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UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

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MEMORANDUM FOR: John G. Davis, Director
Office of Nuclear Material Safety
and Safeguards

FROM: Robert B. Minogue, Director
Office of Nuclear Regulatory Research

SUBJECT: RESEARCH INFORMATION LETTER # 143 - GASTROINTESTINAL ABSORPTION OF PLUTONIUM IN MICE, RATS, AND DOGS

Introduction:

This memorandum transmits the results of experimental studies of the gastrointestinal absorption of plutonium in mice, rats, and dogs. The results have direct application to calculation of doses from plutonium ingestion. The research project was initiated in response to a request from the former Office of Standards Development, RR-SD-79-6, to determine the fraction of radionuclide transferred from gut to blood. This fraction, f_1, is used in calculating doses to internal organs resulting from ingestion of plutonium. Several investigators, working independently, have shown that the previously accepted value (ICRP-2) for f_1 (1×10^{-5}) was incorrect because the Pu(IV) used in the earlier experiments hydrolyzed, a phenomenon which does not always occur, and which reduces solubility. Consequently, the calculated doses were too low. In recognition of this fact, the International Commission on Radiological Protection in 1979 raised its value to 1×10^{-4} (The National Radiological Protection Board in England later adopted a value of 5×10^{-4}.). However, the subject experimental results suggest that 1×10^{-4} is still too low by a factor of ten. The work was performed by Drs. Maryka Bhattacharyya and Robert Larsen of the Division of Biological and Medical Research at the Argonne National Laboratory. The report describing these studies, entitled "Gastrointestinal Absorption of Plutonium in Mice, Rats, and Dogs: Application to Establishing

Values of f_1 for Soluble Plutonium," NUREG/CR-4208, has been transmitted to your staff.

Methodology:

Mice and rats were exposed to solutions of plutonium either ad libitum via drinking water or by gavage (direct administration into the stomach). Plutonium solutions were administered to dogs via gelatin capsules. Plutonium concentrations were 1×10^{-10} M, the molar concentration of Pu-239 at the MPC, the maximum permissible concentration in drinking water (5 pCi/ml). The administration medium was 0.01 M sodium bicarbonate, a medium similar to Lake Michigan water. The oxidation state was, except where noted, Pu(VI), the oxidation state present in chlorinated drinking water. At sacrifice of mice and rats, between 2 and 6 days after administration, pelts were removed, bodies were eviscerated, and plutonium was assayed in lungs, livers, and skinned eviscerated carcasses. Dogs were sacrificed 5 weeks after administration and their pelts and gastrointestinal tracts were removed; livers, lungs, and skeletons were removed and assayed. Plutonium concentrations in tissues were determined by gamma spectroscopy for Pu-237 and by alpha spectrometric isotope dilution for Pu-236, Pu-238, and Pu-239.

Results and Discussion

1. Effect of Plutonium Oxidation State

To determine the effect of the oxidation state of plutonium on GI absorption, two groups of adult female mice were fasted for 24 hours and administered Pu(IV) or Pu(VI) by gavage. The fraction of plutonium

retained at 6 days was 2×10^{-3} and was the same for both Pu(IV) and Pu(VI).

2. Effect of Plutonium Concentration

To determine the effect of plutonium concentration on the GI absorption of plutonium, three groups of fed mice were administered Pu-236 at a concentration of 1×10^{-12} M, Pu-238 at 1×10^{-10} M, and Pu-239 at 1×10^{-8} M. The fraction of Pu(VI) retained by fed mice at 21 days was independent of concentration over four orders of magnitude.

3. Effect of Administration Medium and Hydrolysis

To determine the effect of administration medium, tetravalent Pu-237 was administered to three groups of fasted adult female mice as nitrate, citrate, or bicarbonate solutions. The retention of Pu-237(IV) was not significantly affected by the nature of the anionic species of the solutions.

Additional experiments examined the effect of hydrolysis of Pu(IV) characterized by the degree of ultrafilterability (low UF values indicate polymerization). A decrease from 70% UF to 10% UF resulted in a decrease in GI absorption from 2×10^{-3} to 3×10^{-4} in the fasted mouse.

4. Effect of Animal Species

To determine the effect of animal species on the GI absorption of plutonium, a solution of Pu(VI) was administered to fasted mice by gavage, to fasted rats via drinking water, and to fasted dogs via gelatin capsule.

The fraction of plutonium retained at 6 days was 1.5×10^{-3} for mice, 3.2×10^{-3} for rats, and 6.6×10^{-4} for dogs at 5 weeks.

5. Effect of Feeding Regimen and Time of Administration

To determine the effect of food deprivation on the GI absorption of plutonium, a group of adult male mice was administered Pu-236 via drinking water with food available and 2 days later Pu-238 via drinking water following a fasting period. The fraction of plutonium retained 7 to 9 days after GI absorption of Pu(VI) in the fasted mouse (1.9×10^{-3}) was 13-fold higher than in the fed mouse (1.4×10^{-4}). A similar experiment showed that uptake during the active cycle (night) was the same as during the inactive cycle (day).

6. Effect of Age of the Animal

To determine the effect of the age of the animal, Pu-238 solutions were administered to groups of fed rat pups who were 1,2,10,19,29,52, and 100 days old. The fraction of Pu-238 retained by the fed rat at 1 day of age was 7.4×10^{-3}, seventy-fold higher than the value of 1×10^{-4} for the 100 day old adult. At 19 days, just prior to weaning, the fraction retained was 3.1×10^{-3}, approximately the same as the fasted adult rat. By 29 days, 1 week after weaning, the fraction retained had decreased to adult levels, 1×10^{-4}.

Conclusions and Recommendations

The objective of these studies was the determination of f_1, the fraction of radionuclide transferred from gut to blood. Two cases must be considered for application: workers and the general population.

For consideration of exposure to plutonium in the workplace, the most likely situation would be an accident; i.e., a single exposure. However, two groups of individuals are considered: those who eat a normal breakfast and those who skip breakfast. For the fed worker, a value of f_1 of 2×10^{-4} is recommended based on the results for the fed adult mouse. For the fasted worker, a value of 2×10^{-3} is recommended.

In considering the environmental exposure to plutonium in drinking water, two approaches were developed. The first involved calculating the amounts of Pu-239 and the doses accumulated with age for a concentration of 1 Bq/l.

Age-dependent values of f_1, fluid consumption, and body weight were used to produce the curves given in Appendix C of NUREG/CR-4208. A single f_1 was determined by calculating the value that would give the same lifetime dose.

The second approach involved calculating the dose commitment over a 70-year lifetime from each year's uptake of Pu-239 from drinking water containing Pu-239 at 1 Bq/l. Since the first year of human life is the year during which uptake of plutonium from drinking water results in the greatest commitment of lifetime dose (14.4%) due to high GI absorption, low body weight, and long residence time, a single value of f_1 for the first year of life is limiting.

Using the first approach, an $f_1 = 3 \times 10^{-4}$ would protect fed individuals of all ages and $f_1 = 6 \times 10^{-4}$ would protect fasted individuals. The second approach, which limits exposure by applying an ALI (annual limit on intake) to the first year of human life, would produce an $f_1 = 4 \times 10^{-3}$.

We recommend that NMSS consider the above f_1 values in conducting regulatory assessments. With regard to NRC regulations (10 CFR Part 20), we are proposing

SEP 18 1985

to adopt current ICRP intake recommendations (f_1 of 1×10^{-4} for class D plutonium). This question will be reviewed following confirmation of the results of this study through ongoing experiments using a non-human primate.

Future Work

In collaboration with investigators at New York University, four baboons have been administered isotopes of plutonium, uranium and neptunium. Results should be available in FY 1986. At that time we expect to inform ICRP of the results and to initiate any necessary action to change the maximum permissible concentration for plutonium in liquid effluents. For further information, please contact Dr. Judith D. Foulke (427-4563).

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