eventual regeneration of stem-cell reproductive activity (Bond et al., 1965).

Radiation-induced hematologic changes in mammals are qualitatively similar. Quantitative comparisons between species are difficult to make using published data because of differences in radiation doses, dose rates, and quality. In general, the concentration of circulating erythrocytes is lowest between 14 and 21 days after exposure, decreasing to approximately 75% of normal in gamma-irradiated beagle dogs, and gradually returning to normal values by 80 days after exposure (Norris et al., 1968). Anemia caused by external gamma-ray exposure is considered less critical than is depletion of the blood elements such as granulocytes, lymphocytes, and platelets (Bond et al., 1965). Granulocytes are depleted more rapidly than erythrocytes and reach minimal concentrations (5 to 15% of normal) within a few days of exposure. In rodents, lowest levels occur within 2 to 3 days of exposure; this is followed by a plateau of 1 to 2 weeks and, in survivors, normal values are reached by approximately 30 days after exposure (Carsten and Noonan, 1964; Ainsworth and Mitchell, 1968). In dogs, minimal concentrations occur after 2 to 3 weeks, with higher-than-normal values recorded by 5 to 6 weeks after exposure (Norris et al., 1968; Ainsworth and Mitchell, 1968). Concentrations of circulating lymphocytes decrease sharply after exposure to minimal levels (between 0 and 10% of normal) within 1 to 3 days in both dogs and rodents (Carsten and Noonan, 1964; Ainsworth and Mitchell, 1968). They usually remain at low levels for 1 to 2 weeks before a gradual increase in numbers is observed. Reported concentrations of lymphocytes, relative to normal values, in different species exposed to nearly lethal radiation doses include 44% at 42 days and 70% at 73 days after exposure in mice (Ainsworth and Mitchell, 1968), 70% at 27 days in rats (Carsten and Noonan, 1964), 35% at 36 days in dogs (Ainsworth and Mitchell, 1968) and 40% at 85 days, also in dogs (Norris et al., 1968). Blood platelet concentrations are at lowest levels between 2 and 3 weeks after exposure and generally reach normal values by 4 to 5 weeks after exposure. Death from bone-marrow radiation syndrome is associated with bacterial infection that is allowed to progress because of depleted circulating leukocytes and hemorrhage that is precipitated by the severely depressed blood platelet concentrations. The role of either event in lethality is quite species-specific, as is the degree of damage caused by a given radiation dose (Bond et al., 1965).

Hematologic effects were noted in early experiments with inhaled, relatively soluble forms of beta-emitting radionuclides. Animals died relatively early (within 2 months of exposure) as a result of bone-marrow aplasia (Benjamin et al., 1973). This has not generally been reported as an effect of inhalation of less soluble aerosols, although another hematologic change, lymphocytopenia, has been noted. Lymphocytopenia is a hematologic effect consistently reported from studies of animals with plutonium ILB, regardless of whether or not they developed radiation pneumonitis (Ragan et al., 1976).

Stuart et al. (1964) reported lymphocytic depression in all dogs studied after exposure to $^{144}\text{CeO}_2$ aerosols. They observed that the severity of depression was directly related to ILB. Hobbs et al. (1972) noted lymphocytopenia in beagle dogs exposed to ^{90}Y (FAP). It was also dose-dependent in those dogs, but with ILB less than 0.6 MBq (17 μCi)/g lung, numbers of circulating lymphocytes were back to normal within a month of exposure. With ILB greater than 3.4 MBq (91 μCi)/g lung, values remained at 50% or less of the pre-exposure values up to 9 months after exposure.

The data of Scott et al. (1987b) indicate depressed lymphocyte concentrations in circulating blood of rats at 7 and 14 days after inhalation of ^{90}Y (FAP). By 30 days after exposure, however, values had returned to normal. According to the same report, there was very little perturbation of lymphocyte concentration in rats that had inhaled ^{90}Sr (FAP) or ^{90}Y plus 25% ^{90}Sr (FAP). Promethium-147 (FAP) caused lymphocytopenia similar to that caused by ^{90}Y (FAP) but, again, values were back to normal by 30 days after exposure. Lung burdens of ^{147}Pm (FAP) that caused lymphocytopenia were in the range of 1.6 to 13.6 MBq (43 to 368 μCi)/g lung (Scott et al., 1987b).

Pulmonary-Function Impairment

Much effort has been expended to quantitate functional impairment of lungs by radiation pneumonitis as it develops from inhaled radioactive materials as well as from upper-body X- or gamma-irradiation. Because of the wide variety of measurement techniques, this discussion will be limited to subjective evaluations, with no attempt made to compare results quantitatively.

In a study of 15 humans who received thoracic radiation therapy for breast or lung carcinomas, lung volume measurements, such as inspiratory capacity (IC), vital capacity (VC), residual volume (RV), and total lung capacity (TLC), were reduced as radiation pneumonitis progressed. The tidal volumes (V_T) decreased, and respiratory rates (RR) increased, with a corresponding increase in minute volumes (V_m). The increase in V_m , however, was considered to be caused by an increased ratio of physiological dead space to V_T , with no change in alveolar ventilation, because there was no change in the carbon-dioxide tension of arterial blood (Emirgil and Heinemann, 1961). Two other manifestations of radiation pneumonitis were measured in those patients: reduced carbon-monoxide diffusing capacity (DL_{CO}), a measure of the effectiveness of air-to-blood gas transfer; and decreased lung compliance (C_L), a measure of the "stiffness" of lungs. The decrease in DL_{CO} was greatest between 50 and 100 days after exposures, and the reduction in C_L was also greatest in the first 100 days. The changes were considered irreversible in patients with bilateral lung irradiation, although DL_{CO} did improve with time in those patients with only one irradiated lung.

Many of the same pulmonary-function parameters have been measured in dogs exposed (upper-body) to X- or gamma-radiation. Functional residual capacity (FRC), DL_{CO} , and C_L were found to decrease progressively after 3000 to 4800 R of 260-kVp X-ray exposure, given in increments of 200 to 300 R/week. The most obvious changes occurred approximately 3 months after exposure (Sweany et al., 1959). In another study, dogs received unilateral, thoracic, 200-kVp X-irradiation (4500 R over 23 to 27 days), and pulmonary function was tested in each lung of each dog. Comparing irradiated with nonirradiated lungs indicated a radiation-induced reduction of IC and C_L , with an associated decrease in V_m ; these changes became apparent within 2 months of exposure. DL_{CO} was also reduced, although there was an initial (within 3 weeks of exposure) increase in diffusing capacity of the irradiated lung. An explanation for the transient increase involved increased capillary surface area and capillary volume, resulting from hyperemia, an acute stage of inflammation (Teates, 1965).

Lung compliance, the change in lung volume per unit pressure (ml or L/cm H_2O pressure) is a measure of the distensibility of the lungs and, as such, is the favored technique for measuring the degree of radiation-induced pulmonary fibrosis. In a study of beagle dogs that received 12.5 Gy (1250 rad) of thoracic ^{60}Co gamma-irradiation,

C_L was significantly reduced by 10 weeks after exposure and was reduced still further by 3 months after exposure (Tyree et al., 1966).

The same pulmonary-function parameters used to detect damage induced by thoracic X- and gamma-irradiation have been used to characterize functional impairment induced by inhaled radionuclides. Studies of beagle dogs with lung burdens of beta-particle-emitting radionuclides indicated that C_L and DL_{CO} were sensitive indications of radiation-induced fibrosis and loss of alveolar gas-exchange capacity, respectively (Mauderly et al., 1973; 1980a). Two other tests were used in those studies: 1) the multiple-breath nitrogen washout (MBN_2), which was used to generate a lung clearance index (LCI), and nitrogen (N_2) dilution constant; and 2) specific ventilation, ml of V_m required for each ml O_2 consumption, measured while dogs were on a treadmill run at 4.5 mph. The latter two tests were considered valuable in characterizing the progression of radiation pneumonitis but did not correlate well with histologic changes observed after the deaths of the dogs. The functional index that best correlated with those changes was lung compliance. The dogs had relatively high lung burdens: sufficient ^{90}Y to kill most of the dogs within a year of exposure and enough ^{144}Ce to kill many of them within 2 years (Mauderly et al., 1973; 1980a).

The progress of radiation pneumonitis, as indicated by pulmonary-function measurements, was compared in dogs that inhaled aerosols of 1.5- μm monodisperse $^{238}PuO_2$ and polydisperse ^{144}Ce in FAP (Mauderly et al., 1980b). For dogs with lung burdens of $^{238}PuO_2$, the altered breathing pattern previously described (Lustgarten et al., 1976) first appeared at 500 days (mean) after exposure. Decreased C_L , changes in N_2 washouts, and reduced DL_{CO} occurred 674 days (mean) after exposure. Pulmonary insufficiency, as indicated by the alveolar-arterial PO_2 gradient, first appeared at 812 days after exposure. Using the stated mean initial dose rate for the whole lung and the stated effective half-life in the lung (Mauderly et al., 1980b), the estimated cumulative lung dose for the dogs is between 40 and 45 Gy (4000 and 4500 rad) at 500 days, and approximately 50 Gy (5000 rad) at 674 days.

The progression of pulmonary-function changes was different in dogs that inhaled ^{144}Ce (FAP). The altered breathing patterns, changes in C_L , and reduced DL_{CO} occurred sooner and nearly simultaneously (325-day mean postexposure time). Changes in gas distribution occurred only in the later stage of radiation pneumonitis (572 days after exposure).

Differences in the progression of lung changes in the two groups of dogs were attributed to two major factors: 1) the initial lung dose rate with ^{144}Ce (FAP) was nearly 20 times that for $^{238}PuO_2$, and 2) a much smaller fraction of the total lung was irradiated by the monodisperse $^{238}PuO_2$ than by the polydisperse ^{144}Ce (FAP). Fractions of lung irradiated were reported to be 6 and 100%, respectively, for ^{238}Pu and ^{144}Ce (Mauderly et al., 1980b).

Pulmonary-function testing of rodents has developed more slowly; published reports generally deal with animals exposed to inhaled toxicants other than radioactive materials. A review of techniques for use with five species of rodents was made by Likens and Mauderly (1979) and included tables of data acquired by them and others. The data acquired from various laboratories were considered only qualitatively comparable because of differences in techniques and equipment used.

Among the first efforts to relate diminished lung function with radiation was an experiment by Travis et al. (1979, 1980). They used a whole-body plethysmograph

to measure breath rate and amplitude in mice that had been thoracically irradiated. A dose-dependent response was determined (decrease in amplitude and increase in frequency) within 16 weeks after doses above 11 to 12 Gy (1100 to 1200 rad). Increased frequency, noted between 14 and 24 weeks after exposure, corresponded with radiation pneumonitis, determined by histological evaluations. At doses of approximately 14 Gy (1400 rad), values were returning to normal in animals that survived. However, at higher doses, there was a steady increase in frequency until death. It was concluded that the increased frequency after the onset of pulmonary fibrosis reflected decreased compliance of the lungs, although compliance was not directly measured (Travis et al., 1980).

Many of the same respiratory-function tests used with dogs have been adapted for use with rats. Pressure-volume (P-V) curves obtained by inflation and deflation of rats' lungs to predetermined pressure at slow rates (usually 1 to 5 ml/second) can be used to determine divisions of lung volumes such as IC and VC as well as quasistatic compliance (C_{QS}). Recently, these have been used to demonstrate the effects of anesthetics (Mauderly and Likens, 1979), pure oxygen (Harkema et al., 1982), oxidant gases (Mauderly, 1984), starvation, and intratracheally instilled elastase (Harkema et al., 1984), injected 4-ipomeanol (Sabo et al., 1983), mineral dusts (Hatch et al., 1984), diesel engine exhaust (Mauderly et al., 1983), and ammonium sulfate and ammonium nitrates (Loscutoff et al., 1985). The DL_{CO} was considered a sensitive indicator of pulmonary impairment in the same studies.

The use of N_2 washout tests in rodents has been less frequently reported. However, single-breath nitrogen washout (SBN_2) tests were used to evaluate the effects of elastase and histamine (Likens and Mauderly, 1982) and ammonium sulfate and ammonium nitrate (Loscutoff et al., 1985) in rat lungs. The MBN_2 tests were used in the study of mineral dusts (Hatch et al., 1984), which included Mount St. Helen's ash and silica dust.

Scott et al. (1987b) performed pulmonary-function tests on rats exposed to ^{90}Y (FAP) and ^{90}Sr (FAP). Relating DL_{CO} to dosimetric parameters, they concluded that only sublethal lung doses delivered at high dose rates over a short time, such as those from ^{90}Y (FAP), led to impaired pulmonary function. Doses as low as 150 Gy (15,000 rad; 65% of the median lethal dose) could cause functional impairment. Rats exposed at lower dose rates and over a long period of time would likely have pulmonary-function impairment but would eventually die from radiation pneumonitis.

In another investigation, Scott et al. (1988) performed pulmonary-function tests on rats 1.5 years after exposure to aerosols of ^{147}Pm and found reduced VC, diminished DL_{CO} , increased slopes of the alveolar plateau of the SBN_2 , and decreased C_{QS} . They estimated the ILB_{50} (lung burden at which 50% of the rats showed impairment of three of the four parameters) to be 1.5 MBq (40 μCi)/g lung. That corresponded to a 1.5-year lung dose of approximately 75 Gy (7500 rad). Median lethal lung burdens in that same study were 6.0 MBq (160 μCi)/g lung, resulting in lung doses of 300 Gy (30,000 rad). Of the four pulmonary-function parameters measured, their data did not indicate any single parameter to be a more sensitive indicator of radiation pneumonitis than any other.

OBJECTIVES

The general objective of this research was to provide data to derive and verify a model to predict acute morbidity and mortality in laboratory animals from combined radiation exposures. "Acute" effects are defined as those that occur within 1 year of exposure in the two organ systems that were of primary interest: the respiratory system and the bone marrow.

The experiment was designed so that three specific objectives could be fulfilled:

1. To determine the effect of total-body gamma irradiation and/or inhalation of beta-emitting, insoluble aerosol of ^{147}Pm in FAP on acute mortality of laboratory animals
2. To determine the extent of acute morbidity induced in laboratory animals by total-body gamma irradiation and/or inhalation of ^{147}Pm (FAP). Measurement of morbidity included results of pulmonary-function testing, determining hematologic changes, and monitoring changes in body weight.
3. To investigate the validity of models in which the effects of each kind of radiation are added to predict the effect of both radiation results combined

Promethium-147 was the radionuclide used for inhalation exposures because it emits relatively low energy beta radiation. Thus, there would be little or no cross-organ irradiation, and the effects would be confined to the lung.

MATERIALS AND METHODS

EXPOSURE

Fischer-344 (F-344) rats (Charles River Laboratories, Kingston, NY) were randomly assigned to groups and exposed to ^{60}Co gamma radiation and/or an aerosol of ^{147}Pm (FAP) as shown in Table 1. All rats were approximately 15 weeks of age at exposure. Numbered metal tags were attached to each rat (one in an ear and one in the dorsal skin of the neck) for positive identification throughout the experiment.

TABLE 1. Experimental Design for Exposure of Rats to Total-Body ^{60}Co Gamma Irradiation and/or an Aerosol of ^{147}Pm (FAP)

^{147}Pm (FAP) Exposure		^{60}Co Gamma Exposure			
		0	Low	Medium	High
0	Group number	21	22	23	24
	Number of rats	60	30	60	30
	Pulmonary-function testing	60		60	
	Hematologic testing	30		30	
Low	Group number	25	26	27	28
	Number of rats	35 ^a	70	35	35
	Pulmonary-function testing		70		
	Hematologic testing		35		
Medium	Group number	29	30	31	32
	Number of rats	70 ^b	35	35	35
	Pulmonary-function testing	70			
	Hematologic testing	35			
High	Group number	33	34	35	
	Number of rats	35	35	35	
Medium-High	Group number		39		
	Number of rats		35		

^aFive of each group of 35 rats exposed to ^{147}Pm (FAP) were killed after the 5-day whole-body count

^bTen of each group of 70 rats exposed to ^{147}Pm (FAP) were killed after the 5-day whole-body count

The low, medium, and high gamma-radiation exposures listed in Table 1 correspond to the LD_{20/30}, LD_{40/30}, and LD_{60/30}, respectively. These values were previously determined by graded exposures of groups of rats, which resulted in the mortality curve of Figure 1. The ILB of ^{147}Pm (FAP) were intended to correspond to the LD_{20/200}, LD_{40/200}, and LD_{60/200} for the low, medium, and high exposures, respectively. These were based on dose/mortality data from previous experiments (Hahn et al., 1987; personal communication) at ITRI, Albuquerque, NM.

The experiment was designed as a 4 x 4 matrix (Table 1), with certain modifications; for example, Groups 21, 23, 26, and 29 contained twice as many rats as the other groups. This was done because mortality was expected to be approximately equal within Groups 23, 26, and 29 if the effects of the two kinds of radiation exposure were equal, and larger numbers were desired to increase statistical validity. Also, at the indicated position within the matrix, an additional 60 to 70 rats were exposed for evaluation of pulmonary function, and an additional 30 to 35 rats were exposed for blood sampling and hematologic examination. The reason for including these animals was that blood sampling might affect mortality, and because rats subjected

to lung-function tests were killed immediately after testing. These tests will be discussed in detail later in this report.

FIGURE 1. Mean Mortality Fraction (with 95% Confidence Limits) of Fischer-344 (F-344) Rats Exposed to Graded Doses of ^{60}Co Gamma Radiation

Exposure to gamma radiation was accomplished with a 12,000-Ci ^{60}Co source (Gammabeam 650, Atomic Energy of Canada, Ltd.). Rats were confined to cylindrical, high-impact polystyrene tubes; the main body of the tube had an outside diameter (OD) of 5.7 cm and was 11.5 cm in length. The head end of each tube was conical, decreasing to 2.7 cm over a 6.4-cm length, and the end containing the nose of the rat was 2.7 cm OD x 1.6 cm in length. The wall thickness of the entire tube was 3.2 mm. Tubes containing the rats were placed (nose upward) on a horizontal arc 270 cm from the radiation source, with the ventral side of the rats facing the source. The dose rate along this arc was measured before exposures with ionization chambers traceable to the U.S. National Bureau of Standards (NBS) and, during exposures, with thermoluminescent dosimeters (TLD). Data collected by TLD were used only as verification of doses on the arc during each exposure session. The exposure rate was between 22 and 26 rad/minute, depending on the time exposure was performed; the rate varied along the arc by 2 to 3%. Exposure times were varied to achieve the required doses, listed in Table 2.

Immediately (within 1 hour) after gamma irradiation, the nose ends of the containment tubes were inserted into a central aerosol chamber, and the rats were exposed to an aerosol of ^{147}Pm (FAP) as described below.

The inhalation exposures of rats were performed using the flow-past nose-only exposure system described by Cannon et al. (1983). The animals, in the containment tubes, were inserted into the central aerosol chamber for inhalation exposure to the

radioactive aluminosilicate aerosol. Three of the exposure ports at the top, center, and bottom tiers of the chamber were occupied by filter samplers operating at flow rates of approximately 0.1 L/min while a cascade impactor (Mercer et al., 1970), drawing a sample flow of approximately 0.15 L/min, occupied a port in the next to the bottom tier. The chamber exhaust was filtered by three HEPA filters in series as was the exhaust air from the glove boxes containing the generation and exposure equipment.

TABLE 2. Mean ^{147}Pm (FAP) Initial Lung Burdens (ILB) with Ranges of Values for each Group of Rats Exposed to ^{147}Pm (FAP) With or Without ^{60}Co Gamma Irradiation ($\pm$ = Standard Deviation)

	^{60}Co Gamma Exposure (Total Body)			
	0	Low (850 rad or 8.5 Gy)	Medium (890 rad or 8.9 Gy)	High (915 rad or 9.2 Gy)
Group number	25	26	27	28
Total ^{147}Pm (FAP) ILB range, both sexes	115-232 ^a (4.3-8.6) ^b	7-319 (0.3-11.8)	6-272 (0.2-10.1)	25-281 (0.9-10.4)
Mean ^{147}Pm (FAP) ILB/g lung, males	85 $\pm$ 13 (3.1 $\pm$ 0.5)	85 $\pm$ 31 (3.1 $\pm$ 1.1)	68 $\pm$ 31 (2.5 $\pm$ 1.1)	95 $\pm$ 29 (3.5 $\pm$ 1.1)
Mean ^{147}Pm (FAP) ILB/g lung, females	105 $\pm$ 20 (3.9 $\pm$ 0.7)	109 $\pm$ 25 (4.0 $\pm$ 0.9)	94 $\pm$ 18 (3.5 $\pm$ 0.7)	95 $\pm$ 29 (3.5 $\pm$ 1.1)
Group number	29	30	31	32
Total ^{147}Pm (FAP) ILB range, both sexes	214-620 (7.9-23.0)	7-487 (0.3-18.0)	60-397 (2.2-14.7)	177-387 (6.6-14.3)
Mean ^{147}Pm (FAP) ILB/g lung, males	186 $\pm$ 52 (6.9 $\pm$ 1.9)	147 $\pm$ 55 (5.4 $\pm$ 2.0)	112 $\pm$ 48 (4.1 $\pm$ 1.8)	136 $\pm$ 21 (5.0 $\pm$ 0.8)
Mean ^{147}Pm (FAP) ILB/g lung, females	225 $\pm$ 65 (8.3 $\pm$ 2.4)	186 $\pm$ 47 (6.9 $\pm$ 1.7)	156 $\pm$ 30 (5.8 $\pm$ 1.1)	159 $\pm$ 26 (5.9 $\pm$ 1.0)
Group number	33	34	35	
Total ^{147}Pm (FAP) ILB range, both sexes	89-610 (3.3-22.6)	221-694 (8.2-25.7)	309-713 (11.4-26.4)	
Mean ^{147}Pm (FAP) ILB/g lung, males	215 $\pm$ 45 (8.0 $\pm$ 1.7)	199 $\pm$ 70 (7.4 $\pm$ 2.6)	267 $\pm$ 60 (9.9 $\pm$ 2.2)	
Mean ^{147}Pm (FAP) ILB/g lung, females	310 $\pm$ 94 (11.5 $\pm$ 3.5)	285 $\pm$ 48 (10.6 $\pm$ 1.8)	273 $\pm$ 40 (10.1 $\pm$ 1.5)	
Group number		39		
Total ^{147}Pm (FAP) ILB range, both sexes		166-531 (6.1-19.7)		
Mean ^{147}Pm (FAP) ILB/g lung, males		190 $\pm$ 34 (7.0 $\pm$ 1.3)		
Mean ^{147}Pm (FAP) ILB/g lung, females		205 $\pm$ 54 (7.6 $\pm$ 2.0)		

^aMicrocuries

^bMegabecquerels

A suspension of Montmorillonite clay, obtained from ITRI, was spiked with ^{147}Pm at 1.036×10^{10} Bq (280 mCi)/ml by cation exchange. A small amount of ^{137}Cs -spiked clay was added to give a ratio of 1:10,000 ^{137}Cs : ^{147}Pm in the suspension. The ^{137}Cs was added to facilitate whole-body counts. The mass concentration of the original clay suspension was 20.3 mg/ml. The clay suspension was diluted to an activity concentration of 6.845×10^9 Bq (185 μCi)/ml before generating exposure aerosols. Prior

to aerosol generation, the suspension was ultrasonicated for several minutes and stirred to prevent the clay from settling out.

With a Lovelace nebulizer, an aerosol of clay containing the two radionuclides was generated into an air stream of approximately 1.5 L/min and immediately passed through a 1-in. (2.54-cm)-diameter quartz tube in a horizontal tube furnace, which was heated to a temperature of 1150°C at the outer wall of the tube. As the clay particles reached 500°C inside the furnace, the water of crystallization was driven off, and the attached radionuclides were fixed in the lattice of the clay. As the particles reached approximately 1000°C, the clay particles fused into aluminosilicate ceramic spheres, firmly fixing the ^{137}Cs and ^{147}Pm . When the aerosol emerged from the furnace, it cooled to near room temperature as it was diluted to a 10 L/min flow rate and transported to the aerosol exposure chamber via 0.95-cm (3/8-in.) copper line.

The aerosol generator was turned off after 5 minutes of generation and, after a 1-minute chamber clearing time, the three filter samplers were changed. The ^{137}Cs gamma activity on the 5-minute filters was analyzed immediately, and the concentration of ^{147}Pm in the aerosol was determined by calculation. Based on the aerosol concentration during the first 5 minutes, the additional exposure time was that required to assure that the rats received the desired ILB of ^{147}Pm . After exposure, the filter samplers and cascade impactor were removed, and those samples were analyzed for gamma activity.

As data from exposed rats became available, we calculated the factor relating activity deposition in the rats to the product of average aerosol concentration and duration of exposure. This factor, called the effective V_m , was used to estimate the aerosol concentration and exposure duration needed to achieve the target ILB for subsequent exposures.

The average chamber concentration varied from 18 MBq (483 μCi)/L to 44 MBq (1200 μCi)/L, with a mean of 27.6 MBq (747 μCi)/L and a standard deviation (SD) of 10 MBq (268 μCi)/L. The activity mean aerodynamic diameter (AMAD) and the geometric standard deviation (GSD) for each exposure were determined from cascade impactor data. They were $1.59 \pm 0.29 \mu\text{m}$ for AMAD and 1.81 ± 0.1 for GSD.

Because of the very high mortality rate of rats from Groups 25 through 39 within the first 150 days after exposure, we concluded that their body burdens of promethium were too large. It was evident, at that time, that there would not be enough survivors to provide meaningful mortality or morbidity data to the end of the 365-day experiment. More rats were procured from the same source, and Groups 41, 43, 46, and 49 (Table 3) were exposed by the same methods as Groups 21, 23, 26, and 29, respectively, but with lower ILB. Additional rats were also exposed for pulmonary-function testing.

With two exceptions, exposure conditions were identical for the first and second series of exposures. The ^{60}Co gamma radiation source used for the previous exposures was out of order, so another source was used. The alternative was a 5000-Ci source located in a building approximately 0.5 miles from the building in which the aerosol exposures were done. It was assembled onsite for the purpose of calibrating thermoluminescent dosimeters (TLD) so its beam characteristics were well known. Rats were exposed (35 rats at each time) in a three-tier wooden shelf 160 cm distant from the source. The dose rate was 30 R/min, and sufficient test expo-

tures were conducted to ensure that all rats received equivalent doses. As before, TLD were placed with the rats during exposures as a dosimetry check.

TABLE 3. Mean ^{147}Pm (FAP) Initial Lung Burdens (ILB) with Ranges of Values for Additional Groups of Rats Exposed to ^{147}Pm (FAP) With or Without ^{60}Co Gamma Irradiation ($\pm$ = Standard Deviation)

	^{60}Co Gamma Exposure (Total Body)			
	0	Low (850 rad or 8.5 Gy)	Medium (890 rad or 8.9 Gy)	High (915 rad or 9.2 Gy)
Group number/(number of rats)	41(53)		43(59)	
Total ^{147}Pm (FAP) ILB range, both sexes	0		0	
Mean ^{147}Pm (FAP) ILB/g lung, males	0		0	
Mean ^{147}Pm (FAP) ILB/g lung, females	0		0	
Group number/(number of rats)		46(59)		
Total ^{147}Pm (FAP) ILB range, both sexes		74-250 ^a (2.7-9.3) ^b		
Mean ^{147}Pm (FAP) ILB/g lung, males		61 $\pm$ 23 (2.3 $\pm$ 0.9)		
Mean ^{147}Pm (FAP) ILB/g lung, females		72 $\pm$ 18 (2.7 $\pm$ 0.7)		
Group number/(number of rats)	49(54)			
Total ^{147}Pm (FAP) ILB range, both sexes	105-293 (3.9-10.9)			
Mean ^{147}Pm (FAP) ILB/g lung, males	98 $\pm$ 25 (3.6 $\pm$ 0.9)			
Mean ^{147}Pm (FAP) ILB/g lung, females	133 $\pm$ 46 (4.9 $\pm$ 1.7)			

^aMicrocuries

^bMegabecquerels

Aerosol exposure chamber concentrations for the second exposure were: 29.5 MBq (527 μCi) $\pm$ 4 MBq (104 μCi)/L. The mean and SD of the AMAD were 0.99 $\pm$ 0.085 and 1.8 $\pm$ 0.024 for GSD, respectively. The particle sizes were slightly smaller, and the chamber concentrations were slightly lower than those of the first exposure.

For both series, rats were housed in solid-bottom cages with wood-shavings bedding following exposure. At approximately 13 weeks after exposure, when fecal concentration of promethium had subsided, the rats were transferred to wire-bottom cages for the duration of the experiment. They were housed five rats/cage and fed Wayne Lab Blox rat chow (Wayne Pet Food Division, Continental Grain Co., Chicago, IL) and purified and filtered water *ad libitum*. Rooms were maintained on a 12-hour light/dark cycle. Control rats were "sham-exposed" by confining them in the containment tubes for a period of time similar to that required for gamma irradiation and inhalation exposure.

DOSIMETRY

The total-body radiation dose for rats was estimated from the gamma exposure, using information reported by Sinclair (1963) and by NBS Handbook 85 (1964).

Sinclair proposed a rad/R conversion factor of 0.885 with rats confined in 5-cm-diameter tubes (5.7-cm-diameter tubes were used in these exposures). The NBS Handbook 85 indicated an f-factor of 0.96 and a tissue-absorption factor of 0.91 for a combined rad/R factor of 0.874. Thus, average midline absorbed radiation doses of 8.5, 8.9 and 9.2 Gy (850, 890, and 915 rad) were estimated from exposures of 970, 1015 and 1045 R, respectively.

In vivo determination of promethium body burdens was accomplished by whole-body counting (gamma emissions of the ^{137}Cs tag) with a modified version of the instrumentation described by Swinth et al. (1967) and Swinth and Griffin (1970). Rats were confined in 1-quart (0.95 L), paper, ice-cream cartons and placed between two arrays of radiation detectors, each consisting of 13 photomultiplier tubes behind 4.4-cm- (1.75-in.-) diameter, 1-mm-thick, sodium iodide crystals. Frozen rat carcasses with known ^{147}Pm sources with the ^{137}Cs tag implanted in their thoracic cavities were used as standards. Determinations of the body burden of each rat were made at 5 days after exposure, and at 14, 28 and 56 days after exposure (or as long as the rat lived), with a final count at 1 year after exposure. Detailed methods of determining ILB and lung doses are discussed in Appendix A.

BODY-WEIGHT DETERMINATION

Rats were weighed prior to exposure and every 2 weeks after exposure for 52 weeks. This was done with a small-animal balance (Toledo Model 3165), interfaced to a Texas Instruments (TI700) terminal, which recorded the weights on magnetic tape for future input to the main-frame computer (VAX 11-780; Digital Equipment Corporation). All rats were also weighed prior to necropsy if they were killed or had died between scheduled measurements.

PULMONARY-FUNCTION TESTS

Four groups of rats (60 rats/group; 30 males and 30 females) were exposed to gamma radiation and/or ^{147}Pm (FAP) specifically for pulmonary-function testing; the groups are listed in Table 1. The testing regimen included a P-V maneuver, and SBN_2 , DLCO and MBN_2 tests. Tests were made at 60, 100, 130, 210, 270 and 360 days after exposure. The original plan was to test five males and five females of each group each time, but mortality within some groups required modification of the numbers tested.

Additional control rats and rats exposed to gamma radiation were tested at 370 days after exposure; these were the rats exposed for pulmonary-function testing that had survived to the end of the experiment. Rats initially exposed to promethium and/or gamma radiation for the mortality experiment that had survived for 1 year were also tested for pulmonary function just before the final sacrifice. That included rats from Groups 26 and 46 (promethium plus gamma) and from Groups 29 and 49 (promethium only). Because these rats were housed and otherwise treated identically to those exposed for pulmonary-function testing, they were used to provide greater numbers from which to assess pulmonary impairment at 1 year after exposure.

Each rat was anesthetized with an intraperitoneal (IP) injection of 1 ml/kg body weight of pentobarbital sodium (50 mg/ml, Nembutal®, Abbott Laboratories). The trachea was exposed by an incision in the ventral neck and was cannulated with polyethylene tubing (2.0 mm inside diameter; ID). The rat was placed in a supine

position on a concave tray and the esophagus was cannulated, through the mouth, with polyethylene tubing (1.5 mm ID) filled with water and positioned to provide an optimal transpulmonary pressure (Ptp) signal. An IP injection of 0.1 ml succinylcholine chloride (20 mg/ml, Sucostrin®, Squibb) was administered for paralysis of respiratory musculature. The rat was then sealed into a whole-body plethysmograph, with the esophageal cannula inserted through the cover plate, and the tracheal cannula connected to a port through the cover plate. The animals were artificially ventilated with a Harvard Model 681 rodent respirator until the testing regimen was begun and also between tests.

The esophageal cannula was connected to a Statham P-37B differential pressure transducer (± 2 cm H₂O) connected to a Validyne CD-90 demodulator. A "tee" junction at the point where the airway port passed through the door of the plethysmograph allowed monitoring of airway pressure by means of a Validyne MP-45 differential pressure transducer connected to a Validyne CD-19 demodulator. Signals from the CD-90 and CD-19 demodulators were subtracted by a signal conditioner (manufactured in-house), resulting in the Ptp, which was displayed on a Nicolet Explorer 1 digital oscilloscope and recorded by a Hewlett-Packard (HP7046B) X-Y-Y plotter.

The rat was sealed within a two-chamber, equalized plethysmograph (volume of each chamber = 2.3 L), and each chamber had a 2.54-cm-diameter opening, covered with three layers of 400-mesh stainless-steel screen. A differential pressure transducer (Setra Systems, Model 239E) mounted between chambers was used to measure the pressure differential between chambers, which corresponded to the flow of air into and out of the lungs as they were inflated or deflated. The signal from the Setra 239E was processed by a preamplifier (Calex 176), displayed on the oscilloscope, and integrated by a Validyne FN156 integrator to indicate the volume of air used to inflate and deflate the lungs of the rat.

For the P-V maneuver and the SBN₂, the airway port was disconnected from the rodent respirator and connected to an automatically regulated air/vacuum/ oxygen supply. This apparatus inflated the lungs to 25 cm H₂O Ptp (TLC), at which time relays switched the system to a deflation mode. At -10 cm H₂O Ptp (RV), relays switched the system back to the inflation mode, then repeated the cycle. Audible signals were also activated at each end of the P-V curve. Both inflation and deflation were at 2.5 ml/sec. After four or five cycles to establish a constant-volume history, the P-V curves for both inflation and deflation were traced by the X-Y-Y plotter. Near the end of deflation of the second P-V curve, the air supply was switched (by a solenoid valve) to pure oxygen, and a Hewlett-Packard 47302A N₂ analyzer was activated. This resulted in simultaneous tracing of a third P-V curve and the SBN₂ curves by the X-Y-Y plotter. After this test, rats were reconnected to the respirator for a short period of time while preparations were made for the next test, DL_{CO}.

The VC, estimated from the P-V curves, was the volume of test gas used for testing DL_{CO}. Three syringes (A, B and C; Figure 2) were used in the process. Syringe B was filled to the desired volume with the test gas, which consisted of 0.5% carbon monoxide and 0.5% neon in breathing air (primary standard; Matheson Gas Products). When the end of the apparatus was connected to the airway port, Syringe A was used to withdraw air from the lungs to RV (-10 cm H₂O Ptp), as indicated by an audible signal from the monitoring system. The bolus of test gas was injected into the lungs and held there for 10 seconds. At the end of that time, the first few milliliters of the bolus were withdrawn into Syringe B, and the remainder of the sample was

drawn into Syringe C. The sample from Syringe C was injected into a Carle AGC-III gas chromatograph, in two separate fractions if the volume was sufficient. The monitoring system was set to provide a time-volume trace on the X-Y-Y plotter. Again, the rat was artificially ventilated until the final test (MBN₂) was begun.

FIGURE 2. Syringe Apparatus for Carbon Monoxide Diffusing Capacity Measurements on Rats

To perform the MBN₂ test, the respirator was momentarily disconnected from the airway port, and a valve was opened to provide pure O₂ to the respirator intake for 10 cycles of the respirator. This assured that all atmospheric N₂ was cleared from the apparatus. The respirator was then reconnected to the airway port, and the monitoring system was set to trace the N₂ concentration in each breath as it was withdrawn by the respirator. This procedure was allowed to continue until the N₂ concentration of withdrawn air was less than 2%. Approximately 15 to 30 minutes generally elapsed between the beginning of the P-V maneuver and the end of the MBN₂ test. After the MBN₂ was completed, the rat, still under anesthesia and paralyzed, was allowed to die.

The monitoring system was calibrated for flow, pressure, and volume parameters at the beginning of each day. The N₂ analyzer and gas chromatograph were also checked periodically throughout the day in addition to the initial calibration. Examples of the tracings obtained during the testing procedure are shown in Figures 3 through 6. They were analyzed with a digital image analyzer (MOP-1.2.3; Carl Zeiss, Inc.) to measure distances (mm) on the graphs, and the distances were converted to time, pressure, volume, concentration, etc. in a small dedicated computer (MIN;[®] Digital Equipment Corp.) interfaced with the image analyzer. Data were stored on disks, and hard copies were printed; all data were entered into files on the main-frame computer (VAX 11-780) for statistical analysis.

A template was superimposed over the P-V curve as shown in Figure 3. Two of the respiratory parameters derived from this curve were VC (ml), and C_{Q5} (ml/cm H₂O Ptp) between 2 and 5 cm H₂O Ptp on the deflation curve, generally referred to as the "chord" compliance.

FIGURE 3. Traced Curve Showing Measured Parameters of the Pressure-Volume Maneuver with a Control (Sham-Exposed) Rat

Two lines were drawn over the SBN_2 curve (Figure 4), and two parameters were estimated from them: 1) the closing volume, and 2) the slope of the alveolar plateau (Phase III) of the curve.

Data from the DL_{CO} test were analyzed according to the methodology of Takezawa et al. (1980). The curve shown in Figure 5 is a tracing of lung volume for the time period during which the test was performed. The breath-holding time was measured as the time between a point one-third of the way up the ascending portion to the point halfway down the descending portion, after withdrawal of a volume of air to compensate for the physical dead space. A factor of 0.9 was used to convert the VC at ambient temperature and pressure (saturated) to an alveolar volume at standard temperature and pressure (dry). The equation that gave the DL_{CO} (ml CO/min) was, therefore:

$$DL_{CO} = 0.9 \times VC \times \frac{\text{Inspired Ne}}{\text{Expired Ne}} \times \frac{60}{(713 \times t)} \ln \left| \frac{\text{Inspired CO}}{\text{Expired CO}} \times \frac{\text{Expired Ne}}{\text{Inspired Ne}} \right|$$

where "t" is the breath-holding time from curves such as those shown in Figure 5, and 713 is the barometric pressure corrected for altitude.

The same data were used for determining TLC:

$$TLC = 1.08 \times VC \times \frac{\text{Inspired Ne}}{\text{Expired Ne}}$$

The factor 1.08 was used to correct from ambient temperature and pressure (saturated) to standard temperature and pressure (dry; Takezawa et al., 1980).

FIGURE 4. Traced Curve Showing Measured Parameters of the Single-Breath Nitrogen Washout test with a Control (Sham-Exposed) Rat

FIGURE 5. Traced Curve Showing Measured Parameters from the Carbon Monoxide Diffusing Capacity Test with a Control (Sham-Exposed) Rat

A curve traced during the MBN₂ test is shown in Figure 6. To analyze these curves, the concentrations at each peak were summed until a peak indicated less than 2% N₂ in expired air. In Figure 6, 10 cycles of the respirator were required to achieve a level of less than 2% N₂, and adding the peak concentration resulted in an "area" under the curve (Area N₂) of approximately 190.

HEMATOLOGY

Four groups of 30 rats each were exposed specifically for hematopoietic testing (see Table 1). Blood was drawn from 10 rats of each group before exposure and at 7, 14, 30, 60, 90, 180 and 365 days after exposure. The rats (five males and five females) were selected from survivors at each of those times. Ten rats from the control and gamma-only groups (Groups 21 and 23, Table 1) were also sampled at 2 days after exposure and four control rats were sampled at 120 days after exposure. Samples were not taken from the promethium-exposed rats at some of the earlier times because of the radiation hazard present for some time after exposure.

FIGURE 6. Traced Curve from the Multiple-Breath Nitrogen Washout of Lungs in a Control (Sham-Exposed) Rat

Blood samples were collected from an incision in the tail of each rat, which was confined in a plastic stanchion. Smears were made from fresh blood, stained with Wright-Giesma with an automatic slide stainer (Gam-Rad, Inc.), and microscopically evaluated for concentrations of segmented neutrophils, lymphocytes, monocytes, eosinophils, band neutrophils and nucleated red blood cells. Samples used for determination of platelet concentrations were diluted in ammonium oxalate and enumerated microscopically, using a stage hemacytometer. Reticulocyte concentrations were determined from smears stained with new methylene blue. A sample of heparinized fresh blood was diluted in Isoton (Coulter Instruments) and processed with a Coulter Model S counter to determine concentration of total nucleated cells, red blood cells and hemoglobin. Analyses with this instrument also included the

volume of packed red cells (VPRC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC).

MORBIDITY DATA ANALYSIS

Measured values of pulmonary-function parameters, hematologic parameters and body weights from control rats measured throughout the 1-year observation period of the experiment were plotted against time. Mean regression lines, with 95% confidence intervals, were derived for each of these plots and were used to determine which of the values for exposed rats were considered abnormal. For the N₂ concentration measurements, values above the upper 95% limit were considered as indicative of respiratory illness; for all other pulmonary-function parameters and body weights, values below the lower 95% limit indicated illness. Values for hematologic parameters, which were either above or below the 95% limits were noted (Appendix B).

NECROPSY AND HISTOPATHOLOGY

Necropsy was performed on all rats that died during the experiment and on those that survived to the end (365 to 370 days). Rats were killed by an overdose of pentobarbital sodium (Abbott Labs). All organ systems were grossly examined; lungs were routinely removed and fixed in formalin, and other grossly abnormal tissues were also fixed and saved. A longitudinal section from the left lobe of each lung and sections from other abnormal tissues were selected for histopathologic evaluation. Tissue samples were embedded in paraffin, sectioned at approximately 5- μ m thickness, and stained with hematoxylin and eosin for examination by light microscopy. Radiation pneumonitis was graded according to severity on a scale of 0 to 5; 5 was most severe.

ANALYSIS OF PULMONARY FUNCTION

The primary pulmonary-function parameters, which were derived from the data collected included: TLC, VC, DL_{CO}, C_{QS}, Slope III, and Area N₂. The Area N₂ was not used in the final analysis of morbidity for reasons that will be discussed later. The TLC was not used because it was considered redundant to use both TLC and VC, both lung volume parameters.

Analysis of variance (ANOVA) was used to analyze the pulmonary-function data. If a significant treatment effect occurred, Tukey's multiple comparison test (Tukey, 1953; Kramer, 1957) was used to delineate intergroup differences. The general linear model (GLM) procedure in the Statistical Analysis System (SAS, 1985) was employed to carry out these analyses.

Animals were considered morbid if values for three or more of the four parameters were outside the 95% confidence interval for control values. This allowed for one potentially aberrant measurement per animal and resulted in very few control animals being considered morbid (see Results Section).

DOSE/MORBIDITY AND DOSE/MORTALITY ANALYSIS

Comparisons between groups of animals were made by fitting the modified Weibull model to the plots of morbidity (as defined above) versus dose and to mortality versus dose. This model has been used to describe acute responses of experimental animals to radiation from inhaled radionuclides and from external radiation sources

(Scott et al., 1987; Scott and Hahn, 1980). The equation used to describe the Weibull distribution function was:

$$F(D) = R_o + (1 - R_o)[1 - \exp(-0.693X^V)]$$

where

$F(D)$ = fraction of mortality (morbidity) at a given dose, D

R_o = baseline mortality or morbidity not caused by beta radiation

X = D/D_{50} , the dose in units of the D_{50} (the dose resulting in 50% mortality or morbidity)

V = shape parameter (related to the slope of the curve).

This model was used to determine morbidity and mortality differences between animals exposed to promethium aerosols only and those that were exposed to the promethium aerosols with gamma irradiation. The comparison was based on lung doses from inhaled promethium; therefore, the term R_o was used to represent morbidity or mortality resulting from gamma irradiation. Mortality and morbidity were minimal in animals of the control groups and were not considered in the application of the model.

RESULTS

MORTALITY

The mortality fraction of each of the exposure groups at 30 days after exposure is presented in Table 4. None of the control rats (Group 21) and none of the rats exposed to promethium only (Groups 25, 29 and 33) died within 30 days of exposure. There was little mortality within groups of rats exposed to gamma radiation only (Groups 22, 23 and 24), regardless of dose, much less than that anticipated on the basis of the data from which Figure 1 was constructed.

TABLE 4. Mortality of Rats Within 30 Days of Exposure to ^{60}Co Gamma Irradiation and/or ^{147}Pm (FAP) Aerosol (Mortality Study)

	^{60}Co Gamma Radiation (Total Body)			
	0	Low (850 rad or 8.5 Gy)	Medium (890 rad or 8.9 Gy)	High (915 rad or 9.2 Gy)
0 ^{147}Pm (FAP)				
Group number/(Number of rats)	21(60)	22(30)	23(60)	24(30)
Percent mortality, males	0	0	7	0
Percent mortality, females	0	0	3	0
Percent mortality, both sexes	0	0	5	0
Low ^{147}Pm (FAP)				
Group number/(Number of rats)	25(30)	26(60)	27(30)	28(30)
Percent mortality, males	0	3	13	0
Percent mortality, females	0	10	53	13
Percent mortality, both sexes	0	7	33	17
Medium ^{147}Pm (FAP)				
Group number/(Number of rats)	29(60)	30(30)	31(30)	32(30)
Percent mortality, males	0	20	0	33
Percent mortality, females	0	33	7	7
Percent mortality, both sexes	0	27	3	20
High ^{147}Pm (FAP)				
Group number/(Number of rats)	33(30)	34 and 39(60)	35(30)	
Percent mortality, males	0	30	0	
Percent mortality, females	0	13	60	
Percent mortality, both sexes	0	22	30	
Mortality Summary (Excluding gamma-only groups)				
Percent mortality, males	0	17	4	17
Percent mortality, females	0	16	40	20
Percent mortality, both sexes	0	17	22	18
Overall Mortality (^{147}Pm (FAP) + gamma)				
Percent mortality, males	0	14	5	11
Percent mortality, females	0	13	25	13
Percent mortality, both sexes	0	14	15	12

Statistically Significant Differences

Groups 22, 23 and 24: males versus females ($P < 0.018$)

Groups 26-28, 30-32 and 34-39: males versus females ($P < 0.0001$)

Groups 26-28, 30-32 and 34-39 versus Groups 22, 23 and 24: males ($P < 0.044$)

Groups 26-28, 30-32 and 34-39 versus Groups 22, 23 and 24: males and females ($P < 0.0001$)

Survival of rats exposed to ^{60}Co gamma radiation only (Groups 22, and 23 and 43 combined), is graphically illustrated compared to control groups (Groups 21 and 41 combined) in Figures 7 and 8. In general, males (Figure 7) that survived more than 30 days after exposure lived longer than 250 days after exposure. Mortality increased after approximately 300 days, especially in the two highest dose groups. The survival pattern of females (Figure 8) was similar except that a few rats died between 150 and 200 days after exposure. Also, mortality in females appeared to be inversely related to dose. No groups, male or female, had greater than 25% mortality during the 400-day duration of the experiment. The late deaths were not considered an acute response to exposures; the probable causes of death will be discussed later.

In Groups 26 through 28, 30 through 32, and 34 through 39 (gamma plus promethium), mortality within 30 days of exposure was greater than that in Groups 22 through 24 (gamma only; $P < 0.0001$). Promethium lung burdens did enhance the effect of total-body gamma doses. In some groups there was a difference in mortality rate between sexes; female mortality was greater ($P = 0.018$) than male mortality when all groups exposed to promethium and gamma radiation were combined. As in Groups 22 through 24, there was no apparent mortality increase with increasing gamma dose, nor was there a consistent mortality increase with increasing promethium lung burden.

Mortality fractions within the groups of rats exposed for hematologic and pulmonary-function evaluations are shown in Table 5. These data also show the influence of promethium lung burden on 30-day mortality: Group 26 had higher mortality rates than did Group 23, even though their gamma doses were somewhat lower. There was no significant difference in mortality between the sexes, and mortality was lower than that expected, based on the data shown in Figure 1.

FIGURE 8. Survival Curves for Groups of Female Rats Exposed to ^{60}Co Gamma Radiation

TABLE 5. Mortality of Rats Within 30 Days of Exposure to ^{60}Co Gamma Radiation and/or ^{147}Pm (FAP) Aerosol

	^{60}Co Gamma Radiation (Total Body)			
	0	Medium (890 rad or 8.9 Gy)	Low (850 rad or 8.5 Gy)	0
Hematologic Testing				
Group number	21	23	26	29
^{147}Pm (FAP) ILB, males	0	0	$97 \pm 30 (3.6 \pm 1.1)$	$230 \pm 39 (8.5 \pm 1.4)$
Percent mortality, males	0	20	27	0
^{147}Pm (FAP) ILB, females	0	0	$143 \pm 31 (5.3 \pm 1.1)$	$262 \pm 47 (9.7 \pm 1.7)$
Percent mortality, females	0	7	7	0
Pulmonary-Function Testing				
Group number	21	23	26	29
^{147}Pm (FAP) ILB, males	0	0	$128 \pm 36 (4.7 \pm 1.3)$	$130 \pm 38 (4.8 \pm 1.4)$
Percent mortality, males	0	0	13	0
^{147}Pm (FAP) ILB, females	0	0	$161 \pm 51 (6.0 \pm 1.9)$	$137 \pm 57 (5.1 \pm 2.1)$
Percent mortality, females	0	0	30	0
Overall Percent Mortality				
Males	0	7	11	0
Females	0	7	22	0

^aILB = Initial lung burden; mean $\pm$ standard deviation, μCi and (MBq)/g lung for each group

Mortality data of the groups of rats exposed during the second series are shown in Table 6. With one exception, 30-day mortality fractions are very similar to those of rats exposed in the first series. Two control rats and two rats of the gamma-plus-promethium groups died at 5 days after exposure. These rats were approximately 2

weeks older (and therefore larger) than those of the first series of exposures, and the males fit quite snugly in the exposure tubes. That, coupled with the longer times in the tubes because of transport between buildings for gamma exposure, caused some mortality during exposures. These factors are considered responsible for the deaths at 5 days after exposures in Groups 41 and 46.

TABLE 6. Mortality of Rats Within 30 Days of Exposure to ^{60}Co Gamma Radiation and/or ^{147}Pm (FAP) Aerosol (Second Series of Exposures)

	^{60}Co Gamma Radiation (Total Body)			
	0	Medium (890 rad or 8.9 Gy)	Low (850 rad or 8.5 Gy)	0
Mortality Groups				
Group number	41	43	46	49
^{147}Pm (FAP) ILB ^a , males	0	0	61 ± 23 (2.3 ± 0.9)	98 ± 25 (3.6 ± 0.9)
Percent mortality, males	8 ^b	3	7 ^b	0
^{147}Pm (FAP) ILB, females	0	0	72 ± 18 (2.7 ± 0.7)	133 ± 46 (4.9 ± 1.7)
Percent mortality, females	0	0	3	0
Pulmonary-Function Testing				
Group number			46	49
^{147}Pm (FAP) ILB, males			56 ± 10 (2.1 ± 0.4)	95 ± 26 (3.5 ± 1.0)
Percent mortality, males			9 ^b	0
^{147}Pm (FAP) ILB, females			77 ± 15 (2.9 ± 0.6)	153 ± 25 (5.7 ± 0.9)
Percent mortality, females			0	0
Overall Percent Mortality				
Males	8 ^b	3	8 ^b	0
Females	0	0	0	0

^aILB = Initial lung burden; mean $\pm$ standard deviation, μCi and (MBq)/g lung for each group

^bIncludes rats whose deaths were not considered radiation-induced (see text).

Survival times of rats exposed to promethium only and to promethium with gamma radiation are shown versus promethium ILB in Figures 9 through 12. Data for males and females were plotted separately in these figures, although the mortality patterns of the two sexes were similar. There were no deaths in the promethium-only groups before 50 days after exposure (Figures 9 and 10). Thereafter, survival time was dependent on ILB, but with a wide range of biological variation. For example, an ILB between 3.7 and 5.6 MBq (100 to 150 μCi)/g lung resulted in survival times ranging between 50 and 350 days. There were 28 survivors past the 365-day duration of the experiment, and their ILB were between 1.9 and 4.8 MBq (50 and 130 μCi)/g lung. Although the number of rats surviving past 1 year is small, Figures 9 and 10 indicate that survival past 1 year was likely with an ILB of less than 2.2 MBq (60 μCi)/g lung for both males and females.

The mortality rates of rats exposed to both gamma radiation and promethium were slightly different from those of rats exposed to promethium only. In addition to the deaths from gamma radiation within 10 to 20 days of exposure, most other deaths in both males and females occurred between 30 and 120 days after exposure. After 120 days, rats died at various times between 120 and 365 days after exposure, and their survival appeared to be more a result of individual variation than of the amount of promethium in their lungs. There were 19 survivors past 1 year of exposure, and most had ILB between 1.9 and 3.7 MBq (50 and 100 μCi)/g lung; however, 14 rats with similar ILB died between 150 and 365 days after exposure. Many

more rats in that same ILB range died between 30 and 120 days. Six females in that ILB range survived past 1 year of exposure, and they also had ILB between 1.9 and 3.7 MBq (50 and 100 μCi)/g lung, as did eight of the male survivors.

FIGURE 9. Survival Times of Male Rats with Varying Lung Burdens of ^{147}Pm (FAP)

FIGURE 10. Survival Times of Female Rats with Varying Lung Burdens of ^{147}Pm (FAP)

An attempt was made to analyze the data from rats exposed to both promethium and gamma radiation, according to the gamma dose received. Ultimately, this approach was not considered feasible because no gamma dose effect could be demonstrated. Thereafter, regardless of the gamma dose, analyses were confined to a group of rats exposed to promethium only and a group exposed to promethium with gamma radiation.

Deaths in the promethium-only groups (Figures 9 and 10) were attributed to radiation pneumonitis. Deaths within the first 30 days in the promethium-plus-gamma groups (Figures 11 and 12) were attributed to bone-marrow syndrome; however, radiation pneumonitis was the cause of death in those animals that died after 30 days. Evidence for these interpretations will be presented later in this report in the form of hematological data, pulmonary-function data, necropsy observations, and histopathologic evaluations.

FIGURE 11. Survival Times of Male Rats with Varying Lung Burdens of ^{147}Pm (FAP) and ^{60}Co Gamma Irradiation

Mortality rates from inhaled promethium with no exposure to gamma radiation are graphically illustrated in Figures 13 and 14. Three intervals of ILB, represented in each plot, are roughly similar between the sexes in terms of promethium/g lung. The curves show no definite dose dependence, except for the slower rate of mortality with the lowest ILB ranges. Regardless of ILB, both males and females began to die as a result of radiation pneumonitis at approximately 100 days after exposure. With high ILB, most rats died before 200 days after exposure, as illustrated in Figures 9 and 10.

Comparisons of mortality rates in groups of rats that received approximately equal lung burdens of promethium, with and without gamma doses, are made in Figures 15 and 16. Median lung burdens of males and females whose survival curves are shown in Figures 15 and 16 were 4.4 MBq ($120 \mu\text{Ci}$)/g lung and 3.7 MBq ($100 \mu\text{Ci}$)/g lung, respectively. The curve for rats exposed to gamma radiation only is a com-

posite curve based on mortality within all three dose groups. Males and females exposed only to promethium began to die after approximately 70 and 110 days, respectively. Thereafter, female mortality rates were lower than male rates, reflecting the slightly lower medium ILB of the females.

FIGURE 12. Survival Times of Female Rats with Varying Lung Burdens of ^{147}Pm (FAP) and ^{60}Co Gamma Irradiation

Mortality among the groups that received both kinds of radiation insult occurred at a much more rapid rate. For rats that survived past 30 days, there was a high mortality rate during the subsequent period up to 120 days after exposure, after which nearly all were dead. Mortality curves of control rats are included in Figures 7 and 8; there were few deaths among controls for the 1-year duration of the experiment.

Cumulative percent mortality (within 365 days of exposure) was plotted against the 365-day dose commitment from inhaled promethium, using the Weibull cumulative distribution function as described by Scott et al. (1987; Figure 17). Data from all rats are included, therefore the curve for rats exposed to promethium with gamma irradiation begins at 22% mortality, which was the mortality that resulted from exposure to gamma radiation only (Groups 22, 23, 24 and 43). The LD_{50} values were approximately 160 Gy (16,000 rad) and 290 Gy (29,000 rad) for the promethium-plus-gamma and promethium-only groups, respectively. Gamma doses were not added to the lung doses of the promethium-plus-gamma groups; however, the difference between LD_{50} values of the two groups is approximately 16 times the doses received from gamma exposure.

The LD_{50} values for males and females were not significantly different within either exposure group, therefore the curves in Figure 17 include data from both sexes combined.

The differences between mortality responses of rats exposed to promethium and gamma radiation and those exposed to promethium only are highly significant.

FIGURE 13. Survival Curves for Groups of Male Rats with Three Ranges of Lung Burdens ($\mu\text{Ci/g}$ Lung) of ^{147}Pm (FAP)

FIGURE 14. Survival Curves for Groups of Female Rats with Three Ranges of Lung Burdens ($\mu\text{Ci/g}$ Lung) of ^{147}Pm (FAP)

FIGURE 15. Survival Curves for Three Groups of Male Rats, One with Exposure to ^{60}Co Gamma Radiation, One with Exposure to an Aerosol of ^{147}Pm (FAP), and One with Exposure to Both (Median ILB of Promethium Groups = 4.4 MBq (120 μCi)/g Lung)

FIGURE 16. Survival Curves for Three Groups of Female Rats, One with Exposure to ^{60}Co Gamma Radiation, One with Exposure to an Aerosol of ^{147}Pm (FAP), and One with Exposure to Both (Median ILB of Promethium Groups = 3.7 MBq (100 μCi)/g Lung)

FIGURE 17. Comparison of Weibull Cumulative percent Mortality Distributions with Dose from ^{147}Pm (FAP) Lung Burdens in Male and Female Rats Exposed to a Promethium Aerosol With and Without Additional Exposure to ^{60}Co Gamma Radiation

PATHOLOGIC EVALUATIONS

Tissues of 252 rats were histopathologically evaluated; included in the total were: (1) 4 rats from Groups 21 and 41 (Controls), (2) 20 rats from Groups 22, 23, 24 and 43 (gamma irradiation only), (3) 158 rats exposed to gamma irradiation and the promethium aerosols (Groups 26-28, 30-33, 34, 35, and 39), and (4) 70 rats exposed to promethium only (Groups 25, 29, and 33). The primary objective of microscopic examination was to determine the incidence and severity of radiation pneumonitis; therefore, only lung sections were examined unless changes in other systems were noted at necropsy.

Of six control rats (Groups 21 and 41) that died during the experiment, two died 5 days after exposure of apparent exposure-related stress, as previously mentioned. Two other rats had no grossly or microscopically visible lesions, one rat had a diaphragmatic hernia; and one had a carcinoma involving the skin of its right front shoulder. The latter four rats died at times ranging between 187 and 375 days after exposure. No other control rats had grossly observable lesions when sacrificed at the end of the experiment.

Thirty-four rats of Groups 22-24 and 43 (gamma irradiation only) died during the experiment, and tissues from 19 of them were microscopically examined. The lungs of three of the four rats that died within 30 days of exposure contained no remarkable changes. They died between 11 and 17 days after exposure, most probably from the bone-marrow radiation syndrome. A rat that died 26 days after exposure (Group 23) had severe radiation pneumonitis and extensive intra-alveolar hemorrhage.

There were no deaths within those groups between 30 and 150 days after exposure; however, 26 rats died between 150 and 365 days after exposure. Lungs of 15 of those rats (generally, those that died between 150 and 280 days after exposure) contained inflammatory cells and/or varying degrees of pulmonary fibrosis. Thirteen of the rats that died within 1 year of exposure (generally, between 280 and 365 days after exposure) had tumors, 10 of which were skin tumors such as dermal fibromas; two other tumors (in different animals) were of visceral origin (see Appendix C). Because there were so few tumors within the control groups, the skin tumors must be considered exposure-related. Four other rats died between 365 and 388 days after exposure (terminal sacrifice), and two of those also had skin tumors.

Lungs of all rats exposed to only the promethium aerosol (Groups 25, 29, and 33) had microscopic characteristics associated with radiation pneumonitis. Alveoli contained necrotic debris, neutrophils, and macrophages; many of the latter were of the large "foamy" type, indicating a high degree of phagocytic activity. In the rats that died earlier in the experiment (100 days or less after exposure), many lungs contained edema and/or a fibrinous exudate. Alveolar septal fibrosis was a characteristic of most rats that died later than 100 days after exposure.

In many rats that died between 150 to 200 days after exposure, lungs revealed an intimal thickening in small pulmonary blood vessels. The two rats of Group 25 that died at 338 and 400 days, respectively, after exposure also had foci of bronchiolo-alveolar hyperplasia and cuboidal-to-squamous metaplasia. This change was not present in most of the rats examined, presumably because few lived long enough to develop the lesion. Hemorrhagic foci were present in lungs of 8 of the 70 rats examined after exposure to promethium only.

The pulmonary changes described above were also present in rats exposed to ^{147}Pm (FAP) with gamma irradiation. In general, the changes occurred sooner and pulmonary hemorrhaging was more prevalent than in the groups exposed to ^{147}Pm (FAP) without gamma radiation doses.

One indication of radiation pneumonitis noted at necropsy was the presence of extrapulmonary serous exudate within the pleural cavity. Measured amounts of 10 ml or more were frequently observed, primarily in animals that died between 60 and 150 days after exposure. This change was reported for nearly 80% of the rats that died within that time span and for which a radiation pneumonitis severity grade of 2 or greater was subsequently assigned on microscopic examination.

Figure 18 contains plots of the cumulative incidence of extrapulmonary exudate at various times after exposure for groups of rats exposed to ^{147}Pm (FAP), alone or with gamma irradiation. The curves illustrate two points: (1) that the change was quite specific to the 60- to 150-day time frame, and (2) that the higher the gamma radiation dose, the earlier the onset of the change.

Table 7 contains a summary of histopathologic data from the rats that died during the experiment; mean ILB and survival times are included. Values in the table indicate: (1) the influence of gamma irradiation on reduction of survival time, even though the ILB were similar (e.g., Groups 25-28 and 29-32), and (2) the influence of longer survival time on increased severity of radiation pneumonitis (e.g., Groups 27, 30, 34, and 35 versus Groups 25, 29, and 33). The influence of gamma irradiation on

the induction of pulmonary hemorrhaging is also indicated in that the change was not prevalent in the rats exposed to $^{147}\text{Pm}(\text{FAP})$ alone.

FIGURE 18. Plots of the Cumulative Incidence of Extrapulmonary Exudate at Various Times after Exposure for Groups of Rats Exposed to $^{147}\text{Pm}(\text{FAP})$, Alone or with Gamma Irradiation. (Numbers in parentheses indicate the total number of rats evaluated.)

TABLE 7. Group Mean Survival Times, Selected Histopathology Data, and Mean ILB of Rats Exposed to $^{147}\text{Pm}(\text{FAP})$ With or Without Gamma Radiation ($\pm$ = Standard Deviation)

	^{60}Co Gamma Radiation			
	0	Low (850 rad or 8.5 Gy)	Medium (890 rad or 8.9 Gy)	High (915 rad or 9.2 Gy)
Group number (Number of rats)	25(13)	26(18)	27(14)	28(16)
Mean ILB ($\mu\text{Ci/g}$ lung)	99 $\pm$ 13	109 $\pm$ 22	91 $\pm$ 20	97 $\pm$ 19
Mean survival time (days)	179 $\pm$ 105	82 $\pm$ 35	41 $\pm$ 22	68 $\pm$ 32
Mean severity (pneumonitis)	3.0 $\pm$ 0.8	2.6 $\pm$ 0.9	1.6 $\pm$ 0.8	3.3 $\pm$ 1.6
Pulmonary hemorrhage (%)	15	22	14	50
Group number (Number of rats)	29(37)	30(21)	31(16)	32(18)
Mean ILB ($\mu\text{Ci/g}$ lung)	198 $\pm$ 53	178 $\pm$ 48	151 $\pm$ 28	149 $\pm$ 25
Mean survival time (days)	137 $\pm$ 39	66 $\pm$ 40	73 $\pm$ 28	54 $\pm$ 28
Mean severity (pneumonitis)	3.1 $\pm$ 0.5	2.0 $\pm$ 0.9	3.4 $\pm$ 1.5	3.3 $\pm$ 1.1
Pulmonary hemorrhage (%)	14	33	88	67
Group number (Number of rats)	33(20)	34(21)	35(16)	
Mean ILB ($\mu\text{Ci/g}$ lung)	245 $\pm$ 73	253 $\pm$ 66	294 $\pm$ 49	
Mean survival time (days)	133 $\pm$ 30	66 $\pm$ 36	63 $\pm$ 33	
Mean severity (pneumonitis)	2.9 $\pm$ 0.5	2.1 $\pm$ 1.1	2.1 $\pm$ 1.2	
Pulmonary hemorrhage (%)	5	10	15	
Group number (Number of rats)		39(18)		
Mean ILB ($\mu\text{Ci/g}$ lung)		201 $\pm$ 47		
Mean survival time (days)		73 $\pm$ 38		
Mean severity (pneumonitis)		2.1 $\pm$ 1.1		
Pulmonary hemorrhage (%)		6		

MORBIDITY MEASUREMENTS

Body Weights

Weight gains of male and female control rats (Group 1) are shown in Figures 19 (male) and 20 (female). Even though the rats were approximately 15 weeks old at the beginning of the experiment, their weight increased steadily. The curves represent mean percent of exposure weight, with 95% confidence intervals.

FIGURE 19. Mean Body Weight Gains (with 95% Confidence Interval) of Male Control Rats for 1 Year after Sham Exposure

Corresponding curves (without the confidence intervals) for the first 20 weeks after exposure for rats exposed to gamma radiation are shown in Figures 21 and 22. Mean weight gain was reduced in all gamma-exposed groups of both sexes during the first 50 days after exposure when compared to that of control rats. However, the curves fell below the lower confidence limit (LCL) of controls for only three groups of rats: males with medium and high gamma doses (Figure 21) and females with high gamma doses (Figure 22). After the first 50 days, survivors gained weight at a nearly normal rate.

For rats exposed only to promethium, body weights were not significantly different from those of controls (Figures 23 and 24). All promethium-exposed rats were divided into three ILB groups for comparison purposes. Whenever possible, ILB ranges were selected to include rats that survived through the time frame illustrated because mortality perturbed the body-weight data. For example, mortality in high-ILB males was sufficient to cause artificial increases in mean weights because the rats that lost the most weight died.

Weight loss was most severe in rats that received gamma exposure and promethium (Figures 25 and 26), although dependence of weight loss on ILB was not demonstrable. The curves for groups with lowest ILB of both sexes indicate a reduced

weight gain. The curves reflect the immediate effect of the gamma radiation on body weight; however, rather than recovering like those rats exposed to gamma radiation only, their weight continued to remain below normal throughout their lives. The curves of rats with greater ILB were artificially raised because of the mortality of sick rats, as discussed previously. Rats exposed to promethium, with or without gamma irradiation, generally began losing weight 4 to 6 weeks before they died. Weights at death were between 60 and 80% of the peak weight.

FIGURE 20. Mean Body Weight Gains (with 95% Confidence Interval) of Female Control Rats for 1 Year after Sham Exposure

Hematology

Four groups of rats were exposed to gamma radiation and/or ^{147}Pm (FAP) specifically for hematologic evaluation (Tables 1 and 5) so that the blood-sampling process would not interfere with dose/mortality data obtained from Groups 21 through 35. Exposure histories of these groups included: Group 21 (Hematology), a sham-exposed control group; Group 23 (Hematology), the medium gamma dose (890 rad or 8.9 Gy); Group 26 (Hematology), a low gamma dose (850 rad or 8.5 Gy) with a low range of promethium ILB; and Group 29 (Hematology), a medium range of ^{147}Pm (FAP) ILB. There were 30 rats per group, with equal numbers of male and females. At each time of evaluation, five males and five females were selected from among the survivors in such a way that an individual rat was not tested at two consecutive times unless the small number of survivors in a group made it necessary.

For each hematologic parameter, the mean values, with 95% confidence intervals, were plotted against time for controls, and the data from exposed rats were compared with these plots. Hematologic values of control and exposed rats are listed in tables in Appendix B, and values that were above or below the 95% confidence interval of controls are so marked. Appendix B also contains the plots of control values.

FIGURE 21. Mean Body Weight Gains (or Losses) for the First 20 Weeks after Exposure in Three Groups of Male Rats Exposed to ^{60}Co Gamma Radiation Compared with Mean Control Values

FIGURE 22. Mean Body Weight Gains (or Losses) for the First 20 Weeks after Exposure in Three Groups of Female Rats Exposed to ^{60}Co Gamma Radiation Compared with Mean Control Values

FIGURE 23. Mean Body Weight Gains (or Losses) for the First 12 Weeks after Exposure in Three Groups of Male Rats Exposed to ^{147}Pm (FAP) Compared with Mean Control Values. ILB ranges are in $\mu\text{Ci/g}$ lung.

FIGURE 24. Mean Body Weight Gains (or Losses) for the First 12 Weeks after Exposure in Three Groups of Female Rats Exposed to ^{147}Pm (FAP) Compared with Mean Control Values. ILB ranges are in $\mu\text{Ci/g}$ lung.

FIGURE 25. Mean Body Weight Gains (or Losses) for the First 12 Weeks after Exposure in Three Groups of Male Rats Exposed to ^{147}Pm (FAP) and ^{60}Co Gamma Radiation (850 rad or 8.5 Gy) Compared with Mean Control Values. ILB ranges are in $\mu\text{Ci/g}$ lung.

FIGURE 26. Mean Body Weight Gains (or Losses) for the First 12 Weeks after Exposure in Three Groups of Female Rats Exposed to ^{147}Pm (FAP) and ^{60}Co Gamma Radiation (850 rad or 8.5 Gy) Compared with Mean Control Values. ILB ranges are in $\mu\text{Ci/g}$ lung.

Concentrations of circulating red blood cells (erythrocytes) in control rats are plotted against time in Figures B1 and B2. The mean concentration of erythrocytes was slightly, but not significantly, higher in males (Figure B1) than in females (Figure B2). Values for two control rats were slightly below the LCL: a male and a female at 120 days after sham exposure (Table B1). Another female at 365 days after exposure had a value nearly 10% of control values. This rat also had abnormally high lymphocyte and neutrophil concentrations, suggesting hematologic morbidity.

Gamma-irradiation resulted in a severe depression in erythrocyte concentration, as indicated by data collected at 14 and 30 days after exposure (Table B2). Subsequent measurements indicated a return toward control values; however, values for one of five males and four of five females had not yet reached control values (above the LCL) by 180 days after exposure. Three of five males and two of five females were also below the LCL of control rats at 365 days after exposure.

Promethium lung burdens caused a slight reduction in erythrocyte concentrations during the first 30 days after exposure (Table B3). All males and half of the females had values slightly lower than the LCL of control rats at 18 and 30 days after exposure. At 60 days after exposure, all but one male were within the control range, but, again, two males and two females had slightly lower values at 90 days after exposure. All rats of this group (Group 29, Hematology) died between 90 and 180 days after exposure, so no further measurements could be performed.

In the combined exposure group, erythrocyte concentrations in all rats dropped below the LCL of control rats by 7 days after exposure (Table B4) and remained there through 90 days after exposure with the exception of two females at 60 days after exposure. Mean values at 60 and 90 days after exposure, while below the LCL, indicated recovery and, in survivors, values were at or above control values at 180 and 365 days after exposure.

There was a steady decline in concentration of circulating lymphocytes in control animals (both males and females) during the course of the experiment (Figures B3 and B4). Mean values at 365 days were nearly half of the mean values at the beginning. Two males, at 120 days after sham exposure, had lymphocyte concentrations below the LCL (Table B5), and two females had values above the upper confidence limit (UCL), one at 7 days and the other at 365 days after exposure.

Gamma exposure resulted in a severe and immediate depression of lymphocyte concentration, with nearly complete absence of the cells in circulating blood 2 days after exposure (Table B6). Recovery began shortly thereafter; although most values were below the LCL of control rats at 60 days after exposure, most were within the limits at 180 days after exposure. The values for four of five males and one female were slightly below the LCL at 90 days after exposure.

Promethium lung burdens resulted in depressed lymphocyte concentrations below the LCL by 18 days after exposure (first measurement), and the concentrations remained below the LCL of control rats until the last measurement (90 days after exposure; Table B7). Only one of five females had a lymphocyte concentration within the control range at 90 days after exposure. All Group 29 rats died between 90 and 180 days after exposure, so no further measurements could be made.

The severe effect of gamma irradiation on lymphocytes was indicated by values for the rats that received combined exposures (Table B8). All values of those rats were

very low at 7 and 14 days after exposure. After that, the values increased slightly but remained below the LCL of control rats through 90 days after exposure. Of the two male rats tested at 180 and 365 days after exposure, values of only one had returned to the control range by the end of the experiment.

Control neutrophil concentrations remained relatively constant throughout the year (Figures B5 and B6; Table B9), although five rats had slight neutrophilia: a male at 30 days after exposure, a male at 180 days after exposure, and a male and two female control rats at 365 days after sham exposure. The primary effect of gamma irradiation on segmented neutrophil concentrations in circulating blood was an early increase in males (2 days after exposure). This was followed by a depression of values. Five of ten measurements made 14 days after exposure resulted in values below the LCL of controls. Values from that time to 1 year after exposure were generally within control limits (Table B10).

Lung burdens of promethium resulted in neutrophil concentrations that were high compared to control values at first and, in three male rats, above the UCL of control rats (Table B11). Values in Group 29 were generally within the control range from 30 days after exposure to the last measurement (90 days after exposure). One female had severe neutrophilia at 90 days after exposure and died shortly thereafter (Table B11).

In Group 26 (promethium-plus-gamma), the neutrophil concentrations of most rats were below the LCL of control rats during the first 14 days after exposure but gradually returned to normal during the remainder of the experiment. Two rats, one male and one female, had slight neutrophilia at 60 days after exposure and died shortly afterward (Table B12).

Monocytes represent a small fraction of the nucleated cells, and determination of their concentration during a routine hematological analysis is not a reliable process unless their numbers are extraordinarily large or unless they are virtually absent from circulating blood. For that reason, the 95% confidence interval about the mean value for control animals (Figures B7 and B8) was large enough to encompass nearly all values from irradiated animals. One female control rat had an abnormally high monocyte concentration at 365 days after sham exposure (Table B13). Values slightly above the UCL of controls were observed in one female at 7 days, two females at 30 days and one male at 60 days after exposure.

Gamma irradiation caused an immediate reduction in mean monocyte concentrations (Table B14); however, by 30 and 60 days after exposure, values were increasing toward control levels. Two females had monocytosis at 30 days after exposure, and both died shortly. One female had severe monocytosis at 60 days after exposure but survived and had a normal concentration of monocytes at the next measurement (90 days after exposure).

Lung burdens from promethium exposure without concomitant gamma irradiation (Group 29; Table B15) had little effect on monocyte concentrations in the blood of rats, except for a slight depression in values for males at 30 days after exposure and in both males and females at 90 days after exposure. With inhaled promethium plus gamma irradiation (Group 26), monocyte concentrations declined during the first 60 days after exposure (Table B16), and the mean values generally remained lower than control means through 90 days after exposure. There were two animals with slight monocytosis, a female at 90 days and a male at 365 days after exposure.

Blood platelets are of myelogenous origin, and changes in their concentrations in circulating blood of irradiated animals closely paralleled changes of the other myelogenous cells (e.g., neutrophils). When compared to control values (Figures B9 and B10; Table B17), platelet concentrations were depressed by gamma irradiation for the first 30 days of the experiment in Group 23 (Hematology; Table B18). By 90 days after exposure, concentrations were within limits of control rats. There was no discernible effect of promethium lung burden on platelet concentration (Table B19), and the effect of promethium with gamma exposure (Table B20) was similar to that of gamma exposure alone (Table B18), except that two males had very low values at 180 days after exposure. Values for those two rats were within the control range at the end of the experiment (Table B20).

Pulmonary Function

Measurements made on gamma-irradiated animals and/or those with lung burdens of promethium are compared, in the following section, with the corresponding parameters measured in control rats. Values shown for controls are plotted as mean values, with 95% confidence intervals. The figures generated for rats of Groups 23/43 (Pulmonary Function; gamma-exposed only) are directly comparable with those of Groups 21/41 (Pulmonary Function; controls), since the independent variable (abscissa) is time for both groups. For those rats with promethium lung burdens, the independent variable is lung dose, therefore the figures are not directly comparable with those for control rats. To provide a general indication of which rats were considered "sick" for each parameter, the appropriate confidence limit has been included in figures for rats with promethium lung burdens (Groups 26/46 and 29/49, Pulmonary Function). Most parameters varied with time in control rats as did lung dose in promethium-exposed rats. In general, therefore, those rats with the greatest lung doses were measured at the later times. Lung doses shown are those resulting from the promethium lung burdens; they do not include gamma dose. The detailed information concerning which rats were considered abnormal for each parameter is included in Table 8.

For Groups 26/46 and 29/49 gamma and promethium, and promethium only, respectively), there were not enough survivors available for the pulmonary-function tests after 100 days (Table 8). Surviving rats from the corresponding groups exposed for hematologic examination and mortality information were given pulmonary-function tests at 360 days after exposure to provide additional data.

Data from control rats in a previous experiment (Filipy et al., 1988) were included with those of this experiment for the purpose of generating the figures for control values. The other rats were acquired from the same supplier and were exposed and tested at approximately the same ages with the same procedures and equipment as rats in this experiment. Data from both groups of control rats were first analyzed separately to determine that the mean values and ranges of values for each parameter were unaffected. The net effect of including data from the other control rats was reduction of the size of the 95% confidence intervals because of the increase in the number of statistical degrees of freedom.

TABLE 8. Detailed Data for Rat Pulmonary-Function Parameters at each Time of Measurement after Exposure to ^{60}Co Gamma Irradiation and/or an Aerosol of ^{147}Pm (FAP). (Numbers in parentheses are the 95% Confidence Limit.)

Groups 21 and 41 (Control)

Males

Females

Animal Number	60 Days					Animal Number	60 Days				
	VC (5.6)	Slope (0.78)	C_{QS} (0.15)	DL_{CO} (0.07)	TLC (8.0)		VC (5.2)	Slope (1.16)	C_{QS} (0.10)	DL_{CO} (0.03)	TLC (6.0)
5202	11.9	0.40	0.72	0.43	17.9	3706	7.1	0.73	0.17	0.05	9.4
5218	10.5	0.37	0.70	0.18	13.5						

Animal Number	100 Days					Animal Number	100 Days				
	VC (5.8)	Slope (0.76)	C_{QS} (0.17)	DL_{CO} (0.08)	TLC (8.3)		VC (5.2)	Slope (1.14)	C_{QS} (0.12)	DL_{CO} (0.04)	TLC (6.4)
4721	9.5	0.48	0.57	--a	--a	4761	7.5	0.45	0.24	0.10	9.5
4725	9.4	0.53	0.50	0.25	12.0	4762	6.5	0.71	0.24	0.17	8.6
4726	10.6	0.41	0.84	--a	--a	4763	7.6	0.59	0.56	0.13	9.8
4729	11.3	0.34	0.63	0.17	14.9	4764	7.8	0.61	0.46	0.18	9.7
4730	10.5	0.50	0.75	0.25	13.6	4767	7.0	0.62	0.39	0.15	9.4
4734	10.1	0.36	0.52	0.14	17.0	4768	7.7	0.81	0.42	0.26	10.3
4739	9.8	0.52	0.70	--a	--a	4770	7.3	0.67	0.29	0.14	10.2
4742	11.7	0.43	0.89	0.18	14.7	4775	8.0	0.35	0.50	0.26	10.7
4747	5.2^b	1.27^b	0.32	0.10	6.9	4779	6.9	0.54	0.38	0.17	9.5
4749	8.6	0.81	0.80	0.14	11.3	4780	7.4	0.62	0.40	0.15	9.5

Animal Number	130 Days					Animal Number	130 Days				
	VC (5.9)	Slope (0.75)	C_{QS} (0.18)	DL_{CO} (0.08)	TLC (8.5)		VC (5.2)	Slope (1.13)	C_{QS} (0.13)	DL_{CO} (0.04)	TLC (6.6)
5208	10.1	0.45	0.75	0.23	13.1	5251	6.9	0.73	0.45	0.17	9.8
5215	9.9	0.39	0.59	0.15	13.1	5252	7.3	0.64	0.45	--a	--a

Animal Number	210 Days					Animal Number	210 Days				
	VC (6.1)	Slope (0.70)	C_{QS} (0.28)	DL_{CO} (0.11)	TLC (8.8)		VC (5.2)	Slope (1.10)	C_{QS} (0.17)	DL_{CO} (0.05)	TLC (6.8)
4723	9.4	0.53	0.39	--a	--a	4765	6.9	0.69	0.58	0.13	9.7
4724	4.8^b	2.18^b	0.19	0.13	6.8	4766	6.7	0.89	0.52	0.14	9.7
4728	9.1	0.50	0.46	0.17	12.6	4769	8.2	0.55	0.71	0.11	10.9
4735	8.4	0.57	0.66	0.18	12.7	4771	6.4	0.91	0.45	0.13	9.1
4743	9.1	0.50	0.76	0.16	11.8	4772	7.3	0.55	0.49	0.11	10.0

^aMeasurement not obtained

^bValues were not included in the definition of 95% confidence limits (see text)

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{QS} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

TABLE 8. (Continued)

Groups 21 and 41 (Control) cont'd

Males						Females					
Animal Number	270 Days					Animal Number	270 Days				
	VC (6.3)	Slope (0.68)	C _{Q5} (0.31)	DL _{CO} (0.12)	TLC (9.1)		VC (5.2)	Slope (1.07)	C _{Q5} (0.20)	DL _{CO} (0.05)	TLC (6.9)
4733	11.8	0.28	0.92	0.23	15.6	4751	7.2	0.49	0.38	0.14	9.2
4736	7.3	0.78	0.34	0.24	10.3	4755	7.5	0.52	0.45	0.13	9.8
4737	11.2	0.33	0.92	0.25	15.7	4756	7.2	0.66	0.32	0.14	9.9
4738	10.5	0.39	0.70	0.20	14.7	4758	7.3	0.57	0.44	0.14	9.4
4746	11.6	0.27	1.00	0.18	15.2	4778	7.1	0.69	0.50	0.13	9.8

Animal Number	360 Days					Animal Number	360 Days				
	VC (6.4)	Slope (0.64)	C _{Q5} (0.37)	DL _{CO} (0.14)	TLC (9.4)		VC (5.2)	Slope (0.97)	C _{Q5} (0.23)	DL _{CO} (0.06)	TLC (7.2)
5201	10.6	0.31	0.80	0.19	12.0	5233	5.8	2.01^a	0.36	0.18	10.2
5203	10.8	0.42	1.19	0.30	14.4	5236	7.4	0.78	0.59	0.15	8.3
5204	5.7^a	1.40^a	0.30	0.16	6.9	5238	6.0	0.79	0.35	0.03	6.7
5205	6.3^a	1.13	0.37	0.19	7.5	5242	6.1	0.85	0.45	0.15	7.3
5223	9.2	0.59	0.66	0.21	10.9	5245	5.7	1.03	0.38	0.18	7.1

Animal Number	370 Days					Animal Number	370 Days				
	VC (6.4)	Slope (0.63)	C _{Q5} (0.38)	DL _{CO} (0.14)	TLC (9.5)		VC (5.2)	Slope (0.96)	C _{Q5} (0.23)	DL _{CO} (0.06)	TLC (7.2)
4731	12.7	0.27	0.96	0.26	16.1	4752	7.9	0.54	0.51	0.13	10.1
4732	11.2	0.31	0.83	0.24	13.9	4753	7.7	0.45	0.52	0.15	9.9
4740	9.8	0.34	0.80	0.16	12.6	4757	7.1	0.58	0.37	0.12	9.1
4741	12.1	0.21	0.94	--b	--b	4759	7.9	0.50	0.54	0.12	10.6
4744	11.2	0.28	0.85	0.25	14.7	4760	7.9	0.50	0.59	0.16	10.2
4748	11.6	0.29	0.99	0.15	14.9						
4750	14.6	0.30	--b	0.38	--b						

^aValues were not included in the definition of 95% confidence limits (see text)^bMeasurement not obtained

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{Q5} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

TABLE 8. (Continued)

Groups 23 and 43 (Gamma only)**Males****Females**

Animal Number	60 Days					Animal Number	60 Days				
	VC (6.3)	Slope (0.68)	C _{QS} (0.31)	DL _{CO} (0.12)	TLC (9.1)		VC (5.2)	Slope (1.16)	C _{QS} (0.10)	DL _{CO} (0.03)	TLC (6.0)
						5297	6.6	0.70	0.16	0.15	9.3
Animal Number	100 Days					Animal Number	100 Days				
	VC (5.8)	Slope (0.76)	C _{QS} (0.17)	DL _{CO} (0.08)	TLC (8.3)		VC (5.2)	Slope (1.14)	C _{QS} (0.12)	DL _{CO} (0.04)	TLC (6.4)
4782	8.6	0.48	0.53	0.14	10.8	4811	6.7	0.67	0.40	0.03	9.6
4788	10.5	0.58	0.66	--a	13.9	4816	6.1	0.78	0.35	0.15	7.7
4792	11.3	0.34	0.84	0.18	16.2	4818	7.3	0.66	0.20	--a	9.6
4793	10.8	0.47	0.48	0.23	14.0	4821	6.8	0.61	0.46	0.16	8.8
4795	8.3	0.82	0.64	0.17	11.0	4827	7.4	0.50	0.39	0.16	10.3
4801	6.0	0.81	0.14	0.14	8.0	4829	6.4	0.48	0.28	0.21	8.7
4803	9.5	0.48	0.60	0.32	14.1	4830	6.4	0.55	0.35	0.33	8.6
4805	9.5	0.69	0.67	0.28	12.7	4834	6.9	0.68	0.47	0.16	9.2
4807	8.4	0.60	0.53	0.20	11.2	4839	6.8	0.60	0.28	0.23	10.4
Animal Number	210 Days					Animal Number	210 Days				
	VC (6.1)	Slope (0.70)	C _{QS} (0.28)	DL _{CO} (0.11)	TLC (8.8)		VC (5.2)	Slope (1.10)	C _{QS} (0.17)	DL _{CO} (0.05)	TLC (6.8)
4789	9.2	0.40	0.60	0.13	12.5	4812	6.3	0.77	0.35	0.14	8.5
4790	10.7	0.34	0.89	0.18	14.6	4813	6.0	0.76	0.28	0.09	9.3
4791	10.0	0.47	0.87	0.14	13.2	4822	6.2	1.05	0.29	0.13	8.8
4794	9.3	0.48	0.59	0.15	12.7	4823	6.2	1.01	0.41	0.10	8.4
4796	8.6	0.54	0.59	0.15	11.6						
Animal Number	270 Days					Animal Number	270 Days				
	VC (6.3)	Slope (0.68)	C _{QS} (0.31)	DL _{CO} (0.12)	TLC (9.1)		VC (5.2)	Slope (1.07)	C _{QS} (0.20)	DL _{CO} (0.05)	TLC (6.9)
4783	9.5	0.40	0.79	0.20	13.2	4828	6.7	0.54	0.38	0.13	9.0
4787	10.0	0.40	0.77	0.20	12.8	4831	6.3	0.53	0.28	0.14	8.6
4798	11.3	0.29	0.58	0.25	15.0	4833	6.1	0.53	0.46	0.14	8.9
4799	10.0	0.35	0.65	0.17	13.5	4836	5.0	0.90	0.68	0.12	7.1
4809	8.5	0.28	0.55	0.21	11.2	4837	6.3	0.68	0.41	0.15	8.5

^aMeasurement not obtained

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{QS} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

TABLE 8. (Continued)

Groups 23 and 43 (Gamma only) cont'd

Males						Females					
Animal Number	360 Days					Animal Number	360 Days				
	VC (6.4)	Slope (0.64)	C _{QS} (0.37)	DL _{CO} (0.14)	TLC (9.4)		VC (5.2)	Slope (0.97)	C _{QS} (0.23)	DL _{CO} (0.06)	TLC (7.2)
5277	8.1	0.50	0.75	0.06	11.0	5301	6.1	0.72	0.47	0.12	7.8
5280	5.7	1.93	0.35	0.24	10.1	5303	5.9	0.61	0.41	0.12	7.3
5283	9.0	0.64	0.72	0.19	10.2	5311	6.6	0.83	0.43	0.13	8.7
5285	8.2	1.06	0.20	0.25	11.8	5314	5.9	0.74	0.44	0.11	7.1
5286	8.3	0.69	0.53	0.21	10.4	5318	6.0	0.74	0.43	0.13	7.9
5290	7.8	0.61	0.48	0.16	9.3						

Animal Number	370 Days					Animal Number	370 Days				
	VC (6.4)	Slope (0.63)	C _{QS} (0.38)	DL _{CO} (0.14)	TLC (9.5)		VC (5.2)	Slope (0.96)	C _{QS} (0.23)	DL _{CO} (0.06)	TLC (7.2)
4786	11.5	0.39	0.89	0.14	14.9	4824	7.2	0.53	0.45	0.09	9.5
4797	7.3	0.81	0.35	0.11	10.3	4832	5.8	0.93	0.38	0.12	7.7
4800	9.9	0.38	0.77	--a	--a	4835	6.3	0.78	0.25	0.13	8.7
4802	11.4	0.30	0.82	0.16	15.0	4838	7.2	0.69	0.44	0.14	10.0
4806	8.7	0.55	0.50	0.18	11.8	4840	6.4	0.78	0.32	0.10	7.7

^aMeasurement not obtained^bLung dose from promethium, exclusive of gamma dose

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{QS} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

Groups 26 and 46 (Promethium and Gamma, 8.5 Gy or 850 rad)

KEY: C_{QS} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

TABLE 8. (Continued)

Groups 26 and 46 (Promethium and Gamma, 8.5 Gy or 850 rad) cont'd

Males							Females						
Animal Number	360 Days						Animal Number	360 Days					
	Dose ^a	VC (6.4)	Slope (0.64)	C _{Qs} (0.37)	DL _{CO} (0.14)	TLC (9.4)		Dose ^a	VC (5.2)	Slope (0.97)	C _{Qs} (0.23)	DL _{CO} (0.06)	TLC (7.2)
5324	160	6.0	1.12	0.42	0.16	8.3	5351	241	2.1	7.31	0.15	0.05	2.6
5329	200	4.0	2.05	0.28	0.10	4.7	5352	161	4.5	1.08	0.28	0.11	6.3
5330	144	4.9	1.34	0.29	0.06	5.7	5355	232	1.8	13.80	0.10	0.06	3.2
5331	211	5.4	1.65	0.34	0.13	6.9	5359	172	4.1	1.81	0.22	0.08	5.3
5333	135	6.8	0.77	0.40	0.09	9.7	5363	191	1.8	11.62	0.11	0.02	2.5
5334	133	6.8	0.57	0.57	0.15	8.7	5372	204	3.6	2.76	0.23	0.10	5.0
5346	264	2.8	4.07	0.17	0.08	3.9							
5348	175	6.5	0.71	0.46	0.14	9.0							

^aLung dose from promethium, exclusive of gamma dose

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{Qs} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

TABLE 8. (Continued)

Groups 29 and 49 (Promethium only)**Males**

Animal Number	60 Days					
	Dose	VC (5.6)	Slope (0.78)	C _{Qs} (0.15)	DL _{CO} (0.07)	TLC (8.0)
3713	133	10.3	0.47	0.46	0.21	13.5
5475	99	10.8	0.24	1.13	0.17	13.7
5477	197	9.5	0.50	0.67	0.23	14.8
5479	171	7.0	0.67	0.12	0.02	9.7
5480	104	6.8	0.85	0.08	0.13	10.4

Females

Animal Number	60 Days					
	Dose	VC (5.2)	Slope (1.16)	C _{Qs} (0.10)	DL _{CO} (0.03)	TLC (6.0)
3719	212	7.2	0.77	0.43	0.13	9.7
5481	188	7.6	0.74	0.49	0.05	10.2
5482	196	6.4	0.89	0.20	--a	--a
5488	252	7.1	0.90	0.24	0.16	9.6
5490	195	7.3	0.71	0.42	--a	--a

Animal Number	90 Days					
	Dose	VC (5.8)	Slope (0.77)	C _{Qs} (0.17)	DL _{CO} (0.08)	TLC (8.2)
4346	267	7.3	0.71	0.35	0.13	10.1
4347	248	8.1	0.75	0.34	0.14	10.7
4348	110	2.1	9.60	0.10	0.03	3.3
4349	175	9.0	0.67	0.59	0.15	10.0
4350	222	3.7	4.96	0.16	0.08	5.3
4351	311	5.3	1.99	0.28	0.08	7.0
4352	230	7.9	0.71	0.47	0.06	10.3
4354	219	7.7	0.77	0.57	0.12	10.3
4355	178	6.2	1.20	0.23	0.08	8.4
4359	208	2.7	4.24	0.11	0.01	5.0

Animal Number	90 Days					
	Dose	VC (5.2)	Slope (1.14)	C _{Qs} (0.12)	DL _{CO} (0.04)	TLC (6.3)
4376	248	5.2	1.66	0.13	0.06	7.2
4377	418	4.0	3.51	0.22	0.06	5.6
4378	222	4.2	1.96	0.19	0.07	5.8
4380	391	6.1	0.83	0.24	0.08	7.9
4381	229	5.7	1.07	0.29	0.09	7.6
4382	269	5.5	3.04	0.43	0.06	8.0
4384	163	7.0	0.71	0.37	0.13	9.1
4385	182	6.0	0.89	0.32	0.11	8.2
4387	280	3.4	5.65	0.17	0.06	5.1
4390	335	4.1	1.62	0.22	0.08	5.7

Animal Number	130 Days					
	Dose	VC (5.9)	Slope (0.75)	C _{Qs} (0.18)	DL _{CO} (0.08)	TLC (8.5)
3711	97	9.0	0.48	0.86	0.22	11.6
3714	204	8.0	0.61	0.42	0.14	10.4
3715	185	5.7	0.40	0.40	0.12	8.6
5471	154	8.0	0.76	0.49	0.15	10.6
5476	194	7.8	0.82	0.52	0.16	10.7

Animal Number	130 Days					
	Dose	VC (5.2)	Slope (1.13)	C _{Qs} (0.13)	DL _{CO} (0.04)	TLC (6.6)
3716	337	2.8	6.33	0.11	0.01	4.1
3718	288	4.3	1.42	0.17	0.05	6.1
3720	218	6.2	1.20	0.47	0.07	8.4
5487	315	4.3	2.30	0.26	0.05	6.1

aMeasurement not obtained

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{Qs} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

TABLE 8. (Continued)

Groups 29 and 49 (Promethium only) cont'd

Males							Females						
Animal Number	180 Days						Animal Number	180 Days					
	Dose	VC (6.1)	Slope (0.71)	C _{Qs} (0.27)	DL _{CO} (0.10)	TLC (8.7)		Dose	VC (5.2)	Slope (1.11)	C _{Qs} (0.16)	DL _{CO} (0.05)	TLC (6.8)
4511	314	4.8	1.74	0.23	0.10	6.9	4388	242	4.8	1.69	0.48	0.07	7.4
4513	267	6.0	0.97	0.31	0.10	7.9	4529	298	2.4	3.85	0.16	0.03	3.7
4514	251	7.6	0.83	0.53	0.13	11.0	4536	394	3.9	2.28	0.30	0.05	5.0
4516	94	7.8	0.57	0.62	0.12	10.5	4538	266	5.5	1.07	0.26	0.08	7.6
4521	64	10.6	0.38	0.95	0.19	12.9							

Animal Number	360 Days						Animal Number	360 Days					
	Dose	VC (6.4)	Slope (0.64)	C _{Qs} (0.37)	DL _{CO} (0.14)	TLC (9.4)		Dose	VC (5.2)	Slope (0.97)	C _{Qs} (0.23)	DL _{CO} (0.06)	TLC (7.2)
5382	169	6.5	1.17	0.41	0.18	9.3	5411	228	2.9	3.62	0.13	0.06	3.9
5383	214	6.5	0.97	0.43	0.19	8.0	5413	326	2.8	5.17	0.19	0.08	3.9
5387	211	4.2	1.73	0.29	0.11	5.5	5415	467	1.6	10.88	0.04	0.06	2.7
5400	307	4.2	2.73	0.28	0.11	5.5	5418	352	2.6	3.47	0.17	0.06	4.2
5402	396	4.2	2.54	0.26	0.12	6.6	5419	352	2.8	4.13	0.15	0.05	4.2
5404	315	4.0	2.59	0.24	0.10	5.7	5420	315	2.4	4.37	0.15	0.07	3.7
5405	338	3.9	3.74	0.23	0.13	6.4	5437	302	4.1	2.81	0.26	0.09	6.4
5409	250	4.3	1.54	0.21	0.13	6.2	5438	334	2.7	4.57	0.17	0.07	3.4

^aLung dose from promethium, exclusive of gamma dose

NOTE: Boldface values are those less than or equal to (or greater than or equal to, if slope) the 95% confidence limits of controls.

KEY: C_{Qs} = Quasistatic compliance (ml/mm H₂O); DL_{CO} = Carbon-monoxide diffusing capacity (ml/min/mm Hg); Slope = alveolar plateau of the single-breath nitrogen washout curve (% N₂/ml); TLC = Total lung capacity (ml); VC = Vital capacity (ml)

Generating the confidence intervals ultimately used for control values in the figures was a two-step process. First, all data were plotted with the resultant 95% confidence limits. Next, points outside of those limits were dropped from the data set and new confidence intervals were defined. The points that were eliminated from the data set were usually quite disparate with respect to the retained points. Values for those points were included in Table 8 and are identified there, but they are not plotted in the figures. The purpose of this exercise was to avoid using an occasional aberrant value and values from functionally impaired control rats to define the confidence intervals. Because of this procedure and because values for control rats of the previous experiment (Filipy et al., 1988) are included in the plots, the plotted values in the figures do not match the values in Table 8.

Vital capacity increased slightly with time in male (Figure 27) but not in female (Figure 28) control rats. Values for four males were lower than the LCL (Table 8). Three of the males were considered functionally impaired (i.e., three of four parameters measured were outside the confidence interval).

FIGURE 27. Mean Vital Capacities (Including Individual Data and the 95% Confidence Interval) of Control Male Rats for 1 Year after Sham Exposure

FIGURE 28. Mean Vital Capacities (Including Individual Data and the 95% Confidence Interval) of Control Female Rats for 1 Year after Sham Exposure

Exposure to gamma radiation had little effect on VC in males (Figure 29) or in females (Figure 30). The value for one male was below the LCL 360 days after exposure, and one female had a VC below the LCL 270 days after exposure. Otherwise, all values for both sexes were well within the normal range throughout the experiment.

FIGURE 29. Vital Capacities of Individual Male Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

In general, lung doses of approximately 250 Gy (2500 rad) or more from promethium only (Groups 29 and 49) were sufficient to reduce VC (Figures 31 and 32). Rats of both sexes exposed to promethium with gamma irradiation (Groups 26 and 46) generally had diminished VC with lung doses from promethium of 100 to 150 Gy (10,000 to 15,000 rad; Figures 31 and 32). Eleven of 14 rats tested from Groups 26 and 46 (promethium plus gamma) had VC below the LCL at 360 days after exposure, and 14 of 16 rats from Groups 29 and 49 (promethium only) were similarly impaired. Lung doses of the latter groups were considerably higher, however (Table 8).

For the SBN_2 test, a greater slope of Phase III of the curve (alveolar plateau) indicates functional impairment. Therefore, animals whose values were above the upper 95% confidence limit were considered impaired. Figures 33 and 34 show the control mean values, with 95% confidence intervals. Six male and two female control rats were considered impaired with respect to slope (Table 8); four of the males were considered functionally impaired. Values for rats exposed to gamma radiation only (Groups 23 and 43) are shown in Figures 35 and 36. Two males had slightly increased slopes at 100 days after exposure, and five males had increased slopes at 360 and 370 days after exposure. Only two of the five were impaired with respect to three of the four parameters used to assess functional impairment. No females of these groups had slopes above the UCL. The scales on the ordinates of Figures 35

and 36 are greater by a factor of four than those for control values because the slopes of gamma-exposed rats were greater than those of control rats.

FIGURE 30. Vital Capacities of Individual Female Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

The ordinates of the figures containing slope data for Groups 26/46 and 29/49 (promethium plus gamma and promethium, respectively; Figures 37 and 38) are on a scale 20 times greater than for control animals to accommodate the data. Virtually all rats with promethium lung burdens, whether or not they were also exposed to gamma radiation, had greater-than-normal slopes of alveolar plateaus at 360 days after exposure. For most rats of Groups 29 and 49, promethium lung doses greater than 200 Gy (20,000 rad) increased slopes at 90 days or more after exposure. Rats of Groups 26 and 46 (promethium plus gamma) had slopes greater than the UCL at the first measurements if their lung doses were 100 Gy (10,000 rad) or more (Table 8).

The data for C_{Qs} of control rats are plotted in Figures 39 and 40; three males had values lower than the LCL for this parameter; all three were otherwise functionally impaired. Gamma-irradiation had little effect on C_{Qs} . Three of 11 male rats measured at 360 and 370 days after exposure had values lower than the LCL of control rats, but no females were so affected (Figures 41 and 42; Table 8).

In general, C_{Qs} was not severely affected by inhaled promethium until a year after exposure. At that time, 9 of 14 rats exposed to promethium with gamma irradiation (Groups 26 and 46) had C_{Qs} values below the LCL of control rats and 13 of 16 rats in Groups 29 and 49 (promethium only) were so affected (Table 8). As shown by the data in Figures 43 and 44, lung doses of 250 and 350 Gy (25,000 and 35,000 rad) reduced C_{Qs} values to below the LCL of control rats in males and females, respectively, in Groups 29 and 49 (promethium only). Corresponding lung doses of 200

and 300 Gy (20,000 and 30,000 rad) caused similar reduction of C_{Q5} in males and females, respectively, in Groups 26 and 46 (promethium plus gamma).

FIGURE 31. Vital Capacities of Individual Male Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

Mean values, with 95% confidence intervals, for DL_{CO} are shown in Figures 45 and 46. Comparing these data with those of rats exposed to gamma radiation only (Figures 47 and 48) indicates that gamma irradiation had very little effect on DL_{CO} until a year after exposure and only 3 of 11 males had diminished values at that time. Promethium exposure, without gamma irradiation (Groups 29 and 49), resulted in DL_{CO} values below the LCL of control rats with lung doses of 250 and 350 Gy (25,000 and 35,000 rad) for males and females, respectively (Figures 49 and 50). For rats exposed to promethium with gamma irradiation (Groups 26 and 46), the same effect was caused by lung doses approximately 50 Gy (5000 rad) lower. In Groups 26 and 46, 9 of 14 rats had impaired DL_{CO} at 360 days after exposure, and 10 of 16 rats of Groups 29 and 49 had impaired DL_{CO} at that time (Table 8).

In all exposure groups, the effect on TLC (Figures 51 through 56) was essentially the same as on VC (Figures 27 through 32). For that reason, and because both parameters were closely related as divisions of lung volume, only VC was considered when deciding which animals were functionally impaired.

FIGURE 32. Vital Capacities of Individual Female Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 33. Mean Slopes of the Alveolar Plateaus from the Single-Breath Nitrogen Washout (Including Individual Data and the 95% Confidence Interval) of Control Male Rats Within 1 Year of Sham Exposure

FIGURE 34. Mean Slopes of the Alveolar Plateaus from the Single-Breath Nitrogen Washout (Including Individual Data and the 95% Confidence Interval) of Control Female Rats Within 1 Year of Sham Exposure

FIGURE 35. Slopes of the Alveolar Plateaus of Individual Male Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; UCL = Upper Confidence Limits of Controls)

FIGURE 36. Slopes of the Alveolar Plateaus of Individual Female Rats Exposed to ⁶⁰Co Gamma Radiation (890 rad or 8.9 Gy; UCL = Upper Confidence Limits of Controls)

FIGURE 37. Slopes of the Alveolar Plateaus of Individual Male Rats Exposed to ¹⁴⁷Pm (FAP) With or Without Additional Exposure to ⁶⁰Co Gamma Radiation (850 rad or 8.5 Gy; UCL = Upper Confidence Limits of Controls)

FIGURE 38. Slopes of the Alveolar Plateaus of Individual Female Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; UCL = Upper Confidence Limits of Controls)

FIGURE 39. Mean Quasistatic Lung Compliance Between 2 and 5 cm H_2O Transpulmonary Pressure (Including Individual Data and the 95% Confidence Interval) of Control Male Rats Within 1 Year of Sham Exposure

FIGURE 40. Mean Quasistatic Lung Compliance Between 2 and 5 cm H₂O Transpulmonary Pressure (Including Individual Data and the 95% Confidence Interval) of Control Female Rats Within 1 Year of Sham Exposure

FIGURE 41. Quasistatic Lung Compliance Between 2 and 5 cm H₂O Transpulmonary Pressure of Individual Male Rats Exposed to ⁶⁰Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 42. Quasistatic Lung Compliance Between 2 and 5 cm H₂O Transpulmonary Pressure of Individual Female Rats Exposed to ⁶⁰Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 43. Quasistatic Lung Compliance Between 2 and 5 cm H₂O Transpulmonary Pressure of Individual Male Rats Exposed to ¹⁴⁷Pm (FAP) Lung Burdens With or Without Additional Exposure to ⁶⁰Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 44. Quasistatic Lung Compliance Between 2 and 5 cm H₂O Transpulmonary Pressure of Individual Female Rats Exposed to ¹⁴⁷Pm (FAP) Lung Burdens With or Without Additional Exposure to ⁶⁰Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 45. Mean Carbon Monoxide Diffusing Capacities (Including Individual Data and the 95% Confidence Interval) of Control Male Rats Within 1 Year of Sham Exposure

FIGURE 46. Mean Carbon Monoxide Diffusing Capacities (Including Individual Data and the 95% Confidence Interval) of Control Female Rats Within 1 Year of Sham Exposure

FIGURE 47. Carbon Monoxide Diffusing Capacities of Individual Male Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 48. Carbon Monoxide Diffusing Capacities of Individual Female Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 49. Carbon Monoxide Diffusing Capacities of Individual Male Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 50. Carbon Monoxide Diffusing Capacities of Individual Female Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 51. Mean Total Lung Capacities (Including Individual Data and the 95% Confidence Interval) of Control Male Rats Within 1 Year of Sham Exposure

FIGURE 52 Mean Total Lung Capacities (Including Individual Data and the 95% Confidence Interval) of Control Female Rats Within 1 Year of Sham Exposure

FIGURE 53. Total Lung Capacities of Individual Male Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 54. Total Lung Capacities of Individual Female Rats Exposed to ^{60}Co Gamma Radiation (890 rad or 8.9 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 55. Total Lung Capacities of Individual Male Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

FIGURE 56. Total Lung Capacities of Individual Female Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy; LCL = Lower Confidence Limits of Controls)

For statistical analysis of exposure effects on pulmonary function, data for each parameter were placed into four groups, reflecting the times after exposure when the tests were performed:

- A = 60-130 days after exposure,
- B = 180-210 days after exposure,
- C = 270 days after exposure,
- D = 340-370 days after exposure.

In some exposure groups, few, if any, animals survived to be tested at the later times and, as indicated previously, tests at 360 and 370 days after exposure were made on rats of the mortality groups that had survived to the end of the experiment (1 year). Results of the statistical analyses are presented in Table 9.

In the table, superscripts over mean values are used to indicate statistical significance of differences between the means of each group within each time range. Differences were significant only between those means that have dissimilar superscripts. In females of range A, for example, the means of Groups 21/41 and 23/43 (superscript 1) are not statistically different. Each of the means of Groups 26/46 (superscript 3) and 29/49 (superscript 2) is different from those of Groups 21/41 and 23/43, and they are also statistically different from each other. The superscripts are used in this manner only in horizontal rows of data; they do not indicate differences between means of different time ranges.

Generally, means of groups exposed to gamma radiation alone were not significantly different from those of control groups regardless of the times at which the tests were performed. Means of Groups 29/49 (promethium alone) are different from control means at nearly all times after exposure for each parameter except CQs

and Phase III slopes at the earlier times. At the time of the last measurements, however, those values were also different from the control values. Means of Groups 26/46 (promethium and gamma) were consistently different from control means throughout the experiment for each pulmonary-function parameter measured.

For the slope of Phase III, the numbers of rats included in the means were different from those for other parameters because all slope values above 10.0 were excluded from the statistical analysis. They were so far above the normal slope (usually less than 1.0) that they increased variance from the means and made the analysis less sensitive. Including data from those rats resulted in no indicated effect of promethium, with or without gamma irradiation, on slopes. Slope data of seven rats were excluded on that basis; five of those rats were from Groups 26/46.

The two other pulmonary-function parameters measured were the area beneath the MBN₂ curve (Area N₂) and closing volumes from the SBN₂ curve. Analyses of control values and values from exposed rats indicated that these parameters were not appropriate for use. The Area N₂ measurement resulted in clearly defined mean values for control rats; however, analysis of values from exposed rats were not outside the 95% confidence interval, regardless of impairment with respect to the other parameters. Analysis of closing volumes, from the SBN₂ curve, did not result in clearly defined control values because of a large degree of individual variation.

The boldface values in Table 8 are those that were below the lower 95% confidence limit (or above, for Slope III) for the listed parameters at the time of measurement. When a rat was indicated as "sick" for three or four of the four parameters (VC, slope, CQ₅ and DLCO), its lungs were considered functionally impaired, and the animal was considered morbid.

Cumulative morbidity fractions for lung dose intervals were fitted to Weibull distribution curves, which are shown in Figure 57. As with mortality curves, only the lung dose from promethium exposure was considered; the gamma dose was not included. The D₅₀ values were approximately 300 Gy (18,000 rad) for rats exposed to promethium only and 180 Gy (32,000 rad) for rats exposed to promethium with gamma radiation. The difference between D₅₀ values was over 14 times that for the gamma dose of 8.5 Gy (850 rad) to the rats that received both radiation insults.

Threshold doses for morbidity can be approximated by extrapolating the curves of Figure 57 toward the abscissa. For rats exposed only to promethium, a lung dose of 240 Gy (24,000 rad) could be considered that at which they became morbid. For rats exposed to promethium-plus-gamma, the corresponding value is 100 Gy (10,000 rad).

TABLE 9. Statistical Comparison of Pulmonary Function Parameters over Time

Time Range After Exposure	Control (21/41)		Gamma (23/43)		Gamma + Promethium (26/46)		Promethium (29/49)	
	Number	Mean	Number	Mean	Number	Mean	Number	Mean
Vital Capacity								
Females								
A 60-130 d	13	7.31 ¹	10	6.74 ¹	13	4.05 ³	19	5.49 ²
B 180-210 d	5	7.10 ¹	4	6.18 ^{1,2}	1	2.60 ³	4	4.15 ^{2,3}
C 270 d	6	7.37 ¹	5	6.08 ²				
D 340-370 d	10	6.84 ¹	10	6.34 ¹	6	2.98 ²	8	2.74 ²
Males								
A 60-130 d	14	9.94 ¹	9	9.21 ^{1,2}	13	5.76 ³	20	7.14 ^{2,3}
B 180-210 d	5	8.16 ¹	5	9.56 ¹			5	7.36 ¹
C 270 d	5	10.48 ¹	5	9.86 ¹				
D 340-370 d	12	10.48 ¹	11	8.72 ¹	10	4.95 ²	8	4.72 ²
Slope								
Females								
A 60-130 d	13	0.62 ¹	10	0.62 ¹	12	3.26 ²	19	1.91 ¹
B 180-210 d	5	0.72 ¹	4	0.90 ¹	1	4.47 ²	4	2.22 ¹
C 270 d	6	0.57 ¹	5	0.64 ²				
D 340-370 d	9	0.84 ¹	10	0.74 ¹	4	3.24 ²	7	4.02 ²
Males								
A 60-130 d	14	0.52 ¹	9	0.59 ¹	12	1.10 ¹	19	1.15 ¹
B 180-210 d	5	0.86 ¹	5	0.45 ¹			5	0.90 ¹
C 270 d	5	0.41 ¹	5	0.34 ¹				
D 340-370 d	12	0.49 ¹	11	0.71 ¹	9	1.64 ²	8	2.13 ²
Quasistatic Compliance								
Females								
A 60-130 d	13	0.38 ¹	10	0.33 ¹	13	0.22 ²	19	0.28 ^{1,2}
B 180-210 d	5	0.55 ¹	4	0.33 ^{1,2}	1	0.17 ²	4	0.30 ^{1,2}
C 270 d	6	0.43 ¹	5	0.44 ¹				
D 340-370 d	9	0.46 ¹	10	0.40 ¹	6	0.19 ²	8	0.16 ²
Males								
A 60-130 d	14	0.66 ¹	9	0.57 ^{1,2}	13	0.34 ²	20	0.42 ²
B 180-210 d	5	0.49 ¹	5	0.45 ¹			5	0.53 ¹
C 270 d	5	0.78 ¹	5	0.67 ¹				
D 340-370 d	11	0.79 ¹	11	0.58 ¹	10	0.32 ²	8	0.29 ²
Carbon Dioxide Diffusing Capacity								
Females								
A 60-130 d	12	0.16 ¹	9	0.18 ¹	13	0.07 ²	17	0.08 ²
B 180-210 d	5	0.12 ¹	4	0.12 ¹	1	0.05 ²	4	0.06 ²
C 270 d	6	0.13 ¹	5	0.14 ¹				
D 340-370 d	9	0.14 ¹	10	0.12 ¹	6	0.07 ²	8	0.07 ²
Males								
A 60-130 d	11	0.20 ¹	8	0.21 ¹	13	0.12 ²	20	0.12 ²
B 180-210 d	4	0.16 ¹	5	0.15 ¹			5	0.13 ¹
C 270 d	5	0.22 ¹	5	0.21 ¹				
D 340-370 d	11	0.23 ¹	10	0.17 ^{1,2}	10	0.11 ²	8	0.13 ²

FIGURE 57. Comparison of Weibull Cumulative Distribution Curves of Percent Morbidity with Lung Dose in Male and Female Rats Exposed to ^{147}Pm (FAP) With or Without Additional Exposure to ^{60}Co Gamma Radiation (850 rad or 8.5 Gy)

DISCUSSION

MORTALITY

Rats of the Fisher strain are quite resistant to gamma-irradiation compared to rats of other strains. The $LD_{50/30}$ ranges for rats, in general, are reportedly between 7 and 8 Gy (700 to 800 rad; Bond et al., 1965; Jones, 1981). In our first attempt to determine the dose/mortality relationship shown in Figure 1, groups of rats were given graded exposures between 5.5 and 8.0 Gy (550 and 800 rad); all survived. Subsequent series of graded exposures resulted in the mortality shown in Figure 1, which indicates an $LD_{50/30}$ of approximately 9 Gy (900 rad).

Exposures required to produce 20, 40, and 60% lethality were extracted from data shown in Figure 1. In a previous experiment (Filipy et al., 1988), those exposures resulted in 7, 30, and 43% 30-day mortality for low, medium, and high gamma doses, respectively. In this experiment (Tables 4 through 6), 30-day mortality was much lower: 4.8% for rats that received medium gamma doses (8.9 Gy or 890 rad) and no mortality in the low or high gamma-irradiation dose groups.

We can offer no explanation for the reduction in mortality rate from one experiment to the other. Dosimetry was carefully monitored in both experiments. Doses for rats in Groups 21 through 35 and 39 were calculated on the same basis as for the first experiment (Filipy et al., 1988); the same exposure facility was used. Exposures of rats in Groups 41 and 43 were conducted in a facility ordinarily used for dosimeter calibration, and the dose rates were well characterized. Additionally, TLD were used to verify doses for all exposures. Also, rats were obtained from the same source for all exposures and, presumably, were from the same genetic stock.

Generally, rats that survived the first 30 days after gamma exposure lived past 300 days after exposure, when the mortality rate increased. Slight increases in mortality occurred in males at 250 days after exposure and in females at 150 days after exposure; however, approximately 80% of both males and females survived until the experiment was terminated. At 365 days after exposure, mortality of males indicated a slight dose-dependence (Figure 7), although an inverse dose-dependence was indicated for females (Figure 8).

Nearly half the gamma-exposed animals that died at later times had tumors, the majority of which were carcinomas, fibromas, or fibrosarcomas (epidermal and dermal). Because relatively few tumors occurred in control rats, these must be considered radiation-induced. Deaths that occurred during the first 30 days after exposure were from bone-marrow radiation syndrome.

Rats exposed to promethium died from radiation pneumonitis and pulmonary fibrosis. The $LD_{50/365}$ of promethium, without gamma exposure, was determined to be approximately 290 Gy (29000 rad; 365-day lung dose) for rats. This dose corresponds to an ILB of approximately 3.3 MBq (90 μ Ci)/g lung. In terms of ILB, the curve for promethium only (Figure 17) ranges between 2.2 and 4.4 MBq (60 and 120 μ Ci)/g lung, which would result in a range of mortality from very low to nearly complete within a year of exposure. Plots of survival times versus ILB (Figures 9 and 10) also show that only two of the rats that survived for more than 1 year past exposure had ILB greater than 4.4 MBq (120 μ Ci)/g lung.

Curves in Figures 13 and 14 for exposure to ^{147}Pm (FAP), alone, indicate that survival time was dependent on the ILB. In terms of $\mu\text{Ci/g}$ lung, the low, medium, and high ILB used to construct the curves are roughly equivalent for males and females. The lowest ILB range for females (Figure 14) was slightly lower than that for males (Figure 13) and the resultant survival curves reflect that difference with increased survival times for females.

The relationship between lung dose from promethium and mortality within a year of exposure in this experiment was similar to that observed by Scott et al. (1987b, 1988). They noted 365-day, median lethal doses between 260 and 270 Gy (26,000 and 27,000 rad) for rats that died from radiation pneumonitis. The slopes of their dose/mortality curves were also similar to that of the curve in Figure 17 of this report.

Comparison of dose/mortality data from inhaled promethium with those of other inhaled beta-emitting radionuclides indicates similar curves and D_{50} doses for rats exposed to ^{147}Pm (FAP), ^{90}Sr - ^{90}Y (FAP), and ^{90}Y plus ^{90}Sr - ^{90}Y (FAP). These similarities led Scott et al. (1987b) to conclude that the energy of beta emissions from inhaled radionuclides did not affect mortality rates of rats. For ^{90}Y plus 2.3% ^{90}Sr - ^{90}Y (FAP), the median lethal 365-day dose was lower, 190 Gy (19,000 rad), even though the shape of the dose/mortality curve was essentially the same as that for the other radionuclides. The difference in D_{50} was attributed to the more rapid delivery of lung dose by ^{90}Y (Scott et al., 1987b).

A dose/mortality curve for rats with promethium lung burdens plus total-body gamma exposures is included in Figure 17. Lung doses (365-day doses) of 100 and 300 Gy (10,000 and 30,000 rad), respectively, resulted in low to nearly 100% mortality within a year of exposure with a D_{50} of approximately 160 Gy (16,000 rad). This curve, based on the promethium dose to lung only, includes animals of the gamma-exposed groups that died within 30 days of exposure. This early mortality is the reason the curve begins at approximately 20% mortality; however, it had little effect on the slope of the curve compared to that from promethium without total-body gamma exposure.

Consideration was given to one possible mechanism by which the effect of inhaled promethium could be enhanced by total-body gamma irradiation. Logically, impaired lung clearance of promethium caused by the gamma radiation would result in higher lung doses from promethium and, therefore, a higher mortality rate, even though the ILB was similar.

Impaired lung clearance by gamma irradiation has been reported in results of experiments designed for that purpose (Ferin et al., 1965) showed that total-body X-ray exposure of 300 R caused impaired clearance of silicon dioxide from the lungs of rats, but only if the rats were exposed 1 day or less before inhalation of the silicon dioxide. Rhoads et al. (1981) reported decreased clearance of plutonium from the lungs of rats caused by ^{137}Cs gamma irradiation, although the exposure conditions were quite different from those reported by Ferin et al. (1965), in that the rats were exposed to plutonium several months after gamma irradiation. Gamma exposure was to the thoracic regions of the rats, and effects were noted only at doses of 1500 and 1800 R. Decreased clearance from the lungs of rats was also reported by Sanders et al. (1983). In that experiment, plutonium was inhaled only 1 day after exposure to 4 Gy (400 rad) total-body ^{60}Co gamma radiation. The indicated difference in clearance between the exposed and unexposed groups was based on *in vivo* determinations of plutonium content. Added investigations and further analysis of

the data resulted in a conclusion by Rhoads et al. (1988) that total-body gamma irradiation (4 Gy or 400 rad) had no statistically significant effect on lung clearance of inhaled plutonium.

In a previous experiment with inhalation of $^{239}\text{PuO}_2$ after gamma irradiation in rats and beagle dogs (Filipy et al., 1988), no effect of gamma irradiation on lung clearance was demonstrated. Lung clearance in rats was affected, however, by the amount of plutonium inhaled. Two separate clearance curves were used in that study: one for rats with ILB >23 kBq (625 nCi)/g lung and one for rats with ILB less than that. The value was chosen more or less arbitrarily in that there may well have been a continuum of clearance curves between the highest and lowest ILB.

Scott et al. (1988) determined different clearance rates of ^{147}Pm (FAP) and ^{238}Pu (FAP) from the lungs of rats when inhaled individually or together. They used separate clearance curves for each radionuclide when it was inhaled alone and when the two were inhaled together. They did not speculate about the reasons for the lung clearance differences.

On the basis of the results reported above, data from our experiment were analyzed over a wide range of lung burdens, and no consistent effect of the total-body gamma doses between 8.5 and 9.2 Gy (850 and 915 rad) on lung clearance of promethium in rats was demonstrated. Nor was there an apparent effect of the amount of promethium inhaled on lung clearance with this beta-emitting radionuclide.

Mortality rates of rats within 30 days of exposure to promethium with gamma irradiation were significantly greater than those of rats exposed to gamma irradiation alone (Table 4). The acute lethal effect of gamma irradiation is considered to be a result of severely depressed blood cell concentrations (Bond et al., 1965); data in Appendix B indicate that that occurred in this experiment.

Inhaled radionuclides could influence mortality from gamma exposure within 30 days of exposure if there were an effect on hematologic stem cells in the bone marrow, and that has been reported when relatively soluble forms of beta-emitting radionuclides were inhaled. Bone-marrow aplasia was a consistent observation in experiments in which beagle dogs were exposed to aerosols of ^{90}Sr , ^{144}Ce , and ^{91}Y as chlorides (ICRP, 1980). Bone-marrow effects were not reported for dogs that had inhaled the same radionuclides in the form of relatively insoluble FAP (ICRP, 1980); nor were they reported by Scott et al. (1987b) for rats exposed to aerosols of ^{90}Sr , ^{90}Y , or ^{147}Pm (FAP).

Some of the hematologic data collected in our experiment suggested a transient bone-marrow effect of ^{147}Pm (FAP). Erythrocyte concentrations in circulating blood of rats exposed to an aerosol of promethium without gamma irradiation (Table B3) were lower than the LCL of control rats at 18 and 30 days after exposure. Concentrations of other blood elements of myelogenous origin, such as segmented neutrophils (Table B11) and blood platelets (Table B19), were not remarkably depressed at the same times after exposure. Also, concentrations of those blood elements and erythrocytes in the groups of rats exposed to promethium with gamma irradiation were not lower than those exposed to gamma only. Any bone-marrow effect of ^{147}Pm (FAP) was minimal and therefore was probably not a major factor in mortality from promethium with gamma irradiation within 30 days of exposure.

The predicted mortality fractions in Table 10 were calculated using the additive model (U.S. NRC, 1975) with actual mortality fractions from inhaled ^{147}Pm (FAP) with or without gamma exposures (Figure 17) and from gamma irradiation (Figures 7 and 8). Data from the high, medium, and low gamma exposures were combined because 1-year mortality within those groups of rats varied by only a few percent. The values in Table 10 show a great disparity between the predicted mortality and actual mortality rates in rats that received both exposures, especially at the lower promethium lung doses.

TABLE 10. Mortality of Rats Exposed to Gamma Irradiation and/or ^{147}Pm (FAP) Compared with Mortality Predicted Using the Additive Model of the U.S. Nuclear Regulatory Commission (1975)

Promethium Lung Dose (Gy)	Induced Mortality (%)		Mortality (%)	
	Promethium	Gamma	Predicted	Actual
200	9	20	27	72
250	26	20	41	90
300	54	20	63	99
350	81	20	85	100

A more accurate prediction of lethality from radiation pneumonitis resulting from the combined exposures can be determined using the hazard function model of Scott et al. (1989). That model states that for immediate lethal exposure $(X_g)^{2.4} + X_b = 1$, where X_g and X_b are the normalized lung doses from total-body gamma irradiation and inhaled promethium, respectively, the exponent 2.4 is based on the ratio of the shape factors of the dose/mortality curves. For our experiment, the average gamma dose (8.9 Gy or 890 rad) was used; the report of Scott et al. (1989) indicated that lethality from radiation pneumonitis would be expected in rats and mice from an external thoracic dose of 13 Gy (1300 rad) X- or gamma radiation. X_g is equal to $8.9/13.0$ or 0.7, and X_b equals $B/290$, where 290 is the D_{50} for lethal lung doses from promethium without gamma radiation; the variable B represents the D_{50} for combined exposures. The equation for combined exposures thus becomes: $(0.7)^{2.4} + B/290 = 1$, and the solution for B is 170 Gy (17,000 rad), which is very nearly the LD_{50} indicated by the curve for combined exposures in Figure 17.

Comparisons between the $LD_{50/365}$ for rats exposed to promethium and plutonium (Filipy et al., 1988) with or without concomitant gamma exposures, are shown in Table 11. These data indicate that plutonium is five times as effective as promethium when inhaled without gamma exposures. With gamma exposures, the corresponding value is 4.4, not substantially different. Scott et al. (1988) reported an effectiveness ratio between ^{238}Pu and ^{147}Pm of 6.7, based on 1.5-year doses and 1.5-year lethality.

MORBIDITY

Body Weights

Body weight changes were an indicator of radiation-induced morbidity in that weight loss was a predictor of imminent death. Rats exposed to promethium with or without gamma irradiation generally began losing weight 4 to 6 weeks before they died. At death, they weighed between 60 and 80% of their previous peak

TABLE 11. Comparisons of LD_{50/365} Lung Doses from Inhaled Promethium or Plutonium, Each With and Without Additional Gamma Exposure

Exposure	Column 1 LD _{50/365}	Exposure	Column 2 LD _{50/365}	Column 1/ Column 2
Ratio ^a				
¹⁴⁷ Pm (FAP)	290 Gy	¹⁴⁷ Pm (FAP) + Gamma	160 Gy	1.8
²³⁹ PuO ₂	58 Gy	²³⁹ PuO ₂ + Gamma	36 Gy	1.6
Ratio ^a	5.0		4.4	

^aPromethium dose/plutonium dose

weight. Those that survived for the full year gained weight steadily, but their weights rarely approached those of control rats.

A single exposure to gamma radiation caused decreased weight gain in rats (Figures 21 and 22), especially in males (Figure 21); in both sexes, the effect was somewhat dose-dependent. Rats with the greater total-body gamma doses gained weight less rapidly.

Lung burdens of promethium generally had little effect on body weight during the first 3 months after exposure (Figures 23 and 24). The high weight gain shown for the male high-dose group (Figure 23) reflected a mortality effect in that the most severely affected animals died, and the mean values were then based on weights of relatively healthy animals.

The same mortality effect occurred in groups of rats exposed to promethium with gamma irradiation (Figures 25 and 26). In those figures, the curves for low-dose groups reflect reduced weight gain caused by radiation because there were fewer deaths in those groups during the first 12 weeks.

Except for the data in Figure 58, comparisons of body weights were not made beyond 12 weeks after exposure because so few rats survived after that. Figure 58 is a plot of body weights of seven males exposed to gamma radiation that had ILb of less than 3.7 MBq (100 µCi)/g lung and survived for a year after exposure. Those values are compared with weight gains of male controls and consistently show reduced body weights in the exposed rats throughout the year.

The body-weight changes in this experiment were similar to those of the previous experiment with inhaled plutonium and/or gamma irradiation in rats (Filipy et al., 1988) and also similar to those reported by Scott et al. (1988) for rats exposed to promethium aerosols.

Hematology

The effect of gamma-irradiation on circulating blood cells in this experiment was qualitatively the same as that for mammals in general (Bond et al., 1965). Red blood cell concentration was at a nadir between 14 and 30 days after exposure; at that time, values were approximately 35% of normal in female rats and 60% of normal in male rats (Table B2). Values were near normal in survivors at 90 days after exposure.

There was an immediate and severe depletion of circulatory lymphocytes after exposure of rats to ^{60}Co gamma-radiation (Table B6); the lowest concentrations occurred at 2 days after exposure. Thereafter, there was a gradual return toward normal values. At 90 days after exposure, concentrations were still below the lower confidence interval for four of five male rats and one of five females; nearly all were within the normal range by 180 days after exposure. One of the female rats had an elevated lymphocyte concentration at 30 days after exposure, but it was within the normal range at the next measurement (60 days after exposure).

FIGURE 58. Comparison of Body Weights of Control Rats with Those of Male Rats Exposed to ^{147}Pm (FAP) and ^{60}Co Gamma Radiation (850 rad or 8.5 Gy) at 1 Year after Exposure or Sham Exposure

There was a steady decline, throughout the year, of lymphocyte concentrations in control rats (Figures B3 and B4). Values at 365 days after sham exposure were approximately half of pre-exposure values in both males and females. The same time-dependent reduction in concentrations occurred in the previous experiment (Filipy et al., 1988) and also in experiments by Scott et al. (1987b); therefore, we conclude that it is a normal age-related effect.

Gamma irradiation of rats produced only one unexpected effect for the remainder of blood elements measured: All five male rats had a slight neutrophilia at 2 days after exposure (Table B10). No explanation can be offered except for the possibility that it was caused by stress induced during the exposure process. Neutrophil concentrations of control rats (Table B9) were not elevated however, although they were subjected to the same stress (except for the radiation). Unfortunately, the other exposure groups (promethium, with or without gamma radiation) were not measured at 2 days after exposure because of the radiological hazard to technicians, so data are not available for comparison. A slight elevation of neutrophil concentrations was noted in three of four rats exposed to promethium only (Table B11) at

18 days after exposure but, by that time, concentrations were within control ranges in the rats exposed only to gamma radiation.

The effect of combined exposures (inhaled promethium and gamma radiation) on blood cell concentrations closely paralleled that of gamma irradiation alone. The primary difference between the two groups of rats was that the cell concentrations progressed toward control values somewhat less rapidly in the former group; for example, lymphocyte concentrations did not return to control values until a year after exposure.

Inhalation of promethium without gamma irradiation had little effect on blood cell concentrations except for lymphocytes (Table B7). Mean lymphocyte concentrations were below the lower confidence limits of controls for both sexes at all times of measurement. This response was similar to that of beagle dogs exposed to plutonium aerosols (Filipy et al., 1988). The data of Scott et al. (1988a) indicated slight lymphopenia in rats at 7 and 14 days after exposure to ^{147}Pm , although concentrations were nearly normal thereafter.

Pulmonary Function

Three male control rats were considered morbid, based on the four pulmonary-function parameters tested: VC, slope of the alveolar plateau of the SBN_2 , DL_{CO} , and C_{Qs} . Rat #4724, at 270 days after sham exposure, and rats #5204 and #5205, at 360 days after sham exposure, had values for three of the four parameters that were outside the 95% confidence intervals (Table 8). In each case, DL_{CO} was the parameter not affected. The etiology of their morbidity was not established. There were only a few other control rats for which one or two values were outside the confidence intervals.

Only two male rats exposed to ^{60}Co gamma radiation were considered morbid (Table 8). Rats #5280 and #4797, at 360 and 370 days after exposure, respectively, each had three values outside the confidence intervals for control rats. Although, at 360 and 370 days after exposure, 11 male rats had slopes greater than the upper confidence limit (indicative of morbidity for that parameter) only the two listed above were functionally impaired for three of the four parameters. Rats of the gamma-exposed group were generally as healthy as the controls when measured. This observation is consistent with the relatively low mortality in the group when compared to the mortality and morbidity of corresponding groups of the previous experiment in which rats were exposed to gamma radiation (Filipy et al., 1988).

Reduced VC and increased slope were the two most sensitive indicators of impaired pulmonary function. During the course of the study, 98 and 100% of the functionally impaired rats had values for VC and slope, respectively, outside the 95% confidence intervals of controls. Comparing the figures for individual parameters of rats exposed to promethium, with or without gamma irradiation (Figures 31 and 32, 37 and 38, 43 and 44; and 49 and 50), doses that caused impaired VC and slope were generally lower than those that caused impairment of C_{Qs} and DL_{CO} .

Diminished C_{Qs} was the next most sensitive indicator of functional impairment; 88% of functionally impaired rats had C_{Qs} below the 95% confidence limit of control rats. DL_{CO} was an indicator of pulmonary-function impairment, although it was affected primarily at the later measurement times. Seventy-one percent of functionally impaired rats had DL_{CO} values below the 95% confidence limit; most were rats whose pulmonary function was measured 180 days or more after exposure (Ta-

ble 8). Data in Table 9, however, indicate that mean values for nearly all parameters were significantly different from those of control rats regardless of when measurements were made.

In retrospect, a single pulmonary-function test, the SBN₂, would have identified functionally impaired rats. This test gave the slope of the alveolar plateau as well as a P-V curve (from which VC and C_{Q5} could be derived). This would have saved time, because the gas chromatographic analysis of exhaled air was usually the rate-limiting step in the testing procedure.

Lungs from 10 of the rats whose pulmonary function was tested at 360 days after exposure were histologically examined. The data presented in Table 12 indicate good agreement between histological evaluation of radiation-induced lung changes and the results of pulmonary-function testing. Lung sections of all five rats with functional impairment indicated radiation pneumonitis, and four of the five rats had pulmonary fibrosis. The rat without fibrotic changes had a mediastinal tumor, which could have contributed to decreased VC and C_{Q5}, even though no pulmonary metastases were found.

TABLE 12. Comparison of 360-Day Pulmonary-Function Test Results with Microscopic Evaluation of Lung Sections in 10 Rats from the Four Exposure Groups

Males

Rat Number	Group ^a	Promethium Lung Dose (Gy)	Pulmonary Function ^b				Microscopic Evaluation		
			VC	Slope	C _{Q5}	DL _{CO}	Radiation Pneumonitis	Pulmonary Fibrosis	Other ^c
5201	21	0	N	N	N	N	No	No	None
5203	21	0	N	N	N	N	No	No	None
5223	21	0	N	N	N	N	No	No	(1)
5277	23	0	N	N	N	I	No	No	(2)
5283	23	0	N	=	N	N	No	No	(1)

Females

5363	26	191	I	I	I	I	Yes	No	(3)
5355	26	232	I	I	I	=	Yes	Yes	(4)
5351	26	241	I	I	I	I	Yes	Yes	
5411	29	228	I	I	I	=	Yes	Yes	
5420	29	315	I	I	I	N	Yes	Yes	

^a21 = Controls, sham exposed; 23 = Gamma exposure (9.2 Gy); 26 = Gamma exposure (8.9 Gy) & inhalation of ¹⁴⁷Pm (FAP) aerosol; 29 = Inhalation of ¹⁴⁷Pm (FAP) aerosol

^bN, Not impaired; I, Impaired; =, Equal to 95% confidence limit of impairment

^c(1) Slight lymphocytic infiltration of lungs; (2) Focus of bronchioloalveolar hyperplasia & cuboidal metaplasia; (3) Mediastinal tumor; (4) Hemorrhagic foci in lungs

In three of the five functionally impaired rats with histological indications of radiation pneumonitis, DL_{CO} measurement indicated only slight or no impairment. Values for two of the three rats were equal to the lower 95% confidence limit for controls. This is another indication that the reliability of pulmonary-function tests would have been adequate even with the omission of the DL_{CO} measurement.

Figure 57 shows dose/morbidity curves for rats exposed to ^{147}Pm (FAP) with and without gamma irradiation. The curves indicate D_{50} lung doses of 300 Gy (30,000 rad) for promethium inhalation alone and 180 Gy (18,000 rad) for promethium with gamma exposures. Comparison of these curves with those for dose/ mortality (Figure 17) is not entirely valid because the curves of Figure 57 are based on cumulative lung doses to the time of pulmonary-function testing, and the curves of Figure 17 are based on 365-day doses. To address that problem, animals from other exposure groups (with similar promethium ILB and the same gamma doses) were given pulmonary-function tests when the experiment was over (1 year after exposure; Table 8).

For rats that inhaled ^{147}Pm (FAP) with gamma irradiation, nearly all tested for pulmonary function at 340 and 360 days after exposure (Table 8) had lung doses that were within the range of those in the curve for promethium plus gamma in Figure 57. Of 16 rats tested at those times, 11 were functionally impaired. Of eight rats with lung doses less than the D_{50} of Figure 57, three were functionally impaired. Of the eight rats with lung doses greater than the D_{50} , all were functionally impaired and, for all but one rat, all four parameters were outside the 95% confidence intervals of controls. These comparisons indicate that the curve of Figure 57, based on cumulative lung doses to the time of testing, results in a slight overestimation of the D_{50} . Probably, a D_{50} based on a 1-year dose would be closer to the $LD_{50/365}$ (Figure 17) of 160 Gy (16,000 rad).

Of 11 rats exposed only to promethium aerosols whose 1-year lung doses were within the range of the curve for promethium only (Figure 57), 10 were functionally impaired. Of three rats whose 1-year doses were below the "threshold" dose of the same curve, one was functionally impaired. This comparison indicates that the D_{50} obtained on the basis of cumulative doses was too high, but data are not available to estimate the magnitude of the error.

Scott et al. (1988) indicated an effective D_{50} for pulmonary-function impairment of 75 Gy (7500 rad) from inhalation of ^{147}Pm (FAP), based on a 1.5-year dose and morbidity within 1.5 years of exposure. In our study, no rats received ILB low enough to produce such lung doses, so there is no basis for comparison. Our data indicate that the D_{50} for pulmonary-function morbidity within a year of exposure and the $LD_{50/365}$ are essentially the same. Scott et al. (1988) showed that the $LD_{50/1.5 \text{ year}}$ was four times the D_{50} for morbidity within 1.5 years of exposure. For modeling purposes, the $LD_{50/365}$ was considered twice the D_{50} for pulmonary-function morbidity (Scott et al., 1989).

It is difficult to believe that a transient radiation pneumonitis would result from inhalation of a long-lived radionuclide unless there were some way of removing the radionuclide from the lung. In this study, the D_{50} doses for pulmonary-function morbidity and the LD_{50} doses were very similar. With ^{90}Y (Scott et al., 1987b), radiation pneumonitis that did not lead to the immediate death of the animal may have occurred because the radionuclide decayed rapidly and ceased irradiating the lungs. With a relatively long-lived radionuclide such as ^{147}Pm , that would not occur. More likely, much of the radionuclide was naturally removed from the lung during the course of 1.5 years, and the remainder became relatively ineffective because of the proliferative changes, especially fibrosis, that eventually occur in the lung.

CONCLUSIONS

Total-body gamma-irradiation significantly enhanced the effect of inhaled ^{147}Pm (FAP) on the mortality of rats when the animals were exposed to both. Lung doses from promethium that resulted in 54% mortality within a year of exposure and total-body gamma doses that resulted in 20% mortality resulted in 99% mortality. The additive model used in the Nuclear Reactor Safety Study (U.S. NRC, 1975) predicts 63% mortality.

A more accurate prediction of lethality from radiation pneumonitis resulting from combined exposure can be determined using the hazard function model of Scott et al. (1989). When applied to the data from rats exposed either to promethium aerosols or to total-body gamma radiation, the model accurately predicted the $\text{LD}_{50/365}$ lung doses for rats exposed to the combined radiation insults. The model predicted an $\text{LD}_{50/365}$ day of 170 Gy (17,000 rad) compared to experimental results of 160 Gy (16,000 rad).

Acute mortality and morbidity from inhaled promethium was primarily caused by radiation pneumonitis and pulmonary fibrosis that occurred more than 50 days after exposure. Acute mortality and morbidity from total-body gamma irradiation occurred within 30 days of exposure and was a result of bone-marrow irradiation.

An $\text{LD}_{50/365}$ -day promethium lung dose of 290 Gy (29,000 rad) was reduced to 160 Gy (16,000 rad) with additional total-body gamma doses between 8.5 and 9.2 Gy (850 and 915 rad). The data indicated that the opposite effect (promethium enhancement of gamma-induced mortality in the first 30 days after exposure) was also true. Therefore, the effects of the two kinds of radiation were considered synergistic.

Pulmonary-function tests were reliable and sensitive indicators of the onset of radiation pneumonitis (morbidity) in rats exposed to promethium. The morbid effects of inhaled promethium were also enhanced by total-body gamma irradiation. The lung dose from inhalation of promethium that resulted in pulmonary-function impairment in 50% of the rats (D_{50}) was 300 Gy (30,000 rad) and the D_{50} from promethium inhalation combined with total-body irradiation was 180 Gy (18,000 rad). The difference was nearly 14 times the 8.5-Gy (8500-rad) gamma dose received by rats of the latter group.

Hematologic parameters reflected radiation-induced depression of hematopoietic activity from total-body gamma doses. Promethium lung burdens, with and without gamma exposures, caused lymphopenia in rats and, in rats exposed to both kinds of radiation, the concentrations of lymphocytes did not return to normal until a full year after exposure.

Although reduced body weight gain was a transient effect of total-body gamma doses, a severe loss of weight was an indication of imminent death when it occurred in animals exposed to promethium. Weight loss usually preceded death by 4 to 6 weeks.

REFERENCES

- Ainsworth, E. J. and F. A. Mitchell. 1968. "Post Irradiation Leukocyte Pattern in Mice and Dogs Treated with Endotoxin." Radiat. Res. 33: 325-336.
- Benjamin, S. A., B. B. Boecker, T. L. Chiffelle, F. F. Hahn, C. H. Hobbs, R. K. Jones, R. O. McClellan, J. A. Pickrell, and, H. C. Redman. 1973. "Neoplasia in Beagle Dogs after Inhalation of $^{144}\text{CeCl}_3$." In *Radionuclide Carcinogenesis*, eds., C. L. Sanders, R. H. Busch, J. E. Ballou, and D. D. Mahlum, pp. 181-200. CONF-720505, National Technical Information Service, Springfield, VA.
- Bond, V. P., T. M. Fleidner, and J. O. Archambeau. 1965. *Mammalian Radiation Lethality: A Disturbance in Cellular Kinetics*. Academic Press, New York, NY.
- Cannon, W. C., E. F. Blanton, and K. E. McDonald. 1983. "The Flow-Past Chamber: An Improved Nose-Only Exposure System for Rodents." Am. Ind. Hyg. Assoc. J. 44: 923-928.
- Carsten, A. L. and T. R. Noonan. 1964. "Hematological Effects of Partial-Body X-Irradiation in the Rat." Radiat. Res. 22: 136-147.
- Dunjic, H., J. Maisin, P. Maldague, and H. Maison. 1960. "Incidence of Mortality and Dose-Response Relationship Following Partial-Body X-Irradiation of the Rat." Radiat. Res. 12: 155-166.
- Emirgil, C. and H. O. Heinemann. 1961. "Effects of Irradiation of Chest on Pulmonary Function in Man." J. Appl. Physiol. 16: 331-338.
- Ferin, J., G. Urbankova, and A. Vlckova. 1965. "Pulmonary Clearance and the Function of Macrophages." Arch. Environ. Health 10: 790-795.
- Filipy, R. E., J. R. Decker, Y.-L. Lai, K. E. Lauhala, R. L. Buschbom, M. P. Hlastala, D. R. McGee, J. F. Park, E. G. Kuffel, H. A. Ragan, W. C. Cannon, S. S. Yaniv, and B. R. Scott. 1988. *Inhaled $^{239}\text{PuO}_2$ and/or Total-Body Gamma Radiation: Early Mortality and Morbidity in Rats and Dogs*, NUREG/CR-5198. U.S. Nuclear Regulatory Commission, Washington, DC.
- Hahn, F. F. 1979. *Early Mortality Estimates for Different Nuclear Accidents: Final Phase I Report*, NUREG/CR-0774. U.S. Nuclear Regulatory Commission, Washington, DC.
- Hahn, F. F., B. A. Muggenburg, B. B. Boecker, R.G. Cuddihy, W. C. Griffith, R. A. Guilmette, R. O. McClellan, and J. A. Mewhinney. 1987. "Insights into Radionuclide-Induced Lung Cancer in People from Life-Span Studies in Beagle Dogs." In *Life-Span Studies in Animals: What Can They Tell Us?*, eds., R. C. Thompson and J. A. Mahaffey, pp. 521-534. CONF-830951, National Technical Information Service, Springfield, VA.
- Harkema, J. R., J. L. Mauderly, R. E. Gregory, and J. A. Pickrell. 1984. "A Comparison of Starvation and Elastase Models of Emphysema in the Rat." Am. Rev. Respir. Dis. 129: 584-591.

Harkema, J. R. J. L., Mauderly, and F. F. Hahn. 1982. "The Effects of Emphysema on Oxygen Toxicity in Rats." Am. Rev. Respir. Dis. 126: 1058-1065.

Hatch, G. E., J. A. Raub, and J. A. Graham. 1984. "Functional and Biochemical Indicators of Pneumoconiosis in Mice: Comparison with Rats." J. Toxicol. Environ. Health 13: 487-497.

Hobbs, C. H., J. E. Barnes, R. O. McClellan, T. L. Chiffelle, R. K. Jones, D. L. Lundgren, J. L. Mauderly, J. A. Pickrell, and E. W. Rypka. 1972. "Toxicity in the Dog of Inhaled ^{90}Y in Fused Clay Particles: Early Biological Effects." Radiat. Res. 49: 430-460.

ICRP. 1980 *Annals of the ICRP: Biological Effects of Inhaled Radionuclides*. Pergamon Press, New York, NY.

Jones, T. D. 1981. "Hematologic Syndrome in Man Modeled from Mammalian Lethality." Health Phys. 41: 83-103.

Kramer, C. Y. 1957. "Extension of Multiple Range Tests to Group Means with Unequal Numbers of Replications." Biometrics 12: 307-310.

Kurohara, S. S. and G. W. Casarett. 1972. "Effects of Single Thoracic X-Ray Exposure in Rats." Radiat. Res. 52: 263-290.

Likens, S. A., and J. L. Mauderly. 1979. *Respiratory Measurements in Small Laboratory Mammals: A Literature Review*, LF-68. Inhalation Toxicology Research Institute, Albuquerque, NM.

Likens, S. A., and J. L. Mauderly. 1982. "Effect of Elastase or Histamine on Single-Breath N_2 Washouts in the Rat." J. Appl. Physiol. Respir. Environ. Exercise Physiol. 52: 141-146.

Loscutoff, S. M., W. C. Cannon, R. L. Buschbom, R. H. Busch, and B. W. Killand. 1985. "Pulmonary Function in Elastase-Treated Guinea Pigs and Rats Exposed to Ammonium Sulfate or Ammonium Nitrate Aerosols." Environ. Res. 36: 170-180.

Lustgarten, C. S., I. A. Mewhinney, C. H. Hobbs, W. H. Halliwell, R. K. Jones, J. L. Mauderly, R. O. McClellan, T. Mo, and J. H. Pickrell. 1976. "Toxicity of Inhaled $^{238}\text{PuO}_2$ in Beagle Dogs. A. Monodisperse $1.5\ \mu\text{m}$ $^{238}\text{PuO}_2$ Particles. B. Monodisperse $3.0\ \mu\text{m}$ $^{238}\text{PuO}_2$ Particles. III." In *Inhalation Toxicology Research Institute Annual Report*, LF-56, pp. 229-237. Inhalation Toxicology Research Institute, Albuquerque, NM.

Mauderly, J. L. 1984. "Respiratory Function Responses of Animals and Man to Oxidant Gases and to Pulmonary Emphysema." J. Toxicol. Environ. Health 13: 345-367.

Mauderly, J. L., J. M. Benson, D. E. Bice, R. L. Carpenter, M. J. Evans, R. F. Henderson, R. K. Jones, R. O. McClellan, J. A. Pickrell, H. C. Redman, S. G. Shami, and R. K. Wolf. 1983. "Life-span Study of Rodents Inhaling Diesel Exhaust: Results Through 30 Months." In *Inhalation Toxicology Research Institute Annual Report*, LMF-107, pp. 305-316. Inhalation Toxicology Research Institute, Albuquerque, NM.

Mauderly, J. L. and S. A. Likens. 1979. "Respiratory Function of Rats Anesthetized with Halothane or Pentobarbital and Breathing Oxygen or Air." In *Inhalation Toxi-*

cology Research Institute Annual Report, LF-69, pp. 266-272. Inhalation Toxicology Research Institute, Albuquerque, NM.

Mauderly, J. L., J. A. Mewhinney, and B. B. Boecker. 1980a. "A Comparison of the Effects of Inhaled Alpha- and Beta-Emitting Radionuclides on Pulmonary Function in the Dogs." In *Pulmonary Toxicology of Respirable Particles*, eds., C. L. Sanders, F. T. Cross G. E., Dagle, and J. A. Mahaffey. CONF-791002, National Technical Information Service, Springfield, VA.

Mauderly, J. A., B. A. Muggenburg, F. F. Hahn, and B.B. Boecker. 1980b. "The Effects of Inhaled ^{144}Ce on Cardiopulmonary Function and Histopathology of the Dog." *Radiat. Res.* 84: 307-324.

Mauderly, J. L., J. A. Pickrell, C. H. Hobbs, S. A. Benjamin, F. F. Hahn, R. K. Jones, and J. E. Barnes. 1973. "The Effects of Inhaled ^{90}Y Fused Clay Aerosol on Pulmonary Function and Related Parameters of the Beagle Dog." *Radiat. Res.* 56: 83-96.

Mercer, T. T., M. I. Tillery, and A. J. Newton. 1970. "A Multistage Low Flow Rate Cascade Impactor." *J. Aerosol Sci.* 1: 9-15.

Michaelson, S. M. and B. F. Schreiner, Jr., 1971. "Cardiopulmonary Effects of Upper-Body X-Irradiation in the Dog." *Radiat. Res.* 47: 168-181.

National Bureau of Standards. 1964. *Physical Aspects of Irradiation, Recommendations of the International Commission on Radiological Units and Measurements (ICRU)*, Report 10b, 1962, Handbook No. 85. National Bureau of Standards, Washington, DC.

Norris, W. P., T. E. Fritz, C. E. Rehfeld, and C. M. Poole. 1968. "The Response of the Beagle Dog to Cobalt-60 Gamma Radiation: Determination of the $\text{LD}_{50/30}$ and Description of Associated Changes." *Radiat. Res.* 35: 681-708.

Ragan, H. A., J. F. Park,, R. J. Olson, and R. L. Buschbom. 1976. "Lymphocytopenia Induced in Beagle Dogs by Inhalation of $^{239}\text{PuO}_2$." In *Radiation and the Lymphatic System*. CONF-740930, National Technical Information Service, Springfield, VA.

Rhoads, K., J. P. Geraci, J. A. Mahaffey, B. W. Killand, and C. L. Sanders. 1988. "Effect of External Irradiation on the Clearance and Fate of Transuranic Oxides Deposited in Rat Lung." *Ann. Occup. Hyg.* 32: 997-1006.

Rhoads, K., J. P. Geraci, and C. L. Sanders. 1981. "Effect of Prior Neutron or Gamma Irradiation on Pulmonary Clearance of $^{239}\text{PuO}_2$." In *Pacific Northwest Laboratory Annual Report for 1980 to the DOE Assistant Secretary for Environment*, PNL-3700, Pt 1, pp. 93-94. National Technical Information Service, Springfield, VA.

Sabo, J. P., E. C. Kinnel, and L. Diamond. 1983. "Effects of the Clara Cell Toxin, 4-Ipomeanol, on Pulmonary Function in Rats." *J. Appl. Physiol. Resp. Environ. Exercise Physiol.* 54: 337-344.

Sanders, C. L., J. Mahaffey, J. M. Morris, and K. Rhoads. 1983. "Inhaled Transuranics in Rodents." In *Pacific Northwest Laboratory Annual Report for 1982 to the DOE Assistant Secretary for Environment*, PNL-4600, Pt 1, pp. 65-67. National Technical Information Service, Springfield, VA.

Scott, B. R. 1980. "A Model for Early Death Caused by Radiation Pneumonitis and Pulmonary Fibrosis after Inhaling Insoluble Radioactive Particles." Bull. Math. Biol. 42: 447-459.

Scott, B. R. and F. F. Hahn. 1980. "A Model that Leads to the Weibull Distribution Function to Characterize Early Radiation Response Probabilities." Health Phys. 39: 521-530.

Scott, B. R., F. F. Hahn, R. A. Guilmette, B. A. Muggenburg, M. B. Snipes, B. B. Boecker, and R. O. McClellan. 1987a. "Use of Studies with Laboratory Animals to Assess the Potential Early Health Effects of Combined Internal Alpha and Beta Irradiation." In *Life-Span Studies in Animals: What Can They Tell Us?*, eds., R. C. Thompson and J. A. Mahaffey, pp. 521-534. CONF-830951, National Technical Information Service, Springfield, VA

Scott, B. R., F. F. Hahn, G. J. Newton, M. B. Snipes, E. G. Damon, J. L. Mauderly, B. B. Boecker, and D. H. Gray. 1987b. *Experimental Studies of the Early Effects of Inhaled Beta-emitting Radionuclides for Nuclear Accident Risk Assessment: Phase II Report*, NUREG/CR-5025, LMF-117. U.S. Nuclear Regulatory Commission, Washington, DC.

Scott, B. R., F. F. Hahn, M. B. Snipes, G. J. Newton, A. F. Eidson, J. L. Mauderly, and B. B. Boecker. 1988. *Early and Continuing Effects of Combined Alpha and Beta Irradiation of the Lung: Phase II Report*, NUREG/CR-5067, LMF-119. U.S. Nuclear Regulatory Commission, Washington, DC.

Scott, B. R., R. E. Filipy, and F. F. Hahn. 1989. Models for Pulmonary Lethality and Morbidity after Irradiation from Internal and External Sources, NUREG/CR-5351, LMF-122. U.S. Nuclear Regulatory Commission, Washington, DC.

Shively, J. N., S. M. Michaelson, and J. W. Howland. 1958. "The Response of Dogs to Bilateral Whole-Body Co⁶⁰ Radiation. I. Lethal Dose Determination." Radiat. Res. 9: 445-450.

Shively, J. N., S. M. Michaelson, and J. W. Howland. 1961. "The Response of Dogs to Bilateral Whole-Body Co⁶⁰ Irradiation. II. Pathophysiological Manifestations." Radiat. Res. 15: 319-328.

Siemann, D. W., R. P. Hill, and D. P. Penny. 1982. "Early and Late Pulmonary Toxicity in Mice Evaluated 180 and 420 Days Following Localized Lung Irradiation." Radiat. Res. 89: 396-407.

Sinclair, W.K. 1962. "The Relative Biological Effectiveness of 22-MeVp X-Rays, Cobalt-60 Gamma Rays and 200-kVcp X-Rays. VII. Summary of Studies for Five Criteria of Effect." Radiat. Res. 16: 394-398.

Sinclair, W.K. 1963. "Absorbed Dose in Biological Specimens Irradiated Externally with Cobalt-60 Gamma Radiation." Radiat. Res. 20: 288-297.

Smith, D. E. and E. B. Tyree. 1954. "Influence of X-Irradiation Upon Body Weight and Food Consumption of the Rat." Am. J. Physiol. 177: 251-260.

Statistical Analysis System (SAS). 1985. *SAS User's Guide, Statistics Version, Fifth Edition*. SAS Institute Inc., Cary, NC.

Stuart, B. O., H. W. Casey, and W. J. Bair. 1964. "Acute and Chronic Effects of Inhaled $^{144}\text{CeO}_2$ in Dogs." Health Phys. 10: 1203-1209.

Sweany, S. K., W. T. Moss, and F. J. Haddy. 1959. "The Effects of Chest Irradiation on Pulmonary Function." J. Clin. Invest. 38: 587-593.

Swinth, K. L. and B. I. Griffin. 1970. "A Developmental Scintillation Counter for Detection of Plutonium In-Vivo." Health Phys. 19: 543.

Swinth, K. L., B. I. Griffin, and J. F. Park. 1967. "Whole Body Counting of Inhaled Plutonium in Dogs." Health Phys. 13: 1223.

Takezawa, J., F. J. Miller, and J. J. O'Neil. 1980. "Single-Breath Diffusing Capacity and Lung Volumes in Small Laboratory Mammals." J. Appl. Physiol. Respir. Environ. Exercise Physiol. 48: 1052-1059.

Teates, C. D. 1965. "Effects of Unilateral Thoracic Irradiation on Lung Function." J. Appl. Physiol. 20: 628-636.

Thomas, R. L., J. K. Scott, and T. L. Chiffelle L. 1972. "Metabolism and Toxicity of Inhaled ^{144}Ce in Rats." Radiat. Res. 49: 589-610.

Travis, E. L. 1980. "The Sequence of Histological Changes in Mouse Lungs After Single Doses of X-Rays." Int. J. Radiat. Oncol. Biol. Phys. 6: 345-347.

Travis, E. L., J. D. Down, S. J. Holmes, and B. Holson. 1980. "Radiation Pneumonitis and Fibrosis in Mouse Lung Assayed by Respiratory Frequency and Histology." Radiat. Res. 84: 133-143.

Travis, E. L., R. A. Harley, J. O. Fenn, C. J. Klobukowski, and H. B. Hargrove. 1977. "Pathologic Changes in the Lung Following Single and Multi-Fraction Irradiation." Int. J. Radiat. Oncol. Biol. Phys. 2: 475-490.

Travis, E. L., B. Vojnovic, E. E. Davies, and D. G. Hirst. 1979. "A Plethysmographic Method for Measuring Function in Locally Irradiated Mouse Lung." Br. J. Radiol. 52: 67-74.

Tukey, J. W. 1953. *The Problem of Multiple Comparisons*. Princeton University, Princeton, NJ.

Tyree, E. B., A. S. Glicksman, and J. J. Nickson. 1966. "Effect of L-Tri-iodothyronine on Radiation-Induced Pulmonary Fibrosis in Dogs." Radiat. Res. 28: 30-36.

U.S. Nuclear Regulatory Commission. 1975. *An Assessment of Accident Risk in U.S. Commercial Nuclear Power Plants*, WASH-1400, Nuclear Reactor Safety Study. U.S. Nuclear Regulatory Commission, Washington, DC.

Van Dyk, J., T. J. Keane, S. Kan, W. D. Rider, and C. J. H. Dryer. 1981. "Radiation Pneumonitis Following Large Single Dose Irradiation: A Re-evaluation Based on Absolute Dose to Lung." Int. J. Radiat. Oncol. Biol. Phys. 7: 461-467.

APPENDIX A

PROMETHIUM LUNG CLEARANCE KINETICS
AND LUNG DOSIMETRY METHODS

PROMETHIUM DOSIMETRY

A suspension of montmorillonite clay, obtained from ITRI, was spiked with ^{147}Pm at 1.036×10^{10} Bq (280 mCi/ml) by cation exchange. A small amount of ^{137}Cs -spiked clay was added, resulting in an activity ratio of 1:10,000 ^{137}Cs : ^{147}Pm in the suspension. The aerosol was generated from a dilution of this suspension, so that the fused aerosol particles inhaled by the rats contained both radionuclides in that proportion.

In vivo promethium body burdens were determined by whole-body counting (^{137}Cs :662-keV gamma rays) with a modified version of the instrumentation described by Swinth et al. (1967) and Swinth and Griffin (1970). Rats were confined in 1-quart (0.95-L) paper ice-cream cartons and placed between two arrays of radiation detectors, each consisting of 13 photomultiplier tubes behind 4.4-cm-(1.75-in.)-diameter, 1-mm-thick, sodium iodide crystals. Frozen rat carcasses with encapsulated aliquots of the original clay suspension implanted in their thoracic cavities were used as standards to convert counts per minute to μCi (Bq). Determinations of the body burden of each surviving rat by *in vivo* counting were made at 5, 14, 28 and 56 days after exposure and at the end of the 1-year period.

A short experiment was performed to determine the amount of external body contamination and the radionuclide content of the gastrointestinal tracts with respect to the lung content in rats at various times up to 29 days after exposure. A group of 35 rats were exposed to the ^{147}Pm - ^{137}Cs aerosol to produce lung burdens similar to those of the main experiment. The numbers of rats, times after exposure, and mean results of the short experiment are presented in Table A1.

TABLE A1. Design and Mean Results of a Short Experiment to Determine the Influence of External Body Contamination and Gastrointestinal Radionuclide Content on Lung Burdens Determined by Whole-Body Counts in Rats

Time after exposure (days)	5	14	29
Number of rats killed	10	10	15
Mean activity remaining on carcass/5-day whole-body count	0.14	0.06	0.02
Mean activity in gastrointestinal tract/5-day whole-body count	0.11	<0.01	<0.01
Mean activity in lungs/5-day whole-body count	0.80	0.90	0.96

Lungs and gastrointestinal tracts of the rats killed at each time were excised, placed in scintillation vials, and analyzed for ^{137}Cs content in a gamma counter (Beckman Model 310). Activity remaining in the carcass was determined by placing it (without the lungs and gastrointestinal tract) in the whole-body counter.

The total activity was slightly greater than that determined by whole-body counting at 5 days and slightly less than at 14 and 29 days after exposure. This was likely the result of differences in counting efficiencies between the two methods. Nevertheless, the values at 29 days after exposure show that the whole-body count was a reliable indication of the lung content at that time.

The estimate of ILB for rats of the main experiment was derived by using the 28-day whole-body count as a base value, expressing the 56- and 28-day counts as a percent of the 28-day count and extrapolating back to the day of exposure. The ILB for all

rats that survived through 56 days after exposure were estimated using this technique. Relatively consistent relationships were found between the 5-day whole-body count and the 14- and 28-day whole-body counts of rats. There was also a constant relationship between the whole-body counts at those times and the lung content determined by *in vitro* counts. For all rats that died before the 28-day whole-body count, a 28-day value was predicted on the basis of those relationships, and the ILB was estimated by extrapolation along the same clearance curve determined from rats that had survived through the first 56 days after exposure.

The lung clearance curve shown in Figure A1 was constructed using a nonlinear regression analysis curve-fitting technique through the estimated mean ILB, and the lung burdens were determined at 28, 56, and 365 days after exposure. A correction was made for the half-life of ^{147}Pm . There was no consistent difference in clearance rates between the groups exposed to gamma radiation and the groups that were not, nor did the amount of the ILB have an apparent effect on clearance rate. Points in Figure A1 are mean values for 37 rats through 56 days after exposure and for 17 rats that survived for the year's duration of the experiment.

FIGURE A1. Clearance of ^{147}Pm from the Lungs of Rats

The equation for the clearance curves was:

$$y = 78.1 e^{-0.0177t} + 21.9 e^{-0.00165t}$$

where y = percent of ILB remaining in the lung at a time (t) in days.

The lung dose was calculated using the equation:

$$\text{Dose (Gy)} = \frac{3.168 \times \text{ILB}}{100 \times \text{lung wt}} \left[\frac{0.781}{0.0177} (1 - e^{-0.0177t}) + \frac{0.219}{0.00165} (1 - e^{-0.00165t}) \right]$$

Definitions of terms were:

ILB	= initial lung burden in nCi
3.17	= rad/ μ Ci-day/g lung (Kocher, 1977)
100	= conversion from rad to gray
t	= time (in days) for which the dose was calculated.

Lung weights used were 2.1 g for males and 1.5 g for females. These were mean lung weights from approximately 50 rats of each sex determined at approximately 15 weeks of age in a previous experiment (Filipy et al., 1988). Those rats were the same age and strain as those used in this experiment.

REFERENCES

Filipy, R. E., J. R. Decker, Y.-L. Lai, K. E. Lauhala, R. L. Buschbom, M. P. Hlastala, D. R. McGee, J. F. Park, E. G. Kuffel, H. A. Ragan, W. C. Cannon, S. S. Yaniv, and B. R. Scott. 1988. *Inhaled $^{239}\text{PuO}_2$ and/or Total-Body Gamma Radiation: Early Mortality and Morbidity in Rats and Dogs*, NUREG/CR-5198. U.S. Nuclear Regulatory Commission, Washington, DC.

Kocher, D. C. 1977. *Nuclear Decay Data for Radionuclides Occurring in Routine Releases from Nuclear Fuel Cycle Facilities*, ORNL/NUREG/TM-102. U.S. Nuclear Regulatory Commission, Washington, DC.

Swinth, K. L. and B. I. Griffin. 1970. "A Developmental Scintillation Counter for Detection of Plutonium In-Vivo." Health Phys. 19: 543.

Swinth, K. L., B. I. Griffin, and J. F. Park. 1967. "Whole Body Counting of Inhaled Plutonium in Dogs." Health Phys. 13: 1223.

APPENDIX B

HEMATOLOGIC DATA FOR RATS EXPOSED TO AN AEROSOL
OF ^{147}Pm (FAP) AND/OR ^{60}Co GAMMA RADIATION
COMPARED WITH THOSE FROM CONTROL ANIMALS

FIGURE B1. Mean Red Blood Cell Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Male Rats for 1 Year after Sham Exposure

FIGURE B2. Mean Red Blood Cell Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Female Rats for 1 Year after Sham Exposure

TABLE B1. Red Blood Cell Concentrations in Male and Female Sham-Exposed (Control) Rats

Group 21: Red Blood Cells ($\times 10^6/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4606	8.9	4616	7.8
4607	8.6	4617	8.1
4608	8.9	4618	7.6
4609	8.8	4619	8.1
4610	8.9	4620	8.1
Mean	8.8	Mean	7.9

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4601	8.8	4621	8.0
4602	8.5	4622	8.0
4603	8.9	4623	8.0
4604	8.5	4624	7.3
4605	8.3	4625	7.9
Mean	8.6	Mean	7.8

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4606	8.8	4626	7.8
4607	8.2	4627	7.3
4608	8.6	4628	7.8
4609	8.4	4629	8.0
4610	8.7	4630	7.8
Mean	8.5	Mean	7.7

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B1. (Continued)

Group 21: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4601	9.0	4616	7.3
4602	8.7	4617	7.5
4603	8.7	4618	7.3
4604	8.7	4619	7.3
4605	8.6	4620	7.9
Mean	8.7	Mean	7.5

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.0 LCL = 8.0	Animal Number	UCL = 8.2 LCL = 7.2
4601	8.3	4626	7.9
4602	9.0	4627	8.0
4603	8.0	4628	8.2
4604	8.6	4629	8.0
4605	8.4	4630	7.7
Mean	8.5	Mean	8.0

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.0 LCL = 8.0	Animal Number	UCL = 8.2 LCL = 7.2
4611	8.7	4616	8.0
4612	8.8	4617	7.6
4613	8.6	4618	7.7
4614	8.7	4619	7.7
4615	8.4	4620	7.9
Mean	8.6	Mean	7.8

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B1. (Continued)

Group 21: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

120 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.0 LCL = 8.0	Animal Number	UCL = 8.3 LCL = 7.3
4601	8.2	4618	7.1
4605	7.6	4619	7.5
Mean	7.9	Mean	7.3

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.3 LCL = 7.3
4606	8.9	4621	7.7
4607	8.3	4622	8.0
4608	8.6	4623	7.9
4609	9.0	4624	8.1
4610	8.6	4625	7.8
Mean	8.7	Mean	7.9

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 8.5 LCL = 7.5	Animal Number	UCL = 7.9 LCL = 6.9
4603	7.7	4616	7.5
4606	8.3	4620	7.8
4607	8.0	4622	7.3
4612	8.3	4625	7.5
		4627	1.1
Mean	8.1	Mean	6.2

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B2. Red Blood Cell Concentrations in Peripheral Blood of Rats Exposed to ^{60}Co Gamma Irradiation (890 rad or 8.9 Gy)

Group 23: Red Blood Cells ($\times 10^6/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.1
4636	9.2*	4656	8.0
4637	8.2	4657	7.8
4638	8.7	4658	7.6
4639	8.6	4659	7.5
4640	8.5	4660	8.2
Mean	8.6	Mean	7.8

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4641	7.3	4646	6.6
4642	7.9	4647	6.3
4643	8.1	4648	6.2
4644	8.5	4649	5.8
4645	7.8	4650	6.3
Mean	7.9	Mean	6.2

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4636	5.9	4651	3.0
4637	4.4	4652	2.2
4638	5.0	4653	3.0
4639	5.7	4654	2.7
4640	3.7	4655	2.0
Mean	4.9	Mean	2.6

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B2. (Continued)

Group 23: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.2 LCL = 7.2
4641	4.5	4648	5.1
4642	5.1	4649	4.6
4643	5.0	4650	2.8
4644	5.6	4659	3.0
4645	6.3	4676	4.7
Mean	5.3	Mean	4.0

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.0 LCL = 8.0	Animal Number	UCL = 8.2 LCL = 7.2
4636	7.4	4651	5.6
4637	7.1	4657	5.6
6638	6.5	4658	6.5
4639	6.4	4659	6.5
4640	6.6	4660	6.6
Mean	6.8	Mean	6.1

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.0 LCL = 8.0	Animal Number	UCL = 8.2 LCL = 7.2
4631	7.9	4655	7.6
4634	7.6	4657	6.1
4636	7.4	4658	7.1
4637	7.7	4659	7.3
4641	7.5	4660	7.1
Mean	7.6	Mean	7.0

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B2. (Continued)

Group 23: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.1 LCL = 8.1	Animal Number	UCL = 8.3 LCL = 7.3
4631	8.2	4646	6.6
4634	8.2	4648	6.6
4636	8.2	4650	7.6
4637	8.3	4651	6.5
4639	8.0	4653	7.2
Mean	8.2	Mean	6.9

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 8.5 LCL = 7.5	Animal Number	UCL = 7.9 LCL = 6.9
4631	7.7	4648	6.3
4637	7.3	4650	7.7
4641	7.2	4651	6.2
4643	7.5	4653	7.2
4644	7.2	4666	7.1
Mean	7.4	Mean	6.9

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B3. Red Blood Cell Concentrations in Peripheral Blood of Rats Exposed to ^{147}Pm (FAP)

Group 29: Red Blood Cells ($\times 10^6/\text{mm}^3$)

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose (Gy)	UCL = 8.2 LCL = 7.2
4691	110	7.1	4716	133	7.2
4692	103	7.6	4718	140	6.8
4693	139	7.2	4720	144	6.7
4695	78	7.1			
Mean	108	7.3	Mean	139	6.9

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose (Gy)	UCL = 8.2 LCL = 7.2
4691	170	7.5	4706	141	7.2
4692	159	7.4	4707	239	7.1
4693	214	6.9	4708	220	7.3
4694	190	6.9	4709	160	6.9
4695	120	6.5	4710	225	7.4
Mean	171	7.0	Mean	197	7.2

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.0 LCL = 8.0	Animal Number	Dose (Gy)	UCL = 8.2 LCL = 7.2
4691	286	8.0	4706	237	7.6
4692	267	8.1	4707	402	7.4
4693	361	8.1	4708	371	7.3
4694	320	8.4	4710	380	7.3
4695	202	7.9	4717	440	7.2
Mean	287	8.1	Mean	366	7.4

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B3. (Continued)

Group 29: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.0 LCL = 8.0	Animal Number	Dose (Gy)	UCL = 8.2 LCL = 7.2
4691	370	8.5	4713	377	6.7
4692	345	8.6	4716	448	6.9
4693	466	7.3	4717	568	8.4*
4694	413	8.9	4719	494	7.7
4697	389	7.9	4720	485	7.8
Mean	397	8.2	Mean	474	7.5

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B4. Red Blood Cell Concentrations in Peripheral Blood of Rats Exposed to ^{147}Pm (FAP) and ^{60}Co Gamma Irradiation (850 rad or 8.5 Gy)

Group 26: Red Blood Cells ($\times 10^6/\text{mm}^3$)

7 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose ^a (Gy)	UCL = 8.2 LCL = 7.2
4481	15	7.1	4501	38	6.6
4482	25	7.2	4502	35	7.0
4483	25	7.1	4503	26	6.8
4484	23	7.8	4504	18	6.7
4485	17	7.0	4505	33	5.8
Mean	21	7.2	Mean	30	6.6

14 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose ^a (Gy)	UCL = 8.2 LCL = 7.2
4486	30	6.9	4496	37	6.7
4487	50	7.4	4497	48	6.0
4488	21	7.0	4499	65	6.5
4489	36	7.0	4500	47	6.7
4490	23	6.4	4508	51	5.6
Mean	32	6.9	Mean	50	6.3

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose ^a (Gy)	UCL = 8.2 LCL = 7.2
4666	103	4.6	4677	91	4.1
4672	71	4.7	4679	102	2.6
4675	117	5.5	4680	87	3.4
Mean	97	4.9	Mean	93	3.4

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B4. (Continued)

Group 26: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose ^a (Gy)	UCL = 8.2 LCL = 7.2
4490	45	4.5	4500	91	4.4
4491	78	5.8	4506	110	4.5
4492	53	5.0	4508	99	4.8
4493	83	5.8	4509	116	4.6
4494	102	6.0	4510	149	5.1
Mean	72	5.4	Mean	113	4.7

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.0 LCL = 8.0	Animal Number	Dose ^a (Gy)	UCL = 8.2 LCL = 7.2
4486	99	6.5	4497	156	6.9
4487	164	6.2	4499	211	7.2
4488	68	6.7	4500	154	6.8
4489	118	7.3	4501	237	7.4
4490	76	6.5	4502	216	6.3
Mean	105	6.6	Mean	195	6.9

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.0 LCL = 8.0	Animal Number	Dose ^a (Gy)	UCL = 8.2 LCL = 7.2
4485	132	6.5	4504	148	5.1
4487	212	5.4	4506	240	4.4
4488	88	7.6			
4492	115	6.7			
Mean	137	6.6	Mean	194	4.8

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B4. (Continued)

Group 26: Red Blood Cells ($\times 10^6/\text{mm}^3$) cont'd

180 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.1 LCL = 8.1	Animal Number	Dose ^a (Gy)	UCL = 8.3 LCL = 7.3
4485	189	8.5	None		
4488	126	9.6*			
Mean	158	9.1			

365 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 8.5 LCL = 7.5	Animal Number	Dose ^a (Gy)	UCL = 7.9 LCL = 6.9
4485	257	9.7*	None		
4488	142	8.3			
Mean	200	9.0			

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

FIGURE B3. Mean Lymphocyte Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Male Rats for 1 Year after Sham Exposure

FIGURE B4. Mean Lymphocyte Concentrations Including Individual Data and the 95% Confidence Interval) in Control Female Rats for 1 Year after Sham Exposure

TABLE B5. Lymphocyte Concentrations in Peripheral Blood of Male and Female Control (Sham-Exposed) Rats

Group 21: Lymphocytes ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.5 LCL = 6.0	Animal Number	UCL = 10.2 LCL = 5.7
4606	7.8	4616	8.6
4607	6.6	4617	8.9
4608	6.9	4618	8.9
4609	7.1	4619	7.1
4610	7.7	4620	7.1
Mean	7.2	Mean	8.1

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.6 LCL = 6.1	Animal Number	UCL = 10.1 LCL = 5.6
4601	8.3	4621	7.9
4602	7.4	4622	6.8
4603	9.2	4623	7.8
4604	8.1	4624	8.3
4605	7.9	4625	11.8*
Mean	8.2	Mean	8.5

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.6 LCL = 6.1	Animal Number	UCL = 10.0 LCL = 5.5
4606	7.8	4626	8.4
4607	8.6	4627	7.3
4608	7.4	4628	9.2
4609	7.8	4629	9.1
4610	8.2	4630	7.9
Mean	8.0	Mean	8.4

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B5. (Continued)

Group 21: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.7 LCL = 6.2	Animal Number	UCL = 9.8 LCL = 5.1
4601	8.2	4616	5.3
4602	7.3	4617	5.3
4603	8.5	4618	7.6
4604	7.5	4619	7.1
4605	8.6	4620	5.3
Mean	8.0	Mean	6.1

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.6 LCL = 6.1	Animal Number	UCL = 9.4 LCL = 4.5
4601	9.1	4626	7.5
4602	6.1	4627	5.3
4603	8.2	4628	7.1
4604	6.5	4629	7.0
4605	7.4	4630	8.5
Mean	7.5	Mean	7.1

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.5 LCL = 6.0	Animal Number	UCL = 9.0 LCL = 4.1
4611	8.7	4616	6.0
4612	8.6	4617	6.9
4613	7.3	4618	7.7
4614	8.8	4619	9.0
4615	8.0	4620	7.0
Mean	8.3	Mean	7.3

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B5. (Continued)

Group 21: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

120 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.2 LCL = 5.7	Animal Number	UCL = 8.5 LCL = 3.8
4601	5.6	4618	4.3
4605	5.0	4619	5.3
Mean	5.3	Mean	4.8

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 8.3 LCL = 4.8	Animal Number	UCL = 7.9 LCL = 3.0
4606	6.4	4621	4.2
4607	6.7	4622	5.6
4608	6.1	4623	5.7
4609	7.6	4624	5.6
4610	6.2	4625	6.4
Mean	6.6	Mean	5.5

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 5.9 LCL = 2.2	Animal Number	UCL = 5.8 LCL = 0.2
4603	4.9	4616	3.3
4606	3.9	4620	2.6
4607	4.1	4622	2.5
4612	3.2	4625	2.8
		4627	10.4*
Mean	4.0	Mean	4.3

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B6. Lymphocyte Concentrations in Peripheral Blood of Rats Exposed to ^{60}Co Gamma Irradiation (890 rad or 8.9 Gy)

Group 23: Lymphocytes ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.5 LCL = 6.0	Animal Number	UCL = 10.2 LCL = 5.7
4636	0.3	4656	0.1
4637	0.2	4657	0.3
4638	0.2	4658	0.2
4639	0.1	4659	0.3
4640	0.5	4660	0.4
Mean	0.3	Mean	0.3

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.6 LCL = 6.1	Animal Number	UCL = 10.1 LCL = 5.6
4641	0.7	4646	0.2
4642	0.6	4647	0.8
4643	0.8	4648	0.5
4644	0.5	4649	0.5
4645	0.4	4650	0.4
Mean	0.6	Mean	0.5

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.6 LCL = 6.1	Animal Number	UCL = 10.0 LCL = 5.5
4636	0.8	4651	1.0
4637	1.5	4652	0.9
4638	1.2	4653	1.3
4639	0.9	4654	0.6
4640	1.7	4655	1.0
Mean	1.2	Mean	1.0

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B6. (Continued)

Group 23: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.7 LCL = 6.2	Animal Number	UCL = 9.8 LCL = 5.1
4641	5.4	4648	3.4
4642	2.7	4649	9.4
4643	6.1	4659	15.0*
4644	3.5	4676	3.9
4645	2.3		
Mean	4.0	Mean	7.9

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.6 LCL = 6.1	Animal Number	UCL = 9.4 LCL = 4.5
4636	4.7	4651	3.7
4637	2.7	4657	2.7
4638	3.5	4658	3.5
4639	3.7	4659	4.7
4640	3.6	4660	3.7
Mean	3.6	Mean	3.7

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 9.5 LCL = 6.0	Animal Number	UCL = 9.0 LCL = 4.1
4631	6.6	4655	5.2
4634	5.6	4657	3.1
4636	5.4	4658	4.2
4637	5.7	4659	6.6
4641	4.2	4660	4.7
Mean	5.5	Mean	4.8

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B6. (Continued)

Group 23: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 8.3 LCL = 4.8	Animal Number	UCL = 7.9 LCL = 3.0
4631	5.6	4646	3.0
4634	5.6	4648	2.9
4636	5.4	4650	3.3
4637	5.0	4651	3.3
4639	5.2	4653	3.2
Mean	5.4	Mean	3.1

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 5.9 LCL = 2.2	Animal Number	UCL = 5.8 LCL = 0.2
4631	3.7	4648	2.0
4637	3.7	4650	1.8
4641	4.1	4651	2.2
4643	2.9	4643	2.6
4644	3.6	4666	2.6
Mean	3.6	Mean	4.6

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B7. Lymphocyte Concentrations in Peripheral Blood of Rats Exposed to ^{147}Pm (FAP)

Group 29: Lymphocytes ($\times 10^3/\text{mm}^3$)

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.6 LCL = 6.1	Animal Number	Dose (Gy)	UCL = 10.0 LCL = 5.5
4691	110	3.5	4716	133	3.0
4692	103	3.9	4718	140	3.5
4693	139	4.0	4720	144	4.0
4695	78	4.5			
Mean	108	4.0	Mean	139	3.5

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.7 LCL = 6.2	Animal Number	Dose (Gy)	UCL = 9.8 LCL = 5.1
4691	170	3.2	4706	141	4.1
4692	159	3.7	4707	239	3.4
4693	214	2.7	4708	220	3.5
4694	190	3.0	4709	160	5.0
4695	120	3.6	4710	225	4.0
Mean	171	3.2	Mean	197	4.0

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.6 LCL = 6.1	Animal Number	Dose (Gy)	UCL = 9.4 LCL = 4.5
4691	286	2.6	4706	237	3.2
4692	267	2.7	4707	402	3.0
4693	361	2.4	4708	371	3.0
4694	320	2.4	4710	380	2.4
4695	202	3.6	4717	440	2.2
Mean	287	2.7	Mean	366	2.8

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B7. (Continued)

Group 29: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 9.5 LCL = 6.0	Animal Number	Dose (Gy)	UCL = 9.0 LCL = 4.1
4691	370	3.8	4713	377	2.4
4692	345	3.0	4716	448	2.8
4693	466	3.4	4717	568	5.5
4694	413	2.7	4719	494	3.1
4697	389	4.2	4720	485	3.9
Mean	397	3.4	Mean	474	3.5

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B8. Lymphocyte Concentrations in Peripheral Blood of Rats Exposed to an Aerosol of ^{147}Pm (FAP) and ^{60}Co Gamma Irradiation (850 rad or 8.5 Gy)

Group 26: Lymphocytes ($\times 10^3/\text{mm}^3$)

7 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.6 LCL = 6.1	Animal Number	Dose ^a (Gy)	UCL = 10.1 LCL = 5.6
4481	15	0.5	4501	38	0.4
4482	25	0.6	4502	35	0.5
4483	25	0.9	4503	26	0.5
4484	23	0.8	4504	18	0.6
4485	17	0.4	4505	33	0.2
Mean	21	0.6	Mean	30	0.4

14 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.6 LCL = 6.1	Animal Number	Dose ^a (Gy)	UCL = 10.0 LCL = 5.5
4486	30	0.5	4496	37	0.7
4487	50	0.7	4497	48	0.4
4488	21	0.3	4499	65	0.4
4489	36	0.1	4500	47	0.3
4490	23	0.8	4508	51	0.5
Mean	32	0.6	Mean	50	0.5

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.6 LCL = 6.1	Animal Number	Dose ^a (Gy)	UCL = 10.0 LCL = 5.5
4666	103	1.6	4677	91	1.0
4672	71	4.7	4679	102	1.4
4675	117	0.9	4680	87	2.2
Mean	97	2.4	Mean	93	1.5

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B8. (Continued)

Group 26: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.7 LCL = 6.2	Animal Number	Dose ^a (Gy)	UCL = 9.8 LCL = 5.1
4490	45	1.2	4500	91	6.3
4491	78	1.0	4506	110	1.1
4492	53	1.9	4508	99	0.6
4493	83	2.0	4509	116	0.5
4494	102	2.3	4510	149	1.1
Mean	72	1.7	Mean	113	1.9

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.6 LCL = 6.1	Animal Number	Dose ^a (Gy)	UCL = 9.4 LCL = 4.5
4486	99	2.1	4497	156	3.4
4487	164	1.6	4499	211	2.9
4488	68	3.1	4500	154	1.7
4489	118	2.4	4501	237	2.6
4490	76	1.5	4502	216	1.5
Mean	105	2.1	Mean	195	2.4

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 9.5 LCL = 6.0	Animal Number	Dose ^a (Gy)	UCL = 9.0 LCL = 4.1
4485	132	2.9	4504	148	2.9
4487	212	3.9	4506	240	1.5
4488	88	4.4			
4492	115	2.3			
Mean	137	3.4	Mean	194	2.2

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B8. (Continued)

Group 26: Lymphocytes ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 8.3 LCL = 4.8	Animal Number	Dose ^a (Gy)	UCL = 7.9 LCL = 3.0
4485	189	3.7	None		
4488	126	4.3			
Mean	158	4.0			

365 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 5.9 LCL = 2.2	Animal Number	Dose ^a (Gy)	UCL = 5.8 LCL = 0.2
4485	257	2.1	None		
4488	142	3.2			
Mean	200	2.7	Mean		

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

FIGURE B5. Mean Segmented Neutrophil Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Male Rats for 1 Year after Sham Exposure

FIGURE B6. Mean Segmented Neutrophil Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Female Rats for 1 Year after Sham Exposure

TABLE B9. Segmented Neutrophil Concentrations in Peripheral Blood of Male and Female Control (Sham-Exposed) Rats

Group 21: Segmented Neutrophils ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.1 LCL = 0.8	Animal Number	UCL = 4.0 LCL = 0.6
4606	1.0	4616	3.2
4607	1.5	4617	2.2
4608	1.7	4618	1.0
4609	2.2	4619	1.4
4610	2.5	4620	1.2
Mean	1.8	Mean	1.8

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.1 LCL = 0.8	Animal Number	UCL = 3.9 LCL = 0.7
4601	1.8	4621	1.8
4602	2.2	4622	3.4
4603	1.5	4623	1.7
4604	2.1	4624	3.0
4605	2.2	4625	2.2
Mean	2.0	Mean	2.4

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.1 LCL = 0.8	Animal Number	UCL = 3.9 LCL = 0.7
4606	1.9	4626	2.5
4607	3.1	4627	3.6
4605	3.1	4628	2.0
4609	2.5	4629	1.5
4610	1.9	4630	1.6
Mean	2.5	Mean	2.3

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B9. (Continued)

Group 21: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.2 LCL = 0.9	Animal Number	UCL = 3.9 LCL = 0.7
4601	1.4	4616	4.8*
4602	1.4	4617	3.1
4603	1.9	4618	2.0
4604	2.1	4619	2.8
4605	2.2	4620	2.0
Mean	1.8	Mean	2.9

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.2 LCL = 0.9	Animal Number	UCL = 3.8 LCL = 0.6
4601	1.8	4626	1.6
4602	1.7	4627	2.0
4603	2.4	4628	1.8
4604	1.6	4629	2.5
4605	2.6	4630	2.2
Mean	2.0	Mean	2.0

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.3 LCL = 1.0	Animal Number	UCL = 3.6 LCL = 0.4
4611	1.9	4616	2.5
4612	2.5	4617	1.2
4613	3.0	4618	1.6
4614	1.9	4619	2.5
4615	2.6	4620	0.6
Mean	2.4	Mean	1.7

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B9. (Continued)

Group 21: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

120 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.4 LCL = 1.0	Animal Number	UCL = 2.9 LCL = 0.1
4601	1.1	4618	1.0
4605	2.0	4619	0.9
Mean	1.6	Mean	1.0

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.6 LCL = 1.1	Animal Number	UCL = 2.8 LCL = 0.0
4606	2.3	4621	1.6
4607	2.1	4622	1.1
4608	2.0	4623	1.2
4609	3.9*	4624	1.2
4610	2.2	4625	1.4
Mean	2.5	Mean	1.3

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 4.0 LCL = 1.3	Animal Number	UCL = 3.4 LCL = 0.0
4603	5.7*	4616	2.4
4606	3.0	4620	1.2
4607	2.3	4622	1.0
4612	2.7	4625	6.3*
		4627	5.7*
Mean	3.4	Mean	3.3

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B10. Segmented Neutrophil Concentrations in Peripheral Blood of Rats Exposed to ^{60}Co Gamma Irradiation (890 rad or 8.9 Gy)

Group 23: Segmented Neutrophils ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.1 LCL = 0.8	Animal Number	UCL = 4.0 LCL = 0.6
4636	3.3*	4656	1.2
4637	3.4*	4657	3.4
4638	3.7*	4658	2.8
4639	5.3*	4659	2.6
4640	5.5*	4660	2.5
Mean	4.3	Mean	2.5

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.1 LCL = 0.8	Animal Number	UCL = 3.9 LCL = 0.7
4641	1.4	4646	0.2
4642	2.8	4647	1.1
4643	1.5	4648	0.8
4644	1.6	4649	0.7
4645	1.5	4650	0.8
Mean	1.8	Mean	0.7

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.1 LCL = 0.8	Animal Number	UCL = 3.9 LCL = 0.7
4636	0.7	4651	0.9
4637	1.9	4652	0.3
4638	1.0	4653	0.6
4639	0.9	4654	0.5
4640	1.0	4655	0.2
Mean	1.1	Mean	0.5

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B10. (Continued)

Group 23: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.2 LCL = 0.9	Animal Number	UCL = 3.9 LCL = 0.7
4641	1.6	4648	2.6
4642	1.9	4649	1.3
4643	2.5	4659	1.5
4644	2.0	4676	0.6
4645	2.3		
Mean	2.1	Mean	1.5

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.2 LCL = 0.9	Animal Number	UCL = 3.8 LCL = 0.6
4636	1.4	4651	0.8
4637	2.5	4657	0.9
4638	2.3	4658	1.0
4639	1.0	4659	1.4
4640	1.7	4660	1.4
Mean	1.8	Mean	1.1

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.3 LCL = 1.0	Animal Number	UCL = 3.6 LCL = 0.4
4631	1.5	4655	1.0
4634	1.9	4657	0.7
4636	2.0	4658	1.2
4637	3.0	4659	1.0
4641	2.6	4660	1.9
Mean	2.2	Mean	1.2

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B10. (Continued)

Group 23: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 3.6 LCL = 1.1	Animal Number	UCL = 2.8 LCL = 0.0
4631	2.0	4646	1.4
4634	1.8	4648	1.7
4636	2.0	4650	2.6
4637	2.5	4651	1.8
4639	1.5	4653	1.8
Mean	2.0	Mean	1.9

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 4.0 LCL = 1.3	Animal Number	UCL = 3.4 LCL = 0.0
4631	3.0	4648	0.6
4637	4.0	4650	1.4
4641	3.0	4651	1.4
4643	2.6	4653	1.0
4644	1.4	4666	1.6
Mean	2.8	Mean	1.2

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B11. Segmented Neutrophil Concentrations in Peripheral Blood of Rats Exposed to an Aerosol of ^{147}Pm (FAP)

Group 29: Segmented Neutrophils ($\times 10^3/\text{mm}^3$)

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 3.1 LCL = 0.8	Animal Number	Dose (Gy)	UCL = 3.9 LCL = 0.7
4691	110	3.7*	4716	133	1.1
4692	103	3.2*	4718	140	2.2
4693	139	4.1*	4720	144	2.5
4695	78	2.1			
Mean	108	3.3	Mean	139	1.9

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 3.2 LCL = 0.9	Animal Number	Dose (Gy)	UCL = 3.9 LCL = 0.7
4691	170	1.7	4706	141	0.9
4692	159	2.1	4707	239	0.8
4693	214	1.6	4708	220	2.4
4694	190	2.0	4709	160	0.9
4695	120	1.5	4710	225	1.1
Mean	171	1.8	Mean	197	1.2

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 3.2 LCL = 0.9	Animal Number	Dose (Gy)	UCL = 3.8 LCL = 0.6
4691	286	1.8	4706	237	0.9
4692	267	1.8	4707	402	1.5
4693	361	2.9	4708	371	1.4
4694	320	1.6	4710	380	1.2
4695	202	2.2	4717	440	1.2
Mean	287	2.1	Mean	366	1.2

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B11. (Continued)

Group 29: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 3.3 LCL = 1.0	Animal Number	Dose (Gy)	UCL = 3.6 LCL = 0.4
4691	370	3.9*	4713	377	0.7
4692	345	2.4	4716	448	1.1
4693	466	3.0	4717	568	10.7*
4694	413	2.7	4719	494	2.2
4697	389	1.8	4720	485	3.4
Mean	397	2.8	Mean	474	3.6

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B12. Segmented Neutrophil Concentrations in Peripheral Blood of Rats Exposed to an Aerosol of ^{147}Pm (FAP) and ^{60}Co Gamma Irradiation (850 rad or 8.5 Gy)

Group 26: Segmented Neutrophils ($\times 10^3/\text{mm}^3$)

7 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.1 LCL = 0.8	Animal Number	Dose ^a (Gy)	UCL = 3.9 LCL = 0.7
4481	15	0.6	4501	38	0.7
4482	25	0.7	4502	35	0.6
4483	25	0.7	4503	26	0.7
4484	23	1.1	4504	18	0.9
4485	17	0.7	4505	33	0.4
Mean	21	0.8	Mean	30	0.7

14 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.1 LCL = 0.8	Animal Number	Dose ^a (Gy)	UCL = 3.9 LCL = 0.7
4486	30	0.4	4496	37	0.4
4487	50	0.7	4497	48	0.4
4488	21	0.8	4499	65	0.3
4489	36	0.6	4500	47	0.4
4490	23	0.6	4508	51	0.4
Mean	32	0.6	Mean	50	0.4

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.1 LCL = 0.8	Animal Number	Dose ^a (Gy)	UCL = 3.9 LCL = 0.7
4666	103	1.4	4677	91	0.3
4672	71	0.8	4679	102	0.5
4675	117	1.6	4680	87	0.9
Mean	97	1.3	Mean	93	0.6

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B12. (Continued)

Group 26: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.2 LCL = 0.9	Animal Number	Dose ^a (Gy)	UCL = 3.9 LCL = 0.7
4490	45	0.8	4500	91	1.9
4491	78	0.9	4506	110	0.7
4492	53	1.8	4508	99	0.7
4493	83	1.2	4509	116	0.3
4494	102	0.6	4510	149	0.7
Mean	72	1.1	Mean	113	0.9

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.2 LCL = 0.9	Animal Number	Dose ^a (Gy)	UCL = 3.8 LCL = 0.6
4486	99	4.1*	4497	156	1.6
4487	164	1.2	4499	211	6.0*
4488	68	1.0	4500	154	1.6
4489	118	2.4	4501	237	2.4
4490	76	1.8	4502	216	1.5
Mean	105	2.1	Mean	195	2.6

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.3 LCL = 1.0	Animal Number	Dose ^a (Gy)	UCL = 3.6 LCL = 0.4
4485	132	1.4	4504	148	2.2
4487	212	1.9	4506	240	0.6
4488	88	1.0			
4492	115	1.7			
Mean	137	1.5	Mean	194	1.4

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B12. (Continued)

Group 26: Segmented Neutrophils ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 3.6 LCL = 1.1	Animal Number	Dose ^a (Gy)	UCL = 2.8 LCL = 0.0
4485	189	2.7	None		
4488	126	2.7			
Mean	158	2.7			

365 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 4.0 LCL = 1.3	Animal Number	Dose ^a (Gy)	UCL = 3.4 LCL = 0.0
4485	257	3.1	None		
4488	142	1.0			
Mean	200	2.1			

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

FIGURE B7. Mean Monocyte Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Male Rats for 1 Year after Exposure

FIGURE B8. Mean Monocyte Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Female Rats for 1 Year after Exposure

TABLE B13. Monocyte Concentrations in Peripheral Blood of Male and Female Control (Sham-Exposed) Rats^a

Group 21: Monocytes ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.41	Animal Number	UCL = 0.41
4606	0.09	4616	0.06
4607	0.08	4617	0.17
4608	0.13	4618	0.00
4609	0.14	4619	0.00
4610	0.07	4620	0.04
Mean	0.10	Mean	0.05

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.42	Animal Number	UCL = 0.41
4601	0.10	4621	0.10
4602	0.20	4622	0.16
4603	0.34	4623	0.05
4604	0.00	4624	0.42*
4605	0.10	4625	0.00
Mean	0.15	Mean	0.15

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.44	Animal Number	UCL = 0.42
4606	0.30	4626	0.22
4607	0.30	4627	0.06
4608	0.11	4628	0.11
4609	0.38	4629	0.29
4610	0.26	4630	0.30
Mean	0.27	Mean	0.20

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit; * = Values above upper 95% confidence limits

TABLE B13. (Continued)^a**Group 21: Monocytes ($\times 10^3/\text{mm}^3$) cont'd**

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.47	Animal Number	UCL = 0.43
4601	0.30	4616	0.10
4602	0.09	4617	0.17
4603	0.11	4618	0.51*
4604	0.30	4619	0.52*
4605	0.46	4620	0.27
Mean	0.25	Mean	0.31

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.49	Animal Number	UCL = 0.44
4601	0.52*	4626	0.29
4602	0.33	4627	0.07
4603	0.26	4628	0.19
4604	0.28	4629	0.19
4605	0.31	4630	0.05
Mean	0.34	Mean	0.16

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.48	Animal Number	UCL = 0.42
4611	0.05	4616	0.00
4612	0.06	4617	0.04
4613	0.11	4618	0.05
4614	0.16	4619	0.18
4615	0.33	4620	0.12
Mean	0.14	Mean	0.08

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit; * = Values above upper 95% confidence limits

TABLE B13. (Continued)^a

Group 21: Monocytes ($\times 10^3/\text{mm}^3$) cont'd

120 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.43	Animal Number	UCL = 0.39
4601	0.03	4618	0.07
4605	0.07	4619	0.10
Mean	0.05	Mean	0.09

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.33	Animal Number	UCL = 0.29
4606	0.13	4621	0.03
4607	0.23	4622	0.00
4608	0.00	4623	0.03
4609	0.06	4624	0.07
4610	0.09	4625	0.04
Mean	0.26	Mean	0.03

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.5	Animal Number	UCL = 0.5
4603	0.48	4616	0.40
4606	0.26	4620	0.16
4607	0.20	4622	0.15
4612	0.28	4625	0.14
		4627	1.05*
Mean	0.31	Mean	0.38

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit; * = Values above upper 95% confidence limits

TABLE B14. Monocyte Concentrations in Peripheral Blood of Rats Exposed to ^{60}Co Gamma Irradiation (890 rad or 8.9 Gy)^a

Group 23: Monocytes ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.41	Animal Number	UCL = 0.41
4636	0.00	4656	0.01
4637	0.06	4657	0.02
4638	0.08	4658	0.00
4639	0.00	4659	0.01
4640	0.00	4660	0.00
Mean	0.03	Mean	0.01

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.42	Animal Number	UCL = 0.41
4641	0.14	4646	0.02
4642	0.16	4647	0.06
4643	0.06	4648	0.05
4644	0.03	4649	0.05
4645	0.07	4650	0.02
Mean	0.09	Mean	0.04

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.44	Animal Number	UCL = 0.42
4636	0.02	4651	0.12
4637	0.11	4652	0.00
4638	0.03	4653	0.11
4639	0.03	4654	0.13
4640	0.08	4655	0.01
Mean	0.05	Mean	0.07

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit

TABLE B14. (Continued)^a**Group 23: Monocytes ($\times 10^3/\text{mm}^3$) cont'd**

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.47	Animal Number	UCL = 0.43
4641	0.45	4648	0.55*
4642	0.33	4649	0.28
4643	0.00	4659	1.93*
4644	0.11	4676	0.14
4645	0.14		
Mean	0.21	Mean	0.96

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.49	Animal Number	UCL = 0.44
4636	0.36	4651	0.08
4637	0.30	4657	0.27
4638	0.18	4658	2.00*
4639	0.05	4659	0.09
4640	0.28	4660	0.19
Mean	0.23	Mean	0.53

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.48	Animal Number	UCL = 0.42
4631	0.04	4655	0.04
4634	0.00	4657	0.02
4636	0.08	4658	0.08
4637	0.18	4659	0.03
4641	0.10	4660	0.00
Mean	0.08	Mean	0.03

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit; * = Values above upper 95% confidence limits

TABLE B14. (Continued)^a

Group 23: Monocytes ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.33	Animal Number	UCL = 0.29
4631	0.32	4646	0.00
4634	0.11	4648	0.06
4636	0.08	4650	0.00
4637	0.04	4651	0.08
4639	0.07	4653	0.00
Mean	0.12	Mean	0.03

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 0.5	Animal Number	UCL = 0.5
4631	0.24	4648	0.05
4637	0.28	4650	0.15
4641	0.18	4651	0.17
4643	0.20	4653	0.21
4644	0.05	4666	0.32
Mean	0.19	Mean	0.18

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit

TABLE B15. Monocyte Concentrations in Peripheral Blood of Rats Exposed to ^{147}Pm (FAP)^a

Group 29: Monocytes ($\times 10^3/\text{mm}^3$)

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 0.44	Animal Number	Dose (Gy)	UCL = 0.42
4691	110	0.26	4716	133	0.20
4692	103	0.30	4718	140	0.12
4693	139	0.30	4720	144	0.29
4695	78	0.35			
Mean	108	0.30	Mean	139	0.20

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 0.47	Animal Number	Dose (Gy)	UCL = 0.43
4691	170	0.05	4706	141	0.19
4692	159	0.06	4707	239	0.06
4693	214	0.06	4708	220	0.22
4694	190	0.03	4709	160	0.09
4695	120	0.08	4710	225	0.03
Mean	171	0.06	Mean	197	0.12

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 0.49	Animal Number	Dose (Gy)	UCL = 0.44
4691	286	0.11	4706	237	0.13
4692	267	0.21	4707	402	0.24
4693	361	0.11	4708	371	0.05
4694	320	0.40	4710	380	0.09
4695	202	0.29	4717	440	0.09
Mean	287	0.22	Mean	366	0.12

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit

TABLE B15. (Continued)^a

Group 29: Monocytes ($\times 10^3/\text{mm}^3$) cont'd

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 0.48	Animal Number	Dose (Gy)	UCL = 0.42
4691	370	0.32	4713	377	0.03
4692	345	0.03	4716	448	0.04
4693	466	0.02	4717	568	0.08
4694	413	0.08	4719	494	0.03
4697	389	0.06	4720	485	0.23
Mean	397	0.10	Mean	474	0.08

^aLower confidence limits not defined

KEY: UCL = Upper confidence limit

TABLE B16. Monocyte Concentrations in Peripheral Blood of Rats Exposed to ^{147}Pm (FAP) Aerosol and ^{60}Co Gamma Irradiation (850 rad or 8.5 Gy)^a

Group 26: Monocytes ($\times 10^3/\text{mm}^3$)

7 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.42	Animal Number	Dose ^b (Gy)	UCL = 0.41
4481	15	0.00	4501	38	0.04
4482	25	0.00	4502	35	0.00
4483	25	0.00	4503	26	0.06
4484	23	0.08	4504	18	0.00
4485	17	0.01	4505	33	0.06
Mean	21	0.02	Mean	30	0.03

14 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.44	Animal Number	Dose ^b (Gy)	UCL = 0.42
4486	30	0.00	4496	37	0.07
4487	50	0.00	4497	48	0.01
4488	21	0.00	4499	65	0.02
4489	36	0.00	4500	47	0.01
4490	23	0.00	4508	51	0.00
Mean	32	0.00	Mean	50	0.04

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.44	Animal Number	Dose ^b (Gy)	UCL = 0.42
4666	103	0.06	4677	91	0.00
4672	71	0.00	4679	102	0.08
4675	117	0.08	4680	87	0.15
Mean	97	0.05	Mean	93	0.08

^aLower confidence limits not defined

^bDose for inhaled promethium; does not include total-body gamma dose

KEY: UCL = Upper confidence limit

TABLE B16. (Continued)^a**Group 26: Monocytes ($\times 10^3/\text{mm}^3$) cont'd**

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.47	Animal Number	Dose ^b (Gy)	UCL = 0.43
4490	45	0.11	4500	91	0.25
4491	78	0.07	4506	110	0.06
4492	53	0.16	4508	99	0.04
4493	83	0.22	4509	116	0.01
4494	102	0.05	4510	149	0.06
Mean	72	0.12	Mean	113	0.08

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.49	Animal Number	Dose ^b (Gy)	UCL = 0.44
4486	99	0.29	4497	156	0.03
4487	164	0.04	4499	211	0.28
4488	68	0.06	4500	154	0.07
4489	118	0.13	4501	237	0.21
4490	76	0.21	4502	216	0.03
Mean	105	0.15	Mean	195	0.12

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.48	Animal Number	Dose ^b (Gy)	UCL = 0.42
4485	132	0.20	4504	148	0.45*
4487	212	0.41	4506	240	0.29
4488	88	0.22			
4492	115	0.13			
Mean	137	0.24	Mean	194	0.37

^aLower confidence limits not defined^bDose for inhaled promethium; does not include total-body gamma dose

KEY: UCL = Upper confidence limit; * = Values above upper 95% confidence limits

TABLE B16. (Continued)^a

Group 26: Monocytes ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.33	Animal Number	Dose ^b (Gy)	UCL = 0.29
4485	189	0.07	None		
4488	126	0.33			
Mean	158	0.20			

365 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^b (Gy)	UCL = 0.5	Animal Number	Dose ^b (Gy)	UCL = 0.5
4485	257	0.52*	None		
4488	142	0.27			
Mean	200	0.40			

^aLower confidence limits not defined

^bDose for inhaled promethium; does not include total-body gamma dose

KEY: UCL = Upper confidence limit; * = Values above upper 95% confidence limits

FIGURE B9. Mean Blood Platelet Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Male Rats for 1 Year after Exposure

FIGURE B10. Mean Blood Platelet Concentrations (Including Individual Data and the 95% Confidence Interval) in Control Female Rats for 1 Year after Exposure

TABLE B17. Blood Platelet Concentrations in Peripheral Blood of Male and Female Control (Sham-Exposed) Rats

Group 21: Platelets ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 270	Animal Number	UCL = 1150 LCL = 300
4607	637	4616	810
4608	393	4617	1070
4609	450	4619	442
4610	522	4610	702
Mean	501	Mean	756

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 280	Animal Number	UCL = 1150 LCL = 305
4601	915	4621	405
4602	610	4622	685
4603	660	4623	500
4604	852	4624	585
4605	805	4625	830
Mean	768	Mean	601

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 280	Animal Number	UCL = 1150 LCL = 310
4606	642	4626	765
4607	205	4627	585
4608	510	4628	1000
4609	890	4629	855
4610	823	4630	693
Mean	614	Mean	780

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B17. (Continued)

Group 21: Platelets ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 280	Animal Number	UCL = 1150 LCL = 310
4601	860	4616	885
4602	810	4617	1022
4603	842	4618	820
4604	965	4619	1155*
4605	715	4620	760
Mean	838	Mean	328

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 275	Animal Number	UCL = 1160 LCL = 310
4601	570	4626	720
4602	612	4627	562
4603	450	4628	565
4604	572	4629	475
4605	558	4630	460
Mean	552	Mean	556

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 270	Animal Number	UCL = 1150 LCL = 300
4611	160	4616	778
4612	835	4617	848
4613	678	4618	892
4614	635	4619	1072
4615	850	4620	625
Mean	632	Mean	843

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit; * = Values above upper 95% confidence limit of controls

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B17. (Continued)

Group 21: Platelets ($\times 10^3/\text{mm}^3$) cont'd

120 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1040 LCL = 250	Animal Number	UCL = 1130 LCL = 270
4601	483	4618	52
4605	360	4619	500
Mean	771	Mean	753

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1025 LCL = 200	Animal Number	UCL = 1090 LCL = 200
4606	730	4621	578
4607	535	4622	738
4608	835	4623	463
4609	803	4624	733
4610	350	4625	765
Mean	651	Mean	655

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 990 LCL = 150	Animal Number	UCL = 960 LCL = 60
4603	676	4616	494
4606	470	4620	327
4607	579	4622	469
4612	555	4625	775
		4627	103
Mean	570	Mean	434

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B18. Blood Platelet Concentrations in Peripheral Blood of Rats Exposed to ^{60}Co Gamma Irradiation (890 rad or 8.9 Gy)

Group 23: Platelets ($\times 10^3/\text{mm}^3$)

2 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 270	Animal Number	UCL = 1150 LCL = 300
4636	695	4656	560
4637	855	4657	410
4638	612	4658	807
4639	455	4659	627
4640	702	4660	532
Mean	664	Mean	587

7 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 280	Animal Number	UCL = 1150 LCL = 305
4641	75	4646	28
4642	99	4647	24
4643	71	4648	39
4644	24	4649	27
4645	24	4650	29
Mean	59	Mean	29

14 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 280	Animal Number	UCL = 1150 LCL = 310
4636	37	4651	42
4637	43	4652	20
4638	17	4653	40
4639	16	4654	49
4640	57	4655	61
Mean	34	Mean	42

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B18. (Continued)

Group 23: Platelets ($\times 10^3/\text{mm}^3$) cont'd

30 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 280	Animal Number	UCL = 1150 LCL = 310
4641	218	4648	426
4642	195	4649	177
4643	215	4650	94
4644	114	4659	109
4645	640	4676	161
Mean	276	Mean	193

60 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 215	Animal Number	UCL = 1160 LCL = 310
4636	375	4651	306
4637	482	4657	272
4638	352	4658	399
4639	438	4659	343
4640	352	4660	226
Mean	400	Mean	309

90 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1050 LCL = 270	Animal Number	UCL = 1150 LCL = 300
4631	678	4655	408
4634	450	4657	660
4636	682	4658	480
4637	518	4659	460
4641	452	4660	495
Mean	556	Mean	501

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B18. (Continued)

Group 23: Platelets ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 1025 LCL = 200	Animal Number	UCL = 1090 LCL = 200
4631	520	4646	608
4634	510	4648	453
4636	620	4650	630
4637	540	4651	518
4639	585	4653	485
Mean	555	Mean	539

365 Days After Exposure			
MALES		FEMALES	
Animal Number	UCL = 990 LCL = 150	Animal Number	UCL = 960 LCL = 60
4631	406	4648	477
4637	550	4650	418
4641	685	4651	442
4643	422	4653	383
4644	581	4666	297
Mean	529	Mean	403

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B19. Blood Platelet Concentrations in Peripheral Blood of Rats Exposed to ¹⁴⁷Pm (FAP)

Group29: Platelets ($\times 10^3/\text{mm}^3$)

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 1050 LCL = 280	Animal Number	Dose (Gy)	UCL = 1150 LCL = 310
4691	110	673	4616	133	673
4692	103	662	4618	140	595
4693	139	710	4620	144	378
4695	78	420			
Mean	108	616	Mean	139	549

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 1050 LCL = 280	Animal Number	Dose (Gy)	UCL = 1150 LCL = 310
4691	170	485	4706	141	900
4692	159	395	4707	239	645
4693	214	575	4708	220	960
4694	190	985	4709	160	495
4695	120	820	4710	225	495
Mean	171	652	Mean	197	699

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 1050 LCL = 275	Animal Number	Dose (Gy)	UCL = 1160 LCL = 310
4691	286	630	4706	237	520
4692	267	682	4707	402	468
4693	361	668	4708	371	698
4694	320	528	4710	380	388
4695	202	362	4717	440	525
Mean	287	574	Mean	366	520

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B19. (Continued)

Group 29: Platelets ($\times 10^3/\text{mm}^3$) cont'd

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 1050 LCL = 270	Animal Number	Dose (Gy)	UCL = 1150 LCL = 300
4691	370	322	4713	377	360
4692	345	446	4716	448	292
4693	466	303	4717	568	302
4694	413	310	4719	494	592
4697	389	268	4720	485	430
Mean	397	330	Mean	474	395

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B20. Blood Platelet Concentrations in Peripheral Blood of Rats Exposed to ^{147}Pm (FAP) and ^{60}Co Gamma Irradiation (850 rad or 8.5 Gy)

Group 26: Platelets ($\times 10^3/\text{mm}^3$)

7 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1050 LCL = 280	Animal Number	Dose ^a (Gy)	UCL = 1150 LCL = 305
4481	15	23	4501	38	18
4482	25	30	4502	35	12
4483	25	33	4503	26	16
4484	23	13	4504	18	15
4485	17	20	4505	33	14
Mean	21	24	Mean	30	15

14 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1050 LCL = 280	Animal Number	Dose ^a (Gy)	UCL = 1150 LCL = 310
4486	30	32	4496	37	35
4487	50	25	4497	48	25
4488	21	42	4499	65	19
4489	36	20	4500	47	37
4490	23	50	4508	51	17
Mean	32	35	Mean	50	27

18 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1050 LCL = 280	Animal Number	Dose ^a (Gy)	UCL = 1150 LCL = 310
4466	103	52	4677	91	72
4672	71	51	4679	102	21
4675	117	105	4680	87	49
Mean	97	69	Mean	93	47

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B20. (Continued)

Group 26: Platelets ($\times 10^3/\text{mm}^3$)

30 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1050 LCL = 280	Animal Number	Dose ^a (Gy)	UCL = 1150 LCL = 310
4490	45	44	4500	91	191
4491	78	223	4506	110	147
4492	53	130	4508	99	172
4493	83	405	4509	116	11
4494	102	190	4510	149	256
Mean	72	198	Mean	113	155

60 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1050 LCL = 275	Animal Number	Dose ^a (Gy)	UCL = 1160 LCL = 310
4486	99	97	4497	156	263
4487	164	230	4499	211	101
4488	68	225	4500	154	307
4489	118	217	4501	237	153
4490	76	165	4502	216	206
Mean	105	187	Mean	195	200

90 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1050 LCL = 270	Animal Number	Dose ^a (Gy)	UCL = 1150 LCL = 300
4485	132	275	4504	148	140
4487	212	167	4506	240	8
4488	88	244			
4492	115	326			
Mean	137	253	Mean	194	74

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

TABLE B20. (Continued)

Group 26: Platelets ($\times 10^3/\text{mm}^3$) cont'd

180 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose ^a (Gy)	UCL = 1025 LCL = 200	Animal Number	Dose ^a (Gy)	UCL = 1090 LCL = 200
4485	189	6	None		
4488	126	5			
Mean	158	6			

365 Days After Exposure					
MALES			FEMALES		
Animal Number	Dose (Gy)	UCL = 990 LCL = 150	Animal Number	Dose ^a (Gy)	UCL = 960 LCL = 60
4485	257	381	None		
4488	142	485			
Mean	200	433			

^aDose for inhaled promethium; does not include total-body gamma dose

KEY: LCL = Lower confidence limit; UCL = Upper confidence limit

NOTE: Boldface values are those below the lower 95% confidence limit of controls

APPENDIX C
DATABASE FOR RATS OF MORTALITY GROUPS

DEFINITIONS OF EXPOSURE GROUPS AND ABBREVIATIONS

Sex

M = male
F = female

Group

21 & 41 = Control group
22 = Gamma irradiated, 8.5 Gy
23 & 43 = Gamma irradiated, 8.9 Gy
24 = Gamma irradiated, 9.2 Gy
25 = Exposure to promethium aerosol only
26 & 46 = Exposure to promethium aerosol and 8.5 Gy gamma radiation
27 = Exposure to promethium aerosol and 8.9 Gy gamma radiation
28 = Exposure to promethium aerosol and 9.2 Gy gamma radiation
29 & 49 = Exposure to promethium aerosol only
30 = Exposure to promethium aerosol and 8.5 Gy gamma radiation
31 = Exposure to promethium aerosol and 8.9 Gy gamma radiation
32 = Exposure to promethium aerosol and 9.2 Gy gamma radiation
33 = Exposure to promethium aerosol only
34 = Exposure to promethium aerosol and 8.5 Gy gamma radiation
35 = Exposure to promethium aerosol and 8.9 Gy gamma radiation
39 = Exposure to promethium aerosol and 8.5 Gy gamma radiation

* = Data not obtained

Mode

E = Euthanized
D = Died

Pathology

RP = Radiation pneumonitis
PF = Pulmonary fibrosis

Other

BAEH = Bronchioloalveolar hyperplasia and metaplasia
EMP = Pulmonary emphysema
IT = Intimal thickening of small pulmonary blood vessels
NSL = No significant lesion
PUH = Pulmonary hemorrhage
SKTU = Skin tumor (location not specified)
THROMB = Thrombosis in pulmonary blood vessels
(1) = Diaphragmatic hernia
(2) = Anaplastic pulmonary carcinoma
(3) = Malignant lymphoma (abdominal)

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death	Pathology		
							RP	PF	Other
4001	M	21	271.5	435	403	E			
4002	M	21	285.0	435	430	E			
4003	M	21	265.5	435	418	E			
4004	M	21	286.0	435	381	E			
4005	M	21	282.0	435	389	E			
4006	M	21	264.5	435	419	E			
4007	M	21	269.0	435	390	E			
4008	M	21	247.5	266	338	D			SKTU
4009	M	21	282.5	435	416	E			
4010	M	21	280.5	435	423	E			
4011	M	21	286.0	435	424	E			
4012	M	21	270.5	435	366	E			
4013	M	21	260.5	435	391	E			
4014	M	21	288.0	435	436	E			
4015	M	21	286.0	435	429	E			
4016	M	21	284.5	375	375	D			(1)
4017	M	21	262.0	435	365	E			
4018	M	21	281.0	435	445	E			
4019	M	21	285.0	435	430	E			
4020	M	21	275.0	435	412	E			
4021	M	21	283.0	435	409	E			
4022	M	21	285.0	435	430	E			
4023	M	21	279.5	435	416	E			
4024	M	21	288.5	435	419	E			
4025	M	21	251.5	435	356	E			
4026	M	21	257.0	435	397	E			
4027	M	21	235.0	435	339	E			
4028	M	21	290.5	435	397	E			
4029	M	21	307.5	435	425	E			
4030	M	21	291.5	435	447	E			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death	Pathology		
								RP	PF	Other
4061	M	22	311.0	8.5	329	317	D			
4062	M	22	308.5	8.5	411	346	E			
4063	M	22	287.0	8.5	411	332	E			
4064	M	22	322.5	8.5	411	372	E			
4065	M	22	302.5	8.5	411	352	E			
4066	M	22	300.5	8.5	411	338	E			
4067	M	22	306.0	8.5	412	402	E			
4068	M	22	311.0	8.5	412	362	E			
4069	M	22	298.5	8.5	412	350	E			
4070	M	22	339.5	8.5	412	402	E			
4071	M	22	287.5	8.5	412	312	E			
4072	M	22	331.0	8.5	412	397	E			
4073	M	22	291.0	8.5	412	318	E			
4074	M	22	285.5	8.5	412	303	E			
4075	M	22	333.0	8.5	412	387	E			
4076	F	22	201.0	8.5	157	175	D			PUH
4077	F	22	199.0	8.5	412	220	E			
4078	F	22	193.0	8.5	338	151	D			
4079	F	22	187.5	8.5	412	205	E			
4080	F	22	196.0	8.5	412	213	E			
4081	F	22	188.0	8.5	412	199	E			
4082	F	22	197.0	8.5	412	220	E			
4083	F	22	199.5	8.5	412	214	E			
4084	F	22	188.0	8.5	412	209	E			
4085	F	22	189.0	8.5	172	171	D			EMP
4086	F	22	203.0	8.5	412	212	E			
4087	F	22	182.5	8.5	412	191	E			
4088	F	22	198.5	8.5	412	219	E			
4089	F	22	191.0	8.5	412	210	E			
4090	F	22	179.0	8.5	340	193	D	+		

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death	Pathology		
							RP	PF	Other
4031	F	21	173.5	435	241	E			
4032	F	21	175.5	435	235	E			
4033	F	21	180.0	435	266	E			
4034	F	21	182.0	435	255	E			
4035	F	21	174.5	435	237	E			
4036	F	21	176.5	420	261	D			
4037	F	21	167.5	440	214	E			
4038	F	21	173.0	440	254	E			
4039	F	21	186.5	440	232	E			
4040	F	21	176.5	440	250	E			
4041	F	21	175.0	440	273	E			
4042	F	21	159.5	440	223	E			
4043	F	21	175.0	440	236	E			
4044	F	21	173.0	440	232	E			
4045	F	21	177.0	440	264	E			
4046	F	21	175.0	440	237	E			
4047	F	21	175.5	440	276	E			
4048	F	21	156.5	440	209	E			
4049	F	21	165.5	440	231	E			
4050	F	21	176.0	440	269	E			
4051	F	21	169.5	440	241	E			
4052	F	21	169.5	440	219	E			
4053	F	21	181.0	440	284	E			
4054	F	21	172.5	440	227	E			
4055	F	21	182.5	440	270	E			
4056	F	21	173.5	440	223	E			
4057	F	21	181.0	440	249	E			
4058	F	21	169.5	440	224	E			
4059	F	21	171.0	440	262	E			
4060	F	21	172.5	440	254	E			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death	Pathology		
								RP	PF	Other
4091	M	23	258.5	8.9	388	321	E			
4092	M	23	263.5	8.9	388	305	E			
4093	M	23	295.5	8.9	281	262	D			(2)
4094	M	23	288.0	8.9	388	333	E			
4095	M	23	296.5	8.9	185	338	D	+	+	SKTU
4096	M	23	291.0	8.9	388	336	E			
4097	M	23	279.0	8.9	388	335	E			
4098	M	23	276.5	8.9	388	340	E			
4099	M	23	299.5	8.9	228	264	D			
4100	M	23	298.0	8.9	388	360	E			
4101	M	23	278.0	8.9	388	315	E			
4102	M	23	270.0	8.9	317	286	D			
4103	M	23	290.5	8.9	299	205	D			
4104	M	23	267.0	8.9	388	342	E			
4105	M	23	260.0	8.9	339	274	D			(3)
4106	M	23	263.5	8.9	218	229	D		+	EMP
4107	M	23	283.0	8.9	388	350	E			
4108	M	23	256.5	8.9	388	310	E			
4109	M	23	315.5	8.9	339	365	D			SKTU
4110	M	23	289.5	8.9	17	204	D			
4111	M	23	265.5	8.9	388	323	E			
4112	M	23	293.0	8.9	26	186	D	+		PUH
4113	M	23	385.5	8.9	315	229	D			
4114	M	23	303.0	8.9	388	399	E			
4115	M	23	251.5	8.9	388	303	E			
4116	M	23	290.5	8.9	388	350	E			
4117	M	23	258.0	8.9	388	321	E			
4118	M	23	282.0	8.9	388	314	E			
4119	M	23	256.0	8.9	388	341	E			
4120	M	23	248.0	8.9	388	285	E			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death	Pathology		
								RP	PF	Other
4121	F	23	170.5	8.9	388	204	E			
4122	F	23	172.5	8.9	388	215	E			
4123	F	23	176.0	8.9	388	207	E			
4124	F	23	168.0	8.9	388	216	E			
4125	F	23	176.0	8.9	388	210	E			
4126	F	23	174.0	8.9	388	207	E			
4127	F	23	168.0	8.9	378	136	D			
4128	F	23	174.5	8.9	321	160	D			SKTU
4129	F	23	174.0	8.9	388	198	E			
4130	F	23	168.0	8.9	378	175	D			
4131	F	23	170.5	8.9	388	207	E			
4132	F	23	175.0	8.9	367	166	D			
4133	F	23	173.5	8.9	388	208	E			
4134	F	23	164.0	8.9	388	189	E			
4135	F	23	173.0	8.9	169	189	D	+	+	
4136	F	23	171.0	8.9	388	205	E			
4137	F	23	174.0	8.9	394	202	E			
4138	F	23	170.0	8.9	394	212	E			
4139	F	23	170.0	8.9	394	195	E			
4140	F	23	167.5	8.9	394	186	E			
4141	F	23	168.5	8.9	394	197	E			
4142	F	23	175.0	8.9	13	136	D			
4143	F	23	173.5	8.9	394	199	E			
4144	F	23	171.0	8.9	394	202	E			
4145	F	23	170.5	8.9	274	179	D			
4146	F	23	156.5	8.9	394	174	E			
4147	F	23	176.0	8.9	206	170	D	+		
4148	F	23	167.5	8.9	394	194	E			
4149	F	23	154.0	8.9	173	150	D			
4150	F	23	180.5	8.9	394	194	E			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death	Pathology		
								RP	PF	Other
4151	M	24	263.0	9.2	283	173	D	+	+	
4152	M	24	312.5	9.2	304	335	D			
4153	M	24	290.0	9.2	412	312	E			
4154	M	24	293.5	9.2	412	331	E			
4155	M	24	305.0	9.2	412	390	E			
4156	M	24	292.0	9.2	412	329	E			
4157	M	24	315.0	9.2	412	336	E			
4158	M	24	298.0	9.2	412	371	E			
4159	M	24	291.0	9.2	412	306	E			
4160	M	24	291.0	9.2	340	368	D			SKTU
4161	M	24	340.5	9.2	412	389	E			
4162	M	24	317.0	9.2	255	334	D			
4163	M	24	304.5	9.2	412	328	E			
4164	M	24	284.5	9.2	412	334	E			
4165	M	24	299.5	9.2	412	289	E			
4166	F	24	196.5	9.2	413	227	E			
4167	F	24	192.5	9.2	340	244	D			SKTU
4168	F	24	195.0	9.2	413	217	E			
4169	F	24	183.0	9.2	413	202	E			
4170	F	24	192.0	9.2	413	227	E			
4171	F	24	188.0	9.2	413	224	E			
4172	F	24	195.0	9.2	413	189	E			
4173	F	24	184.0	9.2	413	203	E			
4174	F	24	195.0	9.2	364	177	D			
4175	F	24	185.5	9.2	413	209	E			
4176	F	24	182.5	9.2	413	243	E			
4177	F	24	185.0	9.2	413	229	E			
4178	F	24	181.5	9.2	413	198	E			
4179	F	24	189.0	9.2	413	227	E			
4180	F	24	186.5	9.2	413	204	E			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Lung Burden (μ Ci/g)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
											RP	PF	Other
4189	M	25	326.0	64.8	51	216	411	227	414	E			
4186	M	25	287.5	65.7	52	219	355	216	360	D			
4185	M	25	321.0	71.0	56	236	413	249	390	E			
4193	M	25	305.0	72.3	57	241	377	244	246	D			
4194	M	25	304.0	73.8	58	246	411	258	384	E			
4184	M	25	297.5	79.5	63	265	116	157	205	D	+		
4192	M	25	301.5	86.7	68	289	131	182	199	D			
4188	M	25	297.0	87.6	69	292	411	307	381	E			
4181	M	25	313.0	88.6	70	295	92	154	228	D	+		
4190	M	25	336.5	91.0	72	303	411	318	368	E			
4187	M	25	307.5	92.9	73	309	101	170	275	D	+		
4183	M	25	301.1	94.3	74	314	139	204	267	D			
4920	M	29	286.5	102	80	340	204	264	269	D	+	+	
4195	M	25	299.0	102	80	340	287	306	333	D	+	+	
4191	M	25	307.5	104	82	346	120	209	225	D	+		
4182	M	29	294.5	105	83	349	143	230	260	D	+		
4918	M	29	288.5	112	88	373	84	184	304	D			
4921	M	29	285.5	120	94	399	195	304	224	D	+	+	
4929	M	29	297.5	124	98	413	201	319	229	D	+	+	IT
4925	M	29	283.5	127	100	423	148	283	251	D	+	+	
4342	M	29	284.0	130	102	433	227	353	296	D	+	+	
4341	M	29	247.5	135	106	449	117	267	226	D	+	+	
4922	M	29	282.0	148	116	493	170	352	251	D	+	+	
4907	M	33	289.5	155	122	516	142	339	250	D	+	+	
4338	M	29	271.5	156	123	519	102	287	186	D			
4927	M	29	267.5	158	124	526	128	328	256	D	+	+	
4340	M	29	269.5	168	132	559	140	364	232	D	+	+	
4213	M	29	274.5	168	132	559	99	304	242	D			
4926	M	29	283.0	170	134	566	128	352	238	D	+	+	
4917	M	29	275.0	173	136	576	100	314	252	D			
4903	M	33	280.5	177	139	589	138	381	237	D	+	+	IT
4913	M	33	303.5	182	143	606	124	371	240	D	+	+	

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Lung Burden (μ Ci/g)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
											RP	PF	Other
4928	M	29	290.5	183	144	609	134	388	215	D	+	+	
4923	M	29	270.0	184	145	612	136	393	227	D	+	+	
4901	M	33	289.0	185	146	616	198	472	204	D	+		
4344	M	29	276.0	192	151	639	113	373	196	D	+	+	
5027	M	29	*	193	152	642	104	358	*	D			
4916	M	29	285.0	196	154	652	73	295	276	D			
4919	M	29	297.5	198	156	659	114	386	235	D	+		
4914	M	33	295.5	199	157	662	140	432	233	D			
4915	M	33	255.0	200	157	666	114	390	196	D	+	+	PUH
4902	M	33	281.5	200	157	666	210	524	272	D	+	+	
4908	M	33	282.5	205	161	682	130	428	198	D	+	+	EMP
4345	M	29	293.0	206	162	686	101	376	227	D	+	+	
4339	M	29	265.5	210	165	699	112	406	203	D	+		PUH
4911	M	33	291.5	212	167	706	127	438	215	D			
4912	M	33	286.0	213	168	709	114	416	211	D	+	+	EMP
4924	M	29	286.5	214	168	712	105	400	248	D			
4904	M	33	283.5	216	170	719	153	489	218	D	+		
4910	M	33	285.5	220	173	732	109	419	238	D	+	+	
4336	M	29	269.5	220	173	732	92	381	212	D	+	+	
4905	M	33	281.0	233	183	776	118	463	232	D			
4930	M	29	311.0	242	190	806	139	523	172	D			
4214	M	29	297.0	244	192	812	113	474	224	D			
4215	M	29	301.5	254	200	845	103	469	231	D			
4343	M	29	296.5	264	208	879	103	488	207	D	+	+	
4909	M	33	283.5	286	225	952	106	537	192	D			
4211	M	29	279.0	289	227	962	104	537	192	D			
4212	M	29	285.5	295	232	982	103	545	192	D	+	+	
4906	M	33	259.0	337	265	1122	104	626	162	D	+	+	

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Lung Burden (μ Ci/g)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
											RP	PF	Other
4938	F	33	170.0	59	46	196	448	214	233	E			
4203	F	25	188.5	77	61	256	338	248	204	D	+	+	BAEH
4206	F	25	187.5	83	65	276	411	290	232	E			
4207	F	25	179.0	85	67	283	411	297	225	E			
4197	F	25	193.5	93	73	310	411	325	262	E	+	+	
4200	F	25	185.5	97	76	323	411	339	239	E			
4204	F	25	195.0	97	76	323	267	282	203	D			
4208	F	25	192.5	97	76	323	411	339	258	E			
4210	F	25	190.0	99	78	330	411	346	246	E			
4198	F	25	187.5	103	81	343	411	360	237	E			
4196	F	25	183.5	112	88	373	107	211	135	D	+		
4209	F	25	199.5	113	89	376	112	218	131	D	+		
4199	F	25	180.5	120	94	399	277	355	179	D			
4201	F	25	190.5	125	98	416	107	236	144	D			
4205	F	25	188.0	125	98	416	101	228	147	D	+		PUH
4953	F	29	171.5	150	118	499	133	317	143	D	+	+	
4952	F	29	166.5	151	119	503	174	363	139	D	+	+	IT
4202	F	25	174.5	155	122	516	107	292	86	D			
4372	F	29	170.5	167	131	556	141	363	137	D	+	+	
4954	F	29	178.0	171	135	569	89	291	162	D	+		
4960	F	29	175.0	181	142	602	156	414	137	D	+	+	
4951	F	29	168.5	185	146	616	104	344	128	D			
4956	F	29	168.5	186	146	616	114	363	127	D			
4363	F	29	173.5	195	153	649	124	398	111	D	+	+	PUH
4949	F	29	163.0	199	157	662	148	443	139	D	+	+	
4367	F	29	172.0	201	158	669	178	489	136	D	+	+	
4362	F	29	167.5	205	161	682	125	420	125	D	+		
4937	F	33	166.5	213	168	709	150	478	107	D	+	+	EMP
4955	F	29	176.0	213	168	709	119	425	119	D	+	+	PUH
4950	F	29	291.5	219	172	729	111	421	134	D			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Lung Burden (μ Ci/g)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
											RP	PF	Other
4957	F	29	177.0	219	172	729	120	439	110	D			
4361	F	29	175.5	220	173	732	225	594	152	D	+	+	
4932	F	33	172.5	228	179	759	138	491	137	D	+	+	EMP
4947	F	29	156.5	229	180	762	107	432	118	D	+	+	PUH
4370	F	29	176.5	231	182	769	87	387	158	D			
4364	F	29	170.0	235	185	782	116	463	158	D			
4946	F	29	165.5	244	192	812	118	485	123	D			
4948	F	29	168.0	244	192	812	139	527	116	D	+	+	EMP
4958	F	29	170.0	246	194	819	86	410	145	D	+		
4940	F	33	166.0	249	196	829	139	538	123	D	+	+	EMP
4373	F	29	175.5	256	201	852	130	535	134	D	+	+	
4934	F	33	169.0	261	205	869	128	541	107	D	+	+	EMP
4959	F	29	178.5	271	213	902	119	541	119	D	+	+	PUH
4368	F	29	175.0	272	214	905	92	471	130	D			
4369	F	29	167.5	279	220	929	123	567	122	D	+	+	
4375	F	29	172.0	282	222	939	74	428	180	D			
4941	F	33	160.5	295	232	982	107	556	128	D			
4374	F	29	164.5	295	232	982	74	448	182	D	+		
4365	F	29	177.0	298	234	992	113	579	98	D			
4371	F	29	172.0	323	254	1075	113	628	117	D			
4936	F	33	154.0	336	264	1118	82	544	126	D	+		
4933	F	33	156.0	342	269	1138	120	686	115	D	+	+	
4942	F	33	164.5	357	281	1188	100	649	110	D			
4931	F	33	169.0	358	282	1192	118	712	113	D			
4935	F	33	163.5	373	293	1242	97	666	114	D			
4366	F	29	169.5	381	300	1268	111	733	98	D			
4944	F	33	190.0	383	301	1275	114	748	110	D			
4939	F	33	165.0	391	308	1301	95	690	114	D	+		
4945	F	33	165.5	394	310	1311	111	758	89	D	+	+	
4943	F	33	169.0	407	320	1355	117	805	104	D			

Lat #	Sex	Group	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (μ Ci/g)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
												RP	PF	Other
4277	M	27	283.5	8.9	2.9	2	10	30	2	244	D			
4226	M	30	282.5	8.5	3.3	3	11	434	12	337	E			
4464	M	26	280.5	8.5	3.3	3	11	194	8	200	D			
4273	M	27	326.0	8.9	6.2	5	21	75	9	229	D			
4465	M	26	296.5	8.5	8.6	7	29	420	30	363	E			
4584	M	28	296.0	9.2	11.9	9	40	99	22	267	D			
4430	M	26	269.5	8.5	18.1	14	60	420	64	334	E			
4397	M	31	290.5	8.9	28.6	23	95	410	100	312	E			
4572	M	28	296.5	9.2	59.5	47	198	92	103	275	D	+		
4272	M	27	317.5	8.9	62.9	49	209	411	220	348	E			
4454	M	26	282.5	8.5	62.9	49	209	397	217	188	D			
4281	M	27	312.5	8.9	62.9	49	209	34	55	307	D			
4279	M	27	291.5	8.9	65.7	52	219	31	53	253	D			
4451	M	26	266.0	8.5	66.2	52	220	108	126	248	D	+		
4278	M	27	300.5	8.9	67.6	53	225	28	50	268	D	+		
4434	M	26	284.5	8.5	68.1	54	227	117	135	318	D			
4282	M	27	307.5	8.9	68.6	54	228	41	69	235	D	+		
4275	M	27	332.5	8.9	69.0	54	230	69	100	253	D			
4395	M	31	289.0	8.9	69.5	55	231	86	116	259	D			
4455	M	26	285.5	8.5	71.0	56	236	104	132	257	D	+		
4285	M	27	302.0	8.9	72.9	57	243	38	69	237	D			
4422	M	26	286.0	8.5	72.9	57	243	391	250	264	D			
4284	M	27	324.0	8.9	73.8	58	246	36	67	300	D			
4590	M	28	296.0	9.2	77.1	61	257	80	123	250	D			
4280	M	27	301.5	8.9	79.5	63	265	33	68	255	D			
4426	M	26	295.0	8.5	81.9	64	273	117	162	269	D	+		THROMB
4431	M	26	290.5	8.5	82.9	65	276	95	146	234	D	+		
4283	M	27	311.5	8.9	83.3	66	277	33	71	269	D			
4274	M	27	293.0	8.9	86.2	68	287	88	146	238	D	+		
4460	M	26	280.0	8.5	86.2	68	287	61	115	306	D			
4432	M	26	271.0	8.5	88.6	70	295	90	152	251	D	+		
4582	M	28	273.0	9.2	88.6	70	295	83	144	259	D	+		PUH
4423	M	26	310.5	8.5	89.0	70	296	391	305	264	D			
4433	M	26	306.0	8.5	89.0	70	296	66	126	306	D			
4400	M	31	317.0	8.9	92.4	73	308	103	171	238	D			
4456	M	26	281.0	8.5	92.4	73	308	92	160	251	D			
4458	M	26	284.0	8.5	92.4	73	308	111	178	287	D			
4220	M	30	277.5	8.5	92.9	73	309	95	164	188	D	+		PUH
4463	M	26	266.5	8.5	92.9	73	309	109	177	320	D			
4571	M	28	296.5	9.2	93.8	74	312	119	187	251	D	+		
4392	M	31	303.5	8.9	94.3	74	314	70	138	276	D			
4462	M	26	289.5	8.5	94.3	74	314	60	125	268	D			
4421	M	26	298.0	8.5	95.2	75	317	100	173	286	D			
4424	M	26	302.5	8.5	95.7	75	319	420	338	346	E			

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
												RP	PF	Other
4427	M	26	308.0	8.5	95.7	75	319	116	189	297	D			
4453	M	26	294.0	8.5	95.7	75	319	14	39	314	D			
4457	M	26	273.5	8.5	95.7	75	319	90	164	254	D			
4276	M	27	301.5	8.9	96.2	76	320	29	74	276	D	+		
4578	M	28	284.5	9.2	96.2	76	320	79	152	244	D			
4581	M	28	235.5	9.2	97.1	76	323	65	136	201	D	+		PUH
4583	M	28	260.5	9.2	98.6	78	328	82	160	223	D			
4428	M	26	289.0	8.5	99.0	78	330	119	198	257	D			
4459	M	26	278.0	8.5	101	79	336	85	167	244	D	+		
4576	M	28	267.5	9.2	101	79	336	70	148	224	D	+		PUH
4577	M	28	277.0	9.2	101	79	336	64	140	230	D			
4429	M	26	273.0	8.5	102	80	340	134	216	234	D	+		PUH
4313	M	32	296.0	9.2	102	80	340	87	171	178	D			
4842	M	34	254.0	8.5	105	83	349	56	133	222	D	+		
4452	M	26	268.0	8.5	107	84	356	118	213	187	D	+		EMP
4393	M	31	325.0	8.9	109	86	363	84	179	263	D			
4585	M	28	261.5	9.2	111	87	369	78	174	220	D			
4425	M	26	270.5	8.5	112	88	373	76	173	236	D	+		
4573	M	28	266.5	9.2	112	88	373	85	185	242	D			
4574	M	28	272.0	9.2	112	88	373	77	174	206	D			
4399	M	31	310.0	8.9	113	89	376	96	201	245	D			PUH
4403	M	31	319.0	8.9	114	90	379	88	192	256	D	+		PUH
4394	M	31	309.0	8.9	115	90	383	81	185	270	D	+		PUH
4230	M	30	265.0	8.5	116	91	386	47	129	186	D			
4305	M	32	320.5	9.2	119	94	396	13	45	228	D			
4310	M	32	313.0	9.2	121	95	403	92	210	242	D	+		PUH
4222	M	30	286.0	8.5	122	96	406	99	220	251	D	+		
4307	M	32	293.0	9.2	124	98	413	58	160	262	D	+		PUH
4311	M	32	381.0	9.2	124	98	413	83	202	282	D	+		
4221	M	30	268.0	8.5	125	98	416	40	123	192	D			
4302	M	32	307.0	9.2	125	98	416	90	214	227	D	+		PUH
4224	M	30	291.5	8.5	127	100	423	48	144	210	D	+		PUH
4575	M	28	297.0	9.2	127	100	423	72	190	251	D			
4312	M	32	268.5	9.2	128	101	426	87	215	173	D			
4301	M	32	276.0	9.2	128	101	426	68	184	212	D	+		PUH
4271	M	27	303.5	8.9	130	102	433	44	138	246	D	+		
4314	M	32	296.5	9.2	131	103	436	40	129	253	D	+		PUH
4671	M	39	316.5	8.5	132	104	439	117	261	248	D	+		
4405	M	31	311.5	8.9	134	105	446	84	220	232	D			
4579	M	28	276.5	9.2	134	105	446	75	205	235	D			
4309	M	32	311.0	9.2	134	105	446	64	185	262	D	+		PUH
4398	M	31	306.5	8.9	135	106	449	74	205	224	D	+		PUH
4402	M	31	289.0	8.9	136	107	453	37	126	245	D			NSL
4461	M	26	281.5	8.5	137	108	456	99	248	264	D			
4672	M	39	292.5	8.5	142	112	473	86	236	186	D	+		
4391	M	31	291.5	8.9	143	113	476	83	233	193	D			
4217	M	30	299.5	8.5	145	114	483	40	143	242	D			
4396	M	31	300.0	8.9	148	116	493	100	269	213	D	+		PUH

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Cy)	Initial Lung Burden (Cy)	Dose at 30 Days (Cy)	Dose at 365 Days (Cy)	Survival Time (Days)	Dose at Death (Cy)	Weight at Death (Grams)	Mode of Death	Pathology		
												HP	PF	Other
4308	M	32	299.0	9.2	148	116	493	27	107	196	D	+		PUH
4227	M	30	273.5	8.5	150	118	499	42	154	212	D	+		PUH
4304	M	32	304.5	9.2	150	118	499	71	222	243	D	+		
4435	M	26	271.0	8.5	152	120	506	95	268	222	D			
4665	M	39	263.5	8.5	158	124	526	99	285	197	D	+		
4303	M	32	306.0	9.2	160	126	533	13	61	208	D	+		
4673	M	39	274.0	8.5	161	127	536	14	69	256	D	+		
4847	M	34	291.5	8.5	162	127	539	106	304	205	D			
4401	M	31	288.5	8.9	163	128	543	71	241	217	D			
4674	M	39	305.5	8.5	167	131	556	104	310	232	D			
4315	M	32	299.5	9.2	167	131	556	13	64	196	D	+		
4853	M	34	289.5	8.5	168	132	559	34	146	242	D	+		PUH
4668	M	39	290.0	8.5	169	133	563	14	69	250	D			NSL
4663	M	39	288.5	8.5	171	135	569	14	70	258	D			
4218	M	30	292.5	8.5	171	135	569	76	264	282	D	+		PUH
4219	M	30	297.0	8.5	172	135	573	16	79	220	D			NSL
4229	M	30	239.5	8.5	174	137	579	53	211	158	D			
4542	M	35	304.0	8.9	176	138	586	114	344	239	D			
4228	M	30	277.0	8.5	177	139	589	34	154	208	D	+		
4852	M	34	277.5	8.5	180	142	599	57	230	230	D	+		
4670	M	39	309.0	8.5	181	142	602	72	270	289	D	+		
4306	M	32	326.0	9.2	184	145	612	18	94	228	D	+		PUH
4223	M	30	304.5	8.5	188	148	626	12	66	245	D			
4549	M	35	255.5	8.9	188	148	626	76	290	196	D	+		PUH
4404	M	31	329.5	8.9	189	149	629	115	371	219	D	+	+	
4552	M	35	274.5	8.9	191	150	636	84	314	222	D			
4844	M	34	263.5	8.5	194	153	646	14	79	136	D	+		
4667	M	39	278.0	8.5	195	153	649	14	79	236	D			
4849	M	34	267.0	8.5	197	155	656	107	372	201	D			
4547	M	35	309.0	8.9	203	160	676	92	352	173	D			
4843	M	34	282.0	8.5	203	160	676	102	373	193	D	+	+	EMP
4854	M	34	282.0	8.5	203	160	676	65	284	248	D	+		EMP
4846	M	34	290.0	8.5	205	161	682	106	385	143	D	+	+	EMP
4666	M	39	306.0	8.5	206	162	686	115	404	213	D			
4661	M	39	292.0	8.5	210	165	699	51	248	168	D	+		PUH
4662	M	39	304.0	8.5	210	165	699	14	85	260	D			
4225	M	30	269.0	8.5	211	166	702	12	75	188	D	+		
4664	M	39	284.5	8.5	224	176	746	17	109	194	D			NSL
4855	M	34	285.0	8.5	225	177	749	107	424	218	D			
4841	M	34	287.0	8.5	226	178	752	14	92	260	D			NSL
4675	M	39	303.5	8.5	232	183	772	111	446	147	D	+	+	EMP
4216	M	30	273.5	8.5	232	183	772	77	361	201	D	+		PUH
4555	M	35	285.5	8.9	249	196	829	87	418	269	D			
4554	M	35	269.5	8.9	250	197	832	76	386	225	D			
4669	M	39	296.5	8.5	253	199	842	14	730	262	D			
4543	M	35	293.5	8.9	260	205	865	65	363	209	D	+		
4845	M	34	267.0	8.5	260	205	865	70	381	208	D			
4551	M	35	281.0	8.9	268	211	892	87	449	220	D			
4850	M	34	291.5	8.5	269	212	895	110	515	186	D	+	+	
4553	M	35	303.0	8.9	279	220	929	97	498	232	D	+	+	
4851	M	34	260.0	8.5	283	223	942	68	407	170	D			
4546	M	35	281.0	8.9	291	229	969	34	253	284	D			NSL
4848	M	34	302.5	8.5	292	230	972	104	542	214	D	+		
4544	M	35	291.5	8.9	303	238	1009	92	525	236	D	+		
4548	M	35	264.5	8.9	311	245	1035	35	283	250	D	+		
4550	M	35	287.0	8.9	317	249	1055	84	521	193	D	+		
4545	M	35	281.0	8.9	340	268	1132	52	408	214	D			
4541	M	35	287.0	8.9	386	304	1285	98	693	177	D	+		

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
												RP	PF	Other
4288	F	27	180.0	8.9	55	43	183	38	52	175	D			
4472	F	26	164.0	8.5	57	45	190	67	81	138	D			
4595	F	28	181.0	9.2	64	50	213	60	85	139	D	+		
4471	F	26	157.0	8.5	69	54	230	71	102	114	D			
4289	F	27	176.5	8.9	73	57	243	17	35	146	D	+		
4300	F	27	193.0	8.9	77	61	256	32	64	192	D			
4596	F	28	163.0	9.2	81	64	270	64	112	141	D	+		
4469	F	26	168.5	8.5	81	64	270	72	121	129	D			
4290	F	27	183.0	8.9	82	65	273	45	88	140	D	+		
4297	F	27	183.5	8.9	83	65	276	28	62	174	D			
4444	F	26	166.5	8.5	83	65	276	51	98	201	D			
4476	F	26	171.5	8.5	85	67	283	78	133	155	D			
4475	F	26	170.5	8.5	85	67	283	110	163	171	D	+		
4293	F	27	182.5	8.9	87	68	290	29	67	170	D			NSL
4440	F	26	155.0	8.5	87	68	290	46	95	192	D	+		
4448	F	26	168.5	8.5	90	71	300	76	139	150	D	+		PUH
4592	F	28	166.0	9.2	91	72	303	49	105	179	D	+		PUH
4294	F	27	185.0	8.9	93	73	310	76	144	138	D	+		PUH
4292	F	27	203.5	8.9	95	75	316	32	79	190	D			
4446	F	26	174.0	8.5	95	75	316	58	123	162	D			
4594	F	28	184.5	9.2	95	75	316	68	137	131	D	+		PUH
4407	F	31	194.5	8.9	97	76	323	53	118	152	D			
4591	F	28	164.0	9.2	99	78	330	106	186	185	D	+		
4468	F	26	158.0	8.5	100	79	333	60	132	170	D			
4588	F	28	168.5	9.2	100	79	333	14	41	163	D	+		
4589	F	28	169.5	9.2	100	79	333	91	172	178	D	+		
4599	F	28	180.5	9.2	100	79	333	65	140	169	D			
4598	F	28	172.5	9.2	101	79	336	13	38	132	D			NSL
4600	F	28	176.0	9.2	101	79	336	102	186	166	D	+		
4445	F	26	165.0	8.5	102	80	340	70	150	185	D			
4296	F	27	184.0	8.9	103	81	343	34	90	196	D			
4299	F	27	181.0	8.9	103	81	343	32	85	189	D	+		PUH
4286	F	27	180.5	8.9	104	82	346	14	42	138	D			
4593	F	28	173.5	9.2	104	82	346	72	155	163	D			
4479	F	26	166.0	8.5	105	83	349	88	177	171	D			
4287	F	27	185.5	8.9	105	83	349	14	43	126	D			
4467	F	26	172.0	8.5	106	83	353	138	228	170	D	+		EMP
4466	F	26	170.5	8.5	107	84	356	77	167	129	D			
4295	F	27	177.5	8.9	107	84	356	14	44	116	D	+		THROMB
4298	F	27	203.0	8.9	107	84	356	14	44	150	D			
4438	F	26	271.5	8.5	108	85	359	61	145	161	D			
4473	F	26	142.5	8.5	109	86	363	60	144	159	D	+		
4686	F	39	179.5	8.5	111	87	369	97	198	184	D			
4590	F	28	168.5	9.2	112	88	373	15	49	158	D			
4477	F	26	163.0	8.5	113	89	376	12	40	158	D			
4470	F	26	157.0	8.5	114	90	379	16	52	128	D			NSL

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
												RP	PF	Other
4441	F	26	173.5	8.5	115	90	383	100	209	185	D	+		
4450	F	26	174.5	8.5	115	90	383	54	142	204	D			
4586	F	28	173.5	9.2	117	92	389	15	51	146	D	+		PUH
4418	F	31	196.5	8.9	117	92	389	69	170	130	D	+		PUH
4317	F	32	182.0	9.2	118	93	393	78	185	159	D			
4437	F	26	159.0	8.5	118	93	393	98	212	165	D			
4478	F	26	165.0	8.5	121	95	403	93	211	161	D			
4316	F	32	194.0	9.2	122	96	406	72	182	153	D			
4439	F	26	174.5	8.5	122	96	406	66	172	154	D			
4474	F	26	164.0	8.5	122	96	406	67	174	133	D			
4255	F	30	166.0	8.5	124	98	413	12	44	122	D			PUH
4406	F	31	188.5	8.9	126	99	419	40	124	179	D			
4587	F	28	165.0	9.2	128	101	426	14	52	127	D	+		PUH,THROMB
4322	F	32	182.5	9.2	129	101	429	83	210	152	D	+		PUH
4597	F	28	164.5	9.2	129	101	429	75	198	98	D	+		PUH
4291	F	27	173.0	8.9	129	101	429	14	52	116	D	+		
4241	F	30	155.0	8.5	130	102	433	76	201	132	D			
4408	F	31	201.0	8.9	130	102	433	101	238	188	D			
4436	F	26	269.5	8.5	130	102	433	104	241	157	D			
4245	F	30	178.5	8.5	132	104	439	134	280	146	D	+	+	PUH,EMP
4320	F	32	185.5	9.2	134	105	446	67	191	153	D			
4447	F	26	163.0	8.5	134	105	446	18	68	146	D	+		
4242	F	30	169.0	8.5	137	108	456	100	249	119	D	+	+	
4412	F	31	183.0	8.9	138	109	459	40	136	175	D			
4413	F	31	184.5	8.9	138	109	459	35	123	185	D			
4480	F	26	163.5	8.5	140	110	466	63	192	146	D	+		PUH
4449	F	26	184.5	8.5	141	111	469	51	167	174	D	+		
4681	F	39	177.5	8.5	150	118	499	96	266	147	D			
4327	F	32	185.0	9.2	150	118	499	13	57	152	D	+		
4443	F	26	173.0	8.5	152	120	506	90	260	145	D			
4323	F	32	178.5	9.2	153	120	509	39	148	163	D	+		
4325	F	32	200.5	9.2	153	120	509	63	209	158	D	+		
4321	F	32	192.5	9.2	159	125	529	91	274	141	D	+		
4688	F	39	178.5	8.5	161	127	536	39	156	140	D			
4416	F	31	187.5	8.9	163	128	543	94	286	176	D	+		PUH
4251	F	30	172.0	8.5	163	128	543	127	337	139	D	+	+	
4419	F	31	189.0	8.9	163	128	543	56	206	168	D	+		
4409	F	31	185.0	8.9	165	130	549	35	147	179	D	+		PUH
4324	F	32	185.5	9.2	167	131	556	74	254	130	D	+		PUH
4690	F	39	176.0	8.5	167	131	556	115	327	144	D			
4689	F	39	171.0	8.5	168	132	559	119	335	123	D			
4442	F	26	174.0	8.5	171	135	569	90	293	161	D			
4326	F	32	184.0	9.2	172	135	573	35	153	182	D			
4690	F	39	174.0	8.5	173	136	576	120	347	151	D	+		
4420	F	31	181.0	8.9	173	136	576	85	286	130	D			
4414	F	31	188.0	8.9	174	137	579	43	182	139	D	+		PUH
4330	F	32	178.0	9.2	176	138	586	47	196	142	D	+		PUH
4250	F	31	177.5	8.9	178	140	592	9	48	160	D			
4411	F	30	182.5	8.5	178	140	592	71	263	149	D	+		PUH
4248	F	30	176.5	8.5	180	142	599	107	340	143	D	+	+	
4410	F	31	186.0	8.9	181	142	602	13	69	92	D	+		PUH
4677	F	39	176.0	8.5	181	142	602	66	255	168	D	+		

Rat #	Sex	Group #	Pre-exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death	Pathology		
												RP	PF	Other
4318	F	32	193.5	9.2	181	142	602	78	284	150	D			
4319	F	32	185.5	9.2	181	142	602	75	277	146	D			
4883	F	34	156.0	8.5	184	145	612	106	345	123	D			
4329	F	32	187.0	9.2	189	149	629	42	194	141	D			
4254	F	30	173.0	8.5	189	149	629	83	308	135	D	+		
4417	F	31	176.0	8.9	190	149	632	70	279	133	D	+		PUH
4246	F	30	175.5	8.5	191	150	636	9	52	150	D			NSL
4247	F	30	252.0	8.5	191	150	636	12	68	175	D			
4252	F	30	170.0	8.5	191	150	636	12	68	127	D			
4682	F	39	180.5	8.5	197	155	656	107	372	125	D	+	+	EMP
4415	F	31	194.5	8.9	201	158	669	37	187	191	D			
4679	F	39	167.5	8.5	203	160	676	103	375	104	D			
4556	F	35	170.5	8.9	206	162	686	88	348	120	D	+		PUH
4880	F	34	175.0	8.5	206	162	686	65	288	158	D	+		
4328	F	32	178.5	9.2	208	164	692	32	172	183	D	+		PUH, THROMB
4244	F	30	173.5	8.5	209	164	696	50	244	108	D	+		EMP
4678	F	39	170.0	8.5	213	168	709	90	364	120	D	+		
4567	F	35	177.0	8.9	213	168	709	27	154	186	D			
4568	F	35	177.5	8.9	219	172	729	29	168	185	D			
4243	F	30	170.0	8.5	229	180	762	103	423	128	D	+	+	EMP
4884	F	34	170.5	8.5	237	186	789	14	96	180	D			
4566	F	35	163.0	8.9	240	189	799	33	204	170	D	+		
4560	F	35	160.5	8.9	251	197	835	103	464	136	D	+	+	
4687	F	39	169.5	8.5	252	198	839	95	445	98	D			
4885	F	34	177.0	8.5	255	201	849	105	476	104	D			
4684	F	39	172.5	8.5	257	202	855	82	416	126	D	+	+	
4683	F	39	180.0	8.5	265	208	882	109	505	116	D	+	+	
4253	F	30	166.5	8.5	265	208	882	87	444	126	D	+		
4559	F	35	159.0	8.9	267	210	889	18	136	170	D			
4565	F	35	177.5	8.9	272	214	905	25	184	164	D			
4878	F	34	167.5	8.5	272	214	905	102	500	120	D			
4249	F	30	178.0	8.5	272	214	905	70	399	138	D	+		
4685	F	39	174.5	8.5	275	216	915	97	491	128	D	+		
4557	F	35	177.5	8.9	281	221	935	13	107	186	D			
4561	F	35	175.5	8.9	281	221	935	25	190	168	D	+		
4873	F	34	174.5	8.5	281	221	935	14	114	180	D	+		
4876	F	34	172.0	8.5	281	221	935	123	571	108	D	+		PUH
4562	F	35	172.0	8.9	293	231	975	31	237	174	D			NSL
4558	F	35	177.0	8.9	293	231	975	98	526	138	D			
4875	F	34	163.5	8.5	295	232	982	105	551	110	D	+	+	
4879	F	34	179.5	8.5	297	234	989	15	129	129	D	+		
4676	F	39	173.5	8.5	301	237	1002	18	153	174	D			
4564	F	35	180.0	8.9	302	238	1005	27	218	172	D			
4881	F	34	171.5	8.5	302	238	1005	54	372	152	D	+		
4874	F	34	186.0	8.5	311	245	1035	109	593	117	D			
4563	F	35	172.0	8.9	313	246	1042	27	226	162	D			
4882	F	34	177.0	8.5	317	249	1055	37	295	146	D			
4570	F	35	167.0	8.9	323	254	1075	14	131	140	D			
4569	F	35	167.0	8.9	337	265	1122	30	265	170	D	+		
4877	F	34	177.0	8.5	337	265	1122	78	529	148	D			NSL
4871	F	34	167.5	8.5	339	267	1128	113	659	111	D	+	+	
4872	F	34	177.5	8.5	355	279	1182	91	611	120	D	+		

Rat #	Sex	Group #	Exposure Weight (Grams)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death
5201	M	41	282.5	360	459	E
5203	M	41	266.5	360	409	E
5204	M	41	271.0	360	421	E
5205	M	41	268.5	360	429	E
5206	M	41	292.5	371	474	E
5207	M	41	270.0	187	345	D
5209	M	41	267.5	371	470	E
5210	M	41	275.5	371	391	E
5211	M	41	234.5	371	358	E
5212	M	41	252.0	371	401	E
5213	M	41	263.0	371	438	E
5214	M	41	273.0	371	458	E
5217	M	41	255.5	371	445	E
5218	M	41	267.0	371	457	E
5219	M	41	265.5	371	412	E
5220	M	41	268.5	371	413	E
5221	M	41	259.5	371	414	E
5222	M	41	262.0	371	410	E
5223	M	41	252.5	360	392	E
5224	M	41	258.5	5	259	D
5225	M	41	261.0	371	420	E
5226	M	41	254.5	371	408	E
5227	M	41	268.5	5	269	D
5228	M	41	267.0	371	*	E
5229	M	41	277.0	371	461	E
5230	M	41	259.0	371	434	E

Rat #	Sex	Group #	Exposure Weight (Grams)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death
5231	F	41	173.5	371	233	E
5232	F	41	190.0	371	255	E
5233	F	41	179.0	360	226	E
5234	F	41	168.5	371	214	E
5235	F	41	177.0	371	242	E
5236	F	41	191.5	360	266	E
5237	F	41	184.0	371	253	E
5238	F	41	176.0	360	256	E
5239	F	41	185.0	371	231	E
5240	F	41	180.0	371	240	E
5241	F	41	188.0	371	233	E
5242	F	41	193.5	360	277	E
5243	F	41	176.5	371	240	E
5244	F	41	173.0	371	252	E
5245	F	41	184.0	360	243	E
5246	F	41	173.0	371	226	E
5247	F	41	170.5	371	231	E
5249	F	41	193.0	371	280	E
5250	F	41	176.5	371	241	E
5253	F	41	168.0	371	227	E
5254	F	41	178.5	371	283	E
5255	F	41	189.0	371	261	E
5256	F	41	188.0	371	256	E
5257	F	41	178.5	371	283	E
5258	F	41	167.5	371	222	E
5259	F	41	181.5	371	266	E
5260	F	41	168.5	371	229	E

Rat #	Sex	Group #	Exposure Weight (Grams)	Initial Gamma Dose (Gy)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death
5261	M	43	268.0	8.9	252	275	D
5262	M	43	255.0	8.9	371	309	E
5263	M	43	280.5	8.9	371	335	E
5264	M	43	264.5	8.9	371	385	E
5265	M	43	276.5	8.9	315	386	D
5266	M	43	291.5	8.9	340	304	D
5267	M	43	265.5	8.9	365	199	D
5268	M	43	268.0	8.9	322	264	D
5269	M	43	263.0	8.9	309	254	D
5270	M	43	269.5	8.9	371	344	E
5271	M	43	260.0	8.9	371	334	E
5272	M	43	264.5	8.9	371	326	E
5273	M	43	268.0	8.9	371	372	E
5274	M	43	258.5	8.9	371	343	E
5275	M	43	260.5	8.9	371	304	E
5276	M	43	267.0	8.9	371	330	E
5277	M	43	265.5	8.9	360	346	E
5278	M	43	267.0	8.9	339	187	D
5279	M	43	261.5	8.9	371	328	E
5280	M	43	267.0	8.9	360	293	E
5281	M	43	266.5	8.9	11	163	D
5282	M	43	256.0	8.9	356	136	D
5283	M	43	262.0	8.9	360	353	E
5284	M	43	261.5	8.9	371	302	E
5285	M	43	263.5	8.9	360	384	E
5286	M	43	271.5	8.9	360	357	E
5287	M	43	262.0	8.9	371	327	E
5288	M	43	259.5	8.9	371	336	E
5289	M	43	275.0	8.9	371	356	E
5290	M	43	257.5	8.9	360	340	E

Rat #	Sex	Group #	Exposure Weight (Grams)	Initial Gamma Dose (Gy)	Survival Time (Days)	Weight at Death (Grams)	Mode of Death
5291	F	43	167.5	8.9	167	169	D
5292	F	43	177.5	8.9	371	214	E
5293	F	43	180.0	8.9	371	213	E
5294	F	43	178.0	8.9	371	231	E
5295	F	43	173.5	8.9	371	209	E
5296	F	43	182.0	8.9	350	183	D
5298	F	43	169.0	8.9	371	187	E
5299	F	43	187.5	8.9	371	208	E
5300	F	43	177.5	8.9	371	219	E
5301	F	43	171.5	8.9	360	228	E
5302	F	43	177.0	8.9	371	206	E
5303	F	43	170.0	8.9	360	229	E
5304	F	43	181.0	8.9	371	201	E
5305	F	43	179.0	8.9	371	222	E
5306	F	43	175.0	8.9	371	201	E
5307	F	43	171.5	8.9	354	209	D
5308	F	43	185.0	8.9	371	232	E
5309	F	43	182.0	8.9	371	220	E
5310	F	43	180.5	8.9	371	215	E
5311	F	43	187.5	8.9	360	228	E
5312	F	43	172.5	8.9	371	205	E
5313	F	43	180.0	8.9	371	217	E
5314	F	43	168.0	8.9	360	251	E
5315	F	43	180.0	8.9	371	188	E
5316	F	43	177.0	8.9	371	208	E
5317	F	43	184.5	8.9	371	217	E
5318	F	43	172.5	8.9	360	217	E
5319	F	43	171.0	8.9	371	222	E
5320	F	43	180.5	8.9	266	153	D

Rat #	Sex	Group #	Exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death
5334	M	46	269.5	8.5	41	32	136	360	136	343	E
5333	M	46	286.5	8.5	41	32	136	360	136	300	E
5347	M	46	270.0	8.5	44	35	146	357	145	344	D
5330	M	46	258.0	8.5	44	35	146	360	146	285	E
5332	M	46	294.0	8.5	49	39	163	248	138	311	D
5324	M	46	269.0	8.5	49	39	163	360	162	352	E
5348	M	46	268.0	8.5	54	42	180	360	179	337	E
3701	M	46	268.5	8.5	56	44	186	289	169	274	D
5350	M	46	255.5	8.5	56	44	186	347	158	190	D
5325	M	46	257.5	8.5	57	45	190	223	153	257	D
5328	M	46	281.0	8.5	57	45	190	54	70	266	D
5327	M	46	255.5	8.5	58	46	193	324	183	243	D
5322	M	46	265.5	8.5	60	47	200	67	85	243	D
5349	M	46	264.0	8.5	61	48	203	180	149	250	D
5329	M	46	260.5	8.5	61	48	203	360	202	284	E
5331	M	46	274.0	8.5	65	51	216	360	215	352	E
5335	M	46	273.0	8.5	66	52	220	251	187	290	D
5449	M	46	292.0	8.5	69	54	230	319	217	336	D
5454	M	46	267.0	8.5	70	55	233	204	181	312	D
5326	M	46	257.5	8.5	71	56	236	248	200	293	D
5451	M	46	259.5	8.5	73	57	243	353	240	286	D
5321	M	46	259.5	8.5	74	58	246	263	214	335	D
5453	M	46	255.5	8.5	79	62	263	285	237	220	D
5346	M	46	286.0	8.5	81	64	270	360	268	299	E
5450	M	46	252.0	8.5	84	66	280	67	120	190	D
3704	M	46	273.0	8.5	89	70	296	93	155	240	D
5446	M	46	256.0	8.5	107	84	356	45	115	239	D
5337	M	46	265.0	8.5	110	87	366	11	36	171	D
5340	M	46	272.5	8.5	119	94	396	11	39	163	D

Rat #	Sex	Group #	Exposure Weight (Grams)	Initial Gamma Dose (Gy)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death
5352	F	46	179.0	8.5	49	39	163	360	162	238	E
5359	F	46	180.0	8.5	53	42	176	360	175	248	E
3708	F	46	178.0	8.5	56	44	186	141	122	167	D
5370	F	46	177.0	8.5	56	44	186	49	64	149	D
5357	F	46	177.5	8.5	57	45	190	70	84	118	D
5363	F	46	190.5	8.5	59	46	196	360	195	194	E
5360	F	46	180.0	8.5	63	50	210	218	168	140	D
5372	F	46	175.0	8.5	63	50	210	360	208	206	E
5356	F	46	168.5	8.5	67	53	223	22	41	119	D
5378	F	46	173.0	8.5	68	54	226	305	210	203	D
5377	F	46	182.5	8.5	69	54	230	55	86	138	D
5353	F	46	189.0	8.5	70	55	233	62	95	139	D
5355	F	46	181.0	8.5	71	56	236	360	235	206	E
5368	F	46	179.5	8.5	73	57	243	55	91	165	D
5351	F	46	188.5	8.5	74	58	246	360	245	223	E
5457	F	46	172.5	8.5	74	58	246	62	100	131	D
5461	F	46	175.0	8.5	75	59	250	67	107	151	D
5371	F	46	178.5	8.5	78	61	260	97	139	133	D
5354	F	46	187.0	8.5	79	62	263	64	109	130	D
5358	F	46	181.5	8.5	79	62	263	81	127	145	D
5464	F	46	172.0	8.5	79	62	263	71	117	117	D
5458	F	46	175.5	8.5	80	63	266	88	135	140	D
5379	F	46	184.0	8.5	86	68	286	68	124	119	D
3709	F	46	197.0	8.5	87	68	290	110	167	177	D
5380	F	46	176.0	8.5	88	69	293	79	139	143	D
5373	F	46	185.0	8.5	91	72	302	54	112	131	D
5375	F	46	188.5	8.5	92	72	306	292	278	194	D
5374	F	46	207.0	8.5	93	73	310	88	157	170	D
5376	F	46	184.5	8.5	94	74	313	128	195	158	D
5459	F	46	181.5	8.5	103	81	343	78	162	142	D

Rat #	Sex	Group #	Exposure Weight (Grams)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death
5382	M	49	247.5	52	41	173	360	172	349	E
5399	M	49	269.5	56	44	186	190	140	353	D
5387	M	49	267.0	65	51	216	360	215	427	E
5383	M	49	276.5	66	52	220	360	218	433	E
5409	M	49	263.0	77	61	256	360	255	378	E
5393	M	49	284.5	81	64	270	343	263	324	D
5403	M	49	263.5	82	65	273	228	223	342	D
5398	M	49	273.5	84	66	280	359	278	426	D
5407	M	49	270.5	84	66	280	340	271	434	D
5381	M	49	251.5	85	67	283	201	218	321	D
5400	M	49	282.5	94	74	313	360	311	330	E
5404	M	49	259.5	97	76	323	360	321	362	E
5401	M	49	278.5	99	78	330	127	204	269	D
5397	M	49	262.0	103	81	343	274	303	255	D
5405	M	49	278.5	104	82	346	360	344	408	E
5392	M	49	261.0	106	83	353	172	254	253	D
5395	M	49	252.5	118	93	393	141	257	224	D
5391	M	49	266.0	119	94	396	236	328	331	D
5402	M	49	273.5	121	95	403	360	400	380	E
5396	M	49	274.5	126	99	419	270	369	360	D
5410	M	49	270.0	127	100	423	67	181	223	D
5406	M	49	265.5	127	100	423	80	202	202	D
5408	M	49	272.5	133	105	443	278	394	303	D
5394	M	49	272.0	140	110	466	254	399	254	D
5388	M	49	245.0	*	*	*	5	*	245	D

Rat #	Sex	Group #	Exposure Weight (Grams)	Initial Lung Burden (Gy)	Dose at 30 Days (Gy)	Dose at 365 Days (Gy)	Survival Time (Days)	Dose at Death (Gy)	Weight at Death (Grams)	Mode of Death
5411	F	49	168.5	70	55	233	360	232	213	E
5437	F	49	171.0	93	73	310	360	308	210	E
5420	F	49	176.0	97	76	323	360	321	232	E
5413	F	49	170.5	100	79	333	360	331	229	E
5438	F	49	172.0	103	81	343	360	341	210	E
5418	F	49	173.0	108	85	359	360	357	219	E
5419	F	49	182.5	108	85	359	360	357	222	E
5412	F	49	174.0	118	93	393	310	366	216	D
5432	F	49	178.5	121	95	403	138	261	138	D
5417	F	49	177.0	122	96	406	306	377	177	D
5435	F	49	182.0	124	98	413	317	389	185	D
5423	F	49	181.0	125	98	416	134	265	118	D
5439	F	49	177.5	125	98	416	190	313	152	D
5424	F	49	175.0	135	106	449	203	348	157	D
5422	F	49	175.5	138	109	459	167	326	124	D
5431	F	49	183.0	139	109	463	142	304	153	D
5415	F	49	178.5	143	113	476	360	473	205	E
5414	F	49	174.0	144	113	479	172	345	139	D
5416	F	49	182.5	147	116	489	179	358	144	D
5436	F	49	175.0	153	120	509	125	313	116	D
5427	F	49	184.5	155	122	516	53	188	159	D
5430	F	49	166.0	163	128	543	58	211	133	D
5429	F	49	179.0	168	132	559	55	209	148	D
5425	F	49	182.5	169	133	563	114	330	155	D
5440	F	49	177.5	180	142	599	157	413	146	D
5426	F	49	183.0	181	142	602	110	347	139	D
5428	F	49	182.0	182	143	606	96	323	150	D
5421	F	49	189.0	189	149	629	111	364	129	D
5433	F	49	178.5	192	151	639	140	416	119	D
5434	F	49	182.0	195	153	649	102	358	143	D

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