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MASTER

RELATIVE TRANSLOCATION AND DISTRIBUTION
OF Pu AND Am FROM EXPERIMENTAL PuO_2
SUBCUTANEOUS IMPLANTS IN BEAGLES

By

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A Study of the Translocation of Plutonium and
Americium From Puncture Wounds

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ABSTRACT OF
RELATIVE TRANSLOCATION AND DISTRIBUTION
OF Pu AND Am FROM EXPERIMENTAL PuO₂
SUBCUTANEOUS IMPLANTS IN BEAGLES

Estimating plutonium burdens by in vivo measurement of the 59.5 keV ²⁴¹Am gamma ray has been a widespread practice in the nuclear industry. The assumption that plutonium and americium are identically metabolized within the biological system has been the basis for this procedure. A study of simulated puncture wounds in forty beagle dogs contaminated with PuO₂ provided data on the relative translocation and distribution of Pu and Am. Half of the dogs were given chelation therapy with the trisodium calcium salt of diethylene triaminepentaacetic acid (DTPA).

The first major lymph node draining the implant site collected a significant fraction of the implanted material. The kinetics of the lymph node activity accumulation were studied by in vivo measurement. Empirical equations describing the activity buildup were derived. About 10% of the node burden was accumulated in the first two days.

Pu/Am activity ratios served as indices of the relative concentration or retention within each type of sample. The experimental animals were serially sacrificed for tissue sample collection and

radiochemical assay. Relative enhancement of Am concentration was shown in the reticuloendothelial tissues, the major Pu and Am concentrating soft tissues. Relative enhancement of Pu concentration was general in skeletal tissue. The magnitude of the enhancement increased with the blood cell forming activity of the bone. The disintegrations per minute per gram in the thyroid gland was low, but the relative Am enhancement was the largest of all the tissues.

Administration of DTPA increased the relative Pu/Am ratio in urine, femur, and liver tissue. These samples from DTPA treated dogs showed increases of 2, 3, and 5 fold, respectively, in the Pu/Am activity ratio.

The data showed differential translocation and excretion of Pu and Am. Consideration of the relative metabolism of these elements in interpreting in vivo estimations of Pu burdens via Am measurement is needed.

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CHAPTER I

INTRODUCTION

Statement of Problem

The feasibility and economic advantage of plutonium (Pu) as an energy source in power reactors and in other fissile material fueled systems have been widely explored and demonstrated (International Atomic Energy Agency, 1967). Research and refinement of engineering and technical problems in nuclear systems have made possible a rapid expansion in nuclear power and nuclear explosive programs involving plutonium utilization. The importance of plutonium as an energy source due to the projected depletion of fossil fuels and the projected use and depletion of nuclear fuel from natural resources was discussed by Tremmel (1968) and Roddis (1969). It has been estimated that plutonium generation in nuclear power reactors will yield 700 metric tons of total plutonium recovered by 1990 (Tremmel, 1968). Although this estimated plutonium need and rate of production is not unanimously accepted as true (Teller, 1967), it seems certain that plutonium processing will continue to grow in magnitude.

Processing of plutonium has grown from the recovery of microgram quantities in research laboratories by a few individuals to a routine industrial process involving many personnel handling kilogram quantities of this material. As the manufacture and use of plutonium and other transuranic nuclides has increased, the chance of their

deposition within the human body has increased. Radiological health aspects of the chemical and metallurgical processing of plutonium require that a considerable portion of the work be done in gloveboxes or other containment systems. Although effective exposure control methods have been successfully employed in Pu processing plants, industrial experience has shown that the potential for the accidental entrance of Pu into the human body via breaks in the skin is significant.

Several isotopes of Pu occur in its production. Americium-241 (Am) is also present because it is the daughter of the relatively short-lived ^{241}Pu . Since Am is normally present in Pu and has an abundant yield of gamma rays of 59.5 keV, it has been used as a tracer for Pu. The abundance of gamma rays from the isotopes of Pu is extremely low. The present industrial practice for in vivo evaluation of Pu deposited in the body is based on the gamma emission of ^{241}Am . The assumption that Pu and Am are identically metabolized within the biological system has been assumed. There has been no direct research reported regarding this assumption.

Following his review of the literature concerning the hazards and methods of evaluating Pu contaminated wounds, Thompson (1967) wrote: "Little can be said concerning this hazard except to note the urgent need for additional experimental data."

The goal of the present study was to determine the relative translocation of Pu of known Am content from simulated puncture wounds contaminated with PuO_2 in beagle dogs. This objective would make plutonium body burden assessment by in vivo measurement, excreta analysis, or a combination of these methods more meaningful.

The specific objectives of this research were to:

1. Determine the relative translocation of Pu and Am from experimental wounds contaminated with an oxidized form of the elements and thereby test the validity of using ^{241}Am as a tracer for Pu burden assessment in the dog.
2. Measure the perturbation of chelation therapy on the above relationship.

Subcutaneous implants of PuO_2 were made in the paw of forty beagles. Half of the dogs received chelation therapy. External counts were taken on the implant site, on the lymph node draining the experimental wound site, and over the liver area. Tissue and excreta samples were collected and analyzed for Pu and Am content after various lengths of exposure time.

CHAPTER II

REVIEW OF THE LITERATURE

Some Characteristics of Plutonium and Americium

Plutonium occurs in nature, but only in concentrations of the order of one part in 10^{11} parts of uranium (Leonard, 1967). Virtually all plutonium is produced in reactors. Plutonium may be produced from ^{238}U in a reactor with any type of neutron energy spectrum: thermal, intermediate, or fast. There is a large variation in the ratio of the plutonium isotopes produced. The variation results from differences in the average cross sections of the various plutonium isotopes over the neutron energy spectrum.

Plutonium is a silver white appearing metal which undergoes a total of five allotropic modifications below the melting point (Coleman, 1965). The important oxidation states of plutonium are III, IV, and VI. Plutonium in all of its oxidation states exists in aqueous solutions as highly charged ions which undergo hydrolysis reactions in dilute acid solutions. The following reaction is an example of Pu (IV) hydrolysis:

The principle radiochemical characteristics of plutonium have been discussed by Coleman (1965) and Cleveland (1967).

Coleman (1965) and Martell (1960) concluded that the most important hydrolytic reaction of plutonium, from a radiochemical standpoint, is the formation of colloidal aggregates in solution by successive hydrolysis (polymerization) reactions. In aqueous solution, the coordination tendency (chemical linkage of unknown type) of plutonium is satisfied by water molecules. Since plutonium has a coordination number of 8, that number of water molecules presumably surround one atom. The polymer forms with oxygen or hydroxyl bridges and the reaction is apparently irreversible. The formation of Pu (IV) polymer is favored by an increase in Pu concentration and temperature or by a decrease in the acidity. The relative amounts of polymer and monomer influence the distribution of Pu injected accidentally or experimentally into a biological system.

Plutonium oxidizes more readily than does uranium. Superficial oxidation of a freshly prepared surface occurs in a few hours in normal air. The oxide is more or less adherent, and in several days the oxidation reaction accelerates until finally the oxidation to PuO_2 is completed. Cleveland (1967) has pointed out that plutonium dioxide is the most important and most thoroughly studied of all plutonium compounds. This importance stems from its desirable properties - such as high melting point, irradiation stability, compatibility with other metals, and ease of preparation - that make it one of the most promising compounds for use as a nuclear fuel. This importance is

reflected in the fact that a major portion of the accidental exposures to plutonium occurs with the oxide or metal form at processing facilities such as the Rocky Flats Facility (Hammond and Putzier, 1964; ICRP Report 10, 1968).

Americium-241 is a component of all reactor produced plutonium because it is the daughter of the relatively short-lived Pu-241 isotope which is present to a degree dependent on the neutron energy spectra within the reactor and on the total irradiation time. Americium has several valence states of which Am (III) is the predominate one encountered in aqueous solution (Penneman and Keenan, 1960). The chemistry and production of americium has been reviewed by Penneman and Keenan, 1960; and Dawson, Deonigi, and Eschbach, 1965.

A listing of data taken from Lederer, et al. (1968) for the plutonium and americium isotopes commonly encountered in the plutonium production and processing industry appears in Table 1. The X-ray and gamma emissions listed and their abundance have had an influence on the radiological health techniques which have been implemented in evaluation and treatment of contaminated workers. External counting of Pu has been limited to measurement of the X-rays of uranium which occur following the alpha decay of plutonium. This has been necessary due to the low abundance of gamma radiation from the Pu isotopes. However, the X-rays are rapidly absorbed. These factors

Table 1. Characteristics of Selected Pu and Am Isotopes

Isotope	Half Life (yr)	Radiations	Energy	Abundance (%)
^{238}Pu	86.4	α	5.495 MeV	72
		α	5.452 MeV	28
		U L X-rays	17 keV (ave.)	10.55
		γ	43.5 keV	0.038
		γ	99.8 keV	8×10^{-3}
		γ	153.1 keV	10^{-3}
^{239}Pu	24,390	α	5.16 MeV	88
		α	5.11 MeV	11
		U L X-rays	17 keV (ave.)	4
		γ	38.6 keV	0.007
		γ	51.6 keV	0.020
		γ	129.3 keV	0.005
^{240}Pu	6580	α	5.17 MeV	76
		α	5.12 MeV	24
		U L X-rays	17 keV (ave.)	10
		γ	45.28 keV	
		γ	103.6 keV	
^{241}Pu	13.2	Beta	21 keV	99.97
		γ	145 keV	1.6×10^{-4}
^{242}Pu	3.79×10^5	α	4.90 MeV	76
		α	4.86 MeV	24
		U L X-rays	17 keV (ave.)	10
^{241}Am	458	α	5.49 MeV	85
		α	5.44 MeV	13
		Np L X-rays	17 keV (ave.)	37.6
		γ	26.36 keV	2.5
		γ	43.44 keV	0.07
		γ	55.56 keV	
		γ	59.56 keV	36
		γ	99 keV	0.024
		γ	103 keV	0.019
		γ	106 keV	0.001
		γ	122 keV	0.002
		γ	125 keV	0.005
		γ	146 keV	2×10^{-4}

lead to the use of ^{241}Am gamma rays which is commonly present with plutonium. The use of ^{241}Am as a tracer for Pu burden evaluation is discussed below.

Industrial Internal Plutonium Exposure

Thompson (1967) classified industrial plutonium exposure hazards as (a) the biological damage following plutonium distribution within the body by way of the blood stream, (b) the collection of plutonium in the lungs and associated lymph nodes, and (c) the biological uptake and body deposition of plutonium deposited beneath the skin or in muscle in a relatively nonabsorbable form as a result of contaminated puncture wounds. These hazards are obviously interrelated in most exposure cases. For example in a contaminated puncture wound, both items (a) and (c) have a mutual bearing on the internal distribution or transportability of the activity. The mode of entry into the body, the chemical form, the physical form (particle size), and biological processes such as phagocytosis have long been recognized as significant variables in deposition, translocation, and excretion of Pu from the body whether exposure be by inhalation, ingestion, or through a break in the skin (Thompson, 1967).

Contaminated wound cases from Pu handling facilities were apparently not reported in the open literature prior to about 1958. Langham, et al. (1962) discussed the management of potentially contaminated

wounds and recounted the problems and cases encountered during the 1944-45 nuclear bomb building period. With increasing plutonium production and processing effort, the management, measurement, and treatment of plutonium contaminated wounds have been needed. Case histories of plutonium in wounds of workers have been published by Roesch and Baum (1958), Foreman, et al. (1958), Foreman (1960), Sanders (1961), Lushbaugh and Langham (1962), Hammond and Putzier (1964), Swanberg and Henle (1964), Lagerquist, et al. (1965), Heid, et al. (1966), Lagerquist, et al. (1966), Vernon, et al. (1966), Laylee, et al. (1966), Lagerquist, et al. (1967), Fraser (1967), Putzier (1967), Wilson (1967), Larson, et al. (1968), Snyder, et al. (1968), Heid (1969), and Henle and Bramson (1969).

Heid, et al. (1966) reported 123 wounds with measurable plutonium contamination over a 20 year period at Hanford, a major plutonium production facility. Putzier (1967) reported 429 cases of detectable plutonium wounds over a 13 year period at Rocky Flats, a major plutonium processing plant. Hammond and Putzier (1964), Roesch (1964), and Fuqua (1965) concluded that exposure of personnel to Pu by way of contaminated wounds is a major type of exposure and in some plants is the most frequent accidental mode of entry to the body.

Industrial plutonium contaminated wound experience has shown that the wounds occur most frequently on the hands and fingers.

The relatively insoluble oxide and metal chemical forms are most often involved. Few observed pathological changes in the surrounding tissues have been detected (Hammond and Putzier, 1964; Heid et al., 1966). Contaminated wound management has been difficult due to the following variables; different chemical forms, unknown depth of deposition, type of tissue involved, amount of dispersion of plutonium in the wound, particle sizes involved, and variance of individual response (Langham et al., 1962; Norwood, 1962).

Internal Exposure Evaluation

The evolution of the ^{239}Pu maximum permissible body burden from about 5 μg in 1943 to the present 0.6 μg has been reviewed by Langham et al., (1962). Plutonium body burdens have been estimated by excreta analysis. Prior to 1950, this method was based on experimental animal data. In 1950 Langham et al. (1950) published data taken on terminal human patients given intravenous plutonium citrate injections. Power function models for excretion of plutonium were empirically derived from this data. Considerable use has been made of these models by various people to estimate body burdens of plutonium following accidental exposure. Despite the limitations of these expressions including the use of the non-industrial citrate chemical form and the intravenous mode of entry, they have been used to estimate Pu body burdens, e.g. Snyder et al. (1968). These equations

have been used primarily because they represent the only human data where known amounts of plutonium were involved.

A number of articles have been written describing the uncertainties in calculating plutonium body burdens from urine analysis including those of Snyder (1962), Hammond and Putzier (1964), Beach et al. (1966), and Snyder, Ford, and Warner (1967). Lagerquist et al. (1967) found the body burden calculated from the urine data and Langham's equations to be a factor of 5 high when compared to tissue samples analyzed following the natural death of an occupationally exposed employee. Among other sources of error contributing to this discrepancy, they postulated the movement of plutonium from a reservoir, such as a contaminated wound, directly to the urine which would lead to artificially high body burden estimates.

Lister, Morgan, and Sherwood (1963) proposed that urinary elimination of Pu was most simply described in terms of an empirical power function. Major differences in metabolism were expected with different routes of entry into the body. They suggest it was unlikely that the results of experiments in which plutonium was injected directly in a single shot into the blood stream in a complexed form would be similar to data for Pu taken into the body through the skin (due to hold-up of the Pu at the site of entry). Jackson and Dolphin (1966) have said that if material of small particle size enters the body some may be rapidly absorbed even if the total solubility at equilibrium

is low. The rate of solution in body fluids is very dependent on the route of entry as well as on the size of the particles, hence the wide variation in excretion from case to case. Once dissolved, plutonium does not have a known physiological analogue (Jackson and Dolphin, 1966).

The low abundance of gamma emissions of the plutonium isotopes makes in vivo body burden evaluation difficult. However, in the case of contaminated wounds, development of useful detectors has made wound counting a standard practice at most installations using plutonium (Roesch and Baum, 1958; Gruber, 1960; Gale, Peaple, and Richards, 1960; Roesch, 1964). These authors recorded the development and use of thin NaI (Tl) detectors primarily for measurement of the uranium L X-ray emissions which occur following about four percent of the alpha decays of ^{239}Pu (Roesch, 1964). Thin thallium activated sodium iodide detectors have been used to measure less than a maximum permissible lung or liver burden by Boss and Mann (1967).

Other types of detectors have received attention for possible use in internal dosimetry of Pu. The use of proportional detectors has been explored and applied by Taylor and Rundo (1965) and Taylor (1968). The use of silicon diode detectors for wound counting has received recent attention as reported by Bistline and Tyree (1967) and Palmer, Wogman, and Cooper (1967).

As is shown in Table 1, not only are the gamma ray yields low for the plutonium isotopes, but their energies are very nearly matched by the emissions of ^{241}Am . Photons emitted by ^{239}Pu with potentially useful detection energies are the 51.5 and 129 keV gamma rays. Both of these gamma rays have a somewhat low abundance per disintegration and are closely matched in energy by the ^{241}Am emissions making scintillation counter resolution impossible (Boss and Mann, 1967). The recent development of germanium diode detectors which have resolutions of less than 2 keV full width at half maximum for the 60 keV region seem to offer hope for simultaneous in vivo measurement of americium and plutonium. Development of and operation of lithium drifted germanium diode detectors has been reviewed by Heath, Black, and Cline (1966), Ewan, Malm, and Fowler (1966), and Camp (1967). These detectors show promise of usefulness in the above mentioned energy range primarily because of their high resolution capability. With further development and application of these diode detectors together with excreta analysis data, assessment of plutonium body burdens in industrial situations and in uptake studies under laboratory research conditions should be possible.

In addition to the problem of rapid attenuation of the low energy L X-rays of uranium (HVL of 17 keV photons is 0.6 cm of soft tissue) by body tissues, the significant problem of self absorption of the

X-rays by the plutonium particles in a wound was pointed out by Tyler (1966). His data show that a spherical particle of plutonium with a 7 μ diameter, for example, will show a measured activity about 20 percent lower than the actual activity.

Since the relatively abundant X-ray emissions are rapidly attenuated, their measurement has been useful primarily in measuring activity close to the surface such as in the case of a puncture wound or scratch. Attention has been turned to the higher energy gamma rays as a means of measurement of internal activity. Since americium is normally present in plutonium and has a relatively abundant yield of a 59.5 keV photon, it has been used as an in vivo tracer for plutonium. Present industrial practice for in vivo evaluation of internal deposition and translocation of plutonium in the body is based primarily on ^{241}Am . Knowledge of the ppm of Am in the Pu is necessary to the estimate. That this procedure is in widespread usage is attested to by the following citations wherein this technique is advocated or applied: Lister, Morgan, and Sherwood (1963); Bensted, Taylor, and Sowby (1965); Brodsky, et al. (1966); Boss and Mann (1967); Larson and Bramson (1967); Cloutier and Watson (1967); Swinth (1967); Lagerquist, Putzier, and Piltingsrud (1967); Hammond, Lagerquist, and Mann (1968); Caldwell, Potter, and Schnell (1969); Heid (1969); and Henle and Bramson (1969).

Therapy for Contaminated Wounds

Therapeutic removal of plutonium from contaminated wounds has included surgical excision, where practical, as a standard procedure. The industrial surgeon instigates surgical excision when Pu is in the skin or subcutaneous tissue for any amount which is easily accessible (Norwood, 1963; Fuqua, 1965; Heid, Henle, and Selby, 1966). Initiation of this practice was based on the report by Brues, Lisco, and Finkel (1947) of high incidence of malignant fibrosarcoma in mice at the site of subcutaneous injections of plutonium nitrate in doses as low as 0.1 μ Ci. In discussing the diagnosis and treatment of plutonium contaminated wounds with regard to surgical removal, Langham (1959) and Foreman (1960) concluded that the decision is not an urgent one and can be deliberated for several days when dealing with a material such as plutonium since it is absorbed slowly from intramuscular or subcutaneous sites. Thompson (1967) suggested that in view of the fact that standard excision procedures are based primarily on only one study, there is an urgent need for additional experimental data on implants.

Administration of chemical chelating agents has also become standard practice with or without excision (where excision is impractical). Considerable experience with both experimental and industrial plutonium contamination cases treated with therapeutic agents for

removal of Pu has been reported by: Weeks, Oakley, and Thompson (1955); Schubert (1955); Smith (1958); Langham (1959); Foreman (1960); Sowby and Taylor (1960); Norwood (1960); Catsch (1961); Schubert, Fried, Rosenthal, and Lindenbaum (1961); Ballou (1961); Lindenbaum, Markley, Rosenthal (1962); Norwood (1962); Taylor and Sowby (1962); Taylor (1962); Norwood (1963); Cable et al. (1963); Markley (1963); Swanberg and Henle (1964); McClanahan et al. (1964); Lagerquist, Hammond, Putzier, and Piltingsrud (1965); Fuqua (1965); Bokowski and Hammond (1965); Heid, Henle, and Selby (1966); Lagerquist, Putzier, and Piltingsrud (1967); Boss and Mann (1967); Lindenbaum et al. (1967); McClanahan and Kornberg (1967); Lagerquist, Allen, and Holman (1967); and Larson et al. (1968).

The trisodium calcium salt of diethylenetriaminepentaacetic acid (DTPA) currently heads the list in therapeutic effectiveness and is in general use in plutonium handling plants (Fuqua, 1965, and Lagerquist et al. 1965). The effects of DTPA on the relative translocation ratio of plutonium and americium and on their systemic distribution as a function of time is of obvious importance and is presently unknown.

Chelate specificity, affinity for a metal relative to that of body protein, and the distribution of the metal in the body all play significant roles in determining the net action of a particular chelating agent according to Schubert and Lindenbaum (1960). The distribution of a metal in the body depends on its chemical state at the time of entry.

Some metals complex so strongly with proteins that chelate action is impaired. Taylor and Sowby (1962) reported experimental data where DTPA reduced the level of Pu in the liver by a factor of 14 while the Am content was reduced by a factor of 200. In contrast they found that Pu was removed more efficiently from the skeleton than was Am. McClanahan and Ragan (1965) found DTPA was equally effective in reducing liver and femur concentrations of Pu whether it was injected subcutaneously or intravenously.

DTPA may be toxic at higher concentrations (Seven, 1960), and, consequently, administration of therapeutic doses of DTPA range from 0.1 to 2.0 grams per day for man. The usual procedure has been to give 1 gram per day for 5 days by slow intravenous infusion followed by a no treatment period of about two weeks and then a repeat of the treatment (Norwood, 1963; Larson et al. 1968). Catsch (1961) found that DTPA increases both urinary and fecal excretion rate effectively for as long as 8 days. Some question exists as to the effect of chelate therapy on absorption of activity from an implant site. Ballou (1961) observed increased absorption of radionuclides as a result of the external use of chelating agents for wound decontamination. However, there has been no reported absorption acceleration from wound sites following chelate intravenous infusion. McClanahan and Kornberg (1967) reported that rinsing wounds with DTPA had no discernible effect on the subsequent tissue distribution of Pu.

Existing Evidence Regarding the Relative Metabolism of Pu and Am

Evaluation of plutonium burdens via americium measurement is based on the assumption that this natural contaminant of plutonium is metabolized in a similar manner to plutonium once inside the living system. In any exposure case, it is desirable to measure the exposed individual periodically in order to follow changes in body or organ retention. Since all measurements depend upon detecting the characteristic 59.5 keV gamma photon of ^{241}Am , the possible source of error in the uncertainty of Am translocation rate and retention in a given organ relative to that of plutonium could be important. This possible source of error may be compounded by the application of medical therapeutic measures.

Although no experimental evidence has been published regarding the relative metabolism of plutonium and americium, indications that a significant difference in the translocation of these two elements may exist were inferred from the results obtained in a number of industrial and experimental Pu contamination experiences. Taylor (1962) suggests that the distribution of Pu and Am would be expected to differ due to differences in valency states in solution at the biological pH. Pu (IV) and Am (III) are the primary chemical species present in the living system (Taylor, 1962; Thompson, 1967). Am (III) ions are only weakly hydrolyzed in solution whereas Pu (IV) with its smaller ionic

size and higher charge, readily forms complex ions. Therefore, at body pH, Pu exists only as a complex ion or in a colloidal state. The type of anions present with the Pu or Am would have an influence on the subsequent translocation and distribution of these elements.

Durbin (1960) had postulated that the main differences between the metabolism of Pu and Am would be due to the variance in the chemical properties noted above.

Bensted, Taylor, and Sowby (1965) in studying the carcinogenic effect of Am and Pu found Am to be far less effective in producing major pathological changes than Pu, suggesting differential micro-distribution within the biological system. Jackson and Dolphin (1966) concluded after a study of its metabolism and excretion that Pu does not have a physiological analogue. In studying four types of plutonium dioxide, Bair and Park (1966) found the Pu to Am ratio of inhaled material to increase for one of four oxide allotropes in the lung and bronchial lymph node tissues. This suggests either a selective loss of Am or a selective retention of the Pu in these tissues for the one allotrope.

Putzier (1967) and Hammond, Lagerquist, and Mann (1968) observed a shifting plutonium to americium ratio over time in excreta data from some human exposure cases which indicated that these two elements were being handled differently. Turner and Taylor (1968) warned that considerable caution be exercised in equating metabolic

behavior of members of the actinide series. Probable differential metabolism of Pu and Am have been suggested by these observations.

Experimental Metabolism and Distribution
of Pu and Am from Implants

A rather extensive amount of work using laboratory animals for inhalation, ingestion, and intravenous injection of plutonium has been published as noted in Thompson's (1967) review. Much less research on Pu and/or Am in contaminated wounds (intradermal, subdermal or intramuscular implants) in laboratory animals has been reported. As was previously pointed out, Brues, Lisco, and Finkel (1947) implanted Pu nitrate subcutaneously in mice which subsequently showed a high frequency of fibrosarcoma. This study has had a significant influence in the practice of industrial medicine at plutonium processing operations. In 1948, Scott et al. made studies on the metabolism and distribution of Pu and Am following intramuscular injection which showed liver and skeleton to be the major sites of concentration. Jee et al. (1962) has since shown these sites of deposition to be in the reticuloendothelial system and on mineralized bone surfaces. The fate and pathologic effect of Pu metal implanted subcutaneously in rabbits and rats was studied by Lisco and Kisielewski (1953). The metal fragmented soon after introduction with only small amounts absorbed

from the implant sites. A species difference was noted in the fact that the rabbits absorbed more than the rats.

Langham (1959) reported that microgram quantities of PuO_2 placed on abraded areas of rabbit skin failed to show any absorption, but was lost with the scab. Cable et al. (1962) studied intradermally injected $\text{Pu}(\text{NO}_3)_4$ in blonde, miniature swine to determine acute and chronic effects and to determine translocation. A large fraction of the injected dose was lost via the scab within the first few days. Of particular interest was the observation that one week after injection as much as 12 percent of the administered plutonium appeared in the regional lymph nodes.

Intramuscularly injected Pu nitrate in the rat was shown by Taylor and Sowby (1962) to remain mostly at the injection site even after administration of DTPA. Ballou et al. (1964) reported that the Pu deposited in the soft tissues of rats tends to accumulate in cells of the reticuloendothelial system. The work of McClanahan and Ragan (1965 and 1966) on the translocation of subcutaneously administered PuO_2 in swine showed the quantity of the oxide form translocated to be about 100 times lower than that of the nitrate form studied previously by Cable et al. (1962 and 1963). An exception to this was the regional lymph nodes which were concluded to be the major point of translocation of PuO_2 from the implants. Further work on plutonium contaminated wounds in rats by McClanahan and Kornberg (1967) emphasized

the importance of the chemical form of plutonium on the translocation rate. The translocation of the citrate form from a wound site was much more rapid than that of the nitrate form which in turn was much more rapidly absorbed than the oxide form. Taylor (1969) found that intramuscular injection of plutonium nitrate in rabbits resulted in almost all the Pu being initially retained at the site of injection. He reported subsequent translocation to other organs by way of lymphatic transport as well as slow formation of soluble Pu complexes which migrate directly into the blood stream. These reports point out that the chemical form of the Pu as it enters the body greatly affects the subsequent distribution and concentration of Pu in the tissues.

Work on the nature of the physiological plutonium and americium complex was first reported by Taylor and Sowby (1962). The binding and transport of both Pu and Am by serum proteins, particularly transferrin, has been elucidated by Stevens, Bruenger, and Stover (1965); Boocock and Popplewell (1966, two papers); Stover, Bruenger, and Stevens (1968); Bruenger, Stevens, and Stover (1968 and 1969); Stevens, Bruenger, and Stover (1968); Chipperfield and Taylor (1968, two papers). The plasma clearance rate of Am is much more rapid than that for Pu (Turner and Taylor, 1968). In physiological studies Am formed weaker complexes than did Pu with transferrin, which delivers iron to bone marrow (Stevens, Bruenger, and Stover, 1965). Transferrin probably carried Pu and Am to the bone where

interaction with bone surfaces became possible. Two bone glycoproteins, sailoprotein and chondroitin sulphate-protein, were shown to bind Pu and Am strongly in in vitro studies. Transferrin was thought to be a mechanism of transport since the bone glycoproteins bind both metals much more strongly. Transferrin in normal plasma is only 30 percent saturated with iron, thus many binding sites for transport are available (Stevens, Bruenger, and Stover, 1968). Although both heavy elements are apparently bound by the same proteins, the fact that there is a marked difference in the strength of the complex is evidence for differential metabolism.

Review of the Status of Internal Plutonium Dosimetry

One of the important aspects to an understanding of the translocation, distribution and excretion of Pu and/or Am which may be derived from completed studies and industrial experience is recognition of the importance of the chemical form. Much of the experimental work has been done with plutonium citrate which is a non-industrial form thereby limiting the usefulness of the information obtained from such studies. Since accidental industrial exposures have been predominately to the metal and oxide forms, experimental data from other chemical forms must be related to these chemical forms to be interpreted for industrial application. The work of Schubert (1961) demonstrated the necessity for relating chemical forms. Pu citrate and nitrate injected

into the mouse resulted in a greater retention of Pu in the liver and spleen for the nitrate form while the citrate form showed greater retention in bone (Schubert, 1961).

The modes of experimental introduction of Am and Pu in the case of completed studies have been mostly inhalation or intravenous injection. Except for the few instances of experimental wound studies cited above, there is little information available on the metabolism of Pu or Am from implants and even less information on the differential movement of the two elements in a biological system. The mode of entry of Pu into the body affects its tissue distribution by influencing the form of the Pu translocated from the original site of deposition. For example, Pu introduced into the skin or muscle is translocated to the skeleton as monomeric Pu while Pu introduced intravenously is mostly deposited as polymer in the liver (Lindenbaum et al., 1967).

Little information is available from experiments with respect to the physical form of the implant material and its influence on the uptake and distribution of Pu or Am from implant reservoirs. Because the material has been shown to be moved via both the lymphatic system (Lister, Morgan, and Sherwood, 1963) and by way of the blood, the particle size distribution of the material at a wound site is of importance particularly in the case of the relatively insoluble chemical forms. The importance of both the size and the chemical composition of colloidal or suspended particles was evident from the work of

Honda, Rafter, and Kyker (1963) based on administration of radio-isotopes intralymphatically. They found the effective size for gradual lymph node localization to be less than 3μ in diameter. At or below this size the particles did not move significantly past the first node in their channel of drainage. Based on some experimental data, Thomas (1968) postulated an infinite residence time in the pulmonary lymph nodes for particulate matter trapped there.

Langham et al. (1962) reported that analysis of the tissue of Los Alamos employees at autopsy following death from natural causes show that the order of Pu concentration was usually respiratory lymph nodes, lungs, liver, and bone in descending order. The concentration of Pu in lymph nodes was of the order of 50 times that in bone. Autopsy results on Hanford employees according to Newton et al. (1966) showed that the amount of Pu in the liver was at least 3 times that in the skeleton. These data indicate that in some circumstances the critical organ may be something other than the skeleton.

CHAPTER III

MATERIALS AND METHODS

Experimental Design

Research with laboratory animals has increased our understanding of the metabolism of plutonium in mammalian systems. The use of appropriate experimental animal systems is important in any study where the results may be extrapolated to man. Since most wounds occur on the hands or fingers of workers, an experimental animal should have extremities in about the same proportion to the body as for man. Also, for in vivo measurements of gamma rays, the amount of skeletal absorption should be proportionately similar to man. The dog represents an experimental biological system fulfilling the above needs and in addition has a longevity nearly like man. For the present purpose, the dog was considered a better experimental animal than other laboratory animal systems in current use.

Forty adult, male beagles were obtained from the barrier maintained beagle colony of the Collaborative Radiological Health Laboratory at Colorado State University. Phenotypically they varied considerably from small slender animals to large, robust males, some of whom were very obese. They came from the same breeding stock and were maintained within the same kennels. Records of their immunization and general clinical status were kept, enabling experimental animal medical evaluation.

These animals were randomly divided into ten study groups, four to a group, and then half of each group was randomly selected to receive chelation therapy (DTPA). Animals of the same group were housed one or two to a kennel and were given the animal care described below. The groups were defined by the length of study time that each was to receive. At the time of initiation of the study the youngest dog was 19 months of age and had reached skeletal maturity. Skeletal maturity has been estimated to be approximately 15 months of age for the dog (Dougherty, 1962). Since bone is listed as the critical organ for Pu, adult experimental animals best suit the purpose of this experiment because industrial Pu contaminated wounds occur only in skeletally mature humans.

Animal Care

The animals were maintained in accordance with provisions of the Laboratory Animal Welfare Act (1967). The kennels are located on the Foothills Research Campus of Colorado State University. The kennel design (Collaborative Radiological Health Laboratory, 1963) is as follows: 15 x 15 feet in size, 1 foot gravel base, 4 foot high, 2 inch mesh cyclone fence, and concrete curbs extending 12 inches above the gravel level (Figure 1). Panels of galvanized sheet metal on the fence provided shelter from sunlight and concrete houses with wooden floors provided shelter from storm and cold (Figure 2).

Figures 1 and 2. Dog maintenance facilities.

The dogs were fed a nutritionally adequate dry ration of Purina dog chow. Automatic watering devices insured a constant source of water in the summer while daily filling of water pans was necessary in the winter. Cleaning and sanitation of feed and water containers were carried out as per required standards.

Regular medical diagnosis and treatment of conditions arising in the experimental animals were carried out. An immunization program for rabies was followed for each dog. The veterinary medical personnel and facilities within the College of Veterinary Medicine and Biomedical Sciences at Colorado State University provided a broad capability for the needs associated with the experimental animal research.

Implanting Procedures

The laboratory was prepared for handling radioactive materials by protecting walls, floors and equipment with wax and plastic covering. The usual personnel protective equipment, including respirators, was used during the implanting procedure and as needed following implantation. All plutonium implants were made under the surveillance of radiation monitoring personnel from Rocky Flats. Air samples and contamination surveys were taken to assure adequate containment and control during and after the injections.

The plutonium oxide (oxidized under ambient conditions) used for the implants was prepared and provided by the Rocky Flats Division of Dow Chemical Company. The physical and chemical characteristics of the material are shown in Tables 2 and 3 and in Figure 3. Assuming log normally distributed particles (Kirchner, 1966), the mean count diameter was extrapolated to be 7 microns. The plutonium was contained in rubber diaphragm stoppered vials. Each vial contained about one milligram of PuO_2 .

An ultrashort acting anesthetic (sodium thiamylal for injection N.F. 4% solution) was used to prepare the animals for the implant. Hypodermic needles and syringes were used for making the implants. The standard site selected for the simulated puncture wound contaminated with Pu was the subcutaneous tissue of the left dorsal metacarpal area. A hypodermic needle was positioned in the subcutaneous fascia in the desired region as illustrated in Figure 4 a-d. Proper positioning was determined by palpation and by observing that there was no back flow of blood in the syringe due to intravenous insertion. A milliliter of water was injected into the vial containing the plutonium with a tuberculin syringe and needle. The vial was shaken to suspend the PuO_2 particles and an aliquot of the suspension (about 0.25 ml) was drawn into the syringe. The syringe was joined to the needle previously positioned in the dog's leg and the injection was made (Figure 4 d). This amount of PuO_2 provided an adequate level of Pu and Am in

Table 2. Particle Size Distribution of Implant Material

<u>Geometrical Mean Diameter (microns)</u>	<u>Fraction</u>
<25	0.79
25-50	0.10
50-75	0.04
>75	0.06

Table 3. Quantitative Chemical and Nuclidic Composition of Implant Material

<u>Element</u>	<u>Analysis Date</u>	<u>Quantity Present</u>
Am-241	4-29-68	2200 ppm
Pu	3- -67	0.9986 by weight
Fe	3- -67	30 ppm
C	3- -67	99 ppm
U-238	3- -67	78 ppm
Np-237	3- -67	2 ppm
<u>Plutonium Isotope</u>	<u>Percent Present</u>	
Pu-238	0.035	
Pu-239	86.63	
Pu-240	11.69	
Pu-241	1.51	
Pu-242	0.135

Figure 4 (a-d). Procedural sequence for establishing the experimental PuO_2 contaminated wounds.

b

b

b

c

the excreta and tissues for radioanalytical measurement. Upon withdrawal of the needle, an alpha survey meter was used to determine the extent of surface contamination. The dog's leg was decontaminated at least once and then the procedure was repeated until no alpha activity was detected. In most cases no contamination was detected after needle withdrawal.

DTPA Therapy

Following the implant, the dogs were placed in the metabolism cages illustrated in Figure 5 for urine and feces collection. About two hours after the PuO_2 contaminated simulated wounds were established, the animals designated to receive therapeutic treatment were given DTPA injections. A dose of 0.25 grams of DTPA in 10 ml of physiological saline solution was injected intravenously. The usual level of DTPA administration for industrial workers is 1 gram per infusion (Norwood, 1962; Lagerquist et al. 1965). The 0.25 grams per injection for the dog was selected by comparing the standard blood volume for man (Radiological Health Handbook, 1960) to that of the dog which has been estimated to be 9.5 percent of the body weight by Altman (1961). Blood volume determinations based on a radioiodinated serum albumin method outlined by Chase and Rabinowitz (1967) were made on a few of the dogs. These data shown in Table 4 verify the above cited

Figure 5. Dog metabolism cages for collection of excreta samples.

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CHRISTIAN LIND
80% COTTON FIBER

Table 4. Beagle Blood Volume Determination

Dog	Weight (kg)	Measured Volume (ml)	Fraction of Body Weight (%)
2315	17.5	1385	8.0
1884	16.5	1615	10.0
1688	13.5	1400	10.5
2447	13.0	1220	9.5
3032	13.0	1340	10.0
1367	15.0	1210	8.0
0792	16.5	1530	9.5
Mean Value			9.4 ± 1.0

number and show that the average beagle blood volume is about 25 percent of the standard-man volume.

Sample Collection

Each dog was maintained in a metabolism cage on a standard schedule where blood samples and 24 hour urine and feces samples were collected for two weeks. The blood samples were obtained by jugular venepuncture. The dogs were returned to the outside kennels for two weeks and then placed back in the metabolism unit for three days for sample collections. Until the specified time for euthanasia, each dog was scheduled for a two to three day stay in a metabolism cage each month to collect samples and to administer DTPA, when applicable.

At the time of sacrifice, pentobarbital sodium anesthesia was induced, and euthanasia was performed by bleeding directly from the heart until death. To minimize clotting during the bleeding procedure, a few thousand units of heparin were given intravenously with the anesthesia at the time of sacrifice.

The tissue samples collected at necropsy were as follows: left eye, left testis, left kidney, left adrenal gland, trachea (small piece to represent body cartilage), lung (tip of one lobe), spleen, liver (about a fourth of the organ was chemically analyzed), thyroid gland, sternum, left 10th rib, two lumbar vertebrae, piece of skull bone,

left femur (sectioned into the proximal end, the shaft, and the distal end), left axillary lymph node, right and left superficial cervical lymph nodes, and the implant site (left front paw sectioned at the carpo-metacarpal joint).

Sample cross contamination was controlled by using new glassware, plastic bags, and syringes for each sample collected. The metabolism cages and instruments were decontaminated between collection with KW solution. KW solution is a specially formulated mixture of citric acid, detergent, and ethylenediaminetetraacetic acid (EDTA) which has proven effective at the Rocky Flats plant as a radioactivity decontaminating agent (Putzier, 1967).

All samples collected were radiochemically assayed for plutonium and americium in the Rocky Flats laboratories. The general chemical procedures for each sample type are outlined in Appendix A.

In Vivo Counting Equipment and Procedures

External counting of the dogs was done with a thin NaI (Tl) crystal wound counter, a body counter located at Rocky Flats, and with a lithium drifted germanium diode detector. Wound counter measurements were taken at the time of blood sampling. Body counter measurements were made on each dog in the first few days following implantation primarily for the purpose of estimating the quantity of

Figure 6. Schematic drawing of the scintillation wound counter.

Figure 7. Triple probe, thin NaI (Tl) pullout detector system.

Figure 8. Scintillation counter measurement of the superficial cervical lymph node activity.

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material at the implant site. Germanium detector counts were also obtained during sample collection periods.

The wound counter has three thin NaI (Tl) scintillation detectors. A schematic diagram of the electronic components of the wound counter is shown in Figure 6. The detector diameters are $3/4$, 1, and $1\ 1/2$ inches. The $1\ 1/2$ inch diameter detector was used for the present study. This triple probe, pullout detector is pictured in Figure 7. The wound counter was used to measure the activity at the wound site and in the left superficial cervical lymph node. The wound counter was operated in the integral counting mode thereby counting all electromagnetic radiations above about 10 keV which reached the detector. The left superficial cervical lymph node is the first major node draining the area in the dog's foot and leg which contained the plutonium (Miller, 1965). The count rate as a function of time was recorded. The counter is shown in use in Figure 8 for a lymph node count.

The body counter detector is a 4 inch diameter by 4 mm thick sodium iodide detector connected with a multi-channel spectroscopy system. Body counter measurements included implant site and liver area counts. The implant sites were measured shortly after their establishment. Estimation of the amount of Pu present was made by measurement of the Am-241 in the wound and by comparison with a standard Am-241 reference source. The liver area counts were taken just prior to necropsy for comparison with the chemical assay results.

The Am-241 tracer technique was also used for derivation of estimated liver burdens from these counts.

The germanium diode detector was a top mounted, right angle to the horizontal plane, planar model with an active entrance area of 10 cm² and a lithium drifted depth of 7.5 mm. It was housed in an evacuated chamber 12 mm behind a 0.25 mm beryllium window and maintained at "liquid-nitrogen" temperature. The resolution of the detector is about 2.0 keV for full width at half maximum for the 59.5 keV ²⁴¹Am gamma ray. A schematic diagram of the electronic components of this system is shown in Figure 9.

Figures 10 and 11 picture the germanium system and shows it in use for a lymph node count. Measurements at the wound site and in the liver area were also obtained using the same system. The dogs were placed in a specially devised sling for counting on the diode detector. Count times usually ranged from 2-5 minutes for the implant site, 15 minutes for a lymph node, and two hours for a liver area measurement. Background counts on unimplanted dogs were taken at the same positions and counting times. The counting system was arranged so that a single channel analyzer was centered on each of three portions of the detector signal representing the 51.5 keV and 129 keV gamma rays from Pu-239 and the 59.5 keV gamma ray from Am-241. Data from this system were used to determine the possibility of

Figure 9. Schematic diagram of the lithium drifted germanium detector system.

Figure 10. Ge(Li) diode detector and associated electronics.

Figure 11. Superficial cervical lymph node activity measurement using the Ge(Li) counting system.

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simultaneous in vivo measurement of Pu and Am and subsequently the relative translocation of these two nuclides as a function of time.

The flow chart in Figure 12 summarizes the entire experimental protocol.

CHAPTER IV

RESULTS AND DISCUSSION

Body Counter Measurements

A quantitative implantation of a pre-determined amount of the air oxidized PuO_2 was not made due to the insoluble nature of the material. To estimate the amount deposited at the wound site, a measurement of the activity on the Rocky Flats body counter was made. The count was taken 8-10 days following establishment of the wound. The ^{241}Am 59.5 keV gamma ray measurement tracer technique was used to estimate the amount of Pu present.

An adjustment for ingrowth of ^{241}Am over the time of the study was necessary. The amount of ^{241}Am present was computed by use of Bateman's equation relating parent-daughter radioactivity:

$$A_2 = \frac{A_1 \lambda_2}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t})$$

This number together with the information provided in Table 4 was used to compute the ppm ^{241}Am for the implant material as a function of time. The result of this computation is graphed in Figure 13.

Measurement and calculation of the micrograms of Pu at the wound site were based on the ^{241}Am present (assuming no differential removal of the two elements from the implant site) and referenced to a 10^{-3} microgram ^{241}Am source. The relationship used was:

Figure 13. Buildup curve for americium activity in the implant material since chemical separation and since the start of the implant study.

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$$\mu\text{g of Pu} = \frac{(10^{-3} \mu\text{g Am}) Y_1}{Y_2 (\text{ppm Am}/\mu\text{g Pu}) (10^{-6} \mu\text{g Am}/\text{ppm})}$$

where

Y_1 = net counts on dog paw per time interval

Y_2 = net counts on ^{241}Am check source per time interval

ppm Am = value for any point in time as per Figure 13

The body counter estimate of the quantity of Pu implanted is listed in Table 5. The data in Table 5 is a chronological sequential listing for the dogs as they were implanted. It shows the amount of implant material in the vial prior to implant as prepared at the Rocky Flats facilities and an idealized amount of material transferred from the vial to the dog assuming a perfect suspension without settling. Based on the body counter estimate, the fractional transfer of the suspended material from the vial was determined. The fraction of material transferred from the vial to the dog ranged from 0.06 to 0.37. The fractional amount transferred tended to increase from the beginning of the study. This probably reflects decreased time needed to accomplish the implant due to experience. The shorter the time used in preparing for implant, the less settling of the suspension and, therefore, a greater fractional transfer.

Results of the chemical assay for Pu of some of the dog paws appears in Table 4 of Appendix B. Due to residual organic materials

Table 5. Estimation of Quantity of Implanted Plutonium

Dog Number	Extrapolated Pu Implant Quantity (1) (μg)	Body Counter Measurement Estimate (2) (μg)	Fractional Transfer from Vial
2315	243	14.8	0.061
1884	159	17.8	0.112
1688	136	13.6	0.100
1689	159	18.3	0.115
2179	278	31.7	0.114
2531	433	59.2	0.137
1991	371	83.5	0.225
2602	742	90.8	0.122
2447	206	61.3	0.298
0792	680	62.5	0.092
1367	402	98.0	0.244
2280	235	47.2	0.201
2894	371	57.4	0.155
2865	402	63.5	0.158
3018	711	82.5	0.116
1308	711	139.0	0.195
2666	711	138.0	0.194
2532	371	100.0	0.270
2853	459	78.3	0.171
2570	459	78.7	0.172
1403	459	86.3	0.188
1219	459	75.2	0.164
0659	370	64.2	0.173
0004	370	59.5	0.161
2761	198	43.5	0.220
1990	198	53.2	0.268
1687	335	58.1	0.173
2325	335	73.0	0.218
2100	212	65.0	0.306
1803	212	64.4	0.304
1696	282	63.2	0.224
1008	282	83.4	0.296
1633	300	111.0	0.370
0650	300	74.6	0.249
1429	264	65.6	0.248
2963	264	68.5	0.260

Table 5., concluded

Dog Number	Extrapolated Pu Implant Quantity (1) (μg)	Body Counter Measurement Estimate (2) (μg)	Fractional Transfer from Vial
0925	229	66.6	0.291
1353	229	65.1	0.284

- (1) Assumed uniform distribution of material in PuO_2 suspension (no settling), multiplied by the gravimetric factor, Pu/PuO_2 .
- (2) Rocky Flats Body Counter wound site measurements estimating amount of implanted Pu by the method of Am gamma ray analysis 8-10 days after implantation.

in the terminal stages of paw sample digestion, the dog paw samples were difficult to prepare for Pu assay. Several paw samples were lost during the chemical digestion step. Internal standards were not used in the analytical procedures for either Pu or Am and an average chemical yield correction for the determinations was applied. There was no consistency in the reported Pu values for the implant sites determined by chemical assay when compared with the amount of Pu estimated by the body counter. The lack of consistency indicated an unknown variation in the data which limited the basis for any inferences from these measurements. A further discussion of experimental errors appears in Appendix A.

The ratio of Pu to Am alpha activity served as an index of the relative translocation of the two elements. The ratio of the Pu/Am alpha activity in the material not implanted was 8.6 at the time of implant site chemical assay. The Pu/Am ratio for the implant sites using the chemical assay data (recorded in Table 4 of Appendix B) ranged from 0.08 to 53.31. The Pu/Am ratio of the material at the implant site was not expected to differ widely from that of the material not implanted. The wide range of Pu/Am ratios reported was viewed as further evidence that the chemical assay data was not reliable.

Body counter measurements of the activity in the liver area of the dogs were made. The detector was positioned over the liver area and

all counts were assumed to be 59.5 keV gamma rays from the liver. The net counts recorded for each of the 20 dogs are listed in Table 6. These counts were made 2-3 days before necropsy. The net counts per minute divided by the Am disintegrations per minute determined by chemical assay following necropsy (Table 4 of Appendix B) provided an observed counting yield. In vivo estimation of the Pu in the liver was based on the observed counting yield, the ppm Am at the given time of analysis, and the current industrial in vivo counting assumption that deposition of material in the liver involved no differential metabolism of Pu and Am. This estimation was compared with chemical assay of the Pu content of the liver at necropsy (Table 4 of Appendix B). Comparison of the estimated liver Pu content with that determined chemically showed an overestimation of the Pu liver burden by the in vivo counting technique for both untreated and DTPA treated dogs. The average factor of overestimation was 4.51 for untreated dogs and 3.61 for DTPA treated dogs (Table 7). These values were not significantly different from each other. This finding correlates with the tendency of the liver to concentrate Am preferentially over Pu as shown in the low Pu/Am ratio for liver tissue discussed below.

NaI (Tl) Wound Counter Measurements

The accumulation of activity with time in the left superficial cervical lymph node was measured with a thin NaI (Tl) detector in 32

Table 6. Body Counter Liver Area Counts Prior to Necropsy

Dog	Net Counts/Min Liver Area (1)	d/m Am in Liver at Assay	Observed Counting Yield
<u>No Treatment</u>			
1633	383	6490	0.059
0650	1110	5950	0.187
0659	408	2770	0.147
0004	1265	2070	0.610
0925	341	4910	0.069
2325	550	2860	0.192
1687	820	10500	0.078
1367	728	21600	0.034
1689	138	2720	0.051
1688	78	803	0.097
<u>DTPA Treatment</u>			
1696	142	1985	0.072
1990	1490	14400	0.103
1429	146	2430	0.060
2963	1050	27400	0.038
1803	69	4050	0.017
2100	124	13500	0.009
3032	99	4400	0.023
2315	24	437	0.055
1884	35	254	0.138

(1) Assumed only ^{241}Am 59.5 keV gamma rays from the liver were counted.

Table 7. Average Overestimation of Liver Pu Burden by Am Tracer Method

<u>Treatment</u>	<u>Mean Factor of Overestimation</u>	<u>± SE</u>
None	4.51	1.21
DTPA	3.61	0.71

experimental animals. Equal quantities of the relatively insoluble implant material were not implanted because the suspension settled rapidly. The inequality of the amounts contaminating the experimental wounds made a normalization procedure necessary. The activity at 120 days post-implant was selected as the normalization reference point. The measured activity at any time divided by the activity observed on day 120 following the implant provided a fraction of the 120 day lymph node activity as a function of time. The mean normalized values with 95 percent confidence intervals are listed in Table 8 for both untreated and DTPA treated animals. The overlapping 95 percent confidence intervals indicates failure to detect any treatment effect on the accumulation of activity at the lymph node. The mean values were compared only at each point of time. No overall comparison was attempted.

The mean normalized lymph node activity values per time interval were used to derive empirical equations describing the buildup of activity. The computer based mathematical modeling methods used in this analysis were developed by Whicker et al. (1968) and Gallegos (1969). Both exponential and power function equation models were generated.

The differential equation describing the rate of change in activity with time for exponential buildup was:

Table 8. Normalized Lymph Node Activity (normalized to 120 days)

Time (days)	No Treatment		DTPA Treatment	
	Mean Value	95% Confidence Interval	Mean Value	95% Confidence Interval
0.0	0	---	0	---
0.083	0.016	0.004-0.028	0.022	0.004-0.040
1	0.072	0.001-0.143	0.065	0.011-0.119
2	0.151	0.000-0.305	0.106	0.018-0.194
3	0.189	0.000-0.478	0.179	0.005-0.353
4	0.264	0.027-0.501	0.167	0.075-0.259
5	0.359	0.025-0.693	0.239	0.066-0.412
6	0.388	0.099-0.677	0.265	0.101-0.429
7	0.343	0.128-0.558	0.284	0.120-0.448
9	0.531	0.268-0.794	0.329	0.121-0.537
11	0.565	0.215-0.915	0.411	0.179-0.643
14	0.564	0.316-0.812	0.278	0.178-0.378
30	0.741	0.583-0.899	0.579	0.473-0.685
60	0.766	0.642-0.890	0.750	0.619-0.881
90	0.833	0.719-0.947	0.876	0.790-0.962
120	1.000	---	1.000	---
150	1.058	0.934-1.182	1.039	0.947-1.131
180	1.229	0.894-1.564	1.046	0.866-1.226
210	1.095	0.890-1.300	1.111	0.981-1.241
240	1.389	0.656-2.122	1.124	0.815-1.433
270	1.138	0.609-1.667	1.142	0.887-1.397
300	1.969	1.022-2.916	1.190	0.545-1.835
330	2.010	1.072-2.948	1.354	0.902-1.806
365	2.076	1.805-2.347	1.306	1.121-1.491

$$\frac{dA}{dT} = I e^{-b_1 T}$$

where A = activity, T = time, I and b_1 are parameters representing the intercept of the curve on a plot of dA/dT versus time (T) at the initial time and the slope of the curve, respectively. The method uses the actual data points to generate approximate slopes (chords) DA/DT . The mid-interval value of the times, T_m , connecting the chords was assumed to have the same approximate instantaneous slopes as the chords. Least squares fit of the logarithm of DA/DT with T_m gives an equation of the form:

$$\ln (DA/DT) = b_0 + b_1 T \quad (1)$$

where b_0 and b_1 are intercept and slope parameters. Transformation and integration of the equation is given in the following steps:

$$DA/DT = dA/dT \quad (2)$$

$$dA/dT = e^{b_0} e^{-b_1 T} \quad (3)$$

$$A = I/b_1 e^{-b_1 T} + C \quad (4)$$

where $I = e^{b_0}$, $C = -I/b_1$ if $A = 0$ at $T = 0$, if $b_1 < 0$

$$A = (I/b_1) (1 - e^{-b_1 T}) \quad (5)$$

The coefficients I and b_1 represent the intercept at the initial time and the slope, respectively, obtained by linear regression of the data with equation (1).

Curvilinear regression of the model exponential equation (5) with the actual data points adjusts the coefficient I and adds an intercept, b_{00} , if $A = 0$ at $T = 0$, or if b_1 is not a fixed parameter through time. If the coefficient b_1 does not demonstrate a constant value in the exponential model, the intercept of the least squares fitted curve is adjusted to compensate for the changing value of b_1 . Where A is known to be zero at the initial time but the intercept of the fitted curve is not equal to zero, the exponential model is not appropriate.

$$A = b_{00} - (b_{11} I / b_1) (1 - e^{-b_1 T}) \quad (6)$$

where b_{11} is the regression coefficient of the model fit; equation (6) is the fitted exponential model.

The analogous model differential equation of a power function is:

$$dA/dT = I T^{-b_1}$$

A procedure similar to that outlined above yields a model equation to compare with the actual data points.

$$A = I / (1 - b_1) (T^{(1 - b_1)} - 1) \quad (7)$$

curvilinear regression of the model power function equation (7) with the data points provides the fitted power function:

$$A = b_{00} - b_{11} I / (1 - b_1) (T^{(1 - b_1)} - 1) \quad (8)$$

where the various symbols have the same definition, except $A = 0$ at $T = 1$.

The fitted exponential and power function equations generated in the above described manner were plotted with their conditional 95 percent confidence interval bands in Figures 14 through 17. The confidence interval bands were termed conditional because the methods used to generate them did not completely account for the variance of the parameters b_0 and b_1 obtained in the linear regression step. Separate equations and plots were obtained for untreated and DTPA treated dogs. The mean normalized data points for a given post-implant day were shown on each graph.

A statistical analysis of the coefficients for the mathematical models fitted to the data using the "t" test has been listed in Table 9. In the case of the exponential model all the coefficients tested were significantly different from zero at the 95 percent confidence level for both untreated and DTPA treated cases. Since A is known to be zero at the initial time, b_1 was thereby demonstrated not to be constant through time. For the power function model, the intercept, b_{00} ,

Figure 14. Exponential activity buildup curve for the superficial cervical lymph node of untreated dogs. Mean values are shown for all dogs measured on a given post-implant day.

Figure 15. Exponential activity buildup curve for the superficial cervical lymph node of DTPA treated dogs. Mean values are shown for all dogs measured on a given post-implant day.

Figure 16. Power function buildup curve for the radioactivity in the superficial cervical lymph node of untreated dogs. Mean values are shown for all dogs measured on a given post-implant day.

Figure 17. Power function buildup curve for the radioactivity in the superficial cervical lymph node of DTPA treated dogs. Mean values are shown for all dogs measured on a given post-implant day.

Table 9. Statistical Parameters for Comparison of Model Fit to Data

Statistical Parameter	Exponential Model	Power Function Model
No Treatment		
$t = b_0/\sigma b_0$	9.84*	5.00*
$t = b_1/\sigma b_1$	3.33*	6.02*
$t_{.05}$	2.08	2.08
Correlation coefficient	0.588	0.796
$t = b_{00}/\sigma b_{00}$	3.12*	1.02
$t = b_{11}/\sigma b_{11}$	11.90*	14.80*
$t_{.05}$	2.074	2.074
Correlation coefficient	0.930	0.953
DTPA Treatment		
$t = b_0/\sigma b_0$	10.80*	5.28*
$t = b_1/\sigma b_1$	5.67*	9.75*
$t_{.05}$	2.086	2.086
Correlation coefficient	0.783	0.909
$t = b_{00}/\sigma b_{00}$	5.40*	1.39
$t = b_{11}/\sigma b_{11}$	2.97*	40.50*
$t_{.05}$	2.074	2.074
Correlation coefficient	0.988	0.993

* Significant at the 5% error level

was not significantly different from zero at the 5 percent error level. The above considerations coupled with larger correlation coefficients made the power function model the best fit of the two models employed for both treated and untreated data.

Biological considerations indicate the probability of a changing rate of uptake. The "walling-off" or encapsulating process following embedding of relatively insoluble material in tissue would most likely preclude a constant value for b_1 in the exponential model. The rate of transfer of material via the lymphatic system would be affected by the thickness of the fibrous sheath surrounding the implanted material. Further, the breaking down and reforming of these nodules at the implant site has been reported by Hammond and Putzier (1963) and observed in the present study indicating that the integrity of the tissue surrounding the implant may vary with time.

The integrated radiation dose for each dog's left superficial cervical lymph node was calculated. The power function equations were integrated over the time from implant to necropsy for each dog. This yielded a total effective number of exposure days. The number of μCi of material in the node at necropsy (see Table 4 of Appendix B) was adjusted to the value at 120 days as predicted by the curves in Figures 16 and 17. Adjustment was necessary because the total effective number of days represents the summation of the fractional 120 day activity or the point of normalization. The average MeV per

disintegration deposited (kinetic energy of alpha particles and recoil nuclei) for the material collected in the lymph nodes was computed to be 5.13 MeV, neglecting the beta emission of ^{241}Pu and the electromagnetic radiations associated with the decay of Am and the Pu isotopes. The number of rads per μCi per day was calculated to be 262 from application of conversion constants. The calculation of the dose to the lymph node assumed a uniform distribution of material in a one gram node. The wet weight of the collected superficial cervical lymph nodes was usually slightly greater than one gram, however, all the associated tissue was not removed due to radioactivity containment considerations. The estimated total integrated dose (rads) for each dog, untreated or DTPA treated, is shown in Tables 10 and 11.

The average fractional transportability of the implanted material from the wound site via the lymphatic system as a function of implant time is indicated in Table 12. By use of the body counter estimate of the amount of material at the implant site (Table 6), the amount of Pu concentrated at the lymph node relative to the total was seen to range up to 26 percent of the estimated initial total. The International Commission on Radiological Protection (ICRP) (1968) recently published a diagrammatic representation of the principle metabolic pathways of radionuclides entering the body. While the lymph nodes associated with the lung were recognized as important sites of radioactivity concentration, there was no pathway indicated from contaminated

Table 10. Estimated Dose to the Left Superficial Cervical Lymph Node (no treatment)

Dog	Exposure Time (days)	Effective Days Exposure ⁽¹⁾	μCi (adjusted to 120 days)	Estimated Integrated Dose (rads)
1991	14	3.91	0.374	383
2602	14	3.91	1.155	1183
2912 ⁽²⁾	31	13.09	0.745	2555
2532	31	13.09	1.420	4870
3018	42	20.74	1.775	9645
2853	62	36.69	0.635	6104
2570	62	36.69	1.255	12064
2865	91	63.85	1.013	16946
1633	125	100.15	0.341	8948
0650	125	100.15	0.379	9945
1353 ⁽³⁾	137	114.54	0.235	7052
0925	153	133.99	0.189	6635
0659	184	173.94	0.218	9935
0004	184	173.94	0.401	18274
1687	212	212.55	0.158	8799
0792	274	304.68	0.392	31292
1688	365	455.06	0.199	23726
1689	365	455.06	0.050	5961

$$(1) \int_1^T (0.255 T^{0.343} - 0.191) dT = 0.19 T^{1.343} - 0.191 T$$

(2) Unplanned intravenous injection.

(3) Lymphosarcoma case.

Table 11. Estimated Dose to the Left Superficial Cervical Lymph Node (DTPA treatment)

Dog	Exposure Time (days)	Effective Days Exposure ⁽¹⁾	μCi (adjusted to 120 days)	Estimated Integrated Dose (rads)
2179	14	3.42	0.946	848
2531	14	3.42	0.406	364
1308	31	12.13	1.320	4195
2666	31	12.13	1.680	5339
1403	62	34.63	1.735	15742
1219	62	34.63	1.177	10679
2280	91	58.93	0.500	7720
2894	91	58.93	0.679	10484
1008	125	90.13	0.117	2763
1696	125	90.13	0.515	12161
1429	153	119.73	0.449	14085
2963	153	119.73	0.933	29268
2761	184	145.13	0.336	12776
1990	184	145.13	0.338	12852
2100	212	178.73	0.598	28003
1803	212	178.73	0.228	10677
2447	274	243.53	0.172	10974
3032 ⁽²⁾	274	243.53	0.415	26479
1884	365	361.13	0.047	4447
2315	365	361.13	0.156	14760

$$(1) \int_1^T (1.65 T^{0.101} - 1.729) dT = 1.5 T^{1.101} - 1.729 T + 0.229$$

(2) Implant surgically removed after 13 days.

Table 12. Average Percent Lymph Node Uptake of Activity from the Implant Site as a Function of Time Implanted

Time Implanted (months)	Percent of Initial Estimated Implant Activity in Lymph Node
0.5	3.3
1.0	6.7
2.0	12.6
3.0	11.0
4.0	6.5
5.0	8.7
6.0	7.5
7.0	6.4
9.0	6.5
12.0	13.3

wounds to lymph nodes. The present experimental data emphasizes the importance of this pathway.

Induction of lymphosarcoma in experimental animals with high concentrations of Pu in lymph nodes was reported by Thompson (1967) and has been observed in the present study (Lebel et al., 1969). Dog number 1353 died prior to the scheduled sacrifice time. Histopathological examination of tissue samples confirmed a diagnosis of lymphosarcoma. This potential further emphasizes the significance of the wound to lymph node pathway.

The count rate of the implant site was measured over time. The count at 60 days following implantation was used as the normalization point. The fractional 60 day count rate of the implant site for treated and untreated animals was listed in Table 13. These data do not demonstrate a measureable chelate effect at the implant site at the 5 percent error level. A general decrease in activity over the first 60-90 days was evident followed by a slight increase in relative activity up to 270 days. The initial decrease may reflect the early translocation of material via the lymph and blood systems. The subsequent increase in relative count rate was believed to be due in part to the buildup of americium. The detector, operated in an integral count mode, detects photons above 10 keV. The L X-rays arising from the daughter nuclides, uranium and neptunium, following the alpha decay of plutonium and americium have energies of about 13-20

Table 13. NaI (Tl) Wound Detector Measurements of Wound Sites:
Normalized to 60 Day Post-Implant Count

Time After Implant (days)	No Treatment		DTPA Treatment	
	Mean Value $\pm$ SE of Mean		Mean Value $\pm$ SE of Mean	
0.083	1.001	0.037	0.992	0.055
1	0.935	0.064	1.098	0.041
14	0.955	0.027	1.027	0.044
30	0.969	0.018	0.966	0.031
60	1.000		1.000	
90	1.042	0.021	1.018	0.022
120	1.049	0.014	1.035	0.030
150	1.064	0.015	1.055	0.020
180	1.115	0.026	1.099	0.039
210	1.100	0.026	1.118	0.049
240	1.122	0.006	1.091	
270	1.113	0.003	1.118	

keV in both cases. However, the abundance of these X-rays per disintegration are reported to be 0.04 for ^{235}U and 0.37 for ^{237}Np by Day (1955), Magnuson (1957), and Swinth (1968). Thus, the ingrowth of ^{241}Am from the decay of ^{241}Pu results in a greater abundance of X-rays following ^{241}Am alpha decay. The ingrowth of ^{241}Am and the resultant greater abundance of L X-rays from Np more than offsets the removal of material to the lymph node and other parts of the body as far as the gross detection of electromagnetic radiations at the implant site was concerned.

Germanium (Li) Detector Counts

Measurements of the implant site, the left superficial cervical lymph node and the liver area were made using the Ge (Li) detector. The objective of the use of this detector was to determine the relative translocation of ^{239}Pu and ^{241}Am externally.

The system energy resolution was ≤ 2.0 keV full width at half maximum at 59.5 keV. The energy resolution capability and energy calibration for the system are illustrated in Figure 18. A gamma ray spectrum of the Pu-Am implant material mounted on a planchet is shown in Figure 19. Both spectra were taken with a single channel analyzer by hand scanning. The 51.5 keV and 129 keV gamma rays from ^{239}Pu are clearly evident. The 51.5 keV gamma ray, though

Figure 18. Gamma ray spectrum of ^{57}Co , ^{109}Cd , and ^{241}Am taken with Ge(Li) detector system.

Figure 19. Gamma ray spectrum of the implant material taken with Ge(Li) detector system.

definitely resolved from the 59.5 keV gamma ray of ^{241}Am , is superimposed on the Compton continuum of the Am gamma ray.

The counts on the dogs were taken with three single channel analyzer windows centered on the 51.5, 59.5, and 129 keV gamma rays with the detector unshielded. The net counts in each channel for each counting position was obtained by making background counts with unimplanted dogs. Subtraction of this background count from the total provided net counts for the 59.5 and 129 keV channels. An additional factor, called the 59.5 keV gamma ray scatter factor, had to be considered for the 51.5 keV channel response evaluation. The count contribution of the 59.5 keV gamma ray to the 51.5 keV channel was determined by surgically implanting a ^{241}Am source in the paw, in the superficial cervical lymph node region, and in the liver of anesthetized dogs. The fraction of the counts from the 59.5 keV channel appearing in the 51.5 keV channel were thereby determined. For the wound site, 5.6 percent of the net counts in the 59.5 keV channel appeared in the 51.5 keV channel. The lymph node and liver area counts showed scatter factors of 7.4 percent and 23.0 percent, respectively.

The abundance of the gamma rays from ^{239}Pu is extremely low (see Table 1). The fraction of the total count attributable to background in the 51.5 and 59.5 keV channels was very large. Subtraction of background and allowance for the 59.5 keV scatter factor in the

51.5 keV channel frequently resulted in zero net counts for both of these channels as shown in the example data listed in Table 14. The data obtained did not allow a quantitative analysis of the relative retention and distribution of Pu and Am from external counting with the diode detector.

The use of the Ge (Li) detector for external measurements of this type could be further optimized by reducing the natural background radiation reaching the detector. This would require shielding both the dog and the counter as well as collimation of the detector during the count. Extending the counting time would provide a greater number of net emissions detected of the two ^{239}Pu gamma rays.

Although quantification of the data from the diode detector was not possible, the potential use of a Ge (Li) system for in vivo counting warrants further investigation. The use of such a system for contaminated wound counting would allow not only gross counting, but with proper calibration it might be used to estimate the amount of ^{241}Am in the contaminating Pu. The amount of americium in the material to which a worker has been exposed is often unknown and must be estimated by analyzing material in the vicinity of the exposure (Putzier, 1967).

Table 14. Ge(Li) Detector Measurements on One Dog

Time Post-Implant (days)	Count Time (min)	Net Counts Channel 51.5 keV ⁽¹⁾	Net Counts Channel 59.5 keV	Net Counts Channel 129 keV
Wound Site				
121	2	0	120802	49
149	2	0	118512	0
183	2	0	131382	38
Lymph Node				
121	15	434	52595	110
149	15	281	48474	22
183	15	443	37005	0
Liver Area				
121	120	0	3945	0
149	120	0	3544	95
183	120	0	4015	0

(1) Net counts in channel 51.5 keV equaled the gross count minus the quantity background plus the scatter factor times the net count in channel 59.5 keV.

Relative Blood, Urine, and Feces

Pu and Am Alpha Activity

The Pu/Am alpha activity ratio for each blood, urine, and feces sample was calculated from the reported sample activity (Tables 1, 2, and 3 of Appendix B) as a means of determining the relative translocation of Pu and Am within each sample type. The ratio was defined as the disintegrations per minute for Pu determined by alpha radiation measurement divided by the disintegrations per minute of Am determined by alpha radiation measurement. This procedure accounted for all the Pu nuclides except ^{241}Pu which was primarily (99%) a beta emitter (see Table 1) and which was only 1.51 percent of the plutonium at the time of chemical separation. The long half lives of all the alpha emitting Pu isotopes present made the Pu alpha activity essentially constant over the time of the present study. The alpha activity of the ^{241}Am increased about 2.5 percent per month during the study time because of the beta decay of ^{241}Pu which has a 13.3 year half life.

The PuO_2 implant material had a Pu/Am alpha activity ratio of 12.0 at the beginning of the present study. The magnitude of this ratio decreased during the experiment due to Am activity buildup (see Figure 13). The change of this ratio is graphed in Figure 20. Although the change of the Pu/Am ratio in the implant material was small over the 365 day study period, adjustment for the buildup of

Figure 20. Pu/Am activity ratio for the implant material as a function of time.

Am activity was made by dividing the Pu/Am ratio in a given sample observation by the calculated Pu/Am ratio in the implant material at the time of sample analysis. This procedure yielded a multiple or corrected ratio of the Pu/Am activity for each observation. A multiple or corrected ratio greater than 1 indicated enhancement of Pu concentration. A multiple or corrected ratio of less than 1 indicated enhancement of Am concentration. The term enhancement indicates only relative changes for the two elements and is meaningful within the in vivo counting frame of reference. The blood, urine, and feces samples were analyzed a few at a time on various dates. An average implant material Pu/Am ratio of 10.0 was assumed for purposes of calculating the multiple of the Pu/Am ratio for these samples. The average value of 10.0 was chosen because it represented the Pu/Am ratio of the implant material at the time when the majority of these samples were being assayed.

Except for the first week following implant, DTPA was not given to the treated animals until after the first 24 hours that the dogs were in the metabolism cages for sample collection. Therefore, the first blood, urine, or feces sample collected during each collection period from the dogs receiving DTPA therapy was radiochemically analyzed but not used in comparing treated and untreated samples. Inspection of the data in Tables 1, 2, and 3 of Appendix B showed a general increase in amount of activity in the urine samples in the

second and third days of the collection periods for the DTPA treated dogs. The DTPA produced a 20 fold average increase in the activity per ml of urine. The increase in concentration of activity in the urine was computed by comparing the level on the first day (pre-treatment) with that on the second or third day following DTPA injection. This indicated that DTPA was effective in increasing the level of removal of Pu and Am at least during the observation period.

The Pu and Am alpha disintegrations per minute per milliliter of blood were measured for each blood sample collected (Table 1 of Appendix B). The possible change of the blood multiple or corrected ratio with post-implant time was determined by linear regression. The data were fit to the mathematical model, $\log M = b_0 + b_1 T$, where M was the multiple or corrected ratio of the Pu/Am activity, T was the post-implant time in days, and b_0 and b_1 were constants representing the curve's intercept and slope respectively. The blood data for untreated and DTPA treated dogs were analyzed separately. The regression coefficients were computed to be significantly different from zero at the 5 percent error level. The regression coefficients were 0.0046 for untreated dogs and 0.0021 for DTPA treated dogs. The correlation coefficients were 0.25 and 0.15, respectively. Since both the regression coefficients and the correlation coefficients were small, the data were not interpreted as indicating a measured change in the blood multiple or corrected ratio with time. The grand mean

blood multiple with the 95 percent confidence interval was calculated for untreated and DTPA treated samples. These values were recorded in Table 15. These data show no measured treatment effect in the Pu/Am blood multiples at the 5 percent error level. The mean blood multiples were less than one indicating enhancement of Am translocation within the blood.

Each urine sample was chemically analyzed for Pu and Am activity. The activity per sample and the Pu/Am alpha activity ratio computed for each sample were listed in Table 2 of Appendix B. A semi-log linear regression of these data as a function of post-implant time similar to that for the blood was completed. The regression coefficients and correlation coefficients were 0.00270 and 0.22 for the untreated urine samples and 0.00426 and 0.33 for the DTPA treated urine samples. The regression coefficients were statistically different from zero at the 5 percent error level. However, due to the small size of the two coefficients in both cases, no measured change in the Pu/Am ratio in the urine with time was deduced. The grand mean Pu/Am urine multiples or corrected ratios with 95 percent confidence intervals for treated and untreated samples were shown in Table 15. The mean values were significantly different at the 5 percent error level indicating a DTPA treatment effect. These data show that DTPA treatment enhanced the relative urine Pu content as compared with the Am content. An increase of about a factor of two in the relative Pu to Am

Table 15. Relative Pu and Am Distribution in Blood, Urine, and Feces

Sample	Treatment	Mean Multiple of Pu/Am Ratio	95% Confidence Interval
Blood	None	0.95	0.80 - 1.09
	DTPA	0.80	0.68 - 0.93
Urine	None	0.79	0.71 - 0.87
	DTPA	1.47	1.28 - 1.65
Feces	None	2.11	0.88 - 3.34
	DTPA	2.24	0.89 - 3.59

urine content was observed for the DTPA treated animals. The untreated urine mean multiple was not significantly different from the mean blood multiples at the 5 percent error level.

The feces sample data were analyzed by the same methods as were the blood and urine samples. A significant change of the feces mean multiple or corrected ratio as a function of time was not detected. The grand mean multiples for fecal samples were determined with the 95 percent confidence intervals and listed in Table 15. These data show no measureable treatment effect on the relative distribution of Pu and Am in the feces. The relative amount of Pu and Am in the feces excreted through the liver or the gastrointestinal tract was not affected by administration of DTPA.

The mean feces multiples shown in Table 15 were significantly larger at the 5 percent error level than either of the blood multiples or the urine multiple for untreated dogs. An increase in the relative amount of Pu in the feces of two fold or more was observed when compared to the blood multiples and the untreated urine multiple.

Relative Pu to Am Activity in Tissue Samples

Activity measurements following chemical analysis of the individual tissue samples for Pu and Am were listed in Table 4 of Appendix B. This table also shows the tissue sample weight, the Pu/Am ratio, and the tissue Pu and Am specific activities for each dog. Inspection of the

tissue specific activities correlates with previous reports (Langham et al., 1962, and Newton et al., 1966) that the lymph nodes, liver, spleen, and bone were the major concentrating tissues in descending order.

The implant material Pu/Am ratio was determined using Figure 20 for the tissue samples at the time of analysis. Using these values, the multiple of the Pu/Am ratio was computed for each sample. The multiple for each tissue together with the total implant time for each dog are listed in Table 16 for the untreated dogs and in Table 17 for the DTPA treated dogs. A linear regression analysis of the multiple versus implant time was completed to determine if a time related change in the multiples for each type of tissue were measureable. The data were fit to the linear, exponential, and power function forms of the mathematical model, $M = b_0 + b_1 T$, where M is the multiple of the Pu/Am ratio, T is the post-implant time, and b_0 and b_1 are constants representing the curve's intercept and slope, respectively. The DTPA treated and untreated tissue sample data were analyzed separately. The $\log M = b_0 + b_1 T$ form of the model was the best fit to the data. Several regression lines were computed for each tissue sample type. Repeated curve fitting was done by deleting data points which were different from surrounding data points by an order of magnitude or more. Like the blood, urine, and fecal regression curves, some of the tissues samples showed regression coefficients different from

Table 16. Multiple of the Pu/Am Ratio for Untreated Tissue Samples

	Implant Time (months)								
	1/2	1/2	1	1.4	2	2	3	4	4
Liver	0.17	0.26	0.05	0.47	3.91*	0.07	0.14	0.47	0.15
Spleen	0.26	0.36	0.10	1.38	2.33	0.74	0.27	1.27	0.35
Kidney	0.50	1.07	0.03	0.01	0.43	0.09	0.20	1.17	0.15
Adrenal gland	2.32	1.79	0.48	0.10	11.10	0.51	1.42	1.35	0.59
Thyroid gland	--	--	--	--	--	--	--	0.075	0.024
Lung	2.15	2.29	0.12	0.16	0.81	0.81	0.15	0.72	0.12
Testis	1.82	0.04	0.12	0.06	1.17	0.05	0.02	0.79	0.30
Eye	0.70	0.46	--	0.15	0.63	0.30	0.26	0.24	0.45
Trachea	0.24	0.01	0.01	0.24	1.35	1.10	0.07	1.60	0.18
L. cervical node	2.76	6.24	0.14	0.93	0.63	1.62	0.21	1.60	1.07
L. axillary node	4.04	0.02	0.84	1.19	4.86	1.23	0.34	0.15	1.66
R. cervical node	--	--	--	--	--	--	--	0.17	0.85
Sternum	3.38	3.88	1.40	7.28	12.65	9.17	0.91	--	2.09
Rib	1.00	1.03	0.29	12.65	1.64	1.63	0.93	8.25	6.30
Vertebrae	16.29	10.28	10.90	7.60	3.92	4.96	1.45	10.69	3.48
Skull	1.10	0.96	2.70	3.20	0.70	1.04	0.84	5.95	1.00
Proximal femur	1.14	6.29	1.31	3.68	2.15	5.05	0.94	0.82	0.57
Shaft femur	2.96	2.82	2.48	0.65	1.08	6.36	0.71	1.54	0.45
Distal femur	1.25	1.98	0.70	0.73	1.13	0.81	1.21	6.84	1.32

Table 16., concluded

	Implant Time (months)									
	4.57	5	6	6	7	7	9	9	12	12
Liver	0.19	0.42	0.65	0.63	0.22	9.00*	0.38	--	0.16	0.07
Spleen	0.32	2.19	0.88	2.00	0.20	0.62	1.00	--	2.78	1.41
Kidney	0.04	--	0.25	0.09	0.05	0.01	0.05	--	0.24	0.32
Adrenal gland	0.22	0.43	3.99	0.84	3.08	4.75	1.41	--	0.18	1.12
Thyroid gland	0.104	0.104	0.040	0.026	0.049	0.071	0.070	0.130	--	0.083
Lung	0.32	0.48	0.20	0.15	0.24	0.11	0.27	--	0.74	1.01
Testis	0.10	--	0.26	0.18	0.04	0.11	0.34	--	--	0.04
Eye	0.05	0.15	0.11	0.20	0.35	0.23	1.15	--	0.12	1.10
Trachea	0.25	0.11	7.90	0.15	0.01	0.11	0.04	--	0.38	0.33
L. cervical node	0.72	0.85	1.38	1.50	0.70	--	--	1.22	--	0.83
L. axillary node	0.11	0.74	0.72	0.40	0.05	0.16	1.60	--	3.92	0.28
R. cervical node	0.45	0.29	2.54	0.28	0.30	0.25	0.21	0.17	1.19	0.43
Sternum	0.59	1.59	1.67	2.79	0.66	1.05	--	--	3.34	2.13
Rib	0.42	0.99	1.84	2.07	0.90	1.03	1.26	--	4.95	8.75
Vertebrae	1.16	0.75	1.67	2.07	0.41	3.80	1.97	--	20.69	1.29
Skull	0.88	0.64	0.86	0.39	0.40	0.49	0.78	--	0.54	1.15
Proximal femur	0.95	1.09	2.19	2.07	0.56	2.62	0.84	--	1.78	0.68
Shaft femur	0.77	0.26	0.54	0.79	0.12	0.88	0.38	--	--	3.80
Distal femur	1.60	0.80	0.63	0.53	0.60	0.57	0.60	--	4.09	1.30

* Omitted in computation of mean multiple.

Table 17. Multiple of Pu/Am Ratio for DTPA Treated Tissue Samples

	Implant Time (months)									
	1/2	1/2	1	1	2	2	3	3	4	4
Liver	2.31	0.76	0.44	0.08	0.26	1.16	0.43	0.44	0.27	5.72
Spleen	0.94	0.39	0.06	0.27	2.13	0.79	0.59	0.59	0.27	1.28
Kidney	1.47	4.37*	0.04	0.06	0.09	0.39	0.23	0.17	0.03	1.02
Adrenal gland	--	1.13	0.17	0.03	0.36	0.45	1.01	1.06	0.46	0.92
Thyroid gland	--	--	--	--	--	--	0.011	0.008	0.048	0.115
Lung	0.28	0.50	1.66	--	0.39	0.74	0.03	0.12	0.40	0.90
Testis	0.07	3.52	0.12	0.22	0.19	0.25	0.10	0.10	0.30	0.62
Eye	0.92	0.27	0.54	0.02	0.13	0.12	0.04	0.50	0.38	0.88
Trachea	--	2.37	0.01	0.08	0.06	0.07	0.05	0.11	0.08	0.85
L. cervical node	0.38	0.95	0.89	1.02	0.82	0.96	1.31	0.95	0.75	1.57
L. axillary node	--	--	2.93	0.79	0.39	2.68	1.09	1.11	0.40	1.85
R. cervical node	--	--	--	--	--	--	1.12	6.93	0.62	0.58
Sternum	0.85	10.44	9.21	0.36	6.09	14.97	11.00	2.21	3.36	9.75
Rib	1.94	4.55	2.92	1.72	1.69	0.10	2.41	2.96	1.11	1.26
Vertebrae	1.22	4.75	9.43	1.00	0.54	5.40	7.03	7.53	0.93	1.03
Skull	0.71	1.97	1.43	0.39	0.76	1.68	0.50	0.31	0.39	0.64
Proximal femur	2.25	3.35	14.62	7.44	14.37	15.87	10.25	8.04	3.30	1.53
Shaft femur	0.84	0.66	1.18	0.76	4.88	2.99	1.59	5.71	1.13	1.90
Distal femur	2.16	2.72	10.28	4.38	5.47	2.28	5.13	5.40	2.09	3.14

Table 17., concluded

	Implant Time (months)								
	5	5	6	6	7	7	9	12	12
Liver	0.48	6.42	2.54	0.14	1.90	1.40	0.87	2.06	1.15
Spleen	1.92	1.69	2.52	0.43	0.55	0.69	0.44	2.09	2.99
Kidney	0.19	0.08	4.21*	0.77	0.07	0.03	0.05	0.11	0.13
Adrenal gland	1.11	0.69	1.22	0.79	0.82	1.10	0.12	--	4.68
Thyroid gland	0.064	0.130	0.135	0.155	0.220	0.063	0.108	0.036	--
Lung	0.79	0.92	1.55	0.62	0.77	0.49	0.68	0.86	0.55
Testis	0.13	0.74	0.31	0.93	0.19	0.31	0.33	1.86	0.76
Eye	0.45	0.06	0.96	0.51	0.25	0.15	0.28	--	1.83
Trachea	1.43	0.07	0.46	0.26	0.16	0.16	0.35	1.20	0.37
L. cervical node	0.59	1.15	0.69	1.44	0.87	0.99	1.10	5.08	2.38
L. axillary node	4.64	0.18	2.54	0.79	0.61	0.40	0.48	0.26	1.03
R. cervical node	0.58	0.50	0.31	0.33	0.54	0.22	0.81	1.05	0.08
Sternum	5.83	8.74	3.32	0.80	1.78	1.59	1.54	5.57	9.30
Rib	2.30	2.57	0.89	0.50	1.85	1.86	1.52	4.41	7.17
Vertebrae	0.80	1.52	1.87	4.15	2.39	2.43	4.98	34.70	21.60
Skull	0.65	1.36	1.18	0.18	2.54	2.36	0.80	0.28	1.62
Proximal femur	3.67	2.21	3.21	0.99	5.67	1.13	0.73	11.69	4.13
Shaft femur	2.61	0.83	0.45	0.29	0.28	3.71	0.67	3.58	3.77
Distal femur	1.29	2.18	1.38	0.18	0.47	0.52	0.35	0.64	5.47

* Omitted in computation of mean multiple.

zero at the 95 percent confidence level. However, the correlation coefficients were generally less than 0.50 making definitive time related change determinations not measureable from these data.

Trends in reticuloendothelial tissue and in skeletal tissue having a high trabecular bone content were evident. These trends are illustrated in Figures 21 and 22. The log of the spleen and distal femur multiples were plotted versus implant time for untreated and DTPA treated samples in these figures. While these trends may not be considered statistically significant, the general pattern illustrated was repeated within most soft tissue and skeletal tissue types. Regardless of treatment, there was an increase in the multiple in most of the soft tissue samples and a decrease in the multiple in most of the bone samples as a function of post-implant time. This trend probably reflects a differential binding of the two elements in soft tissue compared to bone regardless of the DTPA chelation treatment.

The mean multiples with 95 percent confidence intervals for the major soft tissue sites of Pu and Am deposition are listed in Table 18. Only the liver tissue shows a significant DTPA treatment effect at the 5 percent error level. The DTPA treated liver mean multiple is about five times that of the liver tissue of untreated dogs. This may reflect preferential Am chelation because of greater availability of Am in the liver. The mean multiples with 95 percent confidence intervals for the major skeletal tissue sites of Pu and Am deposition are listed in

Figure 21. Regression lines with data points for the change of spleen multiple versus post-implant time for untreated and DTPA treated dogs.

Figure 22. Regression lines with data points for the change of distal femur multiple versus post-implant time for untreated and DTPA treated dogs.

Table 18. Mean Multiple of Pu/Am Ratio for Major Sites of Pu and Am Deposition in Soft Tissues

Sample	Treatment	Mean Multiple	95% Confidence Interval
Liver	None	0.28	0.01 - 0.68
	DTPA	1.49	0.68 - 2.31
Spleen	None	1.03	0.61 - 1.45
	DTPA	1.09	0.67 - 1.51
Kidney	None	0.28	0.11 - 0.45
	DTPA	0.29	0.01 - 1.14
Left cervical lymph node	None	1.40	0.63 - 2.17
	DTPA	1.26	0.78 - 1.74

Table 19. These bones have high blood circulation and high blood cell forming activity. As previously reviewed, Pu and Am transport has been reported to be primarily by the blood protein, transferrin. Deposition of Pu and Am at sites of red blood cell formation were not unexpected. The proximal end of the femur is the only skeletal tissue showing a significant DTPA treatment effect at the 5 percent error level. It showed a Pu enhancement factor of about three for the DTPA treated samples.

The mean multiple for the left superficial cervical lymph node does not show a treatment effect at the 95 percent confidence level. The collection of particulate matter in this lymph node would not be expected to entail differential trapping of the elements in the particulate matter. The 95 percent confidence interval included the multiple or corrected Pu/Am ratio of 1.0 which indicated no enhancement of either element with respect to the other. The mean multiple in both cases, however, was greater than one, indicating a trend toward Pu enhancement.

An unplanned intravenous injection of the intended implant material occurred with dog number 2912. The intravenous injection was verified by an extremely low amount of activity measured at the implant site and, following necropsy one month after injection, by the high specific activities of the liver, spleen, and lung tissues. The low specific activity of the left superficial cervical lymph node also

Table 19. Mean Multiple of Pu/Am Ratio for Major Sites of Pu and Am Deposition in Skeletal Tissue

Sample	Treatment	Mean Multiple	95% Confidence Interval
Sternum	None	3.41	1.60 - 5.22
	DTPA	5.62	3.54 - 7.70
Vertebrae	None	5.74	2.83 - 8.65
	DTPA	5.96	1.86 - 10.06
Proximal femur	None	1.93	1.13 - 2.73
	DTPA	6.02	3.60 - 8.44
Distal femur	None	1.48	0.70 - 2.26
	DTPA	2.92	1.68 - 4.16

indicated an intravenous injection. Comparison of the multiples of the several tissues of this intravenously injected untreated dog with the mean multiples (corrected Pu/Am ratios) of the untreated implanted dogs showed some differences which may be attributable to the mode of entry. The multiple or corrected ratio of the Pu/Am sample activity for this dog's soft tissues fell within the 95 percent confidence interval of the soft tissues from implanted dogs. However, the multiples of the skeletal tissue samples were below the 95 percent confidence interval for most bone samples. This single result indicated that the mode of entry of the material to the body had an influence on the relative distribution of the two elements in bone.

The implant site of another dog (dog number 3032) was excised 13 days after the implant was made. Surgical removal of the implanted material became necessary when an exudate appeared at the implant site resulting in external contamination release. By use of the NaI (Tl) wound counter, it was estimated that 99.95 percent of the implanted material was removed. This dog was designated to receive DTPA therapy and remained on the treatment regime the entire nine month study period. The tissue sample analyses showed high activity concentration which indicated a rapid transfer of material from the wound site. The multiples or corrected Pu/Am ratios for the various tissues were generally within the 95 percent confidence intervals for the DTPA

treated dogs. This result indicated that surgical removal of the implanted material 13 days after the implant was established and followed by an uninterrupted chelation therapy regime was not effective in altering the relative distribution of Pu and Am.

The mean multiples with 95 percent confidence intervals for some "curiosity" soft tissues and for some skeletal tissues with low trabecular bone content are shown in Tables 20 and 21. There was no significant DTPA treatment effect measured at the 5 percent error level. Preferential concentration or retention of Am was shown most distinctly by the thyroid gland tissue. Enhancement of Am concentration in the thyroid averaged about 15 fold. The Am specific activity in the thyroid was greater than that in the liver for both untreated and DTPA treated animals. The average Am activity concentration in the liver was 14.2 d/m-g for untreated dogs and 10.1 d/m-g for DTPA treated dogs. The comparable numbers for the thyroid gland tissue were 23.1 and 13.5 d/m-g. The thyroid gland tissue ranks second to the cervical lymph node in Am activity concentration. This finding suggested the need for consideration of the thyroid as a critical organ for internal dosimetry of Am.

With the exception of the thyroid mean multiple, all the "curiosity" soft tissues had mean multiples in the same range with the liver, spleen, and kidney tissues. The mean multiple for the rib was intermediate between the low multiple of the skull bone and the high multiple

Table 20. Mean Multiple of Pu/Am Ratio for Various Types of Soft Tissue

Sample	Treatment	Mean Multiple	95% Confidence Interval
Left axillary lymph node	None	1.24	0.50 - 1.98
	DTPA	1.30	0.66 - 1.94
Right cervical lymph node	None	0.59	0.15 - 1.03
	DTPA	0.56	0.01 - 1.22
Lung	None	0.60	0.33 - 0.87
	DTPA	0.68	0.47 - 0.89
Adrenal gland	None	1.98	0.67 - 3.29
	DTPA	0.95	0.42 - 1.48
Thyroid gland	None	0.071	0.049 - 0.093
	DTPA	0.091	0.051 - 0.131
Eye	None	0.39	0.22 - 0.56
	DTPA	0.46	0.23 - 0.69
Trachea	None	0.78	0.01 - 1.69
	DTPA	0.45	0.13 - 0.77
Testis	None	0.34	0.06 - 0.62
	DTPA	0.58	0.18 - 0.98

Table 21. Mean Multiple of Pu/Am Ratio for Minor Sites of Pu and Am Deposition in Skeletal Tissue

Sample	Treatment	Mean Multiple	95% Confidence Interval
Rib	None	3.11	1.34 - 4.88
	DTPA	2.30	1.50 - 3.10
Skull	None	1.31	0.63 - 1.99
	DTPA	1.04	0.68 - 1.40
Femur shaft	None	1.56	0.71 - 2.41
	DTPA	1.99	1.19 - 2.79

of the vertebrae. This finding may correlate with an intermediate blood cell forming activity in the rib

The range of the mean multiples or corrected ratios in the various tissues provided a measure of the differential metabolism of Pu and Am in canine tissues. Relative enhancement of Am ranged from 15 fold in the thyroid tissue to about 2 fold in most other soft tissues. Relative enhancement of Pu ranged from a mean multiple of slightly greater than one in bone samples with low blood forming activity to greater than six in bone with a large proportion of trabecular bone. A general comparison of the major Pu and Am collecting soft tissues with the major Pu and Am collecting skeletal tissues showed Pu enhancement of about 5 to 20 fold in the bone when compared to the soft tissues. These findings indicate major differential metabolism of the two elements, plutonium and americium, when they were absorbed and distributed from subcutaneous implants of PuO_2 .

CHAPTER V

SUMMARY

The translocation of Pu and Am from PuO₂ implants in the paw of the dog has provided indications of the relative metabolism of these two elements. Two mechanisms of translocation, lymphatic transport and blood distribution, were important in the disposition of the subcutaneously placed material.

The amount of Pu at the implant site and in the liver was estimated by the method of external ²⁴¹Am 59.5 keV gamma ray analysis. This method assumed no differential metabolism of Pu and Am. In vivo estimation of the liver Pu content prior to necropsy by this method was compared to that determined by chemical assay techniques. The ²⁴¹Am tracer method overestimated the Pu liver burden by an average of 4.5 fold for untreated dogs and 3.6 fold for DTPA treated dogs.

Rapid movement of the material from the implant site to the first major lymph node draining the site was observed by in vivo counting. Data on the dynamics of Pu and Am localization in the lymphatic system were obtained. The kinetics of the lymph node concentration of the implanted material were best described by power function equations. The equation fitting the data for untreated dogs was:

$$A = 0.255 T^{0.343} - 0.191$$

and for DTPA treated dogs was:

$$A = 1.65 T^{0.101} - 1.729$$

where A is the activity accumulated at the lymph node and T is the post-implant time in days. About 10 percent of the node burden was accumulated in the first two days. This finding supports the current industrial practice of immediately excising any wound in which measurable amounts of Pu or Am are detected. The movement of the subcutaneously placed material from the implant site to the superficial cervical lymph node ranged from an average of 3.3 percent after 1/2 month of implant time to 13.3 percent after 12 months of implant time of the estimated initial amount implanted.

The International Commission on Radiological Protection's (1968) model showing the principle metabolic pathways of radionuclide intake and absorption in the body did not show a wound site to lymph node pathway. The present experimental data strongly indicated the existence of this pathway.

The left superficial cervical lymph node of the dogs received radiation doses estimated to range from 363 rads for a two week dog to greater than 31,000 rads for a long-term dog. The probable induction of lymphosarcoma in one experimental animal was observed. The potential for induction of lymphosarcoma as a result of a plutonium contaminated wound was indicated by this experimental observation.

The use of a lithium drifted germanium detector for simultaneous in vivo measurement of ^{241}Am and ^{239}Pu gamma rays was investigated. This method of external measurement was in need of further optimization by shielding out background radiation and by detector collimation. The potential use of the Ge (Li) detection system for estimating the ^{241}Am content of the material in a contaminated wound was proposed.

Calculation of the Pu/Am activity ratio in blood, urine, feces, and tissue samples was used as an index for the relative metabolism of these elements in the dog. This ratio was divided by the calculated Pu/Am activity ratio of the implant material at the sample assay time to correct for the buildup of ^{241}Am activity over the course of the experiment. These values, called multiples or corrected ratios, provided a basis for comparison of the relative metabolism of Pu and Am with in vivo counting as the frame of reference. Regression analyses of the multiples or corrected ratios of all sample types as a function of post-implant time were completed. These analyses did not show a significant time relationship at the 95 percent confidence level for any sample type.

Mean multiples for each sample type from both untreated and DTPA treated dogs were computed to measure treatment effect and to compare sample types. A significant DTPA treatment effect was observed in urine, liver, and proximal femur tissue samples. Enhancement of the relative Pu content was observed in these three sample

types following DTPA treatment. Samples from DTPA treated dogs showed mean multiple increases of 2, 3, and 5 fold for urine, proximal femur tissue, and liver tissue, respectively. Most of the other tissue samples showed a trend toward Pu enhancement for DTPA treated dogs.

The magnitude of the multiple differed for sample type. Enhancement of Am collection averaged about 15 in the thyroid tissue while Pu enhancement in the vertebrae averaged about 6. These two tissues represented the two multiple or corrected ratio extremes in the data obtained. The general result was Am enhancement in soft tissues and Pu enhancement in skeletal tissue. In the case of skeletal tissue, there seemed to be a direct relationship between the hemopoetic activity of a bone and its Pu collection enhancement. This finding supported previous work showing transferrin transport of Pu and Am to the bone where they were transferred to bone glycoproteins.

These data suggested the need for consideration of the relative metabolism of Pu and Am in interpreting in vivo measurement of Pu burdens via Am measurement. Differential translocation and excretion of these two elements were indicated. The administration of DTPA therapy was shown to have an additional effect on the relative collection of Pu and Am in some body tissues and fluids. The validity of the ^{241}Am tracer method for Pu burden estimation may begin to be assessed as a result of this study.

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APPENDIX A

SAMPLE PREPARATION AND ANALYSIS

Urine Samples

1. Add a known quantity of Pu-236 as an internal standard.
2. Wet digest the sample with concentrated nitric acid and heat ($\sim 400^{\circ}\text{C}$) (to destroy organic compounds and any DTPA present and to solubilize the plutonium and americium).
3. Coprecipitation procedure - Pu and Am precipitated with Ca and Mg (as phosphates) with NH_4OH in a steam bath. Allow settling for 4 or more hours and discard the supernatant.
4. Wet ash the precipitate with concentrated HNO_3 and heat (to destroy any residual organics). Completion of this step yields an ash.

Ash

1. Dissolve the ash in 1 N HNO_3 , add hydroxylamine hydrochloride to reduce the Pu to valence III or IV, and allow to stand overnight.
2. Add concentrated HNO_3 to bring the solution to 7.3 N in HNO_3 and then bring just to boil (to take Pu to valence IV and destroy the hydroxylamine).
3. This solution is passed through a DOWEX 1 x 2 resin column (2% cross-linked anion resin).
4. The effluent is collected for Am analysis as described in steps 9-16.

5. The column is washed with 3 ml of concentrated HCl (to remove any thorium or uranium present), this effluent is discarded.
There should be minimum delay between steps 5 and 6 because of aquaregia formation.
6. Hydroxylamine hydrochloride crystals are added to the top of the column (to prevent oxidation of NH_4I) and a solution of 0.5 N HCl saturated with NH_4I is passed through the column.
7. The column is rinsed with an additional portion of 0.5 N HCl.
8. Portions 6 and 7 are collected for Pu analysis and wet ashed (with HNO_3) to destroy the chloride and iodide ions which attack the planchet. The solution is mounted on a planchet by direct evaporation. The planchet is flamed and an alpha particle pulse height analysis is made providing chemical yield (by use of the Pu-236) and an alpha count is made. The total disintegrations per minute of Pu is reported for the sample.
9. For Am-241 analysis, dissolve the salt residue from step 4 in 75 ml of 1.5 N HCl.
10. Charge a column of DOWEX 50 1 x 8 cation resin with 25 ml of 1.5 N HCl.
11. Pass the sample through the column and discard the effluent.
12. Rinse the column with 75 ml of 2 N HCl and discard the effluent.
13. Ellute the activity with 80 ml of 6 N HCl and collect the ellutrient.

14. Evaporate the ellutrient to dryness and take it up in HNO_3 as in step 8.
15. Quantitatively transfer this solution to a planchet and count to determine the total disintegrations per minute of Am for the sample.
16. Recharge the resin column as in step 10.

Blood Samples

1. Wet digest with concentrated HNO_3 and heat ($\sim 400^\circ\text{C}$). Repeat several times until no further color change takes place.
2. Add a mixture of nitric and perchloric acid (3 : 1) and take to a white ash.
3. Proceed as in urine assay beginning with step 1 of the urine ash procedure.

Tissue Samples

1. Add Pu-236 as an internal standard.
2. All tissue samples are wet digested using the same procedures as those outlined above for blood.

Feces Samples

1. Transfer the sample to a 2 liter beaker and add a known quantity of Pu-236 as an internal standard.

2. Add 400-500 ml of 8 N nitric acid along with glass beads and 1 to 2 ml of octanol to the sample in the beaker. Let the sample stand in the hood for 1 to 2 hours without heating (until mushy).
3. Place a speedy vap on the beaker and set it on the hot plate and slowly bring to a boil. Wash down the sides of the beaker with concentrated nitric acid occasionally to keep the beaker clean and keep the sample from sticking to the sides.
4. Bring to dryness and ash with concentrated nitric acid, enough to wet ash but not burn. Some samples can be ashed to white with nitric acid but stubborn samples have to be ashed with 25-50 ml of 1 : 4 nitric-perchloric acid mixture on a very hot hot-plate.
(Warning: Be sure sample is a light tan in color and not brown or black before using the perchloric acid mixture, as the sample might explode if too many organics are present.)
5. Leave on the hot-plate until all perchloric acid has evaporated from the sides and rim of the beaker and the speedy vap.
6. Add 100 to 400 ml (depending on amount of salts) of 0.5 N HCl and let stand for an hour. Swirl to dissolve as much residue as possible and place on low heat until the sample is brought to dryness. The sample is ready for the centrifuge.

Centrifuging

1. Add 100 ml of distilled water and 15 ml of concentrated nitric acid to the fecal ash. Cover the beaker with a speedy vap and boil one minute.
2. Transfer the solution to a 500 ml centrifuge bottle. Rinse the beaker with 1.5 N nitric acid with heat and transfer to the centrifuge bottle. The rinse is repeated twice more with 100 ml portions of distilled water giving an approximate final volume of 400 ml.
3. The acid solution is allowed to cool completely to room temperature and then centrifuged at 2000 RPM for five minutes.
4. Transfer the supernatant carefully to a one liter beaker. Filter if necessary.
5. Add 15 gm of mono-chloroacetic acid, 5 ml of sulfurous acid, 1 - 2 gm of hydroxylamine hydrochloride, and 10 ml of concentrated phosphoric acid. Stir magnetically for 20 - 30 minutes at room temperature.
6. Add 10 - 15 ml thymol blue indicator and then slowly add concentrated sodium hydroxide to the stirring mixture allowing the white curdy precipitate of calcium phosphate to redissolve between additions. When the yellow-orange end-point is approached, switch to the use of 2 N sodium hydroxide to final neutralization. (If neutralization has proceeded to the yellowish side of the

buffered end-point, without the formation of a flocculent iron phosphate precipitate, then add approximately 20 mg of iron as ferric nitrate solution.) NOTE: The iron phosphate precipitate imparts a cloudy appearance to the solution.

7. The sample can now either be centrifuged or filtered to concentrate the precipitate or the precipitate may be allowed to settle in the beaker over a period of time and the supernatant asperated off.
8. After the precipitate has been dissolved in concentrated HCl, add 10 drops of concentrate nitric acid to the solution. Bring it to a boil and allow to cool to room temperature.
9. The sample is passed through a resin column and planchet mounted for counting as described under urine ash beginning with step 3.

EXPERIMENTAL ERRORS

The PuO_2 implant material was prepared, chemically analyzed, and particle sized in the Rocky Flats Laboratories prior to use in this study. No measure of the reliability of these characterizations was provided. The reported values for the amount of ^{241}Pu and ^{241}Am present were the basis for extrapolation of the Pu/Am ratio in the implant material. A small error in the reported values would not affect any conclusions drawn since the relative Pu/Am ratio in the samples was the objective. A change in the initial Pu/Am ratio value would produce a proportionately constant change in the sample multiples.

The dogs received only a minimal amount of metabolism cage conditioning prior to being placed on experiment. Some of the animals "held back" on urine and feces sample production. This was not considered a significant problem with the untreated dogs. The DTPA treated dogs received treatment after the first 24 hours in the cage. Since there were about 4 weeks between sample collections, the Pu/Am activity ratio in the blood, urine, and feces may have been at the untreated dog level initially. Following application of the DTPA treatment, a different Pu/Am activity ratio may have obtained in the blood, urine, and feces. Those DTPA treated animals "holding back" on sample production for several days were in effect

biologically integrating untreated and DTPA treated blood, urine, and feces Pu/Am ratios. This source of error may be considered part of an overall biological variable.

The most significant potential error may have been in the chemical analysis for americium. A known amount of ^{236}Pu was added to the samples as an internal standard to determine the chemical yield for plutonium. There was no americium isotope available for use as an internal standard. An average chemical yield was measured by spiking uncontaminated samples with known amounts of ^{241}Am . Average chemical yield values were computed and used for all the ^{241}Am determinations. The average chemical recovery values showed a narrow range in the spiked samples. However, some samples have shown a considerable range in the Pu chemical yield values. If the americium recovery varied as widely as the plutonium (30 - 100%) an error in some samples could have been as large as a multiple of three. This possible source of error may partially explain the wide range in Pu/Am ratios observed in the various samples. The use of an average americium recovery value contributed to the data scatter about the regression line of the multiple of the Pu/Am ratio versus post-implant time.

APPENDIX B

Table 1. Blood Sample Data

<u>Time</u> <u>Implanted</u>	<u>Dis/Min-Ml</u>	<u>Dis/Min-Ml</u>	
<u>Days</u>	<u>Pu</u>	<u>Am</u>	<u>Ratio of Pu/Am</u>

Dog No. 1991, no treatment, 1/2 month study time

1	2.573	0.149	17.27
2	0.667	0.569	1.17
3	1.487	0.184	8.08
4	0.433	1.166	0.37
5	1.703	0.018	94.61
6	1.860	0.475	3.91
7	0.241	0.964	0.25
9	0.473	0.073	6.48
11	0.487	0.821	0.59
14	0.978	0.375	2.61

Dog No. 2602, no treatment, 1/2 month study time

1	3.637	0.963	3.78
2	0.507	0.109	4.65
3	0.583	0.215	2.71
4	1.967	0.300	6.56
5	0.927	0.270	3.43
6	1.097	0.171	6.42
7	1.187	0.632	1.88
9	1.093	0.395	2.77
11	1.613	0.487	3.31
14	0.752	0.195	3.86

Dog No. 2179, DTPA treatment, 1/2 month study time

1	0.180	0.046	3.91
2	0.150	0.047	3.19
3	0.263	0.096	2.74
4	0.117	0.124	0.94
5	0.197	0.013	15.15
6	0.427	0.015	28.47
7	0.093	0.078	1.19
9	0.033	1.045	0.03

11	0.470	0.429	1.10
14	0.131	0.024	5.46

Dog No. 2531, DTPA treatment, 1/2 month study time

1	1.077	0.389	2.77
2	0.823	0.078	10.55
3	0.290	0.649	0.45
4	0.677	0.376	1.80
5	0.193	0.155	1.25
6	0.540	0.360	1.50
7	0.903	0.525	1.72
9	0.130	0.495	0.26
11	0.493	0.458	1.08
14	0.671	0.087	7.71

Dog No. 2912, no treatment, 1 month study time

1	58.30	8.353	6.97
2	23.98	3.344	7.17
3	3.679	4.155	0.89
4	6.285	0.580	10.84
5	0.908	0.467	1.94
6	1.008	0.429	2.35
7	0.617	0.408	1.51
9	1.779	0.512	3.47
11	1.958	0.122	16.05
14	0.313	0.089	3.52
30	3.617	0.323	11.20
31	2.025	0.286	7.08
32	0.044	0.267	0.16

Dog No. 2532, no treatment, 1 month study time

1	2.008	0.143	14.04
2	0.890	0.178	5.00
3	0.479	2.091	0.23
4	0.288	1.388	0.21
5	0.858	0.204	4.21
6	1.323	0.146	9.06
7	0.621	0.925	0.67
9	3.146	1.696	1.85

11	2.729	0.284	9.61
14	2.007	0.053	37.87
30	2.835	0.055	51.55
31	2.355	0.047	50.11
32	0.715	0.533	1.34

Dog No. 1308, DTPA treatment, 1 month study time

1	5.096	1.263	4.03
2	2.413	2.568	0.94
3	0.829	0.933	0.89
4	1.113	1.545	0.72
5	1.165	1.033	1.13
6	1.830	0.238	7.69
7	1.100	0.495	2.22
9	4.771	0.935	5.10
11	4.883	0.292	16.72
14	8.037	0.023	349.40
30	7.500	0.086	87.21
31	4.415	0.086	51.34
32	2.816	0.204	13.80

Dog No. 2666, DTPA treatment, 1 month study time

1	4.721	1.100	4.29
2	2.517	0.663	3.80
3	1.315	0.736	1.79
4	1.179	1.615	0.73
5	1.288	0.746	1.73
6	9.713	0.679	14.30
7	0.860	0.424	2.03
9	2.363	--	--
11	4.433	0.158	28.06
14	5.933	0.642	9.24
30	3.360	0.642	5.23
31	2.740	0.072	38.06
32	2.232	0.201	11.10

Dog No. 3018, no treatment, 1.4 months study time

1	0.163	0.094	1.73
2	0.125	0.543	0.23

3	0.842	0.591	1.42
4	3.396	0.245	13.86
5	contaminated	0.582	--
6	5.008	4.127	1.21
7	3.208	2.485	1.29
9	0.192	3.047	0.06
11	0.167	2.541	0.07
14	0.200	1.294	0.15
29	1.296	0.495	2.62
30	1.940	3.684	0.53
31	0.060	0.043	1.40
42	wound site 1.1×10^7		
	washing 6.4×10^4		

Dog No. 2853, no treatment, 2 months study time

1	0.500	0.158	3.16
2	lost	lost	--
3	0.813	0.138	5.89
4	0.975	0.160	6.09
5	1.267	0.172	7.37
6	1.925	0.261	7.38
7	2.004	0.258	7.77
9	0.437	0.191	2.29
11	0.530	0.099	5.35
14	0.860	0.058	14.83
28	1.254	0.100	12.54
29	1.042	0.163	6.39
30	0.992	--	--
60	0.757	0.638	1.19
61	0.637	0.112	5.69
62	4.033	0.323	12.49

Dog No. 2570, no treatment, 2 months study time

1	2.407	0.420	5.73
2	0.520	0.071	7.32
3	3.571	0.128	27.90
4	3.058	0.210	14.56
5	9.663	0.854	11.31
6	2.379	0.157	15.15
7	2.975	0.121	24.59
9	2.561	0.156	16.42

11	0.110	0.103	1.07
14	2.610	0.050	52.20
28	1.015	0.241	4.21
29	2.958	0.392	7.55
30	lost	lost	--
60	1.623	0.468	3.47
61	2.167	0.596	3.64
62	contaminated	0.457	--

Dog No. 1403, DTPA treatment, 2 months study time

1	0.910	0.101	9.01
2	0.580	0.053	10.94
3	0.954	0.050	19.08
4	2.083	0.197	10.57
5	1.546	0.213	7.26
6	1.954	0.172	11.36
7	2.075	0.439	4.73
9	1.700	0.156	10.90
11	0.657	1.267	0.52
14	2.250	0.047	47.87
28	0.367	5.070	0.07
29	1.323	0.113	11.71
30	1.727	--	--
60	1.046	0.118	8.86
61	1.130	0.038	29.74
62	5.702	0.265	21.52

Dog No. 1219, DTPA treatment, 2 months study time

1	3.063	0.292	10.49
2	0.130	0.153	0.85
3	0.596	0.150	3.97
4	0.479	0.359	1.33
5	1.346	0.127	10.60
6	0.892	0.511	1.75
7	1.502	0.278	5.40
9	1.253	0.154	8.14
11	1.380	0.809	1.70
14	0.683	0.294	2.32
28	1.983	0.068	29.16
29	1.288	0.056	23.00
30	lost	lost	--

60	0.317	3.185	0.10
61	0.943	0.060	15.72
62	5.032	0.180	27.96

Dog No. 2865, no treatment, 3 months study time

1	0.058	0.122	0.48
2	0.075	0.396	0.19
3	0.875	0.290	3.02
4	0.404	0.235	1.72
5	1.288	0.353	3.65
6	1.875	0.235	7.98
7	1.821	0.812	2.24
9	0.175	1.926	0.09
11	0.433	0.768	0.56
14	0.367	0.629	0.58
29	1.525	0.122	0.13
30	1.280	0.475	2.69
31	0.200	0.474	0.42
55	2.531	0.025	101.24
56	1.717	0.020	85.85
57	0.150	0.216	0.69
89	0.363	0.180	2.02
90	0.158	0.227	0.70
91	lost	lost	--

Dog No. 2280, DTPA treatment, 3 months study time

1	0.292	0.097	3.01
2	0.946	0.063	15.02
3	0.817	0.085	9.61
4	0.613	0.051	12.02
5	0.033	0.169	0.20
6	1.142	1.772	0.64
7	0.388	0.221	1.76
9	0.592	0.665	0.89
11	1.000	0.338	2.96
14	1.821	0.031	58.74
29	0.677	0.384	1.75
30	0.180	0.090	2.00
31	0.973	0.069	14.10
55	1.365	0.017	80.29
56	1.979	0.031	63.84

57	1.233	0.053	23.26
89	0.146	0.313	0.47
90	--	--	--
91	0.354	2.542	0.14

Dog No. 2894, DTPA treatment, 3 months study time

1	0.517	0.043	12.02
2	0.183	0.229	0.80
3	0.088	0.103	0.85
4	0.238	0.118	2.02
5	0.258	0.076	3.39
6	0.933	0.127	7.35
7	0.063	0.482	0.13
9	1.021	1.712	0.60
11	0.329	0.703	0.47
14	1.613	0.062	26.01
29	0.488	0.292	1.67
30	0.270	0.270	1.00
31	0.763	0.793	0.96
55	0.792	0.550	1.44
56	0.825	0.039	21.15
57	0.192	0.153	1.25
89	0.268	0.585	0.46
90	0.329	0.553	0.59
91	1.308	0.858	1.52

Dog No. 1633, no treatment, 4 months study time

1	lost	0.304	--
2	1.758	0.455	3.86
3	0.894	2.932	0.30
4	0.858	0.128	6.70
5	2.254	1.353	1.67
6	0.827	1.010	0.82
7	1.654	0.468	3.53
9	1.875	0.203	9.24
10	--	--	--
11	1.344	0.625	2.15
14	1.888	0.366	5.16
32	1.120	0.110	10.18
33	1.430	1.120	1.28
34	2.512	0.281	8.94

35	--	--	--
60	1.304	0.018	72.44
61	1.121	0.120	9.34
62	--	--	--
88	0.854	0.050	17.08
89	0.900	0.035	25.71
90	--	--	--
123	0.546	0.060	9.10
124	0.697	0.015	46.50
125	2.210	0.110	20.00

Dog No. 0650, no treatment, 4 months study time

1	lost	1.424	--
2	1.702	0.055	30.95
3	0.217	2.280	0.10
4	0.550	1.090	0.50
5	1.890	0.108	17.50
6	0.475	0.990	1.08
7	0.558	0.605	0.92
9	0.900	0.258	3.49
10	--	--	--
11	0.908	0.840	1.08
14	1.922	--	--
32	1.123	0.718	1.56
33	1.500	0.143	10.49
34	2.278	0.163	13.98
35	--	--	--
60	1.117	0.068	16.43
61	1.125	0.045	25.00
62	--	--	--
88	0.670	0.040	16.75
89	0.633	0.058	10.91
90	--	--	--
123	0.420	0.143	2.94
124	0.893	0.040	22.30
125	0.997	0.203	4.90

Dog No. 1696, DTPA treatment, 4 months study time

1	2.860	1.563	1.83
2	0.883	1.403	0.63
3	0.470	0.150	3.13

4	0.863	0.204	4.23
5	0.150	0.035	4.29
6	0.067	none detected	--
7	0.530	0.712	0.74
9	0.916	0.050	18.32
10	--	--	--
11	0.631	7.145	0.09
14	1.325	0.060	22.08
32	1.086	0.770	1.41
33	0.850	0.060	14.17
34	0.596	0.038	15.68
35	--	--	--
60	1.296	0.136	9.53
61	0.850	0.020	42.50
62	--	--	--
88	0.996	0.080	12.45
89	0.718	0.240	2.99
90	--	--	--
123	0.742	0.208	3.57
124	0.530	0.130	4.08
125	1.420	0.105	13.50

Dog No. 1008, DTPA treatment, 4 months study time

1	lost	1.288	--
2	1.077	0.160	6.73
3	0.279	0.094	2.97
4	1.167	0.414	2.82
5	1.309	0.888	1.47
6	0.505	0.258	1.96
7	0.460	0.183	2.51
9	1.017	0.105	9.69
10	--	--	--
11	0.828	3.468	0.24
14	1.179	0.066	17.86
32	0.626	0.400	1.57
33	0.563	0.353	1.59
34	1.229	0.028	43.89
35	--	--	--
60	1.177	0.044	26.75
61	0.983	0.048	20.48
62	--	--	--
88	0.903	0.038	23.76
89	0.870	0.028	31.07

123	0.833	0.200	4.16
124	0.647	2.566	0.25
125	3.238	0.098	33.10

Dog No. 1353, no treatment, 4.57 months study time

1	1.233	0.335	3.68
2	lost	0.160	--
3	0.479	0.250	1.92
4	1.417	2.362	0.60
5	0.353	0.250	1.41
6	0.971	2.738	0.35
7	0.571	2.233	0.26
9	1.917	3.745	0.51
11	0.346	0.620	0.56
14	0.596	0.150	3.97
32	2.090	0.341	6.13
33	1.260	0.364	3.46
34	1.093	0.140	7.81
60	0.196	0.048	4.08
61	1.242	0.048	25.88
88	0.810	0.045	18.00
89	0.923	0.038	24.29
123	0.607	0.033	18.40
124	1.473	0.220	6.69
137	0.165	0.013	12.70

Dog No. 0925, no treatment, 5 months study time

1	lost	0.853	--
2	lost	0.428	--
3	0.374	0.338	1.11
4	0.350	0.294	1.19
5	0.875	0.570	1.54
6	1.429	0.040	35.73
7	1.850	0.103	17.96
9	2.021	0.133	15.20
11	0.864	4.198	0.21
14	0.758	0.886	0.86
32	3.521	0.319	11.04
33	0.588	0.513	1.15
34	1.205	0.095	12.68
60	1.500	0.075	20.00

61	0.688	0.085	8.09
88	1.000	0.035	28.57
89	0.958	0.090	10.64
123	0.526	0.274	1.92
124	0.610	0.073	8.36
153	1.023	0.173	5.92

Dog No. 1429, DTPA treatment, 5 months study time

1	2.840	0.258	11.00
2	lost	0.310	--
3	0.350	0.562	0.62
4	0.879	0.030	29.30
5	0.075	0.163	0.46
6	0.240	0.180	1.33
7	0.446	0.090	4.96
9	1.075	0.740	1.45
11	0.208	0.483	0.43
14	0.503	0.043	11.70
32	1.744	0.096	18.67
33	0.864	0.483	1.79
34	1.042	1.309	0.80
60	0.883	0.073	12.10
61	0.367	0.025	14.68
88	1.078	0.248	4.35
89	1.001	0.120	8.34
123	0.183	0.015	42.20
124	0.437	0.058	7.54
125	0.156	0.018	8.67
151	0.250	0.028	8.93
152	0.167	0.023	7.26
153	0.613	0.060	10.20

Dog No. 2963, DTPA treatment, 5 months study time

1	0.887	0.190	4.67
2	lost	0.718	--
3	0.375	1.142	0.33
5	0.913	1.505	0.61
6	1.746	1.415	1.23
7	1.104	0.258	4.28
9	0.875	0.135	6.48
11	0.354	0.655	0.54

14	2.483	0.296	8.39
32	0.879	0.790	1.11
33	0.363	0.593	0.61
34	1.450	0.080	18.12
60	1.388	0.055	25.24
61	0.363	0.045	8.07
88	1.093	0.080	13.66
89	0.925	0.098	9.44
123	0.723	0.058	12.50
124	0.883	0.103	8.57
125	4.148	0.353	11.70
151	0.377	0.048	7.85
152	0.260	0.035	7.43
153	2.000	0.268	7.46

Dog No. 0659, no treatment, 6 months study time

1	2.703	0.032	84.46
2	0.053	0.573	0.09
3	1.530	0.087	17.58
4	1.638	0.983	1.67
5	0.250	0.158	1.58
6	1.972	0.454	4.34
7	1.867	0.388	4.81
9	1.563	0.088	17.76
11	2.030	0.488	4.16
14	1.697	0.121	14.02
28	1.783	0.103	17.31
29	4.300	0.128	33.59
30	1.317	--	--
60	0.379	0.806	0.47
61	3.696	0.575	6.43
62	1.250	0.295	4.23
91	0.833	0.034	24.50
92	0.417	0.043	9.69
119	0.758	0.065	11.66
120	0.395	0.146	2.71
147	0.308	0.020	15.40
148	0.346	0.043	8.05
184	0.065	0.008	8.14

Dog No. 0004, no treatment, 6 months study time

2	1.370	0.150	9.14
3	0.188	0.038	4.95
4	0.650	0.163	3.99
5	1.771	1.058	1.67
6	1.654	0.192	8.61
7	1.850	0.313	5.91
9	1.107	0.013	85.15
11	0.080	0.079	1.01
14	0.290	0.158	1.83
28	0.129	0.231	0.56
29	0.658	0.467	1.41
30	1.892	0.105	18.02
60	1.196	0.110	10.87
61	1.400	0.092	15.20
62	1.273	0.350	3.64
91	0.785	0.062	12.66
92	0.292	0.034	8.59
119	0.642	0.120	5.35
120	0.254	0.010	25.40
147	0.279	0.088	6.06
148	0.271	0.205	1.32
184	0.165	0.024	6.88

Dog No. 2761, DTPA treatment, 6 months study time

1	1.967	0.747	2.63
2	0.413	0.119	3.47
3	0.804	--	--
4	0.633	0.054	11.72
5	0.588	0.079	7.44
6	0.546	0.040	13.65
7	0.725	0.075	9.67
9	0.720	0.022	32.72
11	0.577	0.137	4.21
14	0.403	0.147	2.74
28	0.788	0.088	8.95
29	0.621	0.041	15.15
30	0.450	--	--
60	1.412	0.222	6.36
61	0.567	0.088	6.44
62	0.757	0.160	4.73
91	0.730	0.208	3.51

92	0.725	0.140	5.18
119	0.500	none detected	--
120	0.217	0.098	2.21
147	0.392	0.015	26.13
148	0.438	0.327	1.34
149	0.304	0.118	2.58
182	0.177	0.040	4.42
183	0.197	0.028	7.04
184	0.076	0.010	7.60

Dog No. 1990, DTPA treatment, 6 months study time

1	1.320	0.581	2.27
2	0.370	1.290	0.29
3	1.171	--	--
4	1.092	0.100	10.92
5	1.288	0.300	4.29
6	0.592	0.071	8.34
7	1.192	0.136	8.76
9	1.247	0.025	49.88
11	1.060	0.227	4.67
14	0.327	0.263	1.24
28	1.392	0.094	14.80
29	1.392	0.128	10.88
30	1.050	--	--
60	0.492	0.198	2.48
61	4.010	0.425	9.44
62	1.210	0.165	7.33
91	0.496	0.220	2.25
92	0.610	0.058	10.51
119	0.354	0.050	7.08
120	0.342	0.048	7.13
148	0.179	0.023	7.78
149	0.175	0.015	11.67
182	0.084	0.004	21.00
183	0.248	0.022	11.30
184	0.041	0.005	8.20

Dog No. 1687, no treatment, 7 months study time

1	1.727	0.400	4.32
2	1.360	0.092	14.78
3	1.676	--	--

4	1.392	--	--
5	0.958	0.395	2.43
6	1.442	0.196	7.36
7	1.767	1.533	1.15
9	1.210	0.281	4.31
11	0.053	0.046	1.15
14	0.120	0.603	0.20
28	1.350	0.176	7.67
29	2.722	0.154	17.68
30	0.508	--	--
60	1.008	0.393	2.56
61	1.043	0.065	16.04
62	1.129	2.543	0.44
91	0.392	1.876	0.21
92	0.150	0.020	7.50
119	0.108	0.030	3.60
120	0.217	0.014	15.50
147	0.204	0.005	40.80
148	0.171	0.050	3.42
182	0.356	0.025	14.20
183	0.144	0.008	18.00
212	2.634	0.200	13.15

Dog No. 2325, no treatment, 7 months study time

1	3.207	0.052	61.67
2	1.047	0.250	4.19
3	4.354	--	--
4	1.013	--	--
5	2.058	1.713	1.20
6	4.854	1.364	3.56
7	4.316	0.503	8.58
9	4.583	3.595	1.27
11	5.047	0.365	13.83
14	5.343	0.503	10.64
28	2.025	0.524	3.86
29	2.671	3.048	0.88
30	3.133	--	--
60	0.679	0.305	2.23
61	1.357	0.392	3.46
62	0.287	0.223	1.29
91	0.548	0.238	2.30
92	0.883	0.043	20.53
119	0.850	0.063	13.49

120	0.883	0.018	49.06
147	0.433	0.025	17.32
148	0.553	0.100	5.53
182	0.253	0.080	3.16
183	0.358	0.018	19.90
212	2.322	0.279	8.32

Dog No. 2100, DTPA treatment, 7 months study time

1	0.903	0.034	26.56
2	1.067	0.272	3.92
3	1.017	--	--
4	0.529	--	--
5	1.067	0.414	2.58
6	1.179	0.133	8.86
7	1.513	0.150	10.09
9	0.227	0.133	1.71
11	1.643	0.041	40.07
14	1.663	0.047	35.38
28	0.227	0.089	2.55
29	1.771	0.108	16.40
30	0.725	--	--
60	1.267	0.230	5.51
61	6.073	0.234	25.95
62	0.890	0.280	3.18
91	0.717	0.010	71.70
92	0.521	0.050	24.76
119	0.433	0.050	8.66
120	0.242	0.046	5.26
147	0.242	0.025	9.68
148	0.196	0.078	2.51
149	0.326	0.102	3.20
182	0.224	none detected	--
183	0.367	0.050	7.34
184	0.123	0.050	2.46
210	0.747	0.141	5.30
211	3.106	0.146	21.30
212	2.104	0.133	15.80

Dog No. 1803, DTPA treatment, 7 months study time

1	2.347	0.303	7.75
2	0.860	0.151	5.70

3	0.053	--	--
4	0.433	--	--
5	0.988	0.271	3.65
6	0.788	0.076	10.36
7	0.942	0.126	7.48
9	1.520	0.069	22.02
11	1.867	0.096	19.44
14	0.389	0.521	0.75
28	0.753	0.450	1.67
29	0.641	0.267	2.40
30	0.888	--	--
60	1.931	0.255	7.57
61	1.110	0.724	1.53
62	6.020	--	--
91	1.513	0.095	15.92
92	1.279	0.932	1.37
119	1.067	0.104	10.26
120	0.754	0.133	5.67
147	0.358	0.030	11.93
148	0.163	0.040	4.07
149	0.388	0.070	5.54
182	0.507	0.230	2.20
183	0.330	0.015	22.00
184	1.670	0.193	8.66
210	5.178	0.255	
211	0.517	0.050	10.35
212	2.963	0.182	16.25

Dog No. 0792, no treatment, 9 months study time

1	0.613	0.797	0.77
2	1.113	0.196	5.68
3	0.120	2.250	0.05
4	0.083	0.928	0.09
5	0.010	0.925	0.01
6	0.760	0.631	1.20
7	0.633	0.766	0.83
9	0.097	1.220	0.08
11	0.372	0.463	0.80
14	0.067	0.781	0.09
30	1.500	0.303	4.95
31	2.342	0.060	39.03
32	1.996	0.075	26.61
66	0.980	0.133	7.37

67	2.308	0.023	100.35
68	0.661	0.008	82.63
99	0.050	0.038	1.32
100	0.788	0.132	5.97
101	0.863	0.183	4.72
132	1.217	0.010	121.70
133	0.977	0.043	22.72
134	0.913	0.350	2.61
160	1.075	0.040	26.88
161	0.871	0.045	19.36
188	0.650	0.033	19.70
189	0.715	0.206	3.47
223	4.708	0.208	22.60
224	0.490	0.213	2.30
251	0.327	0.040	8.18
252	0.347	0.043	8.07
274	2.068	0.025	82.50

Dog No. 1367, no treatment, 9 months study time

1	2.270	0.347	6.54
2	1.000	0.417	2.40
3	1.865	0.339	5.50
4	3.027	0.600	5.05
5	0.290	0.666	0.44
6	0.457	0.728	0.63
7	1.213	1.760	0.69
9	0.550	1.680	0.33
11	2.925	--	--
14	0.533	0.674	0.79
30	4.217	0.279	15.11
31	4.283	0.008	535.38
32	4.354	0.185	23.54
66	0.170	0.292	0.58
67	3.917	0.041	95.54
68	3.515	2.798	1.26
99	0.123	0.120	1.03
100	1.025	3.104	0.33
101	1.225	4.643	0.26
132	0.943	1.080	0.87
133	0.790	0.060	13.17
134	0.954	0.022	43.36
160	0.575	0.070	8.21
161	0.813	0.200	4.07

189	0.970	0.140	6.93
223	0.270	0.045	6.00
224	0.663	0.090	7.37
251	0.330	0.044	7.50
252	0.437	0.030	14.60
274	3.196	0.305	10.45

Dog No. 2447, DTPA treatment, 9 months study time

1	1.353	0.044	30.75
2	0.307	0.161	1.91
3	2/437	0.472	5.16
4	2.150	0.128	16.79
5	0.163	0.480	0.34
6	0.013	0.209	0.06
7	0.387	0.703	0.55
9	0.443	0.519	0.85
11	0.490	0.307	1.60
14	1.104	0.139	7.94
30	1.371	0.153	8.96
31	1.571	0.010	15.71
32	1.729	0.070	24.70
66	0.100	0.261	0.38
67	0.538	0.124	4.34
68	0.796	0.205	3.88
99	0.558	3.143	0.18
100	0.413	0.038	10.87
101	0.246	lost	--
132	0.650	0.022	29.55
133	0.246	0.043	5.72
134	0.317	0.028	11.32
160	0.142	0.025	5.68
161	0.175	0.043	4.07
188	0.333	0.050	6.66
189	0.225	0.075	3.00
223	0.143	0.023	6.22
224	0.110	0.045	2.44
225	0.623	0.068	9.17
251	0.167	0.028	5.97
252	0.117	0.050	2.34
253	0.233	0.100	2.33
272	0.532	0.268	1.99
273	1.286	0.123	10.45
274	2.460	0.030	82.00

Dog No. 3032, DTPA treatment, 9 months study time

1	1.380	0.519	2.65
2	0.210	0.886	0.23
3	0.220	0.483	0.45
4	0.137	0.650	0.21
5	1.125	0.189	5.95
6	0.343	0.081	4.23
7	0.137	0.613	0.22
9	0.620	0.782	0.79
11	0.153	0.114	1.34
13 wound excised			
14	0.308	0.437	0.70
15	0.246	0.063	3.90
16	0.454	0.043	10.56
17	0.129	0.052	2.48
18	0.058	0.200	0.29
19	0.154	0.030	5.13
20	0.279	0.030	9.30
30	0.596	0.332	1.80
31	0.233	0.020	11.65
32	0.413	0.088	4.69
66	1.945	0.317	6.14
67	0.500	0.092	5.43
68	0.203	0.097	2.09
99	0.196	0.240	0.82
100	0.167	0.085	1.96
101	0.298	lost	--
132	0.354	0.258	1.37
133	0.358	0.037	9.68
134	0.213	0.398	0.54
160	0.246	0.053	4.64
161	0.175	0.090	1.94
188	0.183	0.025	7.32
189	0.117	0.043	2.72
223	0.490	0.123	4.00
224	0.243	0.020	12.15
225	0.050	0.010	5.00
251	0.113	0.019	5.95
252	0.093	0.020	4.65
253	0.090	0.012	7.50
272	0.100	0.015	6.67
273	0.427	none detected	--
274	1.883	0.038	49.50

Dog No. 1688, no treatment, 12 months study time

1	0.117	0.113	1.04
2	0.110	0.161	0.68
3	0.267	0.107	2.50
4	0.183	0.023	7.96
5	0.043	0.040	1.08
6	0.150	0.085	1.76
7	0.133	0.055	2.42
9	0.145	0.060	2.42
12	0.081	0.178	0.46
14	0.160	0.013	12.30
31	0.047	0.077	0.61
32	0.140	0.095	1.47
33	0.027	0.089	0.30
65	0.204	0.020	10.20
66	0.250	0.033	7.57
67	0.821	0.373	2.20
100	0.135	0.057	2.37
101	0.667	0.019	35.11
102	0.225	--	--
130	none detected	1.626	--
131	0.033	none detected	--
132	0.025	0.063	0.40
166	0.103	0.015	6.87
167	0.107	0.023	4.65
168	0.071	0.182	0.39
194	0.092	0.080	1.15
195	0.042	0.018	2.33
222	0.129	0.020	6.45
223	0.104	0.052	2.00
257	0.100	0.050	2.00
258	0.100	0.038	2.64
285	0.096	0.035	2.74
286	0.037	0.008	4.62
307	0.127	0.048	2.65
334	0.182	0.014	1.30
335	0.070	0.006	11.65
362	0.094	0.010	9.40
364	0.574	0.010	57.40

Dog No. 1689, no treatment, 12 months study time

1	0.153	0.283	0.54
2	0.463	0.048	9.65
3	0.317	0.036	8.81
4	0.170	0.088	1.93
5	0.103	0.074	1.39
6	0.217	0.025	8.68
7	0.160	0.034	4.70
9	0.177	0.030	5.90
12	0.110	0.009	12.20
14	0.047	0.072	0.65
31	0.113	0.040	2.83
32	0.103	0.101	1.02
33	0.060	0.103	0.58
65	0.188	0.050	3.76
66	0.108	0.074	1.46
67	0.213	0.036	5.92
100	0.740	0.504	1.47
101	0.271	none detected	--
102	0.342	none detected	--
130	none detected	2.400	--
131	0.161	3.978	0.04
132	0.079	0.098	0.81
166	0.134	0.018	7.44
167	0.277	0.054	5.13
168	0.113	0.010	11.30
194	0.117	0.020	5.85
195	0.050	0.008	6.25
222	0.083	none detected	--
223	0.121	0.015	8.07
257	0.310	0.037	8.39
258	0.183	0.085	2.15
285	0.067	0.026	2.58
286	0.077	0.013	5.92
307	0.273	0.030	9.10
334	0.164	0.008	20.50
335	0.130	0.026	5.00
362	lost	lost	--
364	0.588	0.016	36.70

Dog No. 2315, DTPA treatment, 12 months study time

1	0.743	0.178	4.17
2	0.150	0.330	0.45
3	0.020	0.244	0.08
4	0.183	0.051	3.58
5	0.073	0.105	0.70
6	0.187	0.103	1.82
7	0.113	0.058	1.95
9	0.070	0.072	0.97
12	0.303	0.141	2.15
14	0.237	0.124	1.91
31	0.287	0.099	2.88
32	0.303	0.083	3.65
33	0.287	0.082	3.50
62	0.046	0.232	0.20
63	0.133	0.219	0.61
64	0.425	0.016	26.56
100	2.180	0.322	6.77
101	0.167	none detected	--
102	0.342	0.008	42.75
130	0.033	2.198	0.02
131	0.117	0.035	3.34
132	0.275	0.111	2.48
166	0.163	0.043	3.79
167	0.666	0.103	6.47
168	0.103	0.183	0.56
194	0.150	0.023	6.52
195	0.063	0.026	2.74
222	0.125	0.015	8.33
223	0.079	0.018	4.39
257	0.203	0.033	6.15
258	0.113	0.088	1.28
259	0.077	0.025	3.08
285	0.067	0.008	8.37
286	0.190	0.038	5.00
287	0.127	0.018	7.06
306	0.557	0.155	3.59
307	8.060	0.608	13.30
308	0.157	0.045	3.50
334	0.220	0.048	4.58
335	0.173	0.045	3.84
336	3.824	0.230	16.60
362	0.347	0.040	8.67
363	0.107	0.038	2.82
364	0.070	0.012	5.84

Dog No. 1884, DTPA treatment, 12 months study time

1	0.293	0.045	6.51
2	0.223	0.048	4.66
3	0.210	0.282	0.74
4	0.163	0.042	3.88
5	0.097	0.077	1.26
6	0.143	0.018	7.94
7	0.167	0.038	4.39
9	0.107	0.026	4.12
12	0.133	0.055	2.42
14	0.117	0.026	4.50
31	0.070	0.072	0.97
32	0.083	0.020	4.15
33	0.100	0.154	0.65
62	0.142	0.026	5.46
63	0.021	0.105	0.20
64	0.208	0.010	20.80
100	0.160	0.034	4.70
101	0.275	none detected	--
102	0.192	0.014	13.71
130	0.061	3.622	0.02
131	0.013	0.110	0.12
132	0.296	0.250	1.18
166	0.117	0.090	1.30
167	0.121	0.218	0.56
168	0.083	0.010	8.30
194	0.046	0.025	1.84
195	0.033	0.042	0.79
222	0.138	0.033	4.18
223	0.058	0.015	3.87
257	0.170	0.110	1.54
258	0.144	0.079	1.82
259	0.093	0.014	6.64
286	0.037	0.033	1.12
287	0.093	0.023	4.04
306	9.002	0.130	69.30
307	0.380	0.028	13.60
308	none detected	none detected	--
334	0.080	0.020	4.00
335	0.210	0.033	6.37
336	0.877	0.303	2.90
362	0.123	0.016	7.70
364	0.180	0.023	7.83

Table 2. Urine Sample Data

<u>Time</u> <u>Implanted</u> <u>Days</u>	<u>24 Hour Urine</u> <u>Sample</u> <u>Ml</u>	<u>Dis/Min</u> <u>Pu</u>	<u>Dis/Min</u> <u>Am</u>	<u>Ratio of</u> <u>Pu/Am</u>
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Dog No. 1991, no treatment, 1/2 month study time

2		123.	19.	6.47
4		1023.	122.	8.39
5		75.	23.5	3.19
6		99.	34.3	2.89
7		53.2	12.8	4.16
9		70.5	33.2	2.12
11		45.	27.	1.67
14		72.	31.	2.32

Dog No. 2602, no treatment, 1/2 month study time

2		155.	573.	0.27
3		159.	110.	1.45
4		152.	116.	1.31
5		149.	--	--
6		157.	69.1	2.27
7		91.	53.	1.72
9		74.	39.	1.90
11		41.5	53.	0.78
14		65.	32.	2.03

Dog No. 2179, DTPA treatment, 1/2 month study time

3		1019.	1955.	0.52
4		1407.	134.	10.50
5		270.	131.	2.06
6		288.	111.	2.59
7		1086.	196.	5.54
9		528.	23.2	22.76
11		336.	49.	6.86

Dog No. 2531, DTPA treatment, 1/2 month study time

1	100	526.	641.	0.82
2		2563.	837.	3.06
3		3350.	856.	3.91
4		2290.	675.	3.39
5		1584.	824.	1.92
6		2308.	159.	14.52
7		8000.	442.	18.10
9		635.	234.	2.71
11		892.	51.	17.49
14		90.	30.	3.00

Dog No. 2912, no treatment, 1 month study time
(I. V. Injection)

1	300	464.	304.	1.53
2	250	183.	120.	1.53
3	200	68.4	--	--
4	450	108.	65.1	1.66
5	325	204.	128.	1.59
6	375	288.	87.4	3.30
7	250	107.	41.3	2.59
9	475	269.	124.	2.17
11	475	169.	52.4	3.23
14	400	319.	30.4	10.49
30	200	64.3	11.	5.85
31	200	145.	55.5	2.61
32	450	305.	50.	6.10

Dog No. 2532, no treatment, 1 month study time

2	300	200.	221.	0.90
3	425	112.	159.	0.70
4	575	90.7	143.	0.63
5	650	73.6	191.	0.39
6	700	121.	153.	0.79
7	475	89.3	53.7	1.66
9	400	112.	92.1	1.22
11	425	217.	36.7	5.91
14	600	151.	29.	5.21
30	325	417.	25.	16.68

31	425	96.8	45.3	2.14
32	400	69.5	51.1	1.36

Dog No. 1308, DTPA treatment, 1 month study time

2	450	9320.	8340.	1.12
4	400	6140.	--	--
5	1000	11600.	5590.	2.08
6	925	7960.	1040.	7.65
7	650	2870.	815.	3.52
9	850	2480.	755.	3.28
11	575	2590.	1210.	2.14
14	530	1390.	258.	5.39
31	250	580.	386.	1.50
32	750	6890.	1960.	3.52

Dog No. 2666, DTPA treatment, 1 month study time

2	575	lost	2300.	--
3	250	3760.	2060.	1.83
4	375	1740.	2010.	0.87
5	650	4810.	2010.	2.39
6	400	8730.	4480.	1.95
7	250	5480.	696.	7.87
9	225	2190.	755.	2.90
11	425	8620.	1510.	5.71
14	500	539.	188.	2.87
30	250	2730.	225.	1.21
31	200	159.	446.	0.36
32	200	2170	760.	2.86

Dog No. 3018, no treatment, 1.4 months study time
(leaky wound site)

2	250	154.	164.	0.94
3	350	134.	15.	8.93
4	275	118.	--	--
5	375	153.	46.5	3.29
6	500	166.	30.1	5.51
7	450	333.	24.6	13.54
9	550	460.	18.9	24.33

11	375	240.	48.1	4.99
14	300	268.	127.	2.11
29	375	132.	50.5	2.61
30	320	108.	629.	0.17
31	(observed) 450	75.4	9.9	7.62
42		214.	4.2	50.95

Dog No. 2853, no treatment, 2 months study time

1	250	175.	13.8	12.68
2	300	64.9	8.5	7.64
3	250	68.3	111.	0.62
4	350	91.8	42.7	2.15
5	475	109.	36.4	2.99
6	400	132.	1190.	0.11
7	300	159.	44.3	3.59
9	250	288.	63.	4.57
11	200	55.8	10.2	5.47
14	200	73.	17.	4.29
28	350	55.8	3.2	17.44
29	200	40.5	16.8	2.41
30	400	59.9	84.6	0.71
60	100	126.	2.7	46.67
61	100	37.6	12.4	3.03
62	225	46.4	5.1	9.10

Dog No. 2570, no treatment, 2 months study time

1	675	229.	12.3	18.62
2	250	222.	19.8	11.21
3	200	66.2	92.4	0.72
4	270	78.4	118.	0.66
5	275	175.	57.6	3.04
6	250	161.	99.4	1.62
7	350	146.	115.	1.27
9	300	296.	37.9	7.81
11	150	110.	22.8	4.82
14	250	119.	21.	5.67
28	250	141.	30.4	4.64
29	200	122.	22.	5.55
30	250	79.8	18.9	4.22
60	300	87.2	1.5	58.13

61	250	122.	14.	8.71
62	125	67.3	26.9	2.50

Dog No. 1403, DTPA treatment, 2 months study time

1	275	115.	23.3	4.94
2	275	5440.	1700.	3.20
3	450	2940.	2960.	0.99
4	220	2100.	581.	3.61
5	675	944.	567.	1.66
6	280	1970.	728.	2.71
7	450	2840.	1670.	1.70
9	300	1430.	109.	13.12
11	250	491.	246.	2.00
14	225	453.	52.4	8.65
28	575	181.	7.0	25.86
29	400	1110.	232.	4.78
30	600	126.	223.	0.57
60	100	56.2	3.2	17.56
61	425	159.	150.	1.06
62	400	480.	338.	1.42

Dog No. 1219, DTPA treatment, 2 months study time

1	550	55.6	27.1	2.05
2	175	1420.	1110.	1.28
3	300	2140.	2360.	0.91
4	200	2200.	239.	9.21
5	225	1930.	1070.	1.80
6	300	2000.	794.	2.52
7	80	677.	34.2	19.80
9	280	984.	181.	5.44
11	150	524.	213.	2.46
14	150	390.	308.	1.27
28	300	165.	--	--
29	200	1390.	181.	7.68
30	325	1790.	2740.	0.65
61	200	317.	369.	0.86
62	200	2460.	51.7	47.58

Dog No. 2865, no treatment, 3 months study time

2	250	141.	77.	1.83
3	350	67.	55.	1.22
4	600	163.	29.	5.62
5	450	64.4	16.9	3.81
6	275	56.	10.3	5.44
7	650	89.9	21.4	4.20
9	575	96.8	54.7	1.77
11	350	54.4	104.	0.52
14	300	93.6	39.3	2.38
29	250	48.0	13.2	3.64
30	550	79.2	44.6	1.78
31	450	82.3	19.3	4.26
55	550	47.4	7.7	6.16
56	650	53.8	11.2	4.80
57	500	50.5	5.7	8.86
90	600	81.8	13.5	6.06
91	350	66.7	29.4	2.27

Dog No. 2894, DTPA treatment, 3 months study time

2	250	8870.	4380.	2.03
4	300	4670.	726.	6.43
5	250	2700.	321.	8.41
6	250	2800.	389.	7.20
7	275	2020.	286.	7.06
9	400	800.	90.4	8.85
11	250	151.	149.	1.01
14	300	1790.	206.	8.69
30	320	2300.	1060.	2.17
31	250	1760.	127.	13.86
57	300	2100.	444.	4.73
90	275	328.	55.6	5.90
91	200	1920.	399.	4.81

Dog No. 2280, DTPA treatment, 3 months study time
(leaky wound site)

4	400	6500.	1460.	4.45
7	350	4520.	308.	14.68
9	650	1080.	290.	3.72
11	150	273.	116.	2.35

14	300	196.	229.	0.86
56		2600.	211.	12.32
57	850	2580.	153.	16.86
89	leaky wound site observed			
91	350	1890.	135.	14.00

Dog No. 0650, no treatment, 4 months study time

1	185	60.5	93.5	0.65
2	200	65.7	71.6	0.92
3	150	48.8	19.5	2.50
4	150	110.	6.9	15.94
5	225	42.5	43.3	0.98
6	200	50.7	16.2	3.13
9	175	45.1	35.	1.29
11	550	106.	76.3	1.39
14	350	38.	11.3	3.36
33	200	77.7	1.4	55.50
34	200	76.1	2.4	31.71
60	50	15.5	14.7	1.05
61	200	61.9	2.3	26.91
88	200	63.6	6.0	10.60
90	250	87.5	19.8	4.42
124	150	27.4	4.8	5.70
125	175	19.3	5.0	4.86

Dog No. 1633, no treatment, 4 months study time

1	300	98.8	56.1	1.76
3	200	73.	71.3	1.02
5	325	282.	47.6	5.92
6	400	103.	3.2	32.19
9	100	27.	17.5	1.54
11	550	213.	12.1	17.60
14	300	147.	53.	2.77
34	250	85.1	5.4	15.76
61	250	964.	27.	35.70
62	250	1080.	153.	7.06
89	300	80.5	8.7	9.25
90	50	15.1	12.8	1.18
123	300	504.	7.1	71.00
124	300	1.7	0.3	5.67

Dog No. 1696, DTPA treatment, 4 months study time

1	225	27.	4.4	6.14
3	375	4360.	1010.	4.32
5	450	2040.	152.	13.42
6	200	1560.	19.1	81.68
7	150	373.	30.	12.43
9	100	879.	274.	3.21
11	200	1000.	55.8	17.92
14	350	425.	135.	3.15
32	200	138.	14.6	9.45
33	75	603.	68.5	8.80
34	200	955.	--	--
60	50	10.7	9.7	1.10
61	175	81.	152.	0.53
88	100	6.0	2.9	2.07
89	150	610.	190.	3.21
123	300	40.7	--	--
124	650	215.0	--	--

Dog No. 1008, DTPA treatment, 4 months study time

1	210	55.8	29.2	1.91
3	375	681.	863.	0.79
4	200	701.	169.	4.15
5	350	723.	154.	4.69
6	225	1360.	126.	10.79
7	200	482.	144.	3.35
9	250	1060.	97.4	10.88
11	300	1140.	37.8	30.16
14	200	384.	158.	2.43
32	50	lost	20.8	--
33	175	122.	17.2	7.09
34	225	78.	129.	0.60
61	350	1080.	30.8	35.06
62	200	1720.	109.	15.78
89	175	28.2	30.	0.94
90	225	1650.	245.	6.73
123	200	32.2	--	--
124	250	663.	--	--
125	200	995.	--	--

Dog No. 1353, no treatment, 4.57 months study time

1	250	220.	61.9	3.55
2	200	139.	68.4	2.03
3	700	253.	22.8	11.10
4	600	216.	18.6	11.61
5	300	59.7	2.8	21.32
6	550	lost	54.5	--
7	300	80.	33.3	2.40
9	200	46.8	11.2	4.18
11	400	133.	59.5	2.24
14	350	65.7	10.6	6.20
33	225	23.5	1.4	16.79
34	250	86.6	7.5	11.55
60	100	53.2	18.6	2.86
61	125	60.6	6.4	9.47
88	250	38.6	7.8	4.95
89	400	65.3	43.7	1.49
123	50	16.7	6.7	2.50
124	200	52.3	7.1	7.36
137	lymphsarcoma			

Dog No. 0925, no treatment, 5 months study time

1	175	61.1	31.3	1.95
3	400	187.	25.4	7.36
4	400	222.	8.4	26.42
5	400	52.	3.3	15.76
6	425	49.4	17.6	2.81
7	200	41.4	32.1	1.29
9	250	83.5	32.7	2.55
11	450	62.6	59.4	1.05
14	700	61.5	32.7	1.88
32	200	36.9	4.6	8.02
33	150	29.4	10.4	2.83
34	350	70.5	3.6	19.58
60	150	39.4	11.8	3.34
61	100	42.9	15.4	2.79
88	200	27.2	8.2	3.32
89	300	30.2	14.4	2.10
123	150	42.0	4.1	10.25
124	150	24.8	4.1	6.05
151	325	34.2	1.5	22.80
152	125	51.2	1.5	34.13

Dog No. 2963, DTPA treatment, 5 months study time

1	500	2480.	234.	10.60
2	750	1870.	178.	10.50
3	200	1180.	34.5	34.20
4	350	1700.	256.	6.64
5	550	876.	152.	5.76
6	400	1640.	273.	6.00
7	250	340.	228.	1.49
9	400	1510.	123.	12.30
11	200	803.	344.	2.34
14	600	453.	--	--
32	450	200.	45.5	4.40
33	450	1780.	15.	119.00
34	500	1770.	123.	14.40
60	300	97.5	4.4	22.20
61	250	117.	3.7	31.60
88	250	110.	16.1	6.84
89	150	950.	160.	5.94
123	275	81.1	--	--
124	300	904.	22.2	40.70
125	250	645.	--	--
151	100	58.	19.7	2.94
152	450	677.	31.1	21.80
153	100	895.	58.8	15.20

Dog No. 1429, DTPA treatment, 5 months study time

1	300	32.8	23.8	1.38
2	300	3680.	419.	8.78
3	175	1500.	91.4	16.40
4	200	506.	66.1	7.65
5	350	2030.	800.	2.54
6	100	--	125.	--
7	350	466.	25.1	18.57
9	350	647.	121.	5.35
11	150	397.	125.	3.18
14	550	522.	38.7	13.49
32	250	47.6	14.4	3.31
33	350	830.	93.2	8.91
34	300	1330.	16.	83.12
60	250	52.7	3.2	16.47
61	250	670.	22.	30.45
89	325	700.	60.9	11.49

90	250	1260.	407.	3.10
123	225	44.6	2.8	15.93
124	150	547.	--	--
125	300	472.	--	--
151	350	8.9	0.9	9.90
152	150	534.	25.7	20.80
153	150	746.	17.6	42.40

Dog No. 0004, no treatment, 6 months study time

1	250	466.	466.	1.00
2	375	562.	31.3	18.00
3	250	198.	114.	1.74
4	250	131.	19.3	6.80
5	350	79.4	119.	0.67
6	250	79.3	43.9	1.81
7	175	78.5	--	--
9	225	222.	12.5	17.78
11	150	253.	32.1	7.88
14	250	157.	33.6	4.67
28	125	45.2	7.6	5.95
29	280	80.4	13.5	5.96
30	175	78.2	22.8	3.43
60	50	27.2	30.6	0.89
61	150	22.5	1.6	14.10
62	225	72.7	10.9	6.67
91	150	2.7	12.	0.23
92	200	42.4	1.2	35.30
119	175	89.7	36.7	2.44
120	125	22.	11.4	1.93
147	100	71.6	9.	7.97
148	150	45.4	12.3	3.69
182	250	13.3	1.3	10.23
183	200	51.0	5.1	10.00

Dog No. 0659, no treatment, 6 months study time

1	450	49.2	10.	4.92
2	275	151.	45.5	3.32
4	175	110.	68.7	1.60
5	300	127.	48.9	2.60
6	275	91.4	75.1	1.20
7	100	61.1	--	--

9	175	136.	8.8	15.45
11	200	79.9	13.2	6.05
14	270	73.	29.8	2.45
28	25	15.8	3.2	4.94
29	150	29.3	21.	1.40
30	300	101.	19.8	5.10
61	200	93.2	7.2	12.85
62	150	65.9	20.3	3.25
92	425	28.6	2.2	13.00
93	450	28.3	17.0	1.66
119	50	6.4	1.0	6.40
120	250	35.6	6.9	5.17
147	250	75.2	3.4	22.10
148	100	54.4	30.4	1.79
182	350	48.7	6.7	7.27
183	400	18.3	1.8	10.15

Dog No. 1990, DTPA treatment, 6 months study time

1	250	1680.	2880.	0.58
2	475	3830.	566.	6.76
3	550	1780.	1010.	1.76
4	290	1680.	755.	2.22
5	425	1660.	217.	7.65
6	300	1510.	650.	2.32
7	375	1740.	--	--
9	225	654.	82.2	7.95
11	200	420.	84.7	4.96
14	240	274.	135.	2.03
28	250	84.1	4.1	2.05
29	275	1830.	377.	4.86
30	150	284.	191.	1.49
60	300	57.6	1.3	44.40
61	450	326.	241.	1.35
62	275	261.	32.9	7.93
91	375	37.9	4.2	9.03
92	500	1040.	63.7	16.35
119	225	20.5	12.5	1.64
120	275	567.	13.	43.60
147	225	41.4	9.	4.60
148	400	713.	68.7	10.38
149	250	509.	91.3	5.57
182	250	61.2	8.9	6.88

183	200	48.8	13.2	3.70
184	225	73.1	9.2	8.04

Dog No. 2761, DTPA treatment, 6 months study time

1	250	38.	19.8	1.92
2	250	143.	46.8	3.06
3	250	1230.	696.	1.77
4	380	1420.	422.	3.37
5	350	1400.	601.	2.33
6	250	871.	--	--
7	300	890.	--	--
9	350	840.	206.	4.08
11	100	231.	132.	1.75
14	250	292.	47.7	6.13
28	310	78.6	21.8	3.60
29	300	77.4	45.9	1.69
30	225	820.	225.	3.64
60	200	82.	14.3	5.74
61	450	172.	51.6	3.34
62	450	271.	164.	1.65
91	400	20.	5.4	3.70
92	450	407.	126.	3.23
119	300	87.7	5.3	16.55
147	650	73.4	4.5	16.30
148	575	1030.	159.	6.49
149	350	1360.	128.	10.60
182	100	68.0	7.3	9.32
183	250	18.1	4.1	4.41
184	200	115.	11.1	10.40

Dog No. 2325, no treatment, 7 months study time

1	200	189.	3.5	54.00
3	--	122.	145.	0.84
4	450	233.	109.	2.14
5	400	130.	94.9	1.37
6	200	83.8	--	--
7	250	25.1	--	--
9	250	34.3	27.4	1.25
11	330	170.	14.3	11.90
14	200	270.	38.1	7.09
28	200	72.7	2.3	31.60

29	225	85.9	11.6	7.40
30	400	123.	19.3	6.38
60	250	22.6	1.3	17.40
61	300	75.5	5.1	14.80
62	430	130.	13.6	9.55
91	100	4.	17.5	0.23
92	100	28.4	16.2	1.75
119	300	25.	17.9	1.40
120	200	13.8	5.6	2.46
147	200	28.8	13.7	2.10
148	100	42.0	23.	1.83
182	100	45.8	16.6	2.76
183	450	9.8	3.2	3.06
210	250	32.0	6.3	5.08
211	300	16.8	4.4	3.82

Dog No. 1687, no treatment, 7 months study time

1	350	85.5	26.6	3.21
2	300	111.	8.5	13.07
3	375	115.	73.7	1.57
4	200	52.3	40.1	1.31
5	373	49.9	54.1	0.92
6	250	1620.	--	--
7	200	123.	--	--
9	200	65.	25.4	2.56
11	175	57.4	28.	2.05
14	230	65.8	17.6	3.74
28	75	39.4	4.8	8.21
29	225	51.7	16.4	3.15
30	150	34.3	6.	5.72
60	150	26.9	5.8	4.64
61	100	55.7	9.	6.19
62	125	47.	11.9	3.95
91	125	187.	12.8	14.60
92	150	33.2	11.3	2.94
119	300	75.	9.6	7.82
120	125	12.6	0.4	31.5
147	225	31.	19.	1.63
148	300	27.	15.	1.80
182	150	10.1	0.8	12.60
183	350	31.6	3.0	10.50
210	100	27.3	5.7	4.80
211	100	19.1	3.8	5.03

Dog No. 1803, DTPA treatment, 7 months study time

1	175	3.7	31.	0.12
2	275	1430.	798.	1.79
3	375	2170.	1460.	1.49
4	210	1640.	661.	2.48
5	300	1490.	515.	2.90
6	200	271.	--	--
7	150	114.	--	--
11	100	66.4	81.4	0.82
29	250	393.	336.	1.17
30	300	2730.	223.	12.23
60	250	128.	19.9	6.44
61	250	120.	15.5	7.75
62	225	490.	3510.	0.14
92	325	1880	585.	3.22
93	200	124.	2.9	42.75
119	350	123.	15.	8.20
121	--	167.	69.1	2.42
147	100	88.	5.3	16.60
148	350	611.	153.	3.99
149	200	310.	28.8	10.76
183	350	21.9	2.7	8.11
184	150	94.2	12.1	7.78
210	250	21.9	4.7	4.66
211	200	347.	38.0	9.14
212	200	334.	149.	2.24

Dog No. 2100, DTPA treatment, 7 months study time

1	250	46.1	12.	3.84
2	150	3040.	418.	7.27
3	250	866.	1010.	0.86
4	150	1880.	508.	3.70
5	475	1980.	866.	2.29
6	225	841.	--	--
7	150	1700.	--	--
9	150	595.	54.1	11.00
11	75	204.	38.2	5.34
14	250	361.	96.6	3.74
28	25	27.2	4.9	5.55
29	300	758.	153.	4.96
30	310	614.	61.9	9.92
60	250	30.	2.5	12.00

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61	400	212.	95.4	2.22
62	300	895.	245.	3.65
91	375	3.4	4.7	0.72
92	100	47.2	17.	2.78
119	250	115.	7.3	15.80
120	200	51.	19.3	2.64
147	350	91.	4.1	26.40
148	350	759.	98.5	7.70
149	150	483.	125.	3.86
182	150	45.7	6.7	6.83
183	250	11.6	3.4	3.41
184	300	9.8	1.9	5.16
210	100	68.7	10.0	6.87
211	125	398.	50.8	7.84
212	100	360.	35.7	10.10

Dog No. 0792, no treatment, 9 months study time

1	--	165.	32.	5.16
3	--	309.	39.	7.92
5	--	222.	173.	1.28
6	--	290.	95.	3.05
7	--	113.	86.	1.31
9	--	133.	96.	1.39
11	--	180.	115.	1.57
14	--	66.	11.	6.00
30	100	7.5	5.7	1.32
31	350	87.7	39.9	2.20
32	225	56.1	15.3	3.67
66	150	27.6	15.9	1.74
67	175	40.8	10.6	3.85
68	110	28.5	11.	2.59
99	100	28.1	5.	5.62
100	100	10.4	39.4	0.26
101	200	34.1	3.3	10.33
132	50	28.6	1.6	17.88
133	250	38.3	12.5	3.06
134	125	24.	11.4	2.11
160	50	14.3	2.9	4.93
161	350	15.	2.5	6.00
188	300	97.1	16.8	5.78
189	100	53.1	14.6	3.64
223	200	12.6	2.5	5.04
224	200	101.	3.9	25.95

251	150	2.7	0.8	3.37
252	200	43.2	6.5	6.65
272	350	56.5	8.3	6.80
273	100	37.6	6.6	5.70

Dog No. 1367, no treatment, 9 months study time

1	--	134.	53.7	2.50
2	--	84.	36.5	2.55
3	--	102.	54.	1.89
4	--	100.	95.3	1.05
5	--	188.	123.	1.53
6	--	53.	97.	0.55
7	--	87.	39.	2.23
9	--	162.	156.	1.04
11	--	227.	49.	4.63
14	--	85.	38.	2.24
30	--	63.2	28.5	2.22
31	1000	119.	36.6	3.25
32	1000	100.	63.5	1.57
66	325	120.	28.1	4.27
67	650	68.6	94.8	0.72
68	500	83.5	25.2	3.31
99	500	39.1	1.9	20.58
100	350	105.	14.7	7.14
101	375	40.9	6.3	6.49
132	350	2.2	0.4	5.50
133	250	42.	1.5	2.80
134	450	23.7	3.5	6.77
160	625	40.2	3.1	12.97
161	1100	112.	9.	12.44
188	500	97.7	7.5	13.03
189	350	59.	31.2	1.89
223	650	2.6	1.5	1.73
224	900	3.9	0.7	5.58
251	550	60.3	8.8	6.85
252	300	46.6	9.6	4.86
272	550	61.9	11.0	5.64
273	400	28.6	4.3	6.65

Dog No. 3032, DTPA treatment, 9 months study time
(wound excised)

2	--	6170.	1935.	3.19
3	--	3110.	911.	3.41
4	--	3480.	1400.	2.49
5	--	3632.	1700.	2.14
6	--	3300.	1970.	1.68
9	--	2790.	1390.	2.01
11	--	3640.	378.	9.63
13	wound excised	--	--	--
14	--	500.	214.	2.34
15	--	1420.	300.	4.73
17	250	908.	106.	8.57
18	350	1450.	221.	6.56
19	250	623.	61.9	10.06
20	375	466.	33.6	13.87
31	350	447.	25.	17.88
32	200	1430.	416.	3.44
66	300	22.6	8.6	2.63
67	700	419.	63.6	6.59
68	450	588.	74.5	7.89
100	450	470.	82.	5.73
132	350	13.5	1.2	11.25
133	475	83.9	6.2	13.53
134	300	112.	6.4	17.50
160	300	27.2	5.5	4.95
161	500	451.	42.3	10.66
189	450	233.	17.7	13.16
223	50	11.8	4.4	2.68
224	130	41.9	1.4	29.50
251	50	88.2	29.8	2.96
252	200	79.4	8.4	9.45
253	350	102.0	9.4	10.85
272	350	18.4	2.6	7.08
273	100	83.3	14.4	5.78
274	300	243.0	26.0	9.35

Dog No. 2447, DTPA treatment, 9 months study time

1	--	1170.	1590.	0.74
2	--	3510.	2240.	1.57
3	--	2200.	413.	5.33
4	--	2288.	1740.	1.31

5	--	2270.	531.	4.27
6	--	1764.	610.	2.89
7	--	468.	246.	1.90
9	--	90.	38.	2.37
11	--	2190.	620.	3.53
14	--	333.	207.	1.61
30	375	2060.	232.	8.88
31	400	221.	39.3	5.62
32	350	1440.	1090.	1.32
66	250	22.2	10.4	2.13
67	450	809.	166.	4.87
68	450	991.	54.5	18.18
99	50	67.5	30.	2.25
100	175	326.	104.	3.13
101	600	1000.	34.6	28.90
132	550	42.1	1.4	30.07
133	375	13.5	2.3	5.87
134	750	17.6	3.1	5.68
160	350	40.2	8.6	4.67
161	250	625.	52.2	11.97
188	550	32.3	14.7	2.20
189	500	440.	111.0	3.96
223	200	23.8	2.5	9.52
224	300	234.	4.2	55.70
251	125	48.5	3.9	12.40
252	200	218.	10.6	20.60
253	150	365.	53.7	6.80
272	250	5.0	1.9	2.63
273	275	326.	115.	2.84
274	200	234.	69.4	3.37

Dog No. 1688, no treatment, 12 months study time

1	--	60.	334.	0.18
2	--	74.	78.	0.95
3	--	149.	46.	3.24
4	--	96.	41.	2.34
5	--	118.	51.	2.31
6	--	73.	36.	2.03
7	--	80.	9.1	8.80
9	--	31.	4.9	6.33
12	--	61.	9.2	6.63
14	--	104.	13.6	7.65
31	--	38.3	6.0	6.38

32	--	15.6	4.4	3.55
33	--	20.	6.1	3.28
65	300	19.2	5.3	3.62
66	200	8.6	1.0	8.60
67	250	16.9	5.3	3.19
100	200	21.2	3.9	5.44
101	250	12.5	8.3	1.51
102	200	16.	2.8	5.71
130	100	42.9	27.2	1.58
131	200	23.9	1.8	13.28
132	175	17.5	6.9	2.54
166	100	1.6	2.4	0.67
167	300	6.3	0.5	12.60
168	275	9.3	0.6	15.50
194	200	11.4	3.0	3.80
195	100	38.5	6.4	6.02
222	175	33.1	11.4	2.90
223	300	15.5	12.0	1.29
257	100	23.2	5.1	4.55
258	150	3.8	1.1	3.45
285	100	16.2	1.0	16.20
286	100	15.2	4.4	3.45
307	250	8.44	2.4	3.52
335	150	9.8	1.5	6.54
362	50	8.7	0.8	10.88
363	300	14.2	1.1	12.90

Dog No. 1689, no treatment, 12 months study time

1	--	84.	337.	0.25
2	--	238.	411.	0.58
3	--	90.	35.	2.57
4	--	208.	72.	2.89
5	--	37.6	5.7	6.60
6	--	129.	41.	3.15
7	--	103.	16.	6.44
9	--	30.	14.	2.14
12	--	109.	11.	9.91
14	--	146.	7.8	18.72
31	--	23.	2.6	8.85
32	--	43.8	2.7	16.22
33	--	13.	2.9	4.48
65	150	5.4	1.1	4.91
66	400	13.9	3.0	4.63

67	250	22.0	3.1	7.10
101	250	38.1	3.4	11.21
102	150	16.	3.9	4.10
131	275	23.2	0.9	25.77
132	150	20.	1.8	11.11
166	75	8.3	1.4	5.93
167	250	2.8	0.6	4.67
168	300	17.1	3.0	5.70
194	250	1.9	0.4	4.75
195	125	11.4	1.9	6.00
222	250	17.9	3.5	5.11
223	50	9.2	7.6	1.21
257	100	19.8	3.4	5.83
258	350	10.0	2.7	3.70
285	250	4.6	0.7	6.57
286	400	9.3	3.8	2.45
307	250	9.1	1.6	5.69
334	200	10.1	0.6	16.80
335	150	14.8	1.8	8.22
362	50	8.5	1.6	5.32
363	50	9.8	0.9	10.95

Dog No. 1884, DTPA treatment, 12 months study time

1	--	16.	1.6	10.0
2	--	739.	136.	5.43
3	--	1490.	56.	26.61
4	--	623.	219.	2.84
5	--	585.	154.	3.80
6	--	263.	73.	3.60
7	--	386.	113.	3.42
9	--	145.	12.	12.08
12	--	159.	30.	5.30
14	--	204.	72.	2.83
32	--	775.	132.	5.87
33	--	756.	101.	7.49
62	300	32.4	9.7	3.34
63	425	527.	87.2	6.04
64	250	90.6	69.5	1.30
100	250	27.5	2.9	9.48
101	200	260.	23.5	11.06
102	150	332.	64.6	5.14
131	200	210.	1.2	175.00
132	225	120.	7.1	16.90

167	250	64.	18.9	3.39
168	300	79.3	22.7	3.49
194	300	20.8	3.0	6.93
195	150	140.	11.6	12.07
222	100	23.8	26.1	0.91
223	200	192.	18.1	10.61
257	125	17.5	2.0	8.75
258	150	173.	7.3	23.70
259	200	419.	6.0	70.00
286	350	65.0	3.9	16.70
307	300	32.3	13.2	2.45
308	200	206.	36.4	5.66
335	350	112.	16.2	6.91
336	250	75.2	34.2	2.20
362	300	15.0	3.1	4.85
363	300	116.	contaminated	--
364	525	268.	8.5	31.50

Dog No. 2315, DTPA treatment, 12 months study time

1	--	27.	1.0	27.0
2	--	936.	226.	4.14
3	--	610.	256.	2.38
4	--	636.	287.	2.22
5	--	243.	155.	1.57
6	--	278.	90.	3.09
7	--	265.	174.	1.52
9	--	188.	72.	2.61
12	--	189.	56.	3.38
14	--	328.	132.	2.48
31	--	78.4	114.	0.69
32	--	643.	10.4	61.83
33	--	1903.	40.1	47.45
62	325	47.8	21.8	2.19
63	225	660.	281.	2.35
64	275	226.	138.	1.64
100	350	34.3	6.9	4.97
101	600	829.	68.6	12.08
102	400	530.	106.	5.00
130	125	16.	21.4	0.75
131	700	348.	15.1	23.05
132	375	257.	20.	12.85
166	225	6.2	3.2	1.94
167	450	144.	57.5	2.50

168	300	237.	50.3	4.71
194	625	39.4	13.6	2.90
195	250	535.	22.1	24.21
222	600	48.5	8.8	5.51
223	275	417.	41.4	10.07
258	500	16.7	1.1	15.20
259	400	280.	9.9	28.30
285	125	35.0	1.3	26.90
286	400	34.8	3.9	8.93
287	75	lost	lost	--
307	250	114.	14.5	7.87
308	150	227.	30.1	7.54
334	250	15.2	3.5	4.34
335	300	220.	27.4	8.03
336	200	200.	32.9	6.08
362	200	10.1	2.8	3.61
363	150	125.	7.1	17.60
364	600	328.	8.0	41.00

Table 3. Feces Sample Data

<u>Time Implanted Days</u>	<u>24 Hour Feces Sample Grams</u>	<u>Dis/Min Pu</u>	<u>Dis/Min Am</u>	<u>Ratio of Pu/Am</u>
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Dog No. 2179, DTPA treatment, 1/2 month study time

4	494	608.	5.8	104.83
5	479	127.	1.4	90.71
6	305	91.	13.1	6.95
7	396	112.	40.1	2.79
9	19	84.	40.9	2.05
11	315	153.	114.	1.34
14	94	--	11.	--

Dog No. 2531, DTPA treatment, 1/2 month study time

1	72	218.	--	--
2	496	132.	9.2	14.35
3	303	195.	51.1	3.82
4	306	385.	3.7	104.05
5	430	536.	197.	2.72
6	231	471.	193.	2.44
7	191	90.	--	--
9	89	307.	45.2	6.79
11	148	--	209.	--
14	166	385.	5.2	74.04

Dog No. 2602, no treatment, 1/2 month study time

1	81	41.	--	--
5	78	535.	--	--
6	170	720.	6.9	104.35
7	151	124.	21.9	5.66
9	209	150.	66.4	2.26
14	91	174.	120.	1.45

Dog No. 1991, no treatment, 1/2 month study time

4	203	300.	--	--
5	295	236.	1.9	124.21
6	244	159.	4.4	36.13
7	201	95.	5.	19.00
9	183	115.	121.	0.95
11	161	154.	61.4	2.51

Dog No. 2666, DTPA treatment, 1 month study time

2	377	1100.	--	--
3	478	1270.	--	--
4	375	583.	--	--
5	231	698.	--	--
7	198	674.	--	--

Dog No. 1308, DTPA treatment, 1 month study time

4	115	554.	--	--
5	142	357.	--	--
6	302	660.	--	--

Dog No. 2532, no treatment, 1 month study time

7	96	75.	--	--
11	273	320.	--	--

Dog No. 2912, no treatment, 1 month study time
(I. V. Injection)

2	296	210.	--	--
6	222	902.	--	--

Dog No. 3018, no treatment, 1.4 months study time

2	481	136.	--	--
4	206	282.	23.6	11.95
5	157	163.	16.	10.19
7	175	825.	--	--
11	136	392.	--	--
14	280	474.	--	--

Dog No. 1219, DTPA treatment, 2 months study time

7	--	69.	--	--
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Dog No. 2853, no treatment, 2 months study time

9	--	157.	6.6	23.8
11	--	151.	--	--

Dog No. 2280, DTPA treatment, 3 months study time

7	98	97.1	15.	6.47
11	180	272.	--	--

Dog No. 2894, DTPA treatment, 3 months study time

4	185	644.	19.6	32.86
5	207	159.	--	--
9	257	209.	--	--
11	246	345.	--	--

Dog No. 2865, no treatment, 3 months study time

4	155	105.	--	--
5	282	194.	--	--
6	172	184.	--	--
7	305	189.	95.2	1.99
9	350	152.	--	--
14	227	325.	--	--
55	376	128.	--	--
57	252	104.	--	--

Dog No. 1367, no treatment, 9 months study time

4	285	605.	40.9	14.79
5	124	357.	11.1	32.16
6	255	186.	--	--
7	311	746.	21.7	34.38
9	226	765.	71.9	10.64
11	265	208.	32.5	6.40
14	376	256.	--	--
31	305	63.9	--	--

Dog No. 2447, DTPA treatment, 9 months study time

1	128.	15.8	4.1	3.85
4	166	756.	33.4	22.63
5	238	304.	107.	2.84
6	269	315.	10.1	31.19
7	129	97.6	17.1	5.71
9	142	139.	6.5	21.38
11	321	462.	139.	3.32
14	503	396.	5.5	72.00
30	258	671.	--	--
31	314	318.	--	--
32	131	270.	--	--

Dog No. 0792, no treatment, 9 months study time

1	31	1.6	47.1	0.03
2	37	0.1	1.6	16.0
3	17	11.5	--	--
5	112	540.	201.	2.69
6	328	351.	6.3	5.57
7	42	120.	--	--
9	47	238.	28.5	8.35
11	179	315.	--	--
14	296	117.	--	--
30	95	89.	--	--
32	301	183.	--	--

Dog No. 3032, DTPA treatment, 9 months study time

2	492	235.	117.	2.01
3	421	176.	147.	1.20
4	67	5.6	1.7	3.29
5	423	751.	10.8	69.5
7	99	745.	116.	6.42
9	323	1630.	50.2	32.47
11	288	1750.	--	--
13	wound excised	--	--	--
14	92	1150.	52.1	22.07
15	218	287.	--	--
17	252	91.	--	--
20	217	350.	22.3	15.70
30	214	33.3	--	--
31	317	122.	--	--

Dog No. 1884, DTPA treatment, 12 months study time

2	197	2850.	--	--
3	305	365.	--	--
4	326	74.	--	--
5	67	89.	--	--
6	424	1057.	--	--
7	332	133.	--	--
9	157	32.	--	--
12	33	160.	--	--
32	146	117.	6.3	18.57
62	146	21.	--	--

Dog No. 1688, no treatment, 12 months study time

2	400	700.	--	--
3	341	301.	--	--
4	152	6.	--	--
5	500	290.	3.6	80.55
6	400	145.	--	--
7	289	119.	--	--
9	429	78.	--	--
12	205	66.	--	--
14	149	19.	--	--
32	533	17.	6.3	2.70
33	348	11.8	1.2	9.83

66	354	24.4	--	--
67	234	21.5	--	--

Dog No. 2315, DTPA treatment, 12 months study time

2	356	2650.	--	--
4	357	51.	--	--
5	468	970.	--	--
6	260	105.	--	--
7	529	75.	2.5	30.0
9	412	89.	--	--
12	335	84.	--	--
14	349	68.	--	--
32	303	1050.	0.8	1313.0
33	317	117.	--	--
62	80	27.4	--	--
63	298	31.3	--	--
102	373	447.	--	--

Dog No. 1689, no treatment, 12 months study time

2	--	472.	--	--
3	230	311.	--	--
4	287	1280.	--	--
7	217	122.	--	--
9	444	121.	--	--
12	162	131.	--	--
14	299	312.	--	--
32	262	14.	6.5	2.16
33	142	52.	--	--
67	203	43.0	--	--
102	346	19.	--	--

Table 4. Tissue Sample Data

Organ or Tissue Sample	Sample Wet Weight, Grams	Alpha dis/min Pu	Alpha dis/min Am	Ratio Pu/Am	dis/min-g Pu	dis/min-g Am
Dog No. 1991, no treatment, 1/2 month study time						
Liver (368 g)	93	187.	102.	1.83	2.01	1.09
Spleen	87	30.	11.	2.73	0.34	0.13
Kidney	30	156.	30.	5.2	5.20	1.00
Adrenal gland	1	511.	21.	24.4	511.0	21.0
Lung	25	587.	26.	22.6	23.48	1.04
Testis	11	306.	16.0	19.1	27.82	0.15
Eye	5.5	20.	2.7	7.4	3.63	0.49
Trachea	6	6.4	2.5	2.56	1.67	0.42
L. S. C. Node ⁽¹⁾	1	3.2×10^5	1.1×10^4	29.0	3.2×10^5	1.1×10^4
L. A. Node ⁽²⁾	1	2.1×10^5	4960.	42.4	2.1×10^5	496.0
Sternum	24.5	781.	22.	35.5	31.87	0.89
Rib	6.5	101.	9.6	10.5	15.53	1.48
Vertebrae	17.5	341.	2.	171.0	19.48	0.11
Skull	8.5	15.1	1.3	11.6	1.78	0.15
Femur, P. ⁽⁴⁾	8	144.	12.	12.0	18.00	1.50
Femur, Shaft	8.5	46.6	1.5	31.1	5.48	0.18
Femur, D. ⁽⁵⁾	10.	43.1	3.3	13.1	4.31	0.33
Injection Site	--	6.73×10^6	3.00×10^5	22.43	--	--

Dog No. 2602, no treatment, 1/2 month study time

Liver (282 g)	73	2480.	894.	2.78	33.9	12.24
Spleen	62	74.	19.	3.9	1.2	0.31

Kidney	33	42.	3.6	11.7	1.27	0.11
Adrenal gland	1.0	7.8	0.4	19.5	7.8	0.40
Lung	22	726.	29.	25.0	33.0	1.32
Testis	11	1.0	2.2	0.45	0.09	0.20
Eye	8	5.	1.0	5.0	0.62	0.13
Trachea	5	0.6	6.1	0.1	0.12	1.22
L.S.C. Node ⁽¹⁾	1.5	1.02×10^6	1.5×10^4	68.0	6.8×10^5	1.0×10^3
L.A. Node ⁽²⁾	1.0	6.9	28.	0.25	6.9	28.0
Sternum	25	888.	21.	42.3	35.52	0.84
Rib	4.5	45.	4.0	11.25	10.0	0.88
Vertebrae	17	472.	4.2	112.0	27.76	0.25
Skull	10.5	21.	2.0	10.5	2.0	0.19
Femur, P. ⁽⁴⁾	9	686.	10.	68.6	76.22	1.11
Femur, Shaft	10.5	138.	4.5	30.7	13.14	0.43
Femur, D. ⁽⁵⁾	12	28.	13.	2.16	23.33	1.08
Injection Site	--	--	--	--	--	--

Dog No. 2179, DTPA treatment, 1/2 month study time

Liver (411 g)	71	151.	6.	25.2	2.13	0.08
Spleen	25.5	79.	7.7	10.25	3.10	0.30
Kidney	34	16.	1.0	16.0	0.47	0.03
Adrenal gland	1.5	2.	none det.	--	1.33	--
Lung	29	20.3	6.7	3.03	0.70	0.23
Testis	14.5	1.0	1.3	0.77	0.07	0.09
Eye	7	3.	0.3	10.0	0.43	0.04
Trachea	3.5	none det.	0.3	--	--	0.09
L.S.C. Node ⁽¹⁾	1.0	9.5×10^4	2.3×10^4	4.13	9.5×10^5	2.3×10^4
Sternum	33.5	102.	11.	9.27	3.04	0.33
Rib	7.5	57.	2.7	21.1	7.60	0.36
Vertebrae	26.5	110.	8.3	13.3	4.15	0.31
Skull	12.5	10.	1.3	7.7	0.80	0.10

Femur, P. ⁽⁴⁾	13	115.	4.7	24.5	8.85	0.36
Femur, Shaft	14.5	3.0	0.33	9.1	0.21	0.23
Femur, D. ⁽⁵⁾	15.5	54.	2.3	23.5	3.48	0.15
Injection Site	--	7.84×10^6	7.55×10^5	10.38	--	--

Dog No. 2531, DTPA treatment, 1/2 month study time

Liver (370 g)	64	745.	87.	8.57	11.64	1.36
Spleen	97	131.	30.	4.37	1.35	0.31
Kidney	37.5	34.5	0.7	49.4	0.92	0.02
Adrenal gland	1.0	371.	29.	12.8	371.0	29.0
Lung	23	308.	55.	5.6	13.39	2.39
Testis	13	151.	3.8	39.8	11.62	0.29
Eye	8	4.	1.3	3.08	0.50	0.16
Trachea	6.5	134.	5.	26.8	20.61	0.77
L.S.C. Node ⁽¹⁾	1.0	382,000	35,800	10.7	3.82×10^5	3.58×10^4
Sternum	25.5	883.	7.5	118.0	34.63	0.29
Rib	4	92.5	1.8	51.4	23.13	0.45
Vertebrae	18.5	247.	4.6	53.7	13.35	0.25
Skull	10	33.4	1.5	22.3	3.34	0.15
Femur, P. ⁽⁴⁾	10	132.	3.5	37.8	13.20	0.35
Femur, Shaft	10.5	9.	1.2	7.5	0.86	0.11
Femur, D. ⁽⁵⁾	13.5	67.5	2.2	30.7	5.00	0.16
Injection Site	--	--	--	--	--	--

Dog No. 2912, no treatment, 1 month study time
(injected intravenously)

Liver	48	3×10^4	1×10^5	0.3	625.0	2.08×10^3
Spleen	31	8.6×10^5	6.4×10^4	13.45	2.78×10^4	2.06×10^3
Kidney	44	246.	95.	2.59	5.59	2.16
Adrenal gland	1.5	50.	84.	0.6	33.3	56.0

Lung	25	6.2×10^6	8.3×10^5	7.47	2.48×10^5	3.32×10^4
Testis	12	17.	2.1	8.1	1.42	0.18
Eye	7	34.	148.	0.23	4.85	21.14
Trachea	7	22.	197.	0.11	3.14	28.14
L.S.C. Node ⁽¹⁾	1.5	3760.	591.	6.37	2500.	394.
L.A. Node ⁽²⁾	1.5	175.	60.	2.92	116.66	40.0
Sternum	19	1360.	119.	11.4	71.57	6.26
Rib	3.5	195.	5.7	34.2	55.71	1.63
Vertebrae	21.5	591.	51.	11.6	27.48	2.37
Skull	6	30.	2.3	13.0	5.0	0.38
Femur, P. ⁽⁴⁾	10	310.	24.	12.9	31.0	2.40
Femur, Shaft	10	247.	12.	20.6	24.7	1.20
Femur, D. ⁽⁵⁾	13	144.	11.	13.1	11.08	0.85
Injection Site	--	--	--	--	--	--

Dog No. 2532, no treatment, 1 month study time

Liver	96	884.	1740.	0.51	9.21	18.12
Spleen	24	90.	82.	1.1	3.75	3.42
Kidney	26	5.3	16.	0.33	0.20	0.62
Adrenal gland	1	15.	3.	5.0	15.0	3.0
Lung	25	102.	80.	1.28	4.08	3.20
Testis	11	5.9	4.8	1.23	0.54	0.44
Eye	6	none det.	6.1	--	--	1.02
Trachea	5	1.1	24.	0.05	0.22	4.80
L.S.C. Node ⁽¹⁾	2.0	1×10^6	7.6×10^5	1.45	5×10^5	3.8×10^5
L.A. Node ⁽²⁾	1.0	70.	7.9	8.86	70.0	7.9
Sternum	22	1160.	79.	14.7	52.72	3.59
Rib	4.5	318.	106.	3.0	70.66	23.55
Vertebrae	26.5	561.	4.9	114.5	21.17	0.18
Skull	6	54.	1.9	28.4	9.0	0.32

Femur, P. ⁽⁴⁾	12	275.	20.	13.75	22.92	1.67
Femur, Shaft	11.5	26.	1.	26.0	2.26	0.09
Femur, D. ⁽⁵⁾	15.5	213.	29.	7.35	13.74	1.87
Injection Site	--	--	--	--	--	--

Dog No. 1308, DTPA treatment, 1 month study time

Liver	36	1430.	306.	4.67	16.62	3.56
Spleen	29	222.	336.	0.66	7.66	11.59
Kidney	48	13.	30.	0.43	0.27	0.63
Adrenal gland	2	23.	13.	1.77	11.50	6.50
Lung	25	423.	24.	17.6	16.92	0.96
Testis	15	12.	9.4	1.28	0.80	0.63
Eye	7	27.	4.7	5.75	3.85	0.67
Trachea	8	1.2	25.	0.05	0.15	3.12
L.S.C. Node ⁽¹⁾	5	1.7×10^6	1.8×10^5	9.45	3.4×10^5	3.60×10^4
L.A. Node ⁽²⁾	1.0	404.	13.	31.1	404.0	13.0
Sternum	21	908.	9.3	97.6	43.24	0.44
Rib	6	219.	7.1	30.9	36.50	1.18
Vertebrae	16.5	1600.	16.	100	96.90	0.97
Skull	4	32.	2.1	15.2	8.0	0.53
Femur, P. ⁽⁴⁾	9.5	666.	4.3	155.0	70.10	0.45
Femur, Shaft	6.5	85.	6.8	12.5	13.07	1.05
Femur, D. ⁽⁵⁾	13	251.	2.3	109.0	19.31	0.18
Injection Site	--	--	--	--	--	--

Dog No. 2666, DTPA treatment, 1 month study time

Liver (551 g)	143	783.	906.	0.87	5.48	6.34
Spleen	34	414.	145.	2.85	12.18	4.26
Kidney	46	54.	89.	0.61	1.17	1.93

Adrenal gland	4	32.1	112.	0.29	8.03	28.00
Lung	31	none det.	68.	--	--	2.19
Testis	14.5	107.	45.	2.38	7.38	3.10
Eye	8	30.	122.	0.25	3.75	15.25
Trachea	6.	70.	87.	0.81	11.67	14.70
L.S.C. Node ⁽¹⁾	1.5	2.2×10^6	2×10^5	11.0	1.47×10^6	1.33×10^5
L.A. Node ⁽²⁾	0.5	630.	74.	8.5	1260.0	148.0
Sternum	21.5	450.	116.	3.88	20.93	5.40
Rib	7	241.	13.	18.5	34.42	1.85
Vertebrae	27	406.	38.	10.7	15.04	1.41
Skull	4.5	22.	5.3	4.15	4.88	1.18
Femur, P. ⁽⁴⁾	12	400.	5.0	80.0	33.33	0.42
Femur, Shaft	10.5	45.	5.5	8.18	4.29	0.52
Femur, D. ⁽⁵⁾	17.5	316.	6.7	47.1	18.06	0.38
Injection Site	--	2.53×10^7	9.88×10^5	25.60	--	--

Dog No. 3018, no treatment, 1.4 months study time
(implant excised - over anesthetized at surgery)

Liver (427 g)	42.5	1690.	338.	5.0	39.76	7.95
Spleen	122	296.	20.	14.8	2.43	0.16
Kidney	33	11.	89.	0.12	0.33	2.70
Adrenal gland	1.0	19.	17.	1.1	19.0	17.0
Lung	37	93.4	54.	1.73	2.52	1.46
Testis	12	5.4	7.8	0.68	0.45	0.65
Eye	6.5	7.9	4.9	1.61	1.22	0.75
Trachea	4.5	5.9	2.3	2.56	1.31	0.51
L.S.C. Node ⁽¹⁾	1.5	2.3×10^6	2.3×10^5	10.0	1.53×10^6	1.53×10^5
L.A. Node ⁽²⁾	1.0	1.2×10^4	940.	12.8	1.2×10^4	940.
Sternum	14	681.	8.7	78.3	48.64	0.62
Rib	6.5	300.	2.2	136.	46.15	0.34

Vertebrae	24.5	539.	6.6	81.7	22.00	0.27
Skull	6	31.	0.9	34.4	5.17	0.15
Femur, P. ⁽⁴⁾	9	281.	7.1	39.6	31.22	0.79
Femur, Shaft	9	40.	5.7	7.0	4.44	0.63
Femur, D. ⁽⁵⁾	13.5	292.	37.	7.9	21.63	2.74
Injection Site	--	--	--	--	--	--

Dog No. 2853, no treatment, 2 months study time

Liver (390 g)	111	2470.	64.	38.6	22.25	5.80
Spleen	59	5390.	234.	23.0	91.02	3.97
Kidney	34	13.7	3.2	4.28	0.40	0.09
Adrenal gland	2	330.	3.0	110.	165.0	1.50
Lung	23	242.	30.3	8.0	10.52	1.32
Testis	12	931.	80.	11.60	77.58	0.67
Eye	7	24.1	3.9	6.18	3.44	0.56
Trachea	6	298.	22.4	13.3	49.67	3.73
L.S.C. Node ⁽¹⁾	4.0	9.3×10^5	1.5×10^5	6.20	2.33×10^6	3.75×10^4
L.A. Node ⁽²⁾	1.0	345.	7.2	48.0	345.0	7.20
Sternum	23	814.	6.5	125.0	35.39	0.28
Rib	5.5	241.	14.9	16.2	43.82	2.71
Vertebrae	27	561.	14.5	38.7	20.78	0.54
Skull	3.5	25.2	3.6	6.95	7.20	1.03
Femur, P. ⁽⁴⁾	14	351.	16.5	21.2	25.07	1.18
Femur, Shaft	12	46.0	4.3	10.7	3.83	0.36
Femur, D. ⁽⁵⁾	16.5	140.	12.5	11.2	8.48	0.76
Injection Site	--	--	--	--	--	--

Dog No. 2570, no treatment, 2 months study time

Liver	87	1980.	2690.	0.74		
Spleen	12	669.	91.2	7.34	55.75	7.60

Kidney	22	27.6	31.7	0.87	1.25	1.44
Adrenal gland	2	13.5	2.65	5.1	6.75	1.33
Lung	19.5	936.	116.	8.07	48.00	0.59
Testis	14	1.81	3.57	0.51	0.13	0.26
Eye	6	19.7	6.68	2.95	3.28	1.11
Trachea	8	68.8	6.33	10.9	8.60	0.79
L.S.C. Node ⁽¹⁾	2.5	2.00×10^6	1.24×10^5	16.1	8.00×10^5	4.96×10^4
L.A. Node ⁽²⁾	2.0	8.63×10^5	7.06×10^4	12.2	4.32×10^5	3.53×10^4
Sternum	21	1980.	21.7	91.24	94.29	1.03
Rib	7	599.	37.	16.19	85.57	5.29
Vertebrae	31	1160.	23.5	49.36	37.42	0.76
Skull	6	82.7	8.0	10.34	13.78	1.34
Femur, P. ⁽⁴⁾	12	900.	17.9	50.28	75.00	1.49
Femur, Shaft	18	253.	4.0	63.25	14.06	0.22
Femur, D. ⁽⁵⁾	14	170.	21.1	8.07	12.14	1.51
Injection Site	--	--	--	--	--	--

Dog No. 1403, DTPA treatment, 2 months study time

Liver (262 g)	82	743.	291.	2.55	9.06	3.55
Spleen	35	552.	26.1	21.2	15.77	0.75
Kidney	26	17.7	20.9	0.85	0.68	0.80
Adrenal gland	2.0	4.95	1.38	3.58	2.48	0.69
Lung	13	32.4	8.34	3.88	2.49	0.64
Testis	12	7.41	3.87	1.92	0.62	0.32
Eye	7.5	3.64	2.83	1.29	0.49	0.38
Trachea	8.5	9.86	16.7	0.59	1.16	1.96
L.S.C. Node ⁽¹⁾	2.0	2.82×10^6	3.45×10^5	8.17	1.41×10^6	1.78×10^5
L.A. Node ⁽²⁾	1.5	240.	61.9	3.88	160.0	41.30
Sternum	22.5	1030.	17.	60.6	45.77	0.76
Rib	5	256.	15.2	16.85	51.20	3.40
Vertebrae	24	81.5	15.3	5.33	3.40	0.64

Skull	3.5	23.4	3.08	7.6	6.69	0.88
Femur, P. ⁽⁴⁾	9.5	404.	2.83	143.0	42.52	0.30
Femur, Shaft	11	50.0	1.03	48.6	4.55	0.09
Femur, D. ⁽⁵⁾	11.5	181.	3.33	54.4	15.74	0.29
Injection Site	--	1.38×10^7	2.41×10^6	5.73	--	--

Dog No. 1219, DTPA treatment, 2 months study time

Liver (313 g)	94	9090.	791.	11.5	96.70	8.41
Spleen	35	1870.	237.	7.9	53.42	6.77
Kidney	40	79.1	20.2	3.92	1.98	0.51
Adrenal gland	2.0	8.8	1.95	4.5	4.40	0.98
Lung	20	176.	23.8	7.4	8.80	1.19
Testis	14	18.2	7.21	2.53	1.30	0.52
Eye	7	3.7	3.0	1.23	0.53	0.43
Trachea	6	2.35	3.45	0.68	0.39	0.58
L.S.C. Node ⁽¹⁾	3.0	1.94×10^6	2.04×10^5	9.5	6.47×10^5	6.80×10^4
L.A. Node ⁽²⁾	1.0	1510.	56.6	26.7	1510.0	56.6
Sternum	23	894.	6.0	149.0	38.87	0.26
Rib	7	336.	333.	1.01	48.00	47.57
Vertebrae	31	489.	9.15	53.5	15.77	0.30
Skull	4	36.6	2.18	16.8	9.15	0.54
Femur, P. ⁽⁴⁾	10	316.	2.0	158.0	31.60	0.20
Femur, Shaft	14	102.	3.43	29.8	7.29	0.25
Femur, D. ⁽⁵⁾	12.5	213.	9.38	22.7	17.04	0.75
Injection Site	--	--	--	--	--	--

Dog No. 2865, no treatment, 3 months study time

Liver (340 g)	70	2120.	1500.	1.41	30.28	21.4
Spleen	22.5	118.	43.5	2.72	5.24	1.93
Kidney	25	157.	78.8	2.0	6.28	3.15

Adrenal gland	1.0	10.7	0.75	14.3	10.70	0.75
Lung	26	139.	89.6	1.55	5.35	3.45
Testis	10	1.2	6.5	0.19	0.12	0.65
Eye	7	3.15	1.22	2.58	0.45	0.17
Trachea	5	17.6	24.9	0.71	3.52	4.98
L.S.C. Node ⁽¹⁾	1.5	1.34×10^6	6.48×10^5	2.07	8.93×10^5	4.32×10^5
L.A. Node ⁽²⁾	1.0	9.65	2.80	3.45	9.65	2.80
Sternum	20	1170.	129.	9.07	585.0	64.5
Rib	6	362.	39.1	9.26	60.33	6.52
Vertebrae	24	839.	57.5	14.6	34.96	2.40
Skull	5	80.5	9.5	8.47	16.10	1.90
Femur, P. ⁽⁴⁾	12	293.	31.2	9.4	24.42	2.60
Femur, Shaft	9.5	107.	15.1	7.09	11.26	1.59
Femur, D. ⁽⁵⁾	15.5	457.	37.5	12.2	29.48	2.42
Injection Site	--	--	--	--	--	--

Dog No. 2280, DTPA treatment, 3 months study time

Liver (369 g)	69	2240.	522.	4.3	32.46	7.57
Spleen	81	148.	25.1	5.9	1.83	0.31
Kidney	38	92.2	39.7	2.32	2.43	1.04
Adrenal gland	2.0	5.85	0.58	10.0	2.93	0.29
Thyroid gland	1.5	2.0	17.5	0.11	1.33	11.66
Lung	25	17.8	72.2	0.25	0.71	2.89
Testis	19	1.87	1.95	0.96	0.10	0.10
Eye	7	8.33	21.6	0.39	1.19	3.09
Trachea	7	3.13	5.87	0.53	0.45	0.84
L.S.C. Node ⁽¹⁾	2.0	9.45×10^5	7.28×10^4	13.0	4.83×10^5	3.64×10^4
L.A. Node ⁽²⁾	2.0	5.41×10^4	5.2×10^3	10.8	2.71×10^4	2.60×10^3
R.S.C. Node ⁽³⁾	1.5	33.8	3.04	11.1	22.53	2.03
Sternum	26.5	805.	7.35	109.5	30.38	0.28
Rib	7	324.	13.5	24.00	46.28	0.19

Vertebrae	20.5	438.	6.28	69.9	21.37	0.31
Skull	3	27.6	5.6	4.93	9.2	1.9
Femur, P.(4)	12	343.	3.35	102.0	28.58	0.28
Femur, Shaft	9.5	64.5	4.08	15.8	6.79	0.43
Femur, D.(5)	15	181.	3.55	51.0	12.07	0.24
Injection Site	--	--	--	--	--	--

Dog No. 2894, DTPA treatment, 3 months study time

Liver (469 g)	130	2840.	645.	4.40	21.85	4.96
Spleen	41	154.	26.1	5.90	3.76	0.64
Kidney	38	103.	59.4	1.73	2.71	1.56
Adrenal gland	1.0	3.93	0.66	10.50	3.93	0.66
Thyroid gland	1.5	0.43	5.23	0.08	0.29	3.49
Lung	29	49.1	40.4	1.22	1.69	1.39
Testis	20	0.8	0.8	1.0	0.04	0.04
Eye	7.5	5.74	1.15	4.99	0.77	0.15
Trachea	6	10.6	9.55	1.11	1.77	1.59
L.S.C. Node ⁽¹⁾	2.0	1.25×10^6	1.32×10^5	9.47	6.25×10^5	6.60×10^4
L.A. Node ⁽²⁾	2.0	2230.	202.	11.04	1115.0	101.0
R.S.C. Node ⁽³⁾	1.5	6670.	96.7	68.97	4446.0	64.46
Sternum	27	597.	27.1	22.03	22.11	1.00
Rib	8.5	235.	7.98	29.44	27.64	0.94
Vertebrae	32	394.	5.26	74.90	12.31	0.16
Skull	2	27.5	9.0	3.06	13.75	4.50
Femur, P.(4)	17	316.	3.95	80.00	18.59	0.23
Femur, Shaft	15	79.5	1.4	56.79	5.30	0.09
Femur, D.(5)	21	222.	4.13	53.75	10.57	0.20
Injection Site	--	1.76×10^7	8.88×10^5	19.81	--	--

Dog No. 1633, no treatment, 4 months study time

Liver (450 g)	138	9090.	1990.	4.57	65.87	14.42
Spleen	133	210.	17.2	12.21	1.58	0.13
Kidney	38	66.8	5.9	11.3	1.76	0.16
Adrenal gland	3	9.1	0.7	13.00	3.03	0.23
Thyroid gland	2.5	14.2	19.6	0.72	5.68	7.84
Lung	26	109.0	15.8	6.9	4.19	0.61
Testis	10	44.2	5.8	7.62	4.42	0.58
Eye	9	7.5	3.3	2.27	0.83	0.37
Trachea	10	83.2	5.4	15.41	8.32	0.54
L.S.C. Node ⁽¹⁾	4.5	7.3×10^5	4.1×10^4	17.80	1.62×10^5	9.1×10^3
L.A. Node ⁽²⁾	1.5	12.7	8.6	1.48	8.47	5.73
R.S.C. Node ⁽³⁾	2	23.4	14.3	1.64	11.70	7.15
Rib	8	278.	3.5	79.40	34.75	0.44
Vertebrae	28	680.	6.6	103.0	24.29	0.24
Skull	4.5	57.3	1.0	57.3	12.73	57.3
Femur, P. ⁽⁴⁾	11	179.	22.6	7.92	16.27	2.05
Femur, Shaft	13	237.	16.	14.80	18.23	0.12
Femur, D. ⁽⁵⁾	15	270.	4.1	65.9	18.00	0.27
Injection Site	--	1.84×10^7	2.16×10^6	8.52	--	--

Dog No. 0650, no treatment, 4 months study time

Liver (331 g)	74	1910.	1330.	1.44	25.81	17.97
Spleen	71	240.	70.6	3.40	3.38	0.99
Kidney	34	68.3	45.9	1.49	2.01	1.35
Adrenal gland	2	21.	3.7	5.68	10.50	1.85
Thyroid gland	1	25.3	110.	0.23	25.30	110.00
Lung	22	136.	116.	1.17	6.18	5.27
Testis	12	19.4	6.8	2.85	1.62	0.57
Eye	9	11.4	2.6	4.38	1.27	0.29

Trachea	9	23.3	13.5	1.73	2.59	1.50
L.S.C. Node ⁽¹⁾	2	7.8×10^5	7.6×10^4	10.30	3.90×10^5	3.8×10^4
L.A. Node ⁽²⁾	2	17.6	1.1	16.00	8.80	0.55
R.S.C. Node ⁽³⁾	2	14.8	1.8	8.22	7.40	0.90
Sternum	21	309.0	15.3	20.2	14.71	0.73
Rib	7	152.0	2.5	60.8	21.71	0.36
Vertebrae	24	296.0	8.8	33.6	12.33	0.37
Skull	3.5	21.3	2.2	9.68	6.09	0.63
Femur, P. ⁽⁴⁾	10	107.0	19.5	5.5	10.70	1.95
Femur, Shaft	12	16.9	3.91	4.3	1.41	0.33
Femur, D. ⁽⁵⁾	14	112.0	8.8	12.7	8.00	0.63
Injection Site	--	--	--	--	--	--

Dog No. 1008, DTPA treatment, 4 months study time

Liver	70	1780.	676.	2.63	25.43	9.66
Spleen	42	76.3	29.6	2.58	1.82	0.70
Kidney	55	47.	192.	0.24	0.85	3.49
Adrenal gland	3	7.6	1.7	4.47	2.53	0.57
Thyroid gland	0.5	13.3	28.9	0.46	26.60	57.80
Lung	25	122.	31.5	3.87	4.88	1.26
Testis	15	13.5	4.6	2.93	0.90	0.31
Eye	7	9.2	2.5	3.68	1.31	0.36
Trachea	11	11.1	14.2	0.78	1.01	1.29
L.S.C. Node ⁽¹⁾	4.5	2.32×10^5	3.2×10^4	7.26	5.16×10^4	7.11×10^3
L.A. Node ⁽²⁾	3	20.9	5.4	3.87	6.97	1.80
R.S.C. Node ⁽³⁾	3	100.	16.6	6.02	33.33	5.53
Sternum	24	782.	24.1	32.45	32.58	1.00
Rib	8	142.	13.2	10.76	17.75	1.65
Vertebrae	28	93.5	10.4	8.99	3.34	2.69
Skull	4	15.2	4.0	3.80	3.80	1.00
Femur, P. ⁽⁴⁾	10	59.5	1.9	31.5	5.95	1.89

Femur, Shaft	12	52.4	4.8	10.92	4.37	0.40
Femur, D. ⁽⁵⁾	14	103.	5.1	20.19	7.36	0.36
Injection Site	--	1.68×10^6	3.64×10^5	4.62	--	--

Dog No. 1696, DTPA treatment, 4 months study time

Liver (402 g)	94	2560.	46.4	55.2	27.23	0.49
Spleen	59	162.	13.1	12.37	2.75	0.22
Kidney	38	63.	6.4	9.84	1.66	0.17
Adrenal gland	1	49.6	5.6	8.86	49.60	5.60
Thyroid gland	1.5	76.	68.3	1.11	50.67	45.53
Lung	17	42.4	4.9	8.65	2.49	0.29
Testis	14	16.1	2.7	5.96	1.15	0.19
Eye	8	14.5	1.7	8.53	1.81	0.21
Trachea	8.5	10.7	1.3	8.23	1.26	0.15
L.S.C. Node ⁽¹⁾	2	1.09×10^6	7.2×10^4	15.15	5.45×10^5	3.6×10^4
L.A. Node ⁽²⁾	1	28.5	1.6	17.81	28.50	1.60
R.S.C. Node ⁽³⁾	3	17.8	3.2	5.56	5.93	1.67
Sternum	19	1262.	13.4	94.1	66.42	0.71
Rib	5	117.0	9.7	12.18	23.40	1.94
Vertebrae	24	183.0	18.5	9.9	7.63	0.77
Skull	2.5	16.8	2.7	6.22	6.72	1.08
Femur, P. ⁽⁴⁾	10	174.0	11.8	14.75	17.40	1.18
Femur, Shaft	12	78.9	4.3	18.35	6.58	0.36
Femur, D. ⁽⁵⁾	15.5	433.	14.3	30.3	2.79	0.92
Injection Site	--	1.06×10^7	1.11×10^6	9.55	--	--

Dog No. 1353, no treatment, 4.57 months study time
(lymphosarcoma)

Liver (490 g)	156	984.	534.	1.84	6.31	3.42
Spleen	93	140.	45.4	3.08	1.51	0.49

Kidney	37	80.1	205.	0.39	2.16	5.54
Adrenal gland	2	11.1	5.3	2.09	5.55	2.65
Thyroid gland	2.5	12.6	12.6	1.00	5.04	5.04
Lung	12.5	60.6	19.7	3.08	4.85	1.58
Testis	9	6.6	6.9	0.96	0.73	0.77
Eye	7	2.5	5.2	0.48	0.36	0.74
Trachea	5.5	13.0	5.4	2.41	2.36	0.98
L.S.C. Node ⁽¹⁾	31	4.8×10^5	6.9×10^4	6.96	1.55×10^3	2.23×10^3
L.A. Node ⁽²⁾	11.5	10.4	10.1	1.03	0.90	0.88
R.S.C. Node ⁽³⁾	22.5	47.2	10.9	4.33	2.10	0.48
Sternum	19.5	201.	35.6	5.65	10.31	1.83
Rib	6	128.	31.4	4.08	21.33	5.23
Vertebrae	25.5	363.	32.6	11.13	14.24	1.28
Skull	2	34.0	4.0	8.50	17.00	2.00
Femur, P. ⁽⁴⁾	9	224.	24.6	9.11	24.89	2.73
Femur, Shaft	12.5	94.8	12.7	7.46	7.58	1.02
Femur, D. ⁽⁵⁾	12	163.	10.6	15.38	13.58	0.88
Injection Site	--	2.75×10^6	1.22×10^6	2.25	--	--

Dog No. 0925, no treatment, 5 months study time

Liver (346 g)	39	2250.0	554.0	4.06	57.69	14.21
Spleen	30	841.0	40.0	21.08	28.03	1.34
Kidney	28.5	contaminated	2.9	--	--	0.10
Adrenal gland	1	21.6	5.2	4.15	21.60	5.20
Thyroid gland	1	2.6	2.6	1.00	2.60	2.60
Lung	22.5	128.0	27.6	4.64	5.68	1.23
Testis	9	contaminated	2.9	--	--	0.32
Eye	5.5	9.8	6.8	1.44	1.78	1.23
Trachea	6	14.0	13.0	1.08	2.33	2.16
L.S.C. Node ⁽¹⁾	1.5	4.1×10^5	5.0×10^4	8.20	2.73×10^5	3.33×10^4
L.A. Node ⁽²⁾	0.5	34.4	4.8	7.17	68.80	9.60

R. S. C. Node ⁽³⁾	2	10.8	3.9	2.77	5.40	1.95
Sternum	19	1050.0	68.4	15.35	55.20	3.60
Rib	6	243.0	25.5	9.53	40.50	4.25
Vertebrae	24	244.0	33.9	7.20	10.20	1.41
Skull	4.5	57.3	9.3	6.16	12.73	2.06
Femur, P. ⁽⁴⁾	8	244.	23.2	10.50	30.50	2.90
Femur, Shaft	10	26.8	10.6	2.53	2.68	1.06
Femur, D. ⁽⁵⁾	10	128.0	16.6	7.71	12.80	1.66
Injection Site	--	1.33×10^7	1.24×10^6	10.73	--	--

Dog No. 1429, DTPA treatment, 5 months study time

Liver (450 g)	69	1710.	371.	4.61	24.78	5.38
Spleen	55.5	1980.	107.	18.50	35.60	1.92
Kidney	41	27.6	15.2	1.82	0.67	0.37
Adrenal gland	1	7.5	0.7	10.71	7.50	0.70
Thyroid gland	2	14.7	23.6	0.62	7.35	11.80
Lung	5	79.5	10.4	7.64	15.90	2.08
Testis	15	32.7	27.1	1.21	2.18	1.81
Eye	9.5	5.6	1.3	4.31	0.58	0.13
Trachea	9	13.8	1.0	13.80	1.53	0.11
L. S. C. Node ⁽¹⁾	3	9.1×10^5	1.6×10^5	5.69	3.03×10^5	5.33×10^4
L. A. Node ⁽²⁾	3	353.0	7.9	44.68	117.67	2.63
R. S. C. Node ⁽³⁾	2.5	39.3	7.0	5.61	15.72	2.80
Sternum	23	853.0	15.2	56.12	37.09	0.66
Rib	6	173.0	7.8	22.19	28.83	1.30
Vertebrae	31	105.0	13.6	7.72	3.38	0.44
Skull	3.5	19.3	3.1	6.23	5.51	0.89
Femur, P. ⁽⁴⁾	10	336.0	9.5	35.36	33.60	0.95
Femur, Shaft	13	67.8	2.7	25.11	5.22	0.21
Femur, D. ⁽⁵⁾	14	184.0	14.8	12.43	13.14	1.06
Injection Site	--	1.17×10^7	1.08×10^6	10.83	--	--

Dog No. 2963, DTPA treatment, 5 months study time

Liver (404 g)	60	25100.	406.	61.8	418.30	6.8
Spleen	83.5	3940.	242.	16.28	47.19	2.90
Kidney	38	25.	32.5	0.77	0.66	0.86
Adrenal gland	1.5	92.3	13.9	6.64	61.53	9.27
Thyroid gland	2	44.6	35.8	1.25	22.30	17.90
Lung	6	560.	63.4	8.83	93.33	10.57
Testis	16.5	15.6	2.2	7.09	0.95	0.13
Eye	7	7.6	12.7	0.60	1.09	1.81
Trachea	8	11.0	15.9	0.69	1.38	1.99
L.S.C. Node ⁽¹⁾	3	2.0×10^6	1.8×10^5	11.1	6.67×10^5	6.00×10^4
L.A. Node ⁽²⁾	1.5	47.7	27.4	1.74	31.80	18.27
R.S.C. Node ⁽³⁾	2.5	35.7	7.4	4.82	14.28	2.96
Sternum	23	1330.0	15.8	84.18	57.82	0.69
Rib	7	359.0	14.5	24.76	51.28	2.07
Vertebrae	27	226.0	15.4	14.68	8.37	0.57
Skull	4.5	23.5	1.8	13.05	5.22	0.40
Femur, P. ⁽⁴⁾	11	213.0	10.0	21.30	19.36	0.90
Femur, Shaft	11	65.8	8.2	8.02	5.98	0.75
Femur, D. ⁽⁵⁾	15	429.0	20.4	21.03	28.60	1.36
Injection Site	--	6.77×10^7	1.27×10^6	53.31	--	--

Dog No. 0659, no treatment, 6 months study time

Liver (539 g)	88	2810	453.	6.20	31.93	5.15
Spleen	48	891.	106.	8.41	18.56	2.21
Kidney	57	8.8	3.7	2.38	0.15	0.06
Adrenal gland	3	463.	12.1	38.26	154.33	4.03
Thyroid gland	2.5	15.1	39.5	0.38	6.04	15.80
Lung	6.5	28.5	14.7	1.94	4.38	2.26
Testis	15.5	7.1	2.9	2.45	0.46	0.19

Eye	8.5	9.1	8.3	1.10	1.07	0.98
Trachea	7	91.	1.2	75.8	13.00	0.17
L.S.C. Node ⁽¹⁾	4.5	5.3×10^5	4.0×10^4	13.25	1.18×10^5	8.89×10^3
L.A. Node ⁽²⁾	1	92.	13.3	6.92	92.00	13.30
R.S.C. Node ⁽³⁾	3.5	24.9	10.2	24.41	7.11	2.91
Sternum	26	949.0	59.3	16.00	36.50	2.28
Rib	9.5	456.0	25.8	17.68	48.00	2.71
Vertebrae	30	329.0	20.5	16.05	10.97	0.68
Skull	3.5	30.5	3.7	8.24	8.71	1.06
Femur, P. ⁽⁴⁾	12	451.0	21.4	21.07	37.58	1.78
Femur, Shaft	12	27.9	5.4	5.17	2.33	0.45
Femur, D. ⁽⁵⁾	16	73.6	12.1	6.08	4.60	0.76
Injection Site	--	--	--	--	--	--

Dog No. 0004, no treatment, 6 months study time

Liver (342 g)	44.5	1630.	270.	6.04	36.63	6.07
Spleen	49.5	408.	21.2	19.25	8.24	0.43
Kidney	35	60.9	69.4	0.88	1.74	1.98
Adrenal gland	2	29.9	3.7	8.08	14.95	1.85
Thyroid gland	1.5	23.0	93.5	0.25	15.33	62.33
Lung	21.5	51.4	34.9	1.47	2.39	1.62
Testis	9	18.2	10.4	1.75	2.02	1.16
Eye	6.5	9.0	4.7	1.92	1.08	0.72
Trachea	5.5	18.2	12.5	1.46	3.31	2.27
L.S.C. Node ⁽¹⁾	1.5	9.8×10^5	6.8×10^4	14.41	6.53×10^5	4.53×10^4
L.A. Node ⁽²⁾	1.5	31.0	8.1	3.83	20.67	5.40
R.S.C. Node ⁽³⁾	1.5	10.7	3.9	2.74	7.13	2.60
Sternum	18	582.0	21.7	26.82	32.33	1.21
Rib	6	239.0	12.0	19.92	39.83	2.00
Vertebrae	28	245.0	12.3	19.92	8.75	0.44

Skull	3.5	35.2	9.3	3.78	10.05	2.65
Femur, P. (4)	10	461.0	23.2	19.87	46.10	2.32
Femur, Shaft	10	50.4	6.6	7.64	5.04	0.66
Femur, D. (5)	12	133.0	25.9	5.14	11.08	2.16
Injection Site	--	--	--	--	--	--

Dog No. 2761, DTPA treatment, 6 months study time

Liver (410 g)	69	3560.	146.	24.4	51.59	2.1
Spleen	68.5	1030.	42.6	24.18	15.04	0.62
Kidney	33	30.3	0.75	40.40	0.92	0.02
Adrenal gland	1.5	35.	3.	11.67	23.33	2.00
Thyroid gland	2	19.2	14.8	1.30	9.60	7.40
Lung	22.5	310.	20.8	14.90	13.78	0.92
Testis	13	13.4	4.5	2.98	1.03	0.35
Eye	8	16.6	1.8	9.22	2.08	0.23
Trachea	4	29.8	6.7	4.45	7.45	1.68
L.S.C. Node ⁽¹⁾	7.5	7.3×10^5	1.1×10^5	6.64	7.3×10^5	1.1×10^5
L.A. Node ⁽²⁾	1	4.4×10^5	1.8×10^4	24.4	4.4×10^5	1.8×10^3
R.S.C. Node ⁽³⁾	1	23.9	8.0	2.99	23.9	0.8
Sternum	22.5	217.0	6.8	31.91	9.64	0.30
Rib	5.5	124.0	14.5	8.55	22.50	2.63
Vertebrae	6.5	58.9	5.2	11.33	1.96	0.17
Skull	30	3255.0	181.0	17.98	500.70	27.80
Femur, P. (4)	12	284.0	9.2	30.86	23.66	0.77
Femur, Shaft	13.5	14.3	3.3	4.33	1.06	0.24
Femur, D. (5)	14	72.7	5.5	13.22	5.19	0.39
Injection Site	--	5.11×10^4	6.37×10^5	0.08	--	--

Dog No. 1990, DTPA treatment, 6 months study time

Liver (340 g)	61.5	3550.	2600.	1.37	57.72	42.28
Spleen	45	1560.	375.	4.16	34.67	8.33
Kidney	33	49.8	6.7	7.43	15.09	0.20
Adrenal gland	1.5	16.	2.1	7.62	10.67	1.40
Thyroid gland	1.5	4.5	3.0	1.50	3.00	2.00
Lung	18.5	4450.	741.	6.01	240.54	40.05
Testis	13.5	13.5	1.5	9.00	1.00	0.11
Eye	5	8.3	1.7	4.88	1.66	0.34
Trachea	4.5	10.5	4.2	2.50	2.33	0.93
L.S.C. Node ⁽¹⁾	1	7.9×10^5	5.7×10^4	13.86	7.9×10^5	5.7×10^4
L.A. Node ⁽²⁾	1	6.0×10^4	785.	7.64	6.0×10^4	7.85×10^2
R.S.C. Node ⁽³⁾	1.5	9.0	2.8	3.21	6.00	1.87
Sternum	19	425.	55.2	7.70	22.37	2.91
Rib	5	59.3	12.2	4.86	11.86	2.44
Vertebrae	33	664.	16.6	40.00	20.12	0.50
Skull	3	14.5	8.2	1.77	4.83	2.73
Femur, P. ⁽⁴⁾	8	552.	57.6	9.58	69.00	7.20
Femur, Shaft	8	35.6	1.27	2.80	4.45	1.59
Femur, D. ⁽⁵⁾	10	43.1	25.2	1.71	4.31	2.52
Injection Site	--	4.13×10^5	1.11×10^6	0.37	--	--

Dog No. 1687, no treatment, 7 months study time

Liver (315 g)	38	2630.0	1270.0	2.07	69.21	33.42
Spleen	88	262.0	138.0	1.90	2.97	1.56
Kidney	34.5	59.0	138.0	0.43	1.71	4.00
Adrenal gland	2	235.0	8.0	29.37	117.50	4.00
Thyroid gland	2	10.8	22.8	0.47	5.40	11.40
Lung	18.5	101.0	44.6	2.26	5.45	2.41
Testis	11	0.9	2.3	0.39	0.08	0.21

Eye	7	10.8	3.2	3.38	1.54	0.46
Trachea	9	1.3	18.2	0.07	0.14	2.02
L.S.C. Node ⁽¹⁾	4	3.8×10^5	5.7×10^4	6.67	9.5×10^4	1.43×10^4
L.A. Node ⁽²⁾	4	8.1	15.7	0.52	2.03	3.93
R.S.C. Node ⁽³⁾	1	14.8	5.1	2.90	14.80	5.10
Sternum	26	632.0	100.	6.32	24.30	3.85
Rib	9	345.0	40.	8.62	38.33	4.40
Vertebrae	30	120.	31.	3.87	4.00	1.00
Skull	6.5	54.6	14.4	3.79	8.40	2.21
Femur, P. ⁽⁴⁾	13	191.	35.9	5.32	14.69	2.76
Femur, Shaft	14	12.4	11.3	1.10	0.89	0.81
Femur, D. ⁽⁵⁾	18.5	141.	24.6	5.74	7.62	1.33
Injection Site	--	--	--	--	--	--

Dog No. 2325, no treatment, 7 months study time

Liver (374 g)	62	4070.0	47.5	85.7	65.64	0.77
Spleen	88	274.0	46.3	5.92	3.11	0.53
Kidney	31	23.8	200.0	0.12	0.77	6.45
Adrenal gland	3	95.2	2.1	45.33	31.73	0.70
Thyroid gland	1.5	4.6	6.8	0.68	3.06	4.53
Lung	17	106.0	98.1	1.08	6.24	5.77
Testis	13.5	7.5	7.2	1.04	0.56	0.53
Eye	7	6.4	2.9	2.21	0.91	0.41
Trachea	6	15.7	14.6	1.08	2.62	2.43
L.S.C. Node ⁽¹⁾	2	4.2×10^5	4.2×10^4	10.00	2.1×10^5	2.1×10^4
L.A. Node ⁽²⁾	1.5	10.2	6.9	1.48	6.80	4.60
R.S.C. Node ⁽³⁾	1.5	18.7	7.8	2.40	12.46	5.20
Sternum	28	921.0	92.5	9.96	32.89	3.30
Rib	8	520.0	52.7	9.86	65.00	6.59
Vertebrae	32	1100.0	30.4	36.18	34.30	0.95
Skull	7	47.7	10.3	4.63	6.81	1.47

Femur, P. (4)	13	737.	29.4	25.00	56.69	2.26
Femur, Shaft	16	66.5	7.9	8.42	4.16	0.49
Femur, D. (5)	17	191.	35.1	5.44	11.24	2.06
Injection Site	--	--	--	--	--	--

Dog No. 2100, DTPA treatment, 7 months study time

Liver (428 g)	65	3710.0	205.0	18.10	57.07	31.50
Spleen	103	202.0	38.6	5.23	1.96	0.37
Kidney	43	24.0	38.0	0.63	0.56	0.88
Adrenal gland	1.5	3.9	0.5	7.80	2.60	0.33
Thyroid gland	2	7.44	3.58	2.08	3.72	1.79
Lung	25.5	67.7	9.2	7.36	2.65	0.36
Testis	15	5.1	2.8	1.82	0.34	0.19
Eye	6.5	3.3	1.4	2.36	0.51	0.22
Trachea	9.5	7.1	4.6	1.54	0.75	0.48
L.S.C. Node(1)	2	1.4×10^6	1.7×10^5	8.24	7.0×10^5	8.5×10^4
L.A. Node(2)	1.5	11.4	1.96	5.82	7.60	1.31
R.S.C. Node(3)	1	2.98	0.58	5.14	2.98	0.58
Sternum	19	259.	15.2	17.0	13.63	0.80
Rib	7	139.0	7.9	17.59	19.85	1.29
Vertebrae	24	105.0	4.6	22.82	4.38	0.19
Skull	8	14.5	0.6	24.16	1.81	0.08
Femur, P. (4)	10	146.0	2.7	54.07	14.60	0.27
Femur, Shaft	12.5	16.8	6.3	2.67	1.34	0.50
Femur, D(5)	12	52.5	11.7	4.48	4.38	0.98
Injection Site	--	2.97×10^5	5.35×10^5	0.56	--	--

Dog No. 1803, DTPA treatment, 7 months study time

Liver (453 g)	55	656.0	49.6	13.4	11.93	8.90
Spleen	88	40.3	6.1	6.61	2.18	0.07

Kidney	51.5	13.9	54.1	0.26	3.71	1.05
Adrenal gland	2.5	18.8	1.8	10.44	7.52	0.72
Thyroid gland	2.5	13.6	22.7	0.60	5.44	9.08
Lung	27.5	18.1	3.9	4.64	0.66	0.14
Testis	15	11.7	3.9	3.00	0.78	0.26
Eye	7.5	3.8	2.6	1.46	0.51	0.35
Trachea	7	0.6	0.4	1.50	0.09	0.06
L.S.C. Node ⁽¹⁾	5	5.4×10^5	5.7×10^4	9.47	1.08×10^5	1.14×10^4
L.A. Node ⁽²⁾	0.5	12.9	3.4	3.79	25.8	6.8
R.S.C. Node ⁽³⁾	2.5	10.5	5.1	2.06	4.20	2.04
Sternum	23	322.0	21.2	15.19	14.00	0.92
Rib	6	225.	12.7	17.70	37.50	2.12
Vertebrae	27	162.	7.0	23.15	6.00	0.26
Skull	3	27.1	1.2	22.50	9.03	0.40
Femur, P. ⁽⁴⁾	10	174.	16.2	10.75	17.40	1.62
Femur, Shaft	11.5	177.	5.0	35.40	1.54	0.43
Femur, D. ⁽⁵⁾	12.5	42.7	8.7	4.91	3.42	0.70
Injection Site	--	5.86×10^6	1.36×10^5	43.09	--	--

Dog No. 1367, no treatment, 9 months study time

Liver (408 g)	53	10200.0	2800.0	3.64	192.40	52.83
Spleen	93	418.0	44.0	9.50	4.49	0.47
Kidney	39.5	100.0	217.0	0.46	2.53	5.49
Adrenal gland	2	31.0	2.3	13.47	15.5	1.15
Thyroid gland	1.5	4.4	6.6	0.67	2.93	4.40
Lung	24.5	137.0	52.4	2.61	5.59	2.14
Testis	14	48.9	15.1	3.24	3.49	1.08
Eye	9	25.2	2.3	10.96	2.80	0.26
Trachea	11	11.0	28.3	0.39	1.0	2.57
L.S.C. Node ⁽¹⁾	9.5		histopathological examination			

L.A. Node ⁽²⁾	5	3050.0	200.0	15.25	610.0	40.0
R.S.C. Node ⁽³⁾	5.5	14.7	7.3	2.01	2.67	1.33
Sternum	27	lost	lost	--	--	--
Rib	6	401.0	33.5	11.97	66.83	5.58
Vertebrae	34	393.0	20.9	18.80	11.56	0.61
Skull	3	44.8	6.0	7.47	14.93	2.0
Femur, P. ⁽⁴⁾	13	243.0	30.2	8.05	18.69	2.32
Femur, Shaft	12.5	27.4	7.5	3.65	2.19	0.60
Femur, D. ⁽⁵⁾	17	94.1	16.4	5.74	5.54	0.96
Injection Site	--	7.84 x 10 ⁶	8.79 x 10 ⁵	8.92	--	--

Dog No. 0792, no treatment, 9 months study time

Liver	50	5910.0	lost	lost	118.20	--
Spleen	28	773.0	"	"	27.60	--
Kidney	47.5	379.	"	"	7.98	--
Adrenal gland	2	13.	"	"	6.50	--
Thyroid gland	2	129.0	102.	1.26	64.50	51.00
Lung	28	116.	lost	lost	4.14	--
Testis	14.5	20.9	"	"	1.44	--
Eye	8	6.3	"	"	0.79	--
Trachea	10	12.3	"	"	1.23	--
L.S.C. Node ⁽¹⁾	4	1.1 x 10 ⁶	1.0 x 10 ⁵	11.0	2.75 x 10 ⁵	--
L.A. Node ⁽²⁾	2	--	lost	lost	--	--
R.S.C. Node ⁽³⁾	2	31.1	18.9	1.65	15.55	9.45
Sternum	24.5	560.	lost	lost	22.86	--
Rib	9.5	210.	"	"	22.10	--
Vertebrae	31	120.	"	"	3.87	--
Skull	7	16.6	"	"	2.37	--
Femur, P. ⁽⁴⁾	12	176.	"	"	14.67	--
Femur, Shaft	15	27.1	"	"	1.81	--

Femur, D. (5)	15	48.3	lost	lost	3.22	--
Injection Site	--	3.89×10^6	4.26×10^5	9.13	--	--

Dog No. 2447, DTPA treatment, 9 months study time

Liver (316 g)	104	2730.	331.	8.25	26.25	3.18
Spleen	29	1050.	249.	4.22	36.20	8.59
Kidney	35	57.1	125.	0.46	1.63	3.57
Adrenal gland	2	17.3	14.6	1.18	8.65	7.30
Thyroid gland	2	12.5	12.1	1.03	6.25	6.05
Lung	27.5	275.	42.4	6.49	10.00	1.54
Testis	11	114.	36.	3.17	10.36	3.27
Eye	9	5.5	2.1	2.62	0.61	0.23
Trachea	12.5	14.6	4.4	3.32	1.17	0.35
L. S. C. Node ⁽¹⁾	2	4.4×10^5	4.2×10^4	10.48	2.20×10^5	2.10×10^4
L. A. Node ⁽²⁾	1.5	7.8	1.7	4.59	5.20	1.13
R. S. C. Node ⁽³⁾	1.5	17.7	2.3	7.70	11.80	1.53
Sternum	23.5	111.	7.6	14.60	4.72	0.32
Rib	10	91.1	6.3	14.46	9.11	0.63
Vertebrae	28.5	332.	7.0	47.42	11.65	0.25
Skull	6	21.9	2.9	7.55	3.65	0.48
Femur, P. (4)	12	106.	15.3	6.93	8.83	1.28
Femur, Shaft	17	44.2	6.9	6.41	2.60	0.41
Femur, D. (5)	16	43.2	13.0	3.32	2.70	0.81
Injection Site	--	3.62×10^6	7.35×10^5	4.93	--	--

Dog No. 3032, DTPA treatment, 9 months study time
(implant excised after 13 days)

Liver (368 g)	68	6820.	813.	8.39	63.15	11.96
Spleen	117	5510.	3520.	1.57	47.09	30.09

Kidney	30	36.3	16.3	2.23	1.21	0.54
Adrenal gland	4	3.3	3.0	1.10	0.82	0.75
Thyroid gland	2	30.4	18.6	1.63	15.20	9.30
Lung	22	29.7	12.8	2.32	1.35	0.58
Testis	20.5	447.	67.4	6.63	21.80	3.29
Eye	9.5	4.6	2.4	1.92	0.48	0.25
Trachea	8.5	41.8	8.3	5.04	4.92	0.98
L.S.C. Node ⁽¹⁾	3	2.8×10^6	2.1×10^5	13.33	9.33×10^5	7.0×10^4
L.A. Node ⁽²⁾	1.5	2.3×10^5	21.2	1.08×10^4	1.53×10^5	14.13
R.S.C. Node ⁽³⁾	1.5	2.5	3.7	0.68	1.67	2.47
Sternum	29	536.	9.3	57.63	18.48	0.32
Rib	9	73.1	12.4	5.90	8.12	1.38
Vertebrae	30	308.	8.5	36.23	10.27	0.28
Skull	5	15.7	4.0	3.93	3.14	0.80
Femur, P. ⁽⁴⁾	14	97.4	6.3	15.46	6.96	0.45
Femur, Shaft	14	15.0	3.3	4.55	1.07	0.24
Femur, D. ⁽⁵⁾	18	8.7	1.2	7.25	0.48	0.07
Injection Site	--	--	--	--	--	--

Dog No. 1688, no treatment, 12 months study time

Liver (419 g)	57	148.	109.	1.36	2.60	1.91
Spleen	105	321.	13.4	23.95	3.06	0.13
Kidney	39	23.2	11.3	2.05	0.59	0.29
Adrenal gland	1.5	2.5	1.6	1.56	1.67	1.07
Thyroid gland	1	69.3	0.9	77.00	69.3	0.9
Lung	9	13.3	2.1	6.33	1.48	0.23
Testis	11	4.3	none det.	--	0.39	--
Eye	8	2.3	2.3	1.0	0.29	0.29
Trachea	9	5.2	1.6	3.25	0.58	0.18
L.S.C. Node ⁽¹⁾	0.5	6.8×10^5	2.9×10^3	234.40	1.36×10^6	5.8×10^3

L.A. Node ⁽²⁾	0.5	23.6	0.7	33.71	47.2	1.4
R.S.C. Node ⁽³⁾	1	10.2	1.0	10.2	10.2	1.0
Sternum	26	112.	3.9	28.71	4.31	0.15
Rib	9	80.9	1.9	42.58	8.99	0.21
Vertebrae	34	267.	1.5	178.00	7.85	0.04
Skull	7	12.0	2.6	4.62	1.77	0.37
Femur, P. ⁽⁴⁾	11	36.8	2.4	15.33	3.35	0.22
Femur, Shaft	14	40.7	47.0	0.87	2.91	3.36
Femur, D. ⁽⁵⁾	17	35.2	1.0	35.2	2.07	0.06
Injection Site	--	1.14×10^6	2.93×10^5	3.89	--	--

Dog No. 1689, no treatment, 12 months study time

Liver (410 g)	55	203.	365.	0.56	3.69	6.64
Spleen	71	316.	26.	12.15	4.45	0.37
Kidney	40	42.1	15.5	2.72	1.05	0.39
Adrenal gland	1.5	2.9	0.3	9.66	1.93	0.20
Thyroid gland	1.5	1.2	1.7	0.71	0.80	1.13
Lung	23.5	41.6	4.8	8.67	1.77	0.20
Testis	10.5	0.5	1.3	0.38	0.05	0.12
Eye	7	34.1	3.6	9.47	4.87	0.51
Trachea	8	9.4	3.3	2.85	1.18	0.41
L.S.C. Node ⁽¹⁾	2	1.5×10^5	2.1×10^4	7.14	7.5×10^4	1.05×10^4
L.A. Node ⁽²⁾	1	1.7	0.7	2.43	1.7	0.7
R.S.C. Node ⁽³⁾	1.5	2.6	0.7	3.71	1.73	0.47
Sternum	24	254.	13.90	18.3	10.58	0.58
Rib	8	143.	1.9	75.26	17.87	0.24
Vertebrae	30	292.	26.4	11.06	9.73	0.88
Skull	7.5	12.9	1.3	9.92	1.72	0.17
Femur, P. ⁽⁴⁾	14	187.	32.	5.84	13.36	2.29
Femur, Shaft	11	35.9	1.1	32.64	3.26	0.10

Femur, D. (5)	12	16.8	1.5	11.20	1.40	0.13
Injection Site	--	3.13×10^6	3.82×10^5	8.19	--	--

Dog No. 1884, DTPA treatment, 12 months study time

Liver (419 g)	132	140.	7.9	17.70	1.06	0.06
Spleen	131	82.6	4.6	17.96	0.63	0.04
Kidney	50	7.7	8.0	0.96	0.15	0.16
Adrenal gland	1.5	3.1	none det.	--	2.07	--
Thyroid gland	1	1.5	4.8	0.31	1.50	4.80
Lung	11	10.4	1.4	7.43	0.95	0.13
Testis	14	1.6	0.1	16.0	0.11	0.01
Eye	8	8.3	0.1	83.0	1.04	0.01
Trachea	10	20.7	2.0	10.35	2.07	0.20
L.S.C. Node ⁽¹⁾	2	1.4×10^5	3.2×10^3	43.75	7×10^4	1.6×10^3
L.A. Node ⁽²⁾	1	21.5	9.7	2.22	21.5	9.7
R.S.C. Node ⁽³⁾	1	1.8	0.2	9.00	1.8	0.2
Sternum	30	551.	11.5	47.91	18.37	0.38
Rib	7	49.4	1.3	38.00	7.06	0.19
Vertebrae	35	388.	1.3	298.46	11.09	0.03
Skull	5	3.8	1.6	2.38	0.76	0.32
Femur, P. (4)	14	1480.	14.7	100.60	105.71	1.05
Femur, Shaft	16	24.6	0.8	30.75	1.54	0.05
Femur, D. (5)	19	9.4	1.7	5.53	0.49	0.09
Injection Site	--	--	--	--	--	--

Dog No. 2315, DTPA treatment, 12 months study time

Liver (560 g)	91	700.	70.9	9.87	7.69	0.78
Spleen	108	422.	16.4	25.73	3.91	0.15

Kidney	41.5	5.6	5.1	1.09	0.13	0.12
Adrenal gland	2	16.1	0.4	40.25	8.05	0.20
Thyroid gland	2	9.6	1.2	8.00	4.80	0.60
Lung	30	37.8	8.0	4.72	1.26	0.27
Testis	19.5	3.9	0.6	6.50	0.20	0.03
Eye	7	35.5	2.25	15.77	5.07	0.32
Trachea	10.5	11.5	3.6	3.19	1.10	0.34
L.S.C. Node ⁽¹⁾	2.5	4.5×10^5	2.2×10^4	20.45	1.80×10^5	8.80×10^3
L.A. Node ⁽²⁾	1	1.2×10^3	136.	8.82	1.2×10^3	136.
R.S.C. Node ⁽³⁾	1	2.3	3.2	0.72	2.3	3.2
Sternum	33	280.	3.5	80.00	8.48	0.11
Rib	8	148.	2.4	61.66	18.50	0.30
Vertebrae	33	353.	1.9	185.78	10.70	0.06
Skull	6	29.2	2.1	13.90	4.87	0.35
Femur, P. ⁽⁴⁾	13	142.	4.0	35.50	10.92	0.31
Femur, Shaft	14	38.9	1.2	32.42	2.78	0.09
Femur, D. ⁽⁵⁾	16	113.	2.4	47.08	7.06	0.15
Injection Site	--	2.51×10^6	6.35×10^5	3.95	--	--

(1) left superficial cervical lymph node

(2) left axillary lymph node

(3) right superficial cervical lymph node

(4) proximal end of the femur

(5) distal end of the femur