One kilogram of plutonium-239 has a radioactivity level of about 63 curies (or about 2.1 trillion becquerels).

Plutonium-239 is difficult to detect since its gamma radiation is weak and since alpha radiation is rather hard to detect due to its short range. This is especially the case with small quantities of plutonium; nonetheless, such quantities can be lethal.

Nuclear Poison

INTRODUCTION

In the initial years after plutonium was discovered, Colonel Stafford L. Warren called it "the most poisonous chemical known."[17] Although substances other than plutonium produce toxic effects that are more rapidly lethal, and there are other radiological substances with higher specific activity, plutonium can be fashioned into radiological terror weapons because of its carcinogenicity and also into nuclear weapons. These two properties together make plutonium among the most dangerous substances known.

As a metal exposed to the natural environment, plutonium can produce enough heat to boil water and is highly chemically reactive. When in contact with living tissue at high enough levels of exposure, plutonium will cause direct tissue death. Animals experimentally exposed to high concentrations of plutonium by inhalation or injection incur acute damage to the lungs, liver, and hematopoietic (blood-forming) system, and show other manifestations of acute tissue injury.[18] Surviving animals are scarred and develop a number of chronic conditions.[19] Such high level exposure, however, is unlikely to occur to the general public even under a worst-case scenario. Of greatest concern are the radiobiological effects of plutonium, especially cancer, at low levels of exposure.

In the ensuing summary of plutonium toxicity, heavy reliance is made on animal studies, particularly studies of beagle dogs conducted by contractors of the United States Department of Energy (DOE). Investigations of humans exposed solely to plutonium are limited to small case-series studies. Occupational studies of nuclear weapons production workers have provided some data on humans exposed to mixtures of radioactive compounds including plutonium; however, they are few in number and suffer from a number of inaccuracies, omissions, misinterpretations, and other

17 Warren 1946.

18 Thompson 1989.

19 Thompson 1989.

methodological problems. A recent review by a task force of Physicians for Social Responsibility (the United States affiliate of IPPNW) summarized the difficulties posed by the methodological problems as well as the wall of secrecy that surrounded many of these studies in the United States.[20]

CARCINOGENIC MECHANISMS

As a carcinogen, plutonium is dangerous principally because of its alpha (rather than gamma) radiation, and primarily when it is inside the body rather than when outside. When plutonium is in the body, even in small quantities, its alpha radiation causes biological damage. Alpha particles, being heavy, ionize atoms more effectively than electrons and therefore lose their energy and are stopped in a much shorter distance. Because of the relatively many ionizations per unit distance (and per unit of energy lost), alpha radiation is called "high linear energy transfer" radiation ("high LET radiation"), as distinct from the relatively low energy transfer per unit length of photons and electrons ("low LET radiation"). Since alpha particles have a very short range in matter, about 50 micrometers in soft tissue, the energy delivery is more highly concentrated compared to energy from lower LET radiation sources such as beta or gamma radiation emitters. This results in far more biological damage for the same amount of energy deposited in living tissue.

The relative effectiveness of various kinds of radiation in causing biological damage is known as "relative biological effectiveness" (RBE). Over the decades, medical estimates of the dangers of internal alpha exposure have increased with more research. Until the mid-1980s, it was common to use an RBE of 10 for alpha radiation.[21] Since that time, the International Commission on Radiation Protection has recommended that this be increased to 20. (By comparison, gamma radiation has an RBE of 1.)

Very recent research has heightened concern that the true biological damage of alpha radiation may be even higher. Through *in vitro* studies of mouse hematopoietic stem cell colonies, Kadhim et al. found that exposure to a small number of alpha particles (but not X-rays) produced a high frequency of non-clonal aberrations in clonal descendants. This suggests that individual surviving stem cells can transmit to their progeny cells a chromosomal instability that can result in a variety of visible cytogenetic aberrations many cell cycles later.[22] It is well known, in turn, that humans with similar chromoso-

20 Physicians for Social Responsibility 1992.

21 The energy deposited per unit of mass in a medium is measured in units of grays or rads (1 gray = 100 rads), while the biological damage is measured in sieverts or rems (1 sievert = 100 rems). See glossary for fuller definitions of these units.

22 Kadhim et al. 1992.

mal instability defects are more prone to the development of early cancers.[23] This type of transmitted defect is quite distinct from stably induced somatic mutations, which are clonal and readily induced by low LET radiation.

In addition, Nagasawa and Little found that alpha particles at a dose of 0.31 mGy (31 millirads) caused a significant increase in the frequency of sister chromatid exchanges, a marker of genetic damage, in Chinese hamster ovary cells irradiated in the G_1 phase of the cell cycle.[24] A dose of approximately 2.0 Gy was necessary to produce a similar increase in exchanges by X-rays.

These studies suggest that plutonium either has a higher RBE than previously calculated or is more carcinogenic than would be predicted by traditional RBE calculations. If confirmed, this research has implications for both the setting of standards for allowable exposure to plutonium as well as the design and interpretation of epidemiological studies of populations exposed to plutonium.

ROUTES OF EXPOSURE AND BIOKINETICS

In addition to level of dose, the toxicity of plutonium depends on route of exposure, particle size, chemical form, and isotope. The route of exposure of greatest concern is inhalation. Once inhaled, plutonium can become lodged in the sensitive tissues of the lung. Studies in humans and beagle dogs have indicated that such deposits of plutonium remain for years, with gradual absorption into the circulation.[25]

Outside of the body, plutonium is usually less dangerous than gamma-radiation sources. Since alpha particles have a very short range, plutonium on or near the skin deposits essentially all of its energy in the outer, non-living layer of the skin, where it does not cause biological damage. The gamma photons emitted from plutonium decay penetrate the body, but as these are relatively few and weak, a considerable quantity of plutonium would be necessary to yield substantial doses of gamma radiation.[26] (For this reason, plutonium can

23 Evans 1992.

24 H. Nagasawa and J.B. Little. 1992. Induction of sister chromatid exchanges by extremely low doses of alpha particles. *Cancer Research* 52: 6394-6396.

25 Voelz et al. 1976; Thompson 1989; Cuddihy et al. 1976.

26 However, gamma radiation from plutonium increases with age due to the presence of small quantities of plutonium-241 (as an unavoidable contaminant). Plutonium-241 (half life 14 years) decays into americium-241 by emitting a beta particle. Since americium-241 has a far longer half-life (432 years), it builds up as plutonium-241 decays. Therefore, the gamma radiation from americium-241 decay, which is far stronger than that from plutonium-239, also builds up with age.

be transported with minimal shielding, with no danger of immediate serious radiological effects.) A wound, however, would render skin more vulnerable. Studies of beagles indicate that a significant amount of plutonium can be absorbed from a skin wound and enter the general circulatory system.[27]

Ingestion of plutonium is a possible route of exposure, through hand-to-mouth transfer of plutonium-contaminated soil or the consumption of contaminated food and water. However, the gastrointestinal absorption of plutonium oxide is less than 0.1 percent,[28] and the greater part of ingested plutonium is rapidly excreted.

Given the same total amount, plutonium is more dangerous in the form of fine particles than as large ones. When large particles (greater than 5–10 microns) are inhaled, they tend to be trapped in nasal hair or deposited on the surfaces of the bronchial airways, where they can be disposed of by the normal clearance mechanisms of the respiratory tree. These particles are then either ingested, which leads to little, if any, absorption, or excreted by coughing or spitting. Smaller particles (less than 1 micron), however, gain entry into alveoli (terminal air sacs of the lung), where they can become lodged, irradiating the surrounding tissue.

Retained plutonium is gradually absorbed, distributed throughout the body, and excreted via urine. Beagle studies have demonstrated that most plutonium retained in the lung is transferred to pulmonary lymph nodes within months to years. Plutonium is also distributed to hepatic and splenic lymph nodes, ovaries, kidney, other soft tissues, bone, and teeth.[29]

Much of plutonium biokinetics (i.e., rates of absorption and excretion, proportion of tissue distribution, etc.) depends on the chemical form of plutonium. Soluble forms of plutonium, e.g., plutonium nitrate, are absorbed from lung relatively rapidly and are deposited heavily in bone and liver, whereas most of the relatively insoluble plutonium oxide is retained in the lung for years, with gradual internal translocation to pulmonary lymph nodes.[30] Half of deposited plutonium oxide is distributed out of the lung by 4 years, with 75 percent of extraplumonary deposits found in the liver and 21 percent in bone.[31]

27 Dagle et al. 1984.

28 Bair 1975.

29 Thompson 1989; Park et al. 1972; Jee and Arnold 1960.

30 Thompson 1989.

31 Cuddihy et al. 1976.

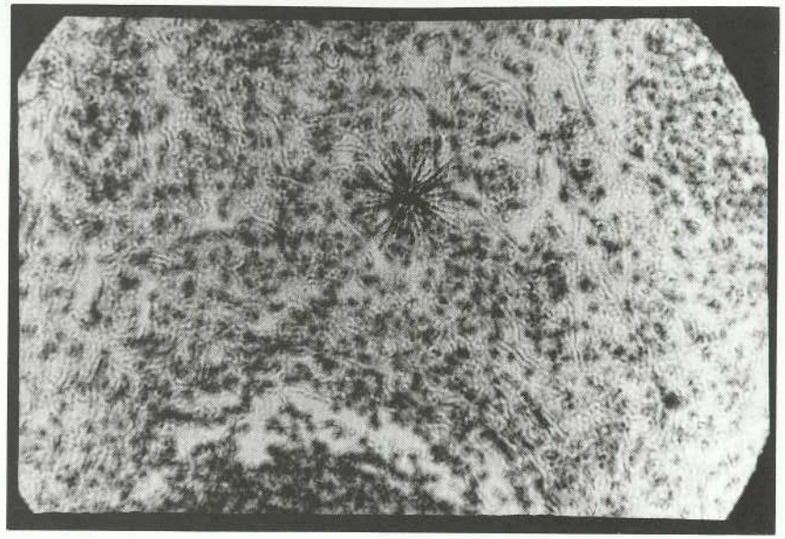

Figure 1.2. Tracks made by alpha radiation emitted by a particle of plutonium in the lung tissue of an ape, magnified 500 times. Photo by Robert Del Tredici.

Unlike radium, another bone-seeking element, which tends to be incorporated exclusively into the calcified mineral matrix of bone, plutonium has an affinity for the non-calcified, non-cartilaginous areas of bone, including the epiphyseum (bone growth plate), the periosteum (outer bone skin), and the endosteum (inner bone in contact with marrow).[32] Deposition is predominantly in trabecular bone (spongy bone in vertebrae and at ends of long bones) rather than in cortical bone.

Species and age are additional factors determining the biological effect of plutonium. For example, younger animals deposit a proportionately larger amount of absorbed plutonium in bone. Studies on monkeys have demonstrated that plutonium deposits in bone concentrate on endosteal surfaces.[33]

Some data are available on the biokinetics of plutonium in humans. In workers who accidentally inhaled plutonium-238 oxide in an insoluble matrix, plutonium was observed to appear in urine within six weeks of

32 Hamilton 1949.

33 Durbin and Jeung 1976.

34 International Commission on Radiological Protection 1972.

35 Voelz et al. 1976.

exposure[34] and then remained measurable in urine for years.[35] Whole body counting cannot be used to estimate body plutonium burden because alpha radiation does not penetrate the skin. Attempts have been made to estimate total plutonium body burden from urinary concentrations and *in vivo* chest counts of plutonium's weak 17-kilovolt X-rays or gamma rays; great variability seems to exist in the relatively sparse data, however, making accurate extrapolation difficult.[36]

The Plutonium Injection Experiment on Humans

Other data on humans derive from an experiment that was begun in April 1945 and carried out on chronically ill patients by Los Alamos National Laboratory in collaboration with the Rochester School of Medicine and Dentistry. The purpose was to gain "adequate information as to the fixation and excretion of plutonium by man [which] is essential to the evaluation and interpretation of the maximum permissible body tolerance."[37] Twelve ill patients were chosen for the experiment whom the authors stated were

> suffering from chronic disorders such that survival for ten years was highly improbable. By adhering to these criteria, the possibility of late radiation effects would be avoided. Furthermore, an opportunity to obtain postmortem material within a few months, or at most a few years, would be much greater.[38]

Two of the subjects were under 45, the youngest being an 18-year-old female with Cushing's syndrome. Each subject was injected with plutonium in the form of plutonium citrate in amounts ranging from 4.6 to 6.5 micrograms. While the subjects were alive, regular physical examinations were performed, and blood, urine and fecal specimens were collected for plutonium measurements and standard clinical assays. At the time of death, samples were collected and analyzed at autopsy.

During the course of the study, the authors did not perceive any sign of clinical toxicity in either the clinical exams or laboratory tests. Monitoring of urine and fecal excretion of plutonium permitted the estimation of the half-life of plutonium in the body — 118 years — as well as the observation that distribution kinetics of plutonium in the human body do not differ substantially from those in animals. The long half-life of plutonium suggests that once absorbed, plutonium poses a lifetime risk due to its neglible excretion rate.

It is difficult, however, to reach firm conclusions from these experi-

36 Voelz et al. 1976.

37 Langham et al. 1950, p. 9.

38 Langham et al. 1950, p. 10.

ments. Inter-individual variations in the observed data were large. The study was performed on ill, mostly elderly subjects who can be expected to have had metabolisms much different than those of young, healthy people.

Finally, we must condemn this experiment as unethical. No therapeutic benefits to the patients were intended, and scientists knew of the toxicity of plutonium even then. Informed consent of the patients was not obtained (since even the word "plutonium" was classified during World War II); surviving patients were only told of their injection with plutonium in 1974.

CARCINOGENICITY OF PLUTONIUM: ANIMAL STUDIES

Experiments on beagles have shown that a very small amount of plutonium inhaled in relatively insoluble form, such as plutonium oxide, will with high probability produce lung cancer. In some experiments, lung tumors arose in 100 percent of the animals. These tumors are predominantly bronchioalveolar carcinomas originating in areas of fibrosis and cell abnormalities in peripheral lung where plutonium is deposited. The data from these animal experiments indicate that the lung burden of plutonium-239 required to induce cancer is very small, and that amounts as small as a millionth of an ounce would cause lung cancer with high probability.[39] Fetter and von Hippel estimated that a single inhalation of 80 micrograms of weapon-grade plutonium (6 percent Pu-240 and 94 percent Pu-239), of which 15 percent would be retained, would lead to a 100 percent risk of death from lung cancer.[40]

Soluble forms of plutonium that have greater systemic absorption, such as plutonium-238 oxide, were found to produce bone tumors in dogs, primarily

39 See, for example, Bair and Thompson 1974. This article reports that 0.003 microcuries of plutonium (in the form of plutonium-239 dioxide particles under 10 microns) deposited per gram of lung is enough to cause bronchio-alveolar cancer (a relatively less common form of lung cancer) in 100 percent of cases of exposed beagle dogs. Thus, 0.003 microcuries per gram x 570 grams of lung per human x 16 micrograms of plutonium-239 per microcurie = 27.4 micrograms to cause lung cancer in the average adult human. However, since this experiment was inadvertently a saturation experiment (i.e., all the dogs, including the lowest dose recipient, got lung cancer), the risk per unit of lung burden may be higher.

The amount of plutonium needed to cause cancer may be smaller in children. In addition, the risk to smokers may well be much higher, as it is for radon exposure, because of synergy.

Also see McClellan, particularly the article in it entitled "Status Report: Toxicity of Inhaled Alpha-Emitting Radionuclides," by B.A. Muggenburg et al.

40 S. Fetter and F. von Hippel. 1990. The hazard from plutonium dispersal by nuclear-warhead accidents. *Science and Global Security* 2: 21-41.

osteogenic sarcomas. These tumors originated predominantly in trabecular bone, usually in the long bones or vertebrae.[41] Incident plutonium dose and rate of bone turnover are factors increasing the risk of osteosarcoma in particular bone sites.

CARCINOGENICITY OF PLUTONIUM: HUMAN STUDIES

Few published studies exist from which one can directly estimate the carcinogenic risk of plutonium in humans. Most relevant published studies have been on cohorts of workers involved in nuclear weapons production who were exposed to multiple sources of radiation in addition to plutonium. Other obstacles to using even these studies to estimate plutonium risk are typical of those encountered in environmental epidemiology:

- uncertainties in identifying exposure times and dose based on records, leading to exposure misclassification
- the difficulty of measuring plutonium in the body and the lack of surrogate biological markers of exposure
- inter-individual variation in the metabolism and excretion of plutonium
- inadequate control of potential confounders, such as smoking, in epidemiological studies
- inadequate follow-up of the morbidity and mortality experienced by a population being studied (e.g., loss to follow-up of retired or transferred workers in occupational studies).

Some of these obstacles are difficult to address in any epidemiological investigation; others, such as follow-up investigation of the morbidity and mortality experience of a study population, require a diligence and concern that were likely absent in the nuclear weapons industry.

Regarding this last point, in 1975, 30 years after large amounts of plutonium began to be handled, thereby causing some exposures to the workers who dealt with it, Dr. George Voelz, the medical director of Los Alamos Scientific Laboratory, noted:

> Formal studies for delayed effects from these [plutonium] exposures have not been reported, so it is only possible to state that no cases of acute human pathology following plutonium exposures have been reported to date. Most of these workers have been followed with regular periodic medical examinations during their employment with AEC contractors. *After termination of employment most workers have not been followed by medical examinations for the*

41 Thompson 1989.

> *specific purpose of determining possible clinical effects from plutonium (or any other hazardous materials they may have encountered in their work). . . .*
>
> It would be nice to be able to report that the long-term studies on plutonium workers have been practiced faithfully throughout the industry. *Unfortunately, the follow-up of workers following termination of their employment in plutonium work has been limited to only a few special situations.* [emphasis added][42]

This paucity of available data on the effects of human exposure to plutonium is both unfortunate and inexcusable. It is unfortunate because it forces plutonium risk estimates to rely on animal studies (which are valuable, but extrapolation to humans is always uncertain) and on human studies with small sample sizes (which means that the sensitivity of the study is low and the uncertainty of the results large). And it is inexcusable given the large number of plutonium workers employed over the last five decades in the U.S. alone, on whom data in fact exist. As concluded by the recent review of the Physicians for Social Responsibility task force, the U.S. government and its contractors have simply failed to set up the studies to properly collect and analyze these data.

Finally, it is noteworthy that, despite the fragmentary and flawed nature of the research that has been performed, the PSR task force reviewing studies of nuclear weapons industry workers in the U.S. identified several cancer types for which five or more study populations had demonstrated a standardized mortality or incidence ratio greater than one (and the occurrence of at least five cases), or a standardized ratio that was significantly higher than expected at the $p < 0.1$ level, or a statistically significant increase in cancer with increased radiation exposure.[43] These cancer types included lymphatic and hematopoietic cancers, non-Hodgkins lymphoma, brain and central nervous system cancer, prostate cancer, and lung cancer.

One of the few attempts to fully follow a cohort of workers exposed mainly to plutonium is a long-term study of 26 white males from the Manhattan Project exposed to plutonium at Los Alamos in 1944 and 1945, where the first nuclear weapons were made. Studies of their health status have been periodically published, most recently in 1991.[44]

The amounts of plutonium deposited in the bodies of the subjects were estimated to range from "a low of 110 Bq (3 nCi) . . . up to 6960 Bq (188

42 Voelz 1975.

43 Physicians for Social Responsibility 1992.

44 Voelz and Lawrence 1991.

nCi)."[45] These quantities corresponded to a weight range of 0.043 micrograms to 3 micrograms. Neither the lung dose initially received nor the route of exposure which resulted in the plutonium body burden is known with certainty. The solubility characteristics of the inhaled plutonium are also not well understood, thereby creating uncertainty as to which organs of the body are being irradiated (insoluble particles stay trapped in the lung for a long time, whereas soluble plutonium is relatively quickly metabolized and translocates to other organs such as bone) and at what dose.[46]

Seven of the subjects had died by 1990. The listed causes of death were three lung cancers (including one where the cause of death was listed as heart disease, but the underlying cause was lung cancer), one bone cancer (bone sarcoma), one myocardial infarction, one pneumonia/heart failure, and one auto-pedestrian accident.[47] While four of the seven deaths were due to cancer, little can be inferred from these small numbers. Interpretation is also complicated by the fact that all three people who had lung cancer had smoked cigarettes.

Unlike lung cancer, however, bone cancer is rare in humans. Its expected occurrence in a group of 26 men over a 40-year timeframe is only about one in 100.[48] The plutonium worker's bone cancer occurred in the sacrum and was diagnosed in 1989, allowing a latency period of 43 years after his exposure. Its occurrence among a population of this size (where the subject, incidentally, received a plutonium dose below that of current occupational radiation protection guidelines)[49] is suggestive, especially in view of plutonium's affinity for bone.

Any other inference from this study is very difficult. Obviously, the small sample size severely limits the power of this study to detect anything but the most grotesquely elevated cancer risk. Nevertheless, this study is one of the very few that has attempted full follow-up of an exposed cohort. The

45 Voelz and Lawrence 1991, p. 186.

46 These aspects of the study are discussed in some detail in Gofman 1981, pp. 510–520 (based on the status of the Manhattan Project workers study as published in Voelz et al. 1979). Gofman notes evidence indicating that the inhaled plutonium was principally in an aerosolized, dissolved form rather than in insoluble particulates, and he concludes that "nothing in Voelz's entire paper... rules out the possibility that these 26 workers inhaled *only* highly soluble plutonium. If that was the case, the Voelz study is irrelevant to the lung cancer hazard of plutonium *particulates*." (Gofman 1981, p. 516.) We note, however, that it would not be irrelevant to the study of other cancer hazards such as bone sarcomas.

47 Voelz and Lawrence 1991, Table 7.

48 Voelz and Lawrence 1991, p. 189.

49 Voelz and Lawrence 1991.

failure of its authors to comment on the lack of statistical power afforded by a sample size of 26 is unfortunately shared by the authors of most of the other occupational mortality studies of the nuclear weapons industry.[50]

Environmental Regulatory Considerations

The danger to human health posed by small quantities of plutonium has given rise to serious concerns about the various ways in which plutonium contaminates soil, water, and air, and the pathways by which it could reach human beings. These concerns have led to restrictions on plutonium and other transuranic materials in radioactive wastes. Notable among these is the special classification for waste materials containing large quantities of transuranic materials.

The maximum amount of plutonium-239 allowed by U.S. regulations in the air for an off-site population is 2×10^{-5} picocuries per liter. The U.S. Nuclear Regulatory Commission calculates that a person exposed to such a concentration for one year would get an effective dose equivalent of 0.5 millisievert (50 millirems). The corresponding limit for plutonium-239 in water is 20 picocuries per liter.[51] The lower allowable concentration of plutonium in air is due in large part to the higher biological uptake through inhalation than through ingestion; an additional reason is the relatively larger volume of air people breathe each year compared to the volume of water consumed.

The U.S. Environmental Protection Agency also has suggested environmental "action levels" to be used in the clean-up of plutonium-contaminated soil.[52] The EPA's principal suggested action level for newly deposited plutonium-239 is 0.1 microcurie per square meter,[53] with a preliminary "screening level" of 0.2 microcurie per square meter in the top centimeter of soil.[54] This matter has assumed some importance because of the contamination of large quantities of soil by plutonium from nuclear weapons production and testing. Areas with plutonium contamination exceeding this level would have to be cleaned up, by removal of topsoil.

Table 1.1 shows the plutonium contamination of various areas in the U.S. nuclear weapons complex, according to official data.

The U.S. Department of Energy classifies wastes containing large quantities of transuranic elements (mainly plutonium, but americium and nep-

50 Physicians for Social Responsibility 1992.

51 U.S. Nuclear Regulatory Commission 1991, Revised 10 CFR Part 20, Appendix B, Table 2. For a summary of standards for radionuclides in air and water, see Saleska 1992a.

52 An "action level" is a guide used to indicate the need for further study of the situation and for the possible initiation of protective actions and restrictions; it is not an enforceable regulatory limit.

53 This is based on a 1 rem dose to the lung over the course of one year due to resuspension of plutonium particles in air and breathing such air. It is conservative in that it assumes 100 percent occupancy for the full year and a resuspension rate derived from the behavior of relatively newly deposited contamination, which is much more mobile and more easily resuspended than old or stabilized contamination (which EPA says may have resuspension rates as much as 1,000 lower than that used to derive the 0.1 microcurie action level). (U.S. Environmental Protection Agency 1990, Vol. 2, pp. 5–11 and 5–12.)

Table 1.1. Inventory of plutonium contamination in soil for selected sites in the U.S.

LOCATION	APPROX. INVENTORY	REMARKS
Hanford Reservation[a] (central Washington)	6.2×10^{14} Bq (16,700 Ci)	Pu production facility (and other activities)
Nevada Test Site (near Las Vegas, Nevada)	$> 5.7 \times 10^{12}$ Bq (> 155 Ci)	Nuclear test site surface and subsurface tests
Rocky Flats Plant (near Denver, Colorado)	$2.9\text{-}3.7 \times 10^{11}$ Bq (8-10 Ci)	Weapons fabrication plant (limited cleanup in progress)
Mound Laboratory (Miamisburg, Ohio)	$1.8\text{-}2.2 \times 10^{11}$ Bq (5-6 Ci)[b]	Pu-238 in sediments in canals
Savannah River Plant (southwest South Carolina)	$1.1\text{-}1.8 \times 10^{11}$ Bq (3-5 Ci)	Pu and higher isotopes production
Los Alamos Lab (northwest of Santa Fe, New Mexico)	$3.7\text{-}7.4 \times 10^{10}$ Bq (1-2 Ci)	Weapons development (high levels in remote canyons)
Trinity Site (near Alamogordo, New Mexico)	1.6×10^{12} Bq (45 Ci)	Site of first atomic bomb test

Source: U.S. Environmental Protection Agency 1990, Vol. 1, Table 1-2, p. 1-11.

Notes:

(a) Total estimated transuranic alpha activity. (U.S. Department of Energy 1991b.)

(b) U.S. Department of Energy (1991b, Table 3.4, p.86) reports a total transuranic alpha activity in soil at Mound of 40 curies.

54 U.S. Environmental Protection Agency 1990, Vol. 2, p. 3–9.