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Sandia Laboratories

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"TOXICITY AND CARCINOGENICITY OF PLUTONIUM-239"

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COMMENTS ON A PAPER ENTITLED
"TOXICITY AND CARCINOGENICITY OF PLUTONIUM-239"

Introduction

The paper "Toxicity and Carcinogenicity of Plutonium-239,"* to which the following pages are a rebuttal, appears as an appendix to a report entitled "Radioactive Waste Transportation Problems and WIPP," by Peter Montague of Albuquerque, New Mexico, dated April 12, 1978. In the following commentary, this appendix is referred to as the Montague Report.

Regarding the Toxicity of Plutonium-239

Threshold Limit Values (TLV's) were developed by the American Conference of Governmental Industrial Hygienists to assist trained hygienists in evaluating industrial environments. In the preface to the Conference's publication concerning TLV's, it is stated that TLV's "are not intended for use, or for modification for use . . . as a relative index of hazard or toxicity . . ." (Ref. 1). Ignoring this disclaimer, the Montague Report uses TLV's to compare workplace exposure limits for plutonium (Pu)-239 to those for chemical substances.

Despite the fact that Reference 1 deals with chemical substances, and therefore does not of course list a TLV for plutonium, Table 1 of the Montague Report gives $0.00000003 \text{ mg/m}^3$ as the workplace limit for plutonium, and identifies this number as a TLV. To accomplish this, Montague converted the radioactivity value of maximum permissible concentration in air (MPC_{air}) to mass-based units, even though MPC values should be expressed as microcuries per cubic centimeter ($\mu\text{Ci/cc}$).

* Southwest Research and Information Center, P. O. Box 4524, Albuquerque, New Mexico 87106, April 4, 1978.

If the logic of comparison used in Table 1 of the Montague Report were followed, it would be necessary to conclude that sugar (sucrose), with a TLV of 10 mg/m^3 , is 6.5 times more toxic than carbon tetrachloride (TLV = 65 mg/m^3), 1.1 times more toxic than hydrogen cyanide (TLV = 11 mg/m^3), and as toxic as the pesticide malathion (TLV = 10 mg/m^3).

After comparing the converted MPC's to TLV's for selected toxic chemicals, the Montague Report concludes that plutonium is ". . . hundreds of thousands to hundreds of millions of times more toxic than any other poison you can name" (p. 3). However, our Table A, in which MPC's for other radioisotopes have been similarly converted to TLV's, demonstrates that except for natural uranium, the exposure limits for these radioisotopes are orders of magnitude below the TLV's for the corresponding stable elements. This vast difference is a result of radiation protection considerations and not of any unique property of plutonium. The Montague Report is therefore incorrect in stating that "Plutonium definitely stands in a class by itself, so far as toxicity goes." In fact, as can be seen in Table A, the same statement could be made about iodine-131, a radioisotope routinely used in thyroid cancer therapy.

TABLE A

Comparison of MPC's (Maximum Permissible Concentrations)
and TLV's (Threshold Limit Values)

Element	Isotope		MPC ^(a) air ($\mu\text{Ci/cc}$)	TLV ^(b) (mg/m^3)	TLV ^(c) (mg/m^3)	Substance
Arsenic	As-76	S ^(d)	1×10^{-7}	6.4×10^{-11}	0.2	Arsine
Beryllium	Be-7	I	1×10^{-6}	2.9×10^{-9}	0.002	Beryllium
Cadmium	Cd-115m	I	4×10^{-5}	1.5×10^{-6}	0.05 as Cd	Cadmium oxide fume
Chlorine	Cl-36	S	4×10^{-7}	1.2×10^{-2}	3	Chlorine
Chromium	Cr-51	I	2×10^{-6}	2.2×10^{-8}	0.05 as Cr	Chromates (insol.) & chromic acid
Cobalt	Co-60	I	9×10^{-9}	7.9×10^{-9}	0.1	Cobalt (metal, dust & fume)
Fluorine	F-18	S	5×10^{-6}	5.3×10^{-11}	2	Fluorine
Iodine	I-131	S	4×10^{-9}	8.1×10^{-9}	1	Iodine
Iron	Fe-59	I	5×10^{-9}	1.0×10^{-10}	0.08	Iron pentacarbonyl
Lead	Pb-210	I	2×10^{-10}	2.4×10^{-9}	0.1 as Pb	Tetraethyl lead
Mercury	Hg-203	I	1×10^{-7}	7.3×10^{-9}	0.01 as Hg	Mercury (alkyl compounds)
Nickel	Ni-65	S	9×10^{-7}	4.8×10^{-11}	0.1 as Ni	Nickel (soluble compound)
Platinum	Pt-197m	S	6×10^{-6}	5.0×10^{-10}	0.002 as Pt	Platinum (soluble salts)
Plutonium	Pu-239	S	2×10^{-12}	3.3×10^{-8}	--	--
Potassium	K-42	S	2×10^{-6}	3.3×10^{-10}	2	Potassium hydroxide
Silver	Ag-110m	S	2×10^{-7}	2.2×10^{-9}	0.01 as Ag	Silver (metal & sol. compounds)
Sodium	Na-22	S	2×10^{-7}	3.3×10^{-8}	0.3	Sodium azide
Sulfur	S-35	S	3×10^{-7}	7.1×10^{-9}	13	Sulfur dioxide
Thallium	Tl-204	S	6×10^{-7}	1.3×10^{-6}	0.1 as Tl	Thallium (sol. compounds)
Uranium	U-nat.	S	7×10^{-11}	0.21	0.2 as U	Uranium (nat. sol. & insol.)
Zinc	Zn-65	S	1×10^{-7}	1.2×10^{-8}	1	Zinc chloride fume

(a) ERDA Manual Chapter 0524, "Standards for Radiation Protection," U.S. Energy Research and Development Administration, 1975.

(b) MPC_{air} converted to TLV units

(c) "Threshold Limit Values for Chemical Substances in Workroom Air Adopted by ACGIH for 1977," (Ref. 1).

(d) S = soluble I = insoluble

The data in Table B are presented to further temper the statements quoted above from Montague.

TABLE B

Acute Toxicity of Citric Acid and Selected Citric Acid Salts in the Mouse by Intraperitoneal Administration

<u>Compound</u>	<u>Median Lethal Dose, LD50</u>
Citric acid	961 mg/kg of body weight
Acetyl triethyl citrate	1150 mg/kg of body weight
Trisodium citrate	1419 mg/kg of body weight
Sodium citrate	1635 mg/kg of body weight
Plutonium citrate	1750 mg/kg of body weight
Disodium citrate	1771 mg/kg of body weight

Source: Registry of Toxic Effects of Chemical Substances (1976 Edition) (Ref. 2)

The prudent examiner of these data would not conclude that plutonium citrate is less toxic than either citric acid -- a normal constituent of the human body -- or trisodium citrate, which is used in foods and as a blood anticoagulant, without a careful review of the experiments that produced the data. On the other hand, under the stated conditions, plutonium citrate is not "hundreds of millions of times more toxic" than, but may be of the same order of magnitude as, citric acid and four of its salts.

Materials with toxic properties as widely varied as Pu-239, iodine-131, carbon tetrachloride, and sugar cannot be compared by any simple number. Furthermore, equating radiotoxicity to chemical toxicity by converting to common units is inappropriate when used to single out a given radioisotope for comparison with non-radioactive toxic substances. Radiotoxicity has to do with the absorption of energy by biological systems, whereas chemical toxicity deals with biochemical reactions. The effects of radiation become critical before any effects are seen on biochemical systems, and this fact is reflected in the stringent controls that are imposed on the handling of radioactive materials. The Montague Report is therefore misleading in its statement that plutonium is "more toxic than any other poison . . .".

Regarding the Carcinogenicity of Plutonium-239

Numerous studies have shown the spectrum of factors that make it difficult to construct valid comparisons between chemically induced carcinogenesis and radiation-induced carcinogenesis. Clayson (Ref. 3), synthesizing earlier work, states that radiation causes a wide variety of deleterious effects on biological systems. Radiation-induced cancer proceeds by a series of specific mutations; there is little evidence that chemical carcinogenesis proceeds by the same series of mutations. A recent analysis of plutonium toxicology (Ref. 4) states that a conscientious search of the literature on chemical carcinogens led to nothing that could be tabulated for comparison to plutonium-induced carcinogenicity.

On page 4 of the Moutague Report, the Research Triangle Study is cited, and on the bottom of that page the comment is made, "Unfortunately, the authors of the study failed to include plutonium-239 in their comparisons." The authors "failed to include" such data because the study was confined to chemical carcinogens. One of the authors (Ref. 5) of that study (Ref. 6), has stated that the data in the Triangle report were not meant in any way to be compared to radiation-induced carcinogenicity. He further commented that he could see no valid reason for comparing the moles of a chemical compound with the alpha particles of plutonium; their carcinogenic effects are derived from different bases.

Studies on carcinogenic effects of Pu-239 on animals have been reviewed often in the literature (Refs. 7, 8, 9). A summary of these studies, which were done primarily with dogs or rats, shows that the inhalation of Pu-239 results in plutonium being retained in highest concentrations in bone, liver, lung, and lymph nodes. This may result in the induction of specific kinds of cancer, primarily lung and bone carcinomas, and to a lesser extent, bile duct tumors (Ref. 7). These animal studies have been extremely useful in the analysis of the limited number of studies available on humans exposed to plutonium (Refs. 7, 10, 11) and in the prediction of plutonium cancer risk to man (Ref. 9). One of the most significant and relevant studies on human exposures to Pu-239 is that of the 1944-45 exposure at Los Alamos Scientific Laboratory. Twenty-five men associated with the Manhattan Project were identified as having had significant plutonium exposures; total initial lung burden across the group was approximately 10 μ Ci. These individuals have been monitored clinically and in laboratory studies for the past 30 years. None of the individuals has shown

cancer incidence (Ref. 7), and none shows medical findings attributable to internally deposited plutonium.

By the use of standard models and theories, Reference 9 predicts that the average risk of death from radiation-induced cancer from inhalation by humans of 1 μ Ci of insoluble Pu-239 is approximately 5%.

So far, no cancer attributable to plutonium has been found in man (Ref. 12). Bair (Ref. 7) reports that there has been no recorded instance of cancer in man resulting from the internal deposition of any plutonium isotope in the more than three decades in which plutonium has been used. This excellent record illustrates the effectiveness of control measures and safety standards imposed on the handling of radioactive materials. These facts lead to a high level of confidence that the transportation of radioactive materials to and around the WIPP would not have a markedly different record.

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