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**Maximum Permissible Body Burdens and Concentrations of Plutonium:
Biological Basis and History of Development**

W. H. Langham and J. Healy

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Maximum Permissible Body Burdens and Concentrations of Plutonium: Biological Basis and History of Development¹

W. H. LANGHAM* and J. W. HEALY

I. Introduction

Any attempt to write an account of the early events and decisions leading to the current protection limits for plutonium will be controversial at best. Many of the early actions and decisions and the reasoning on which they were based were documented only as memoranda among the principal personnel of the various projects, institutions and organizations involved, as monthly progress reports and in the minutes of the various project, group and section council meetings. All exchanges of ideas, information and actions, of necessity, were carried out under strict security regulations.

The present account will be subject to even more controversy because most of the principal participants in these early happenings are still very much alive and each will have his own opinions, views and notes regarding what went on. After 25 years or so, it would be surprising indeed if all who participated would remember the events in exactly the same way and assign to them the same order of importance. Perhaps there is a lesson to be learned by those now faced with making similar decisions that cannot wait for accumulation of unequivocal data. Documentation of the reasoning involved (even if, or particularly if, based on inadequate data) will enable the next generation to more fully understand the inherent uncertainties and basis of the decisions at the time and to proceed compassionately with appropriate modifications and refinements without regarding previous work either as dogma passed down from the most high or as inadequate, irrelevant and immaterial and, therefore, to be completely ignored and rediscovered.

Despite the controversy that may arise, we feel that an attempt to document briefly the early biological basis and history of the development of current protection standards for plutonium is worthwhile, since studies with plutonium and similar work with strontium have constituted the basis for present radiation limits for radionuclides (except radium) that deposit in bone. No attempt will be made to compile a complete review of all excellent research that has been directed toward better understanding of the physiology, toxicology and industrial medical control of plutonium. Previous and following chapters are devoted to such in-depth coverage. Rather, it is our intent to cover in approximate chronological fashion the evolution of protection standards for plutonium, emphasizing those biological observations that had the most impact on the derivation of

¹ Work supported by U.S. Atomic Energy Commission under Contract at the Los Alamos Scientific Laboratory of the University of California, Los Alamos, New Mexico 87544.

* Deceased.

current values. This emphasis seems appropriate as biological considerations and relevant data become somewhat obscure and depersonalized by the formal equations currently used to derive maximum permissible body burdens and concentrations in air and water. In taking the above approach, we extend our profound apologies both to those whom we may annoy by misrepresentation of their views or those we many overlook.

II. Radiation Protection Criteria Prior to 1943

Experience with the biological effects of radiation began within months after the discovery of X-rays and radium. RÖNTGEN discovered X-rays in 1895, and a case of roentgen-dermatitis was reported less than a year later. Several more cases were reported by 1900. PIERRE and Madam CURIE isolated radium in 1898, and in 1900 the occurrence of chronic radium-dermatitis was documented. The first case of occupational roentgen-cancer as well as the first fatality from this disease was reported from Germany in 1902.²

After World War I, a number of committees were organized to recommend protective measures against radiation exposure. These committees were the forerunners of the International Commission on Radiological Protection (ICRP) and the U. S. National Committee on Radiation Protection (NCRP). (Now "Council"—Editor.) The ICRP had its beginning in the Committee on X-ray and Radium Protection authorized by the Second International Congress of Radiology in 1928 (Int. Congr. Radiol. 1928) and the NCRP in the organization in 1929 of a U. S. Advisory Committee on X-ray and Radium Protection (TAYLOR, 1958a). The function of the latter committee was to provide input from the U. S. to the International Committee. It became the NCRP in 1946.

The early history and major recommendations of the NCRP and ICRP have been reviewed by L. S. TAYLOR (1958a and b). Although these groups provided guidance on radiation protection measures, they did not recommend a tolerance dose in their first publications. In 1934 and again in 1937 the International Committee published a recommendation of 0.2 r per day or 1 r per week as the tolerance dose. The U. S. Advisory Committee on X-ray and Radium Protection recommended a tolerance value for X-rays of 0.2 r per day in 1931 (NCRP, 1931), which was subsequently changed to 0.1 r per day in 1936 (NCRP, 1936) and extended to include both X- and gamma-rays in 1938 (NCRP, 1938). The roentgen (r) had been adopted as the international unit of X-ray exposure at the Stockholm Congress of Radiology in 1928. The definition of the roentgen was modified later at the Chicago Congress of Radiology in 1937 to make it include gamma-rays.

During the decade of the 1920's when the various committees were concerned with establishing protection criteria for X-rays and gamma-rays of radium, another human experience attesting to the dangers of radiation and radioactive materials came to light. In 1922, 1923, and 1924, nine girls died who had been employed for several years as luminous watch dial painters in a New Jersey factory (MARTLAND, 1929). No investigations were made as to the cause of death in any of these cases. In September 1924 BLUM (1924), a New York dentist, made the first report suggesting an occupational poisoning associated with the same plant from which the early deaths occurred. He reported before the American Dental Association a case of unusual and intractable osteomyelitis of the mandible and, knowing nothing of the nature of the luminous paint, thought from the unusual clinical behavior that some sort of occupational exposure existed. In May and September 1925, HOFFMAN (1925a and b) reported on his investigations of the New Jersey plant and offered the opinion that an unusual occupa-

² These data and incidences quoted from HUEPER (1942).

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tional poisoning existed and thought that mesothorium in the luminous dial paint might be mainly responsible. In the August issue of the Journal of Industrial Hygiene, CASTLE et al. (1925) reported on "Necrosis of the Jaw in Workers Employed in Applying Luminous Paint Containing Radium". Their report was a result of an investigation of conditions in the New Jersey plant conducted in March 1924 at the request of plant executives, but the findings had not been revealed immediately at company request.

On October 8, 1925, HARRISON S. MARTLAND presented a paper at the New York Pathological Society meeting on "Some Unrecognized Dangers in the Use and Handling of Radioactive Substances", and the paper was published in full in the Journal of the American Medical Association (MARTLAND, 1925) in the same issue as Hoffman's paper on "Radium (Mesothorium) Necrosis". For the next several years MARTLAND and others vigorously pursued the radium poisoning problem and the New Jersey cases in a highly scientific and thorough manner, and within four years MARTLAND and HUMPHRIES (1929) reported the first cases of radium-induced osteogenic sarcoma. By 1932 it was apparent also that industrial uses of radium were not the only potential source of radium poisoning. Radium was being administered by the medical profession and peddled by the nostrum vendors in the form of radium tonics (AMA Bureau of Investigation, 1932; GETTLER and NORRIS, 1933), the most famous being "Radithor." The status of the radium poisoning problem as of 1933 was reviewed by EVANS (1933).

For the next several years efforts were directed toward studies of radium uptake, distribution and excretion and toward development of vastly more sensitive methods of measurement, including quantitation of radium content and elimination rate of living persons (EVANS, 1935, 1937; AUB et al., 1938). Only by knowing the body burdens in exposed individuals with and without overt signs and symptoms of radium poisoning could an approach be made toward establishing a harmful level. In 1934 R. D. EVANS became Assistant Professor of Physics at the Massachusetts Institute of Technology, which resulted in a collaborative effort by EVANS, AUB, and MARTLAND to carefully measure the body burdens of fixed radium in known exposure cases. EVANS has continued the follow-up and measurement of known cases of radium exposure and currently has observations on over 650 cases (1971). By 1941 the observations were that signs of poisoning and even death may occur with body burdens as low as 1 μg of radium fixed in the bone for several years. Seven cases with more than 0.02 but less than 0.5 μg after 7 to 25 years were completely symptom-free. These observations were not referenced until 1943 (EVANS, 1943); however, they were used in 1941 as the basis for the first recommendation of 0.1 μg as the tolerance dose for radium (National Committee on Radiation Protection, 1941)—*a value that is still accepted*. It was recommended also that the radon concentration in the atmosphere of workrooms should not exceed 10^{-11} Ci per liter. Report No. 5 (NBS-27) was prepared, in response to a request from organizations concerned with the dial painting industry, by a special committee³ appointed by LYMAN BRIGGS, Director of the National Bureau of Standards.

³ The committee membership was Dr. L. F. CURTISS, Chairman, representing the National Bureau of Standards, Washington, D.C.; Dr. R. D. EVANS, Physicist, Massachusetts Institute of Technology, Cambridge, Mass.; Dr. G. FALLA, Physicist, Memorial Hospital, New York City; Dr. FREDERICK B. FLINN, Director of Industrial Hygiene, Columbia University, New York City; Dr. HARRISON S. MARTLAND, Chief Medical Examiner of Essex County, Newark, New Jersey; Dr. J. E. PAUL, representing the U. S. Radium Corporation, New York City; Dr. J. S. ROGERS, representing the Division of Labor Standards, Department of Labor, Washington, D.C.; Captain CHARLES S. STEPHENSON (MC), representing the Bureau of Medicine and Surgery, U. S. Department of the Navy, Washington, D.C.; and Dr. G. T. TAYLOR, representing the Radium Chemical Company, New York City.

The quantitative studies of early radium exposure cases during the 1930's by EVANS, AUB and MARTLAND are the most important factor in establishment of present exposure guides for plutonium as well as all other bone-seeking radio-nuclides. Historically, it is interesting to note that the recommendation of 0.1 μg as the tolerance dose for radium (which provided the basis for presently accepted protection standards for plutonium) occurred only two months after the discovery of plutonium and only 18 months prior to the first demonstration of a sustained nuclear reaction.

At the beginning of 1943 (when the Manhattan District's Plutonium Project was just getting underway), only three tolerance values for occupational exposure to radiation and radioactive materials had been established: 0.1 r per day for external X- and gamma-radiation, 0.1 μg of radium as the maximum allowable body deposition and 1×10^{-11} Ci of radon per liter in the air of workrooms. The unit of external radiation exposure was the roentgen and applied only to X- and gamma-rays.

III. Plutonium Occupational Protection Criteria (1943—1946)

During 1943 the Plutonium Project's Health Division under Dr. R. S. STONE had little time to worry about the potential hazards of plutonium *per se*. The external radiation hazards associated with neutrons and gamma-rays from the large-scale chain-reacting piles being planned and the radiation hazards that would be imposed by the large quantities of fission products in the uranium slugs from which the plutonium had to be separated were staggering and had to receive first priority. The hazards imposed by fission products were both external and internal, and little or nothing was known about body uptake, deposition, distribution and excretion of most of them. Dr. G. T. SEABORG (1970) aptly summed up the status of the plutonium hazard problem during 1943 by pointing out that "up to the fall of 1943 the cyclotron-produced plutonium in existence amounted to only 2 mg, a quantity distributed throughout the program over a period of one and a half years—and a quantity so precious we couldn't afford to ingest any of it". The situation changed fast, however; with the start-up of the Clinton (Site X, Clinton, Tennessee) reactor (November 4, 1943), milligram amounts of plutonium became available by the first of the year. Production of plutonium grew to gram amounts by March 1, 1944, and with the start-up of the Hanford piles⁴ (Site W, Hanford, Washington) to kilogram amounts by mid-1945.

Concern over the hazards of plutonium processing developed even more suddenly than did production of plutonium itself; Dr. SEABORG, Head of the Metallurgical Laboratory's Chemistry Division, wrote the following letter (1944a) to Dr. R. S. STONE, Medical Director:

R. S. STONE
G. T. SEABORG

January 5, 1944
(Declassified, July 18, 1969)

Physiological Hazards of Working with Plutonium

It has occurred to me that the physiological hazards of working with plutonium and its compounds may be very great. Due to its alpha radiation and long life it may be that the permanent location in the body of even very small amounts, say one milligram or less, may be very harmful. The ingestion of such extraordinarily small amounts as some few tens of micrograms might be unpleasant, if it locates itself in a permanent position. In the handling of the relatively large amounts soon to begin here and at Site Y, there are many conceivable methods by which amounts of this order might be taken in unless the greatest care is exercised.

⁴ Operation of the first Hanford pile began in September 1944.

practices were already underway at both the Chicago and Clinton laboratories. By January 29, 11 mg of plutonium had been allocated (for shipment on February 1) to Dr. HAMILTON at Berkeley for animal uptake, distribution and excretion studies (PETERSON, 1944). The material was delivered on February 10 (HAMILTON, 1944), and the Metallurgical Laboratory's progress report for February (ALLISON 1944a) contained the following brief announcement:

*"Product Studies—*Oral absorption of all valence states is less than 0.05%; lung retention high; absorbed material predominantly in the skeleton; excretion very small in urine and feces."

This curt announcement coming only a few days after receipt of the plutonium reflects the dedication of Dr. HAMILTON and his group and was the first contribution of plutonium animal experimental data to the establishment of current protection criteria. The importance of these first animal experiments to the biological basis for present plutonium protection criteria can hardly be over-emphasized. They delineated the battlefield: plutonium, like radium, concentrated in bone and would be expected to produce similar types of bone lesions, including osteogenic sarcoma, its initial rate of elimination may be much slower than radium, its fixation in the lungs may be much higher and its absorption in all valence states may be much less. Subsequent experiments by HAMILTON's group and others confirmed these experiments and provided more quantitative information.

What appears to be the first value for a dangerous level of plutonium in air was proposed in a letter dated March 1 (1944 b), from Dr. S. K. ALLISON (Director of the Chicago Metallurgical Laboratory) to Dr. J. R. OPPENHEIMER (Director of Site Y), in which he pointed out that the plutonium problem would exist at Site Y (Los Alamos, New Mexico), and Site X (Clinton Laboratories, Clinton, Tennessee) and Site W (Hanford, Washington). ALLISON proposed that it would be dangerous to work 48 hours per week for two years in an atmosphere that contained 2×10^{-15} g/cm³ (1.2×10^{-10} μ Ci/cm³). Evidently he made the calculation himself based on 5 μ g of plutonium deposited in the lungs as being dangerous. This assumption must have come from an analogy with the 1 μ g harmful level of fixed radium in the skeleton of dial painters. If about 50 μ g of plutonium in the skeleton was equivalent in energy deposition to 1 μ g of radium and the lungs weighed about one-tenth as much as the skeleton, then 5 μ g of plutonium might be a dangerous level if deposited in the lungs. He assumed a breathing rate of 10 liters per minute and evidently 100 percent deposition in the lung with no elimination and translocation. On the basis of these assumptions, the dangerous air concentration for 48-hour occupancy for two years would be:

$$\frac{5 \times 10^{-6} \text{ g}}{10^4 \text{ cm}^3/\text{min} \times 2.8 \times 10^5 \text{ min}/2 \text{ yr}} = \sim 2 \times 10^{-15} \text{ g/cm}^3.$$

ALLISON also proposed some data on an average (standard) man that might be of interest in the plutonium hazard evaluation problem: "In a male of average weight 160 pounds, the weight of the skeleton, where radium is deposited, is 21.6 pounds. The weight of the lungs in this hypothetical average man is 4.34 pounds when they are full of fluid, and 1 pound when the normal fluids are removed. We have taken a factor of 10 as roughly representing the ratio of skeletal weight to lung weight." This tentative air tolerance value was reported at the Project Council Information Meeting (Health) held on March 7, 1944 (NICKSON, 1944). It is of more than casual historical interest that a heated discussion of the effect of particle size on lung deposition and retention ensued in which it was intimated that the majority of particles of less than 1 μ m would stay in the lung. At the

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same meeting, Dr. STONE suggested the use of "rep" for radiation other than X- and gamma-rays (α , β , n , etc.) and "rem" for roentgen equivalent mouse or man. These concepts had been transmitted to him by H. M. PARKER, then at the Clinton Laboratories.

In the Clinton Laboratories report for the month ending April 29, 1944 (Metallurgical Laboratory, 1944a), H. M. PARKER proposed a tentative plutonium air tolerance of $5 \times 10^{-10} \mu\text{g/cm}^3$ ($3 \times 10^{-11} \mu\text{Ci/cm}^3$) for a 1-year exposure based on a comparison with 0.1 r per day tolerance exposure for X- and gamma-rays. He assumed 50 percent retention of dust from the inhaled air. For heavy-particle radiation he assumed the tolerance dose to be 0.01 rep per day (twice as damaging as neutrons, 10 times as damaging as X-rays). Conceptually, this was probably the first use of an RBE (relative biological effectiveness) of 10 for alpha particles, although he did not call it RBE. From these assumptions and the assumption of uniform distribution over the entire lung surface ($\sim 8 \times 10^5 \text{ cm}^2$), he calculated that the lung tissue would receive 0.01 rep per day when the lung burden reached $0.64 \mu\text{g}$ ($0.04 \mu\text{Ci}$). Assuming no elimination mechanism from the lungs, a person could breathe air containing $4.3 \times 10^{-10} \mu\text{g/cm}^3$ for one year before building up to a lung exposure of 0.01 rep per day. A direct quote of the conclusions is interesting: "Thus, a provisional level of $5 \times 10^{-10} \mu\text{g}$ of Pu/cm^3 in air should be a safe temporary limit. In the meantime, improved knowledge of metabolism of the product and of dust particle retention in the lungs should lead to a better value. The tentative figure above is extremely conservative in all respects except for the assumption of uniform distribution through the lung". The value of $5 \times 10^{-10} \mu\text{g/cm}^3$ remained the air concentration guide for the remainder of the Plutonium Project period. J. E. ROSE (1945) reexamined the air tolerance level in the fall of 1945. Working from first principles and preliminary animal data as a basis for more realistic lung deposition and clearance rates, he concluded that there was no compelling justification for changing the air tolerance from PARKER's original value.

With increased availability of plutonium from the Clinton pile, a number of important animal toxicity experiments were started. R. D. FINKLE and E. PAINTER started injecting toxic amounts of plutonium into rats, mice, rabbits and dogs. The first injections at Chicago were on May 22, 1944, and were the beginning of attempts to compare the metabolism and toxicity of plutonium with radium and, through animal experimentation, to provide better guidance for the protection of those working with plutonium. A parallel effort to compare the acute and subacute toxicity of ^{226}Ra , ^{210}Po and ^{239}Pu was started shortly thereafter by FINK et al. (1950) at the Manhattan Project Laboratory (later Atomic Energy Project) of the University of Rochester School of Medicine and Dentistry, Rochester, New York. These early studies and subsequent observations of low-dose, long-term effects (primarily at Chicago) involved many people⁶ and eventually provided the empirical comparison of chronic toxicity of plutonium and radium that is the basis for the currently accepted $0.04 \mu\text{Ci}$ maximum permissible plutonium body burden for man.

By the end of June 1944, studies of deposition, retention, absorption and elimination of plutonium administered to rats via inhalation and tracheal intubation had been or were being initiated both in K. S. Coles' Biological Research

⁶ Among those making contributions to these early studies were R. ABRAMS, W. BLOOM, G. BOYD, A. M. BRUES, G. CASSARETT, K. S. COLE, R. FINK, M. FINKEL, R. FINKLE, D. GARDNER, L. O. JACOBSON, W. KISIELESKI, B. LAWRENCE, H. LISCO, R. METCALF, R. MURRY, W. P. NORRIS, E. PAINTER, C. L. PROSSER, E. RUSSELL, G. SACHER, J. SCHUBERT, H. SILBERTSTEIN, E. L. SIMMONS, R. E. SNYDER, M. N. SWIFT, R. ZIRKLE, and others.

Section (R. ABRAMS et al., 1946) at the Metallurgical Laboratory and in J. G. Hamilton's group (K. G. SCOTT et al., 1945) at the Radiation Laboratory of the University of California. These studies were to provide much of the biological basis for current maximum permissible plutonium air concentrations through their contribution to current models of kinetics of inhaled particulates. These and the early toxicity studies mentioned above were reported from time to time in progress reports and summarized (to date) in a report of a conference on plutonium held in Chicago on May 14-15, 1945 (NICKSON, 1945); however, they did not result in specific reports and analysis of data until the 1946-1950 period.

By the first of March 1945, urine assays were being applied both at Chicago and Los Alamos in attempts to estimate exposure of personnel to plutonium. Body burden was estimated on the assumption that the excretion rate in man was the same as that for the rat and rabbit and at about 20 days after exposure reached a steady state at 0.01 percent of the body burden per 24 hours. In April, tracer studies in subjects with short life expectancy were initiated through both the Chicago and Los Alamos Laboratories (and a little later at the Radiation Laboratory at Berkeley) to establish the human urinary excretion rate (NICKSON, 1945). The first urinary assay results on personnel at Los Alamos suggested that some of the workers in the plutonium recovery group already might have approached or exceeded a body burden of 1 μg . Late in March a meeting was held at Los Alamos with Dr. HYMER FRIEDELLE representing Dr. STAFFORD WARREN (Medical Director of the Manhattan District) to discuss these early results. Other participants were Drs. L. H. HEMPELMANN (Leader of the Los Alamos Health Group), J. W. KENNEDY (Leader of the Los Alamos Chemistry Division), and W. H. LANGHAM. Based largely on apprehension over the autoradiographic studies of J. G. HAMILTON's group at Berkeley (showing plutonium distribution in bone was much more non-uniform than was radium), the decision was made to introduce a safety factor of 5 and to lower the maximum allowable plutonium body burden from 5 μg to 1 μg (0.06 μCi). S. T. CANTRIL and H. M. PARKER (then at Hanford) chose to introduce a safety factor of 10 and introduced a provisional body burden of 0.5 μg (0.03 μCi) for the Hanford Operations. In a memorandum report to CANTRIL, PARKER (1945) proposed a tolerance concentration for plutonium in plant and village drinking water. The tolerance concentration in village drinking water ($\sim 10^{-5}$ $\mu\text{g}/\text{cm}^3$, 6×10^{-7} $\mu\text{Ci}/\text{cm}^3$) was based on a maximum allowable body burden of 0.5 μg , a 60-year effective exposure time, a plutonium absorption rate of 0.05 percent and a water intake of 5 liters per day. The plant water tolerance (5×10^{-5} $\mu\text{g}/\text{cm}^3$ or 3×10^{-6} $\mu\text{Ci}/\text{cm}^3$) was based on the same allowable body burden, a working exposure time of 30 years and a daily water intake of 2 liters.

In summary, during the period 1943 through July 1946 (when the AEC was established) health protection standards for the Manhattan District's plutonium operations evolved from no standards at all to tentatively accepted values for the maximum allowable body burden and tolerance concentrations in air and water. These values were as given in Table 12.1. The maximum allowable body burden was based on comparison of energy deposition from plutonium and 0.1 μCi of radium with a safety factor of 5 or 10 as a precaution against the difference in distribution between radium and plutonium in bone. The comparison axiomatically designated bone as the critical organ. The air tolerance concentration was based on a comparison of dose to the lung from uniformly-deposited plutonium with X- or gamma-ray exposure in which it was assumed that 0.01 rep per day of alpha radiation reached in 1 to 2 years was equivalent in effect to 0.1 r per day of X- or gamma-rays. The water tolerance concentration was based

Table 12.1. Plutonium occupational protection criteria derived during the Manhattan District's plutonium project (1943-1946)

<i>Maximum allowable body burden</i>	
Manhattan District	1.0 μg (0.06 μCi)
Hanford operations	0.5 μg (0.03 μCi)
<i>Air tolerance concentration</i>	
1-2 year exposure	5×10^{-10} $\mu\text{g}/\text{cm}^3$ (3×10^{-11} $\mu\text{Ci}/\text{cm}^3$)
<i>Water tolerance concentration</i>	
Community	1×10^{-5} $\mu\text{g}/\text{cm}^3$ (7×10^{-7} $\mu\text{Ci}/\text{cm}^3$)
Plant	5×10^{-5} $\mu\text{g}/\text{cm}^3$ (3×10^{-6} $\mu\text{Ci}/\text{cm}^3$)

on rate of intake that would result in the maximum allowable body burden in the appropriate time frame. It is interesting to compare the above values with those in current use (see Sec. V).

IV. Plutonium Occupational Protection Criteria (1946-1950)

After the war had ended and about the time of enactment of the Atomic Energy Act (transferring responsibilities from the Manhattan District to the U. S. Atomic Energy Commission) the general urgency relaxed, but studies relevant to the hazardous properties of plutonium continued. HAMILTON's group at Berkeley continued metabolic and inhalation studies, and the Biology Division at Chicago (then a part of the Argonne National Laboratory) continued and expanded studies comparing the chronic or delayed toxicity of ^{89}Sr , ^{226}Ra and ^{239}Pu under the direction of Dr. AUSTIN BRUES.

In 1946 the toxicity, inhalation and metabolic studies initiated earlier began to bear fruit in the form of classified summary and interpretive reports (SCOTT et al., 1945, 1949; ABRAMS et al., 1946; PAINTER et al., 1946; FINKLE et al., 1946; BOYD et al., 1946a and b; FINK, 1950). At about the same time relaxation of security and classification restrictions began, and plutonium could be mentioned outside hallowed halls. Perhaps the credit for the first open disclosure of plutonium as a potential industrial hazard goes to Drs. AUSTIN BRUES, HERMANN LISCO and MIRIAM FINKEL. This disclosure was in a manuscript entitled "Carcinogenic Action of Some Substances which may be a Problem in Certain Future Industries", declassified on July 31, 1946 (BRUES et al., 1946). The paper was presented at a meeting of the Radiological Society of North America (December 1-6, 1946) and published in a very condensed form in a Special Plutonium Project issue of Radiology in September 1947 (LISCO et al., 1947). A direct quote from the concluding remarks of the uncondensed version is interesting indeed: "It is noteworthy, however, that two general principles have been derived from animal experiments which, if true, greatly facilitate extrapolation to longer times: (1) a linear relation between dose, time after latency and tumor expectancy and (2) a logarithmic, or a least gradual, change in latent time with dose. It is of interest that this scheme postulates a true tolerance dose where the latent time exceeds the life span, but in man this would be singularly low (e.g., log dose = -100)". The above quote is referred to affectionately by some as BRUES' Law.

In December 1946 the U. S. Committee on X-Ray and Radium Protection reorganized, extended its scope to respond to the rapid expansion in the radiation field and renamed itself the National Committee on Radiation Protection (TAYLOR, 1958a). During the next three or four years much of the material collected during

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Table 12.2. Plutonium occupational protection criteria resulting from the Chalk River permissible doses conference

<i>US and UK preliminary versions (November 1949)</i>	
Maximum permissible amount in body	0.1 μg (0.006 μCi)
Maximum permissible air concentration soluble and insoluble compounds	5×10^{-12} $\mu\text{g}/\text{cm}^3$ (3×10^{-13} $\mu\text{Ci}/\text{cm}^3$)
Maximum permissible water concentration	4×10^{-6} $\mu\text{g}/\text{cm}^3$ (3×10^{-7} $\mu\text{Ci}/\text{cm}^3$)
<i>Canadian final report (May 1950)</i>	
Maximum permissible amount in body	0.5 μg (0.03 μCi)
Maximum permissible air concentration (24-hour day)	2.5×10^{-11} $\mu\text{g}/\text{cm}^3$ (1.5×10^{-12} $\mu\text{Ci}/\text{cm}^3$)
Maximum permissible drinking water concentration	2×10^{-5} $\mu\text{g}/\text{cm}^3$ (1.2×10^{-6} $\mu\text{Ci}/\text{cm}^3$)

and immediately after the Manhattan Project was issued, with some modification, in unclassified form giving rise to the MDDC and AECD series of documents and appeared in national journals and various volumes of the National Nuclear Energy Series. This multiplicity of reporting of the same material with minor modifications increased immeasurably the problem of reconstruction of the biological bases and history of development of radiation protection criteria. Perhaps the best bibliographical compilation with respect to internal radiation (including plutonium) is that given in the 1959 report of ICRP Committee II on Permissible Dose for Internal Radiation (ICRP, 1960). After the USAEC assumed responsibility from the Manhattan District for the plutonium operations, there were few or no adjustments in plutonium exposure criteria with the self-imposed Hanford levels being approximately a factor of 2 less than elsewhere.

On September 29 and 30, 1949, the first Tripartite (USA, UK, Canada) Permissible Doses Conference⁷ was held at CHALK RIVER, Ontario. At this meeting Dr. BRUES reported that comparative toxicity studies in mice and rats at the Argonne National Laboratory suggested a toxicity ratio between equal microcurie amounts of plutonium and radium of approximately 15 to 1, a very large factor of difference from the earlier anticipated ratio based on energy release (see p. 573). On this basis, the conference adopted a plutonium body burden of 0.1 μg (0.006 μCi) and calculated the corresponding maximum levels for air and water. The US and UK reports of the conference were issued promptly and gave the occupational maximum permissible levels for plutonium given at the top of Table 12.2. Immediately a wave of technical correspondence and telephoning ensued, initiated by Dr. W. LANGHAM and involving Drs. SHIELDS WARREN, AUSTIN BRUES, R. D. EVANS, and K. Z. MORGAN. It was Dr. LANGHAM's contention that (1) the Chalk River values were too restrictive and should not be adopted as the official policy for USAEC operations, (2) comparative chronic toxicity studies of plutonium and radium in dogs should be initiated (at Los Alamos) immediately and (3) chronic plutonium *inhalation* studies in dogs should be initiated (at Los Alamos) also.

This wave of correspondence culminated in a meeting in Washington, D.C., on January 24, 1950, called by Dr. WARREN (Director of the AEC's Division of

⁷ Participants were: from the United States, Dr. SHIELDS WARREN (Chairman) and Drs. A. M. BRUES, G. FAILLA, J. G. HAMILTON, L. HEMPELMANN, F. DE HOFFMAN, W. H. LANGHAM, K. Z. MORGAN, H. M. PARKER, L. S. TAYLOR and B. S. WOLF and Colonel C. A. NELSON; from Canada, Drs. E. A. BRAATEN, H. CARMICHAEL, A. J. CIPRIANI, G. H. GUEST, G. C. LAURENCE, W. B. LEWIS, G. E. MCMURTRIE and E. RENTON; from the United Kingdom, Professor J. S. MITCHELL, Drs. E. F. EDSON and G. J. NEARY and Mr. A. C. CHAMBERLAIN.

n the Chalk River per-

$3 \times 10^{-13} \mu\text{Ci}/\text{cm}^3$

$\times 10^{-7} \mu\text{Ci}/\text{cm}^3$

$(1.5 \times 10^{-12} \mu\text{Ci}/\text{cm}^3)$

$2 \times 10^{-6} \mu\text{Ci}/\text{cm}^3$

h some modification, series of documents he National Nuclear material with minor struction of the bio-ion criteria. Perhaps radiation (including tee II on Permissible EC assumed respon-erations, there were ith the self-imposed elsewhere.

USA, UK, Canada) ario. At this meeting nice and rats at the etween equal micro-15 to 1, a very large ed on energy release ium body burden of um levels for air and d promptly and gave a given at the top of nce and telephoning . SHIELDS WARREN, Dr. LANGHAM's con-e and should not be comparative chronic be initiated (at Los studies in dogs should

in Washington, D.C., he AEC's Division of

EN (Chairman) and Drs. HOFFMAN, W. H. LANG- and Colonel C. A. NEL- CIPRIANI, G. H. GUEST, from the United King- ry and Mr. A. C. CHAM-

Biology and Medicine) to consider whether the Chalk River values would be adopted. A list of those attending this meeting does not seem to be available, but the principals were Drs. BRUES, LANGHAM and WARREN. Dr. LANGHAM gave a 2-hour presentation of all the reasons why the proposed Chalk River values should not be adopted. Dr. BRUES gave a 5-minute presentation in which he pointed out that the 15 to 1 toxicity ratio of plutonium to radium (on a μCi basis) indicated by the Argonne rodent studies was based on injected dose; however, plutonium retention in the rodent was 75 percent compared to 25 percent for radium, and radon retention in the rodent was 15 to 20 percent compared to about 50 percent in man. Assuming the minimal damaging dose of fixed radium in man was 1 μCi and taking the above retention parameters into consideration, the comparable fixed minimal damaging dose of plutonium would be about 6 μg . That is:

$$1 \mu\text{Ci Ra} = \frac{1}{15} \times \frac{0.75}{0.25} \left[\frac{4.8 + 0.5(5.5 + 6.0 + 7.7)}{4.8 + 0.15(5.5 + 6.0 + 7.7)} \right] = \sim 0.4 \mu\text{Ci} (6 \mu\text{g}) \text{ Pu,}$$

where the numbers in brackets represent the ratio of energies imparted to man and rodent from radium and its retained decay products (see Footnote 5 for radium decay scheme—Ed.). Dr. WARREN took 5 minutes to summarize the discussion and announced that the AEC operations could proceed on the basis of a maximum permissible plutonium body burden of 0.5 μg (equivalent in effect to about 0.1 μg radium) and maximum air and water concentrations derived accordingly. The meeting lasted 2 hours and 10 minutes and would have lasted only 10 minutes had Dr. BRUES spoken first.

In May 1950 the Canadian version of the Chalk River Permissible Doses Conference was issued (McMURTRIE, 1950). This report was considered to be the final as it was modified in accordance with suggestions received from the various delegates, including Dr. BRUES' modification of the 15 to 1 toxicity ratio of plutonium to radium. The report gave the maximum permissible levels for plutonium shown at the bottom of Table 12.2.

At a meeting at Buckland House (near Harwell, England) called by Sir JOHN COCKCROFT (August 3-5, 1950) and attended by R. D. EVANS, L. MARINELLI, S. WARREN and J. LOUITT among others⁸, BRUES' derivation of the 0.04 μCi was agreed to. In the Argonne National Laboratory Quarterly Report for February, March and April 1951, BRUES (1951) summarized as follows the animal data on which the 0.04 μCi maximum permissible plutonium body burden for man was based: "The toxicity ratio between radium and plutonium has been evaluated from the data of a large number of experiments. The best available ratios, in terms of injected μc per kg radium to plutonium, are:

- (1) for acute toxicity to small animals, 15
- (2) for chronic survival, 10
- (3) for formation of bone tumors in rats and mice, 15
- (4) for formation of bone tumors in rabbits, 8
- (5) for bone fractures in rats and rabbits, about 10.

"Making appropriate allowance for relative retention of the two elements in rodents and for the greater retention of radon in man, a maximum permissible retained dose of 0.04 μc plutonium in man is the best value available from present biological information. This value depends ultimately on the corresponding permissible dose of radium, presently established as 0.1 μc ."

On the basis of the relative biological effects of plutonium and radium as observed in animal experiments, the 1950 Recommendations of the ICRP (see

⁸ A complete list of attendees is not available.

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ICRP-ICRU, 1951) call attention to the use by the US, UK and Canada of 0.04 μCi as the maximum permissible amount of ^{239}Pu fixed in the body.

In 1950 experiments to compare chronic or delayed toxicity of plutonium and radium in dogs were initiated at the University of Utah School of Medicine under the direction of Dr. J. Z. BOWERS and the guidance of Drs. AUSTIN BRUES, W. CLAUS, R. D. EVANS, and W. LANGHAM. Radium-228 (MsTh_1) was added to the protocol because of its role in exposure of the early radium dial painting cases. Chronic plutonium inhalation experiments in dogs were being initiated also at the University of Rochester School of Medicine and Dentistry and later at Hanford by Dr. W. J. BAIR and colleagues. These efforts marked the end of the era of deriving maximum permissible values for internally-deposited radionuclides through establishing simple empirical relationships and the beginning of the NCRP-ICRP efforts to generalize the methods of deriving such values through calculation of dose to the critical organ and relating this to effect, taking into consideration relevant biological data.

V. Plutonium Protection Criteria (1950—1971)

The value for the maximum permissible plutonium body burden of 0.04 μCi , as derived by biological comparison following the Chalk River Permissible Doses Conference, has not been altered in subsequent years, although attempts to fit the number into the overall framework of dose calculations for internal emitters have tended to becloud somewhat the original concepts described above. The ICRP-NCRP have made changes in the application of the body burden value to derivation of maximum permissible concentrations in air and water and consideration of the dose to the lung. The remainder of this chapter will deal primarily with these changes.

A. The Standard Man

An important development in derivation of maximum permissible quantities was agreement, among those involved, on values of organ weights and other parameters of the "standard man". This agreement provided uniform values for air and water that could be applied to exposure control in general with adequate accuracy. The first formal steps toward agreement were taken at the Chalk River Permissible Doses Conference in 1949 (*op cit*), where earlier work by CIPRIANI and LISCO served as the basis of discussion. Although some detailed changes were made in later years, the values adopted at this meeting have held up well.

Table 12.3. Parameters of the standard man of importance to standards for plutonium

Mass of the bone ^a	7000 g
Mass of the lung ^a	1000 g
Breathing rate	
total day ^a	20 m ³
8 hours at work [after 1960 ^b]	10 m ³
Water intake	
total day [until 1953 ^a]	2.5 l
total day [after 1953 ^c]	2.2 l
8 hours at work [after 1960 ^b]	1.1 l
Time of occupational exposure [until 1960 ^a]	70 yr.
Time of occupational exposure [after 1960 ^{b, c}]	50 yr.

^a Chalk River Conference, 1949; reported by McMURTRIE (1950). ^b ICRP Committee II Report of 1959 (ICRP, 1959). ^c NCRP Report No. 11 (NBS Handbook 52, 1953).

Table 12.3 gives the values which are of primary importance to the derivation of maximum permissible values for plutonium, with indication of the changes which took place over the period under discussion.

B. Changes in Values and Concepts

A summary of the important metabolic constants and resulting MPC's for plutonium as derived from the reports of individual conferences and reports of the NCRP and ICRP is given in Table 12.4. Of necessity, such a summary table must omit some of the concepts, and these will be discussed below. The nomenclature used in Table 12.4 is primarily that introduced by the Subcommittee on Permissible Internal Dose of the NCRP in their 1953 report and later adopted by the corresponding subcommittee of the ICRP. These terms are:

T_b — the biological half life of the material in the organ of concern. The elimination constant ($0.693/T_b$) is additive with the decay constant of the radioactive isotope to give an overall effective elimination rate. In this table it refers to bone for "soluble" forms and lung for "insoluble" forms.

f_1 — the fraction of the material ingested which passes from the gastrointestinal tract to the blood.

f_2 — the fraction of the material present in the whole body which is in the organ of concern. This can change with time depending upon the radioactive half-life of the isotope and the relative rates of uptake and elimination of the isotope.

Table 12.4. Summary of MPC's and Maximum Permissible Body Burdens for Plutonium-239 Showing Changes in Parameters and Derived Figures Over the Period 1949-1960.

	Chalk River (1949)	ICRP (1950)	NCRP No. 11 (NBS-52) (1953)	Harriman Conference (1953)	ICRP (1955)	ICRP ^a (1959)
<i>'Soluble' Forms</i>						
MPBB ^b	0.5 µg: C (0.03 µCi)	0.04 µCi	0.04 µCi	0.04 µCi	0.04 µCi	0.04 µCi
T_b (bone)	6930 d ^d	6930 d ^d	4.3×10^4 d	—	4.3×10^4 d	7.3×10^4 d
f_1	—	—	1.4×10^{-4}	—	1×10^{-4}	3×10^{-5}
			7.0×10^{-5}			
f_3	—	—	0.75	—	0.75	0.9
f_2	—	—	0.7	—	0.7	0.8
f_w	1×10^{-3}	1×10^{-3}	1×10^{-4}	1×10^{-3}	1×10^{-4}	2.4×10^{-5}
MPC _w ^e	1.2×10^{-6}	1.5×10^{-6}	1.5×10^{-6}	—	6×10^{-6}	5×10^{-5}
f_a	0.1	0.1	0.18	0.25 ^f	0.18	0.2
MPC _a ^e	1.5×10^{-12}	2×10^{-12}	2×10^{-12}	—	2×10^{-12}	6×10^{-13}
<i>'Insoluble' Forms</i>						
MPLB ^g	—	—	0.008 µCi	—	0.02 µCi	—
T_b (lung)	—	139 d ^h	360 d	—	360 d	1 yr
f_2	—	—	1.0	—	1.0	—
f_a	—	0.25	0.12	0.10	0.12	0.12
MPC _a ^e	—	7.5×10^{-12} ⁱ	2×10^{-12}	—	2×10^{-12}	10^{-11}

^a Continuous occupational exposure MPC's given. ^b MPBB = Maximum Permissible Body Burden (with bone as the critical organ). ^c Actual comparison gave 0.6 µg which, for purpose of this recommendation, was rounded off to 0.5 µg. ^d Given as a mean life of 10⁴ days. ^e In units of µCi/cm². ^f Retention of soluble material in alveoli. If multiplied by f_1 used by the NCRP (1953), f_a becomes 0.18. ^g MPLB = Maximum Permissible Lung Burden. ^h Given as a mean life of 200 days. ⁱ Not used. Value for insoluble was recommended to be the same as for soluble (see text).

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UK and Canada of n the body. acicity of plutonium School of Medicine Drs. AUSTIN BRUES, sTh₁) was added to dium dial painting being initiated also tistry and later at rked the end of the ly-deposited radio- and the beginning riving such values his to effect, taking

-1971) burden of 0.04 µCi, r Permissible Doses ough attempts to fit or internal emitters scribed above. The dy burden value to ater and considera- will deal primarily

rmissible quantities weights and other uniform values for neral with adequate at the Chalk River ork by CIPRIANI and tailed changes were ave held up well. ndards for plutonium

- 7000 g
- 1000 g
- 20 m³
- 10 m³
- 2.5 l
- 2.2 l
- 1.1 l
- 70 yr.
- 50 yr.

^b ICRP Committee II ok 52, 1953).

For this reason, f_2 is normally taken at a long time when the equilibrium state is reached.

f'_2 — the fraction of the material in the blood which passes to the organ of concern.

f_w — the fraction of the material which reaches the organ of concern following ingestion of the isotope. Since this will equal the product of the quantity passing from the gastrointestinal tract to the blood and the fraction passing from the blood to the organ of concern, $f_w = f_1 f'_2$

f_a — the fraction of the material inhaled which reaches the organ of concern. This will be the sum of the material absorbed directly from the lung and that which is swallowed and absorbed from the gastrointestinal tract.

Discussions at the Chalk River Permissible Doses Conference (*op cit.*) have been summarized earlier with emphasis on derivation of the maximum permissible body burden. The value for the MPC in air was based on a soluble compound with 10 percent retention in the lung, and the material retained with a mean life of 10^4 days once it had passed into the body and been deposited in bone. Thus, the MPC was:

$$\begin{aligned} \text{MPC}_a &= 0.5 \mu\text{g} \times \frac{1}{10^4} \times \frac{1}{0.1} \times \frac{1}{2 \times 10^7} = 2.5 \times 10^{-11} \mu\text{g}/\text{cm}^3 \\ &= 1.5 \times 10^{-12} \mu\text{Ci}/\text{cm}^3. \end{aligned}$$

Similarly, the MPC for water was derived by assuming 0.1 percent absorption in low concentrations and ingestion of 2.5 liters of water per day:

$$\begin{aligned} \text{MPC}_w &= 0.5 \times \frac{1}{10^4} \times \frac{1}{10^{-3}} \times \frac{1}{2.5 \times 10^3} = 2 \times 10^{-5} \mu\text{g}/\text{cm}^3 \\ &= 1.2 \times 10^{-6} \mu\text{Ci}/\text{cm}^3. \end{aligned}$$

These calculations were performed to obtain the MPC which would yield the maximum permissible body burden under equilibrium conditions since, with the elimination constants chosen, the body would be more than 90 percent of the way to equilibrium after the 70-year life-span chosen as the basis of calculation.

No MPC was derived at this meeting based on lung dose, although there was considerable discussion of the problem of lung retention and dose to the lung. In connection with present concern over the single particle problem, it is of interest to note the following quotation from the minutes of the meeting: "Dr. HAMILTON pointed out that the cells in the immediate neighborhood of a dust particle containing 1 or 2% of plutonium would be subjected to a dose of about 400 r/day. The general opinion which emerged from the discussion was that the carcinogenic effect per unit volume is probably considerably less for irradiation of small masses of tissue than for large". Again a prophetic foreshadowing of present concerns is given in the statement: "A brief discussion of the proportion of insoluble particulate material transported from the lung to the lymph nodes merely served to indicate that this factor is rather dependent on the nature and size of the particles". Thus, on a subject which the standards-setting bodies have been accused of ignoring, we find serious discussion in 1949 with, however, the conclusion that more information is needed—the same situation in which we find ourselves today!

An important outcome of the Chalk River Permissible Doses Conference was the formulation of a lung model which, while crude, served as the basis for further

⁹ The fractions in this equation represent in order, (a) mean life t (i.e. $1.44 \times T_b$), (b) f_a and (c) ml of air breathed per day.

¹⁰ The fractions in this equation represent in order, (a) mean life, (b) f_w and (c) ml of water ingested per day.

development. This lung model was given as: "...if specific data were lacking, the convention be adopted that 50% of any aerosol reaches the alveoli of the lungs. If the particles are soluble they are considered to be totally absorbed; if insoluble then the 50% amount is to be regarded as retained for 24 hours, after which only half of it, i.e., 25% of the inhaled amount, is retained *in situ* indefinitely; further, that the particles be assumed spherical." The wording of this model indicates that the originators felt a strong need to give guidance but also felt some unease in providing a definitive statement. Unfortunately, the preface to the statement relating to use when specific data are unavailable seems to have been overlooked or deemphasized in many later considerations of lung dose, although the statement still survives.

The first presentation of these concepts for general use was in the 1950 ICRP recommendations published as ICRU Report No. 6 (NBS Handbook 47) issued June 29, 1951 (op cit.). The values for internal emitters were prefaced by the statement of the Commission that they did not consider that there was sufficient information at the time to make firm recommendations; however, they did indicate that they were bringing to the notice of users values which were commonly used in the US, Canada and Great Britain. The statement on plutonium is of considerable interest and is quoted below:

On the basis of the relative biological effects of plutonium and radium, as observed in animal experiments, it is accepted that

a) *The maximum permissible amount of ^{239}Pu fixed in the body is 0.04 microcurie.*

For soluble compounds of plutonium in the atmosphere, it is estimated that 10 percent of the inhaled material is absorbed, with a mean life of 10^4 days. The maximum permissible concentration in air is, therefore, 2×10^{-12} microcurie/ml

For insoluble compounds, it is estimated that the mean life in the lung is 200 days. If the irradiation of the lungs by alpha rays were limited to the biological equivalent of 0.3r/week, the corresponding concentration of the plutonium in air would be 7.5×10^{-12} microcurie/ml. In view of the possibility of the transference of some of the insoluble material from the lungs to the skeleton, it is suggested that

b) *The maximum permissible concentration of ^{239}Pu in air is 2×10^{-12} microcurie/ml, for soluble and insoluble compounds.*

c) *For ^{239}Pu in liquid media, assuming that 0.1 percent of the ingested amount is retained in the skeleton with a mean life of 10^4 days, the maximum permissible concentrations is 1.5×10^{-6} microcurie/ml.*

The body burdens and MPC's given above are essentially those from the Canadian Chalk River report with the addition of a calculation for "insoluble" plutonium based on dose to the lung, which was not accepted for implementation at that time.

In 1953 the NCRP published the report of their Subcommittee on Internal Emitters as National Committee on Radiation Protection Report No. 11 (NBS Handbook 52) (NCRP, 1953). Although their MPC values remained the same as were derived following the Chalk River Conference and as given by the ICRP, there were some changes in the listed metabolic constants for plutonium as shown in Table 12.4. Chief among these were an increase in half-life for "soluble" forms and a more detailed lung model which is very close to that adopted for and used many years for ICRP calculations of MPC's. This latter is given as: "In dealing with the inhalation of radioisotopes, unless information specific to the radioisotope is available, it is assumed in the case of *soluble* compounds that 25 percent is retained in the lower respiratory tract. From this tract it goes to the blood stream, and a part of this goes to the critical organ within a few days. Fifty percent is held up in the upper respiratory tract and swallowed, so a fraction of that swallowed also reaches the critical organ. In the case of *insoluble* com-

pounds, it is assumed that 12 percent is retained in the lower respiratory tract, which is usually taken as the critical organ when considering the inhalation of insoluble compounds. The rest is eliminated by exhalation and swallowing." Use of this model resulted in changes in the values of f_a for both the "soluble" and "insoluble" materials.

Use of these modified metabolic factors would have led to some changes in the MPC's. Water and air values for soluble plutonium can be calculated from these factors, assuming that exposure is long enough for equilibrium to be reached, as follows:

$$\text{MPC}_a = 0.04 \times \frac{0.693}{4.3 \times 10^4} \times \frac{1}{0.18} \times \frac{1}{2 \times 10^7} = 2 \times 10^{-13} \mu\text{Ci/cm}^3^{11}$$

$$\text{MPC}_w = 0.04 \times \frac{0.693}{4.3 \times 10^4} \times \frac{1}{10^{-4}} \times \frac{1}{2200} = 3 \times 10^{-6} \mu\text{Ci/cm}^3^{11}.$$

However, with the increased retention time for plutonium in the body, the assumption of equilibrium is no longer valid since only about 34 percent of the equilibrium value would be achieved in 70 years. Therefore, the MPC_w could be increased to $9 \times 10^{-6} \mu\text{Ci/cm}^3$ and the MPC_a could be increased over the calculated values to $5 \times 10^{-13} \mu\text{Ci/cm}^3$. For "insoluble" plutonium, use of these metabolic factors and a lung burden of 0.008 μCi would give:

$$\text{MPC}_a = 0.008 \times \frac{0.693}{360} \times \frac{1}{0.12} \times \frac{1}{2 \times 10^7} = 6 \times 10^{-13} \mu\text{Ci/cm}^3.$$

In this case, the equilibrium assumption is valid because of the assumed half life in the lung of 360 days.

It is of interest that the actual MPC's recommended in this document were unchanged from the recommendation of the Chalk River Permissible Doses Conference, in spite of the change in factors utilized to describe the behaviour of Pu in the body. Also, use of the same MPC for soluble and insoluble plutonium indicates that the concern for possible transfer from lung to the body still existed.

The Harriman Tripartite Conference in March 1953 (Tripartite Conference, 1953), about the time of issuance of the NCRP report, gave scant attention to the problem of plutonium *per se* beyond affirming the value of 0.04 μCi derived after the Chalk River Conference. However, an important change was made at this meeting in the RBE factor for alpha particles *viz*: a lowering of the value from 20 to 10 as based on the possibility of carcinogenesis. There also ensued a lengthy discussion on the apparent discrepancy between the bone limit, as based on the comparison with radium, and as based on calculations from the external dose limit assuming a uniform distribution of isotope and an amount limited to give a dose of 0.3 rem per week as was used for other organs. This resulted in a statement concerning the calculation of such doses: "Radium is assumed, for purposes of calculation, to be uniformly distributed. Other alpha emitting bone seekers are assumed to be non-uniformly distributed by a factor of 5". This statement can be interpreted in several ways. First, it could mean that the size of the critical organ should be considered as 1/5 as great as that chosen for radium. In other words, since the calcified portion of bone is taken as 7000 g, the statement could be interpreted to mean that the

¹¹ Editors note: These calculations illustrate the change in MPC values resulting from the slightly different metabolic factors and use the format of previous calculations in this chapter. They do not show the actual approach as in the quoted NBS Handbook. See for example equation G 5 (in NCRP No. 11, NBS, 1953). Also, the values would refer to continuous occupational exposure as in the earlier examples.

critical organ for these calculations should be 1400 g. It can also be interpreted that the alpha radiation is 5 times as damaging for the other alpha emitters as for radium and that the effect considered should be 5 times as large but dispersed in the same size of critical organ. In view of the origin of the factor of 5 in animal experiments with plutonium and its explanation on the basis of non-uniform distribution in bone, the former interpretation would seem to be more reasonable, but later trends seemed to favor the latter interpretation.

Revised recommendations of the ICRP were published in 1955 (ICRP, 1955). Values of the metabolic constants were largely as given in the NCRP report of 1953 (op cit.). The MPC in water for soluble plutonium was revised as a result of the use of these metabolic values, and the maximum permissible lung burden was changed from 0.008 μCi in the NCRP report to 0.02 μCi , to reflect the acceptance of the RBE of 10 rather than 20. In spite of these changes, however, the MPC in air for both soluble and insoluble plutonium remained at a single value as was originally recommended at the Chalk River Permissible Doses Conference ($2 \times 10^{-12} \mu\text{Ci}/\text{cm}^3$, rounded off from the original value at Chalk River of $1.5 \times 10^{-12} \mu\text{Ci}/\text{cm}^3$).

It is of interest that the introduction to the report of the Subcommittee on Internal Emitters states: "In the case of all bone-seeking radioisotopes (with the exception of Ra, ^{32}P and radioisotopes that emit only X- or γ radiation) a factor of safety of 5 is applied to the calculations to take into account the uneven distribution of the radioactive material within the bone, ..." (emphasis added). Thus, the factor for the difference in effectiveness of Pu versus Ra defined by biological experimentation described earlier was described as a "factor of safety". This report also introduced the combination of energy, the RBE, and the distribution factor into one term written as $\Sigma E(\text{RBE})N$ so that this value could be used in place of the energy, with the resulting dose coming out directly in "rems". It may be noted that at this time the ICRU had adopted the rad as an official unit but had not as yet adopted the rem (ICRU, 1954). Therefore, protection organizations such as the ICRP and NCRP were using it as a unit of convenience rather than an officially defined and accepted unit. The definition adopted by the ICRP was that of their Subcommittee on External Dose (ICRP, 1955) and was given as "the rem is the absorbed dose of any ionizing radiation which has the same biological effectiveness as one rad of X- radiation, ...".¹²

An additional feature of this report was the derivation of MPC values as based on the dose to the gastrointestinal tract. Models for the mass of material in the gastrointestinal tract and time of transit through each section were added to the standard man, and the dose was calculated based upon the dose rate at the surface of a semi-infinite mass of material. The concentration was equal to the quantity of the contents of the portion of the gastrointestinal tract of interest which dilutes the amount of radioisotope taken in per day. At this time, the calculations were made on the basis of the full energy of the alpha particle, and the recommended MPC_w based on this dose was $3 \times 10^{-6} \mu\text{Ci}/\text{cm}^3$ or one-half of the value based on

¹² It is noted that this definition implies only the factor of RBE due to differences in specific ionization of the radiations and does not overtly include other factors such as non-homogeneous distribution. Inclusion of this factor in the internal dose energy term had the effect of producing an *ad hoc* definition of the rem for use in estimating the effective dose from bone-seekers. In other words, it seemed to be this step which produced the definition of the non-uniform distribution factor as effectively multiplying the effectiveness of the energy absorbed rather than limiting the size of the critical organ as discussed above. In the cited report, however, it is still clear that the values are based directly on a comparison with radium and that the factor of 5 is still primarily a non-uniform distribution factor, although no description of the derivation of the factor for biological equivalence is given.

uptake into the body. An MPC_a based on exposure of the gastrointestinal tract from material transferred from the upper respiratory tract and lung was calculated also. This value was $5 \times 10^{-10} \mu\text{Ci}/\text{cm}^3$, considerably larger than the value which had been accepted for some years based on transfer from lung to body. In addition, supplementary maximum permissible body burdens based on the gastrointestinal tract were calculated, assuming all of the material to be located there by multiplying the $0.04 \mu\text{Ci}$ based on bone as critical organ by the ratio of the MPC based on the gastrointestinal tract to that based on bone. Values obtained were $0.02 \mu\text{Ci}$ for ingestion and $10 \mu\text{Ci}$ for inhalation. The pertinence and usefulness of these values were not indicated but occasions when they might become the controlling figure can be visualized.

In 1956 the ICRU (1957) accepted the concept of the rem and defined a quantity known as the "RBE dose" which was defined as: "RBE dose is equal numerically to the product of the dose in rads and an agreed conventional value of the RBE with respect to a particular form of radiation effect. The standard of comparison is X- or gamma radiation having a LET in water of $3 \text{ kev}/\mu$ delivered at a rate of about $10 \text{ rad}/\text{min}$." The unit of the RBE dose was taken as the rem with the note that it had the same inherent looseness as the RBE and, in addition, assumed conventional and not necessarily measured values of RBE.

The current values recommended by both the ICRP and NCRP were derived in 1959 and published by both ICRP and NCRP in 1959 (ICRP, 1959; NCRP Report 22 NBS Handbook 69, 1959). As would be expected from the composition of the subcommittees, there is a striking similarity in the numbers; although there are a few differences in philosophy. In discussing the basic standards, the NCRP report indicates for internal emitters: "For bone-seekers the maximum permissible limit is based on the distribution of the deposit, the RBE, and a comparison of the energy release in the bone with the energy release delivered by a maximum permissible body burden of $0.1 \mu\text{g}$ ^{226}Ra plus daughters". The rem is defined as given by the ICRU or equal to rads times RBE with no additional factor for other mechanisms which could result in differences in damage.

In the ICRP report on internal radiation (1959), in the section discussing the basic standards, reference is made to the 1958 recommendations of the main commission (ICRP, 1958) which provided a basic limitation on the dose accumulated in the gonads, the blood-forming organs, and the lenses of the eye, at any age over 18 years, of $5(N-18)$ rems where N is the age of the individual in years. The report¹³ then interpreted this limitation as: "The effective RBE dose delivered to the bone from internal or external radiation during any 13 week period averaged over the entire skeleton shall not exceed the average RBE dose to correspond to the skeleton due to a body burden of $0.1 \mu\text{g}$ of ^{226}Ra . This is considered to a dose rate of $0.56 \text{ rem}/\text{week}$ in the case of ^{226}Ra (derived from a dose rate of 0.06 rad per week, an RBE of 10 and $n = 1$). In computing the effective RBE dose to the skeleton, all absorbed energy shall be weighted by a relative damage factor, n . The relative damage factor is taken as one for all energy absorbed from external radiation and for all internal emitters when the element taken into the body is an isotope of radium. If the isotope taken into the body is not an isotope of radium, the relative damage factor, n , is taken as 1 for all energy absorbed from X- or γ -radiation and as 5 for all other energy components". Later when discussing the basis for their calculations, they state¹⁴: "The first method¹⁵ is

13 Page 3 of ICRP (1959).

14 Page 12 of ICRP (1959).

15 Refers to method of comparison to radium in contrast to calculation of dose.

gastrointestinal tract of lung was calculated from the value which would be obtained for the whole body. In addition, the gastrointestinal tract was treated there by multiple exposures. The ratio of the MPC values obtained were compared and usefulness of the method might become the

and defined a quantitative RBE dose is equal to the conventional value for the effect. The standard dose rate of 3 kev/ μ delivered was taken as the basis for the RBE and, in calculating the values of RBE.

The MPCs were derived from the composition of the bone, although there are standards, the NCRP the maximum permissible RBE, and a committed dose delivered by a source with no additional damage.

In discussing the relations of the main factors on the dose accuracies of the eye, at the individual in effective RBE dose during any 13 week average RBE dose to the eye. This is considered from a dose rate of the effective RBE by a relative damage energy absorbed from the element taken into the body is not an isotope all energy absorbed elements". Later when the first method¹⁵ is

of dose.

the result of a calculation designed to determine (i) the amount (μ c) deposited in the bone that will deliver the same effective RBE dose as delivered by 0.1 μ c of ²²⁶Ra and its daughter products and (ii) the amount (μ c) deposited in bone that will result in damage comparable to that observed from known deposits of ²²⁶Ra in the bone". Thus, it would appear that this subcommittee interpreted the limitation based on blood-forming organs to apply to the skeleton even though the marrow, which is instrumental in blood formation in the bone, is not included in the mass of the organ and the real limitation from human experience with radium would seem to be production of bone cancer rather than effects on the blood-forming organs. It appears that use of the *ad hoc* definition of the rem was continued in this context even though the ICRU at this time had officially recognized the unit as applying only to LET effects. This further implies that the Committee considered the increased effectiveness of these bone-seekers to be due to an enhancement of the effectiveness of the alpha particle rather than a decrease in size of the organ affected, even though they did clearly spell out that the effect was probably due to non-homogeneity in the bone. In fact, the equation used for calculating the body burden simply used the ratios of the quantities and energies, although the factor for 5 was included in the energy term.

It may be noted that the ICRU did later revise their concepts of RBE dose and rem (ICRU, 1968) to correspond to the definition implied by Subcommittee II of the ICRP in 1959. Here they defined the dose equivalent as: "...the product of absorbed dose, (D), Quality Factor, (QF), absorbed dose distribution factor, (DF), and other necessary modifying factors". In addition, several further changes were made in this report in the metabolic constants for soluble plutonium, as is indicated in Table 12.4 (last column). Of particular interest is the increase in fraction of plutonium in bone of that in the total body to 0.9 as a result of the observed distribution of material absorbed from the gastrointestinal tract. This change is of some interest, since it is now known that deposition of plutonium in various organs varies depending upon route of administration and also upon the compound administered (Chap. 9). For example, the dog experiments at Utah using intravenous administration of plutonium as the citrate (MAYS et al., 1970) and the plutonium oxide inhalation experiments with dogs at Hanford (PARK et al., 1968) both show sizable depositions in the liver, as do the few human autopsy cases available (SHIPMAN et al., 1961). The result of these changes for metabolic parameters, plus the decision for the first time to use these revised values in reassessing the maximum permissible concentrations, resulted in a lowering of the MPC in air for soluble plutonium by about a factor of 3 and an increase in the MPC in water value by a factor of about 10.

One of the more interesting changes resulted from the decision to list separate MPC's in air for soluble and insoluble isotopes. These were calculated on the basis of the lung model described earlier and reproduced in Table 12.5. Of particular interest is the footnote which states that the 12 1/2% retained in the lung for a long period is "...taken up into body fluids". The definition of body fluids and ultimate fate of the material seem to be unclear. If one assumes that this uptake is by solubilization and eventual passage to the bone, then breathing air at the recommended level for continuous exposure of 10^{-11} μ Ci/cm³ for 50 years would amount to a total intake in this retained fraction of $10^{-11} \times 365 \times 20 \times 10^6 \times 0.125 \times 50 = 0.46$ μ Ci¹⁶. While this calculation ignores the slow elimination of

¹⁶ The factors in this calculation are the MPC for insoluble plutonium, the number of days per year, the quantity of air breathed per day by the standard man expressed in ml, the fraction of the inhaled plutonium retained for a long period in the lung, and the 50 year time of exposure.

Table 12.5. "Particulates in the Respiratory Tract of the Standard Man. Retention of particulate matter in the lungs depends on many factors such as size, shape and density of the particles, the chemical form and whether or not the person is a mouth breather; however, when specific data are lacking, it is assumed the distribution is as shown below

Distribution	Readily soluble compounds (%)	Other compounds (%)
Exhaled	25	25
Deposited in upper respiratory passages and subsequently swallowed	50	50
Deposited in the lungs (lower respiratory passages)	25 (this is taken up into the body)	25 ^a

^a Of this, half is eliminated from the lungs and swallowed in the first 24 hours, making a total of 62½% swallowed. The remaining 12½% is retained in the lungs with a half life of 120 days, it being assumed that this portion is taken up into body fluids." Taken from ICRP Pub. 2 (1959), Table 10, p. 153.

such material, it can be seen that this assumption would lead to an accumulation of considerably more than a maximum permissible body burden. While the paths of elimination of material in the lung are variable and not always well-established in individual instances, it appears from both animal studies and autopsy results (PARK et al., 1968; SHIPMAN et al., 1961) that the major route of elimination is via the lymphatic system with deposition and long-term retention in the lymph nodes. However, this may vary with different particle sizes of materials and different degrees of "solubility", a term which is difficult to define and which seems to relate more to the metabolic behavior of the material in the body than to the more familiar chemical concept of solubility¹⁷.

The MPC's calculated on dose to the gastrointestinal tract following either ingestion or inhalation were increased over those in the earlier ICRP report because of experiments on mice and rats in which large quantities of the oxide or nitrate were administered orally with little or no indication of damage or histological change (SULLIVAN and THOMPSON, 1957). As a result of these findings, it was concluded that the alpha particle did not penetrate to the sensitive cells of the intestinal lining, and thus only 1 percent of the energy of alpha emitters was used in calculating the dose to the gastrointestinal tract. Parenthetically, it might be noted that this factor was generalized to all alpha emitters, although the work was done only with plutonium. It is not at all certain that other alpha emitters, which are more soluble and less prone to complex, may not penetrate the barrier and produce some damage to the intestinal wall.

In addition to these changes, the 1959 ICRP report also provided MPC's based on exposure to a number of other organs, including the total body where the doses were assessed by assuming uniform distribution in the full 70-kg mass of the standard man. Also, MPC's based on exposure 40 hours per week for 50 weeks per year were suggested for use in occupational situations rather than continuous exposure basis utilized earlier.

¹⁷ Editors note: This problem has been examined in detail by an ICRP Task Force (ICRP, 1966) and a revised lung model with more detailed breakdown of parameters is all but officially adopted.

Standard Man.
such as size, shape and
person is a mouth breat-
hation is as shown below

soluble nds	Other compounds (%)
	25
	50
taken up body)	25 ^a

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VI. Current Situation (1971)

The maximum permissible body burden and the maximum permissible concentrations of plutonium derived by the ICRP-NCRP in 1959 are still the currently recommended values. Both organizations have continued deliberations on the hazards of internal radiation exposure, and revised publications of their deliberations are in preparation. It is expected that such revisions will show no compelling reasons for drastic changes in the 1959 recommendations—they have served their purpose well despite the few inconsistencies in rationale pointed out in the preceding pages. The MPC's have been incorporated into the federal regulations of the AEC not only as limitations on air and water concentrations for occupational exposure but also, when reduced by appropriate factors, for exposure of population groups as limitations on effluents and environmental concentrations. In spite of sporadic criticism of the values and intensive work on plutonium over the past years, there have been no steps taken prior to the preparation of this chapter to make any significant changes in the maximum permissible body burden. In fact, the data from the long-term dog experiments at the University of Utah now indicate little necessity for change in the non-uniform distribution factor (a "relative hazard factor") derived several decades ago by informed judgement based on rodent experiments despite the great difference in life span of the two species.

These safety levels derived from apparently meager information have served as the basis for a protection program leading to the remarkable safety record (despite the unsupported apprehensions of a few) of the extensive plutonium handling operations of the AEC and, more recently, industry in general. There has not been a single known case of damage among those who have worked with plutonium over the past three decades even though many (perhaps 50 to 100) are known to have accumulated approximately "one maximum permissible body burden (0.04 μ Ci)" and, in a few cases, considerably more. This is a record in sharp contrast to that of the early radium industry, or a number of other industries where only the appearance of injury led to institution of proper control. Constant vigilance must be maintained, however, if the projected role of plutonium in the world's future power economy is to become reality without unacceptable risk. Because of the sensitivity of detection of plutonium in air, water and other segments of the environment and the magnitude of discrimination factors along the food chain from soil to man (absolute minimum total discrimination of the order of 10^9), it is almost inconceivable that environmental contamination would be allowed to approach harmful levels from ingestion¹⁸. Chronic inhalation of material discharged directly to the atmosphere or resuspended from accumulated deposition and the long-term effects of such inhaled material on the lungs, lymph nodes and liver are the pressing problems for the immediate future. The oncogenic risk of long-term retention of discrete plutonium particles in these tissues cannot be assessed unequivocally at the present time, although the problem was recognized at the Chalk River Permissible Doses Conference in 1949 and has been considered by the NCRP and ICRP in subsequent years. The future safe handling and use of plutonium, the element frequently and somewhat erroneously called the "most hazardous material known to mankind", are both feasible and necessary and will be accomplished as long as vigilance is maintained and the depth of experience, knowledge and compassion for mankind exhibited by those pioneers is extended and applied by those responsible for future risk assessment and exposure control.

¹⁸ See also Chap. 8.

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Addendum to Chapter 12

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In January 1973 the results of a twenty-seven year study of selected Los Alamos plutonium workers was released as a Los Alamos Scientific Laboratory Informal Report. Since these results have a direct bearing on the validity of the standards for maximum permissible body burden and concentrations in air and water described in this chapter, the abstract of the Los Alamos Report is reproduced below. These findings should be considered also as a supplement to Sec. V, VIII, and Appendix A of Chap. 14 (Editor).

Abstract

Twenty-five male subjects who worked with plutonium during World War II under extraordinarily crude working conditions have been followed medically for a period of 27 years. Within the past year, 21 of these men have been examined at the Los Alamos Scientific Laboratory, and 3 more will be studied in 1973. In addition to physical examinations and laboratory studies (complete blood count, blood chemistry profile, and urinalysis), roentgenograms were taken of the chest, pelvis, knee, and teeth. The chromosomes of lymphocytes cultured from the peripheral blood and cells exfoliated from the pulmonary tract were also studied. Urine specimens assayed for plutonium gave a calculated current body burden (excluding the lungs) ranging from 0.005 to 0.42 μCi , and low-energy radiation emitted by internally deposited transuranic elements in the chest disclosed lung burdens probably of less than approximately 0.01 μCi . To date, none of the medical findings in the group can be attributed definitely to internally deposited plutonium. The bronchial cells of several of the subjects showed moderate to marked metaplastic change, but the significance of these changes is not clear. Diseases and physical changes characteristic of a male population entering its sixth decade were observed. Because of the small body burdens on the order of the maximum permissible level in these men so heavily exposed to plutonium compounds, we conclude that the body has protective mechanisms which are effective in discriminating against these materials following some types of occupational exposures. This is presumably explained by the insolubility of many of its compounds. Plutonium is more toxic than radium if deposited in certain body tissues, especially bone; however, from the practical point of view, plutonium seems to be less hazardous to handle.

Abstract of Los Alamos Scientific Laboratory Informal Report, LA-5148-MS entitled "A Twenty-Seven Year Study of Selected Los Alamos Plutonium Workers" by L. H. HEMPELMANN, C. R. RICHMOND, and G. L. VOETZ.