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NRDC Supplemental Submission

to the

Environmental Protection Agency

Public Hearings

on

Plutonium and the Transuranium Elements

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February 24, 1975

I. INTRODUCTION

On February 14, 1974, the Natural Resources Defense Council (NRDC) petitioned the Atomic Energy Commission (AEC) and the Environmental Protection Agency (EPA) to amend their radiation protection standards applicable to "hot particles" of plutonium and other actinides where hot particles were defined more fully in an accompanying report.[1] The report (referred to herein as the Hot Particles Report) concluded that the existing radiation protection standards are grossly inadequate to protect workers and the public from the high cancer risk posed by exposure to the atmospheric release of plutonium particulates from the nuclear power and weapons industries. The report recommended (and the petition requested) that the current standards be made more restrictive by a factor of 115,000 where hot particles are concerned. In the petition NRDC indicated that matters of importance to the public health and safety such as this require prompt action. Allowing a reasonable period for public comment NRDC recommended that the proposed standards be set within six months (by August 14, 1974).

We have requested that EPA hold adjudicatory type hearings on this matter so that the issues could be properly joined.[2-3] Instead EPA held these hearings with a panel format that developed a record which tends to obfuscate the issues. In the first place it is apparent from the transcript of the hearings on December 10 (pages 1-142 to 1-144) that certain members of the hearing panel were not informed as to the purpose of the hearings as detailed in the Federal Register. Moreover, so far as the hot particle issue is concerned,

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1/ Tamplin, A. R. and T. B. Cochran, "Radiation Standards for Hot Particles," Natural Resources Defense Council, Washington, D.C., 14 February, 1974.

2/ Letter from J. G. Speth to Dr. William D. Rowe, dated July 19, 1974.

3/ Letter from J. G. Speth to Dr. William D. Rowe, dated August 19, 1974.

it is evident from the transcript of the hearings of December 10 (pages 1-148 and 1-149) that the EPA had not ascertained that all members of the panel were prepared to discuss this issue. All of the material which we submitted to the AEC as well as the material prepared by the AEC was available to EPA and should have been reviewed by the panel prior to the hearings. In short, we feel these hearings have only served to reenforce the need for the adjudicatory hearing which we requested.

The purpose of this report is to clarify the issues related to the hot particle problem which the hearing record tends to confuse. We shall first discuss the qualitative aspects of hot particle hypothesis and then its quantitative aspects. This will be followed by a discussion of the points raised by Dr. Edward P. Radford, Jr. during the hearings. These discussions will demonstrate that no information capable of rejecting the hot particle hypothesis was presented in the course of the EPA hearing. In fact, together with the hot particle hazard, the recommendations of Dr. Karl Z. Morgan based on a different approach indicate that overall the transuranic standards should be made substantially more restrictive.

II. The Hot Particle Hypothesis

The "hot particle hypothesis" is relatively simple. Qualitatively, the hypothesis is:

> When a critical tissue mass is irradiated at a sufficiently high dose, the probability of tumor production is high.

A corollary to this is:

> When a critical tissue mass in the lung is irradiated by an immobile particle of sufficient alpha activity the probability of a lesion developing approaches unity, and the probability of this lesion developing into a tumor is high.

In order to quantify this hypothesis, we turned to the available biological data to obtain a) the risk of tumor development once the critical tissue structure has been altered through radiation exposure at high doses, and b) the critical particle activity (or local tissue dose) to significantly alter the tissue structure (or with respect to the corollary, produce a lesion in the lung).

In the Hot Particle Report, with respect to alpha-emitting particles in the lung, the hypothesis was quantified on the basis of the available biological data:

> If a particle deposited in the deep respiratory tissue is of such activity as to expose the surrounding lung tissue to a dose of at least 1000 rem in 1 year, this particle represents a unique carcinogenic risk. The biological data suggest that such a particle may have a cancer risk equal to 1/2000.

This hypothesis implies that if a particle exposes the surrounding lung tissue to a dosage greater than 1000 rem in 1 year, the cancer risk is still 1/2000. (This, of course, causes a large particle to be less effective on a per μCi basis, but not on a per particle basis.) The hypothesis implies nothing about particles that expose the tissue to less than 1000 rem in one year.

In the Hot Particle Report we indicated that much of the basic support for the hypothesis derives from a number of experiments wherein in a small volume of tissue was exposed to high dosage. In these experiments cancer was a frequent, almost inevitable, result. One series of experiments that was discussed

in some detail were those conducted by Dr. Roy C. Albert on rat skin.[4-6] In these experiments, Dr. Albert observed that the radiation induced cancers were remarkably correlated with the disruption of an architectural unit of the skin, the hair follicle. The cancers were induced in the rough proportion of 1 cancer per 2000 atrophied hair follicles when the dosages exceeded some 1000 rem.

The hot particle hypothesis thus suggests that if these skin experiments were performed with small particles, each capable of disrupting a single hair follicle, the observed cancer induction would correspond to one cancer per 2000 particles.

A. Qualitative Aspects

In the Hot Particle Report we indicated that there was qualitative support for the hypothesis in terms of two experimental observations related to hot particles embedded in tissue. Since publication of the Hot Particle Report an additional report on hot particles in hamster lungs has been published. We shall discuss each in turn.

The potential hazard of a single hot particle embedded in human tissue is illustrated by the observation of Lushbaugh

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4/ Albert, R. E., F. J. Burns, and R. D. Heimbach, "The effect of penetration depth of electron radiation on skin tumor formation in the rat," Radiation Res. 30, 1967, pp. 515-524.

5/ Albert, R. E., F. J. Burns, and R. D. Heimbach, "Skin damage and tumor formation from grid and sieve patterns of electron and beta radiation in the rat," Radiation Res. 30, 1967, pp. 525-540.

6/ Albert, R. E., F. J. Burns, and R. D. Heimbach, "The association between chronic radiation damage of the hair follicles and tumor formation in the rat," Radiation Res. 30, 1967, pp. 590-599.

and Langham.[7] They excised a nodule that developed around a Pu-239 particle imbedded in the palm of a machinist. Commenting on the histological examination of the lesion, the authors state:

> The autoradiographs showed precise confinement of alpha-tracks to the area of maximum damage and their penetration into the basal areas of the epidermis, where epithelial changes typical of ionizing radiation exposure were present. The cause and effect relationship of these findings, therefore, seemed obvious. Although the lesion was minute, the changes in it were severe. Their similarity to known precancerous epidermal cytologic changes, of course, raised the question of the ultimate fate of such a lesion should it be allowed to exist without surgical intervention . . . .[8]

Considering the above observations, it would be surprising indeed if a physician would not suggest surgical intervention in a case where a patient had a few such imbedded particles. We feel that this lesion alone should cause one to be very cautious in estimating the hazard of hot particles.

That such lesions can develop in lung tissue is supported by the observations of Richmond, et al., on the lesions induced in experiments wherein hot particles were introduced into blood vessels of the lungs of rats:

> Such a lesion with collagenous degeneration and subsequent liquefaction, due to the large local dose of radiation at a high dose rate, has been reported by Lushbaugh et al., whose description of a plutonium lesion found in the dermis is very similar to that observed for plutonium in the lung.[9]

7/ Lushbaugh, C. C. and J. Langham, "A dermal lesion from implanted plutonium," Archives of Dermatology 86, October 1962, pp. 121-124.

8/ Ibid., p. 462.

9/ Richmond, C. R., et al., "Biological response to small discrete highly radioactive sources," Health Physics 18, 1970, p. 406.

Richmond and co-workers continued these experiments with hamsters and the following appears in their latest progress report (Particular attention is drawn to the last sentence):

> Most of the animals placed on study early in the program have reached the end of their normal life span without developing significant pulmonary lesions. During the past few months, we have observed some histological changes in the lungs of very long-term animals (15-20 months). In these animals, an extension of bronchiolar epithelium into the alveolar ducts and alveoli has occurred. In some cases, the alveoli are lined with cubiodal or columnar epithelial cells (Fig. 1). This lesion has been observed almost entirely in the higher activity levels (levels 4-6) and in animals given relatively small numbers of spheres (2000-6000). An interesting recent observation has been given larger numbers of spheres of approximately 60,000. This group of animals has been exposed only about 6 months. A consistent observation of this lesion after drastically different induction times could lead to speculation that the amount of tissue irradiated is an important element in timing of the tumorigenic response. There has been no increase in frank tumors observed within the past year; however, the epithelial changes described above could be considered as precursors of peripheral adenomas.[10]

The particle activity in these hamster experiments was considerably lower than that associated with the excised palmar lesion and the lesions in the rat experiments. The particle activity from the excised palmar lesion was 5 nCi and those in the rats experiment were 40 nCi and greater. The level 4 particles in the hamster experiment contained only 4.3 pCi and level 6 contained 60 pCi. The initial lesions observed surrounding these lower activity particles were called granulomas measuring

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10/ Richmond, C. R. and Sullivan, E. M., (eds.), Annual Report of the Biomedical and Environmental Research Program of the LASL Health Division for 1973, Los Alamos Scientific Laboratory Report LA-5633-PR, May 1974, p.7.

200-500μ in diameter (about the same size as the excised palmar lesion).[11]

It is of importance to compare the description of the lesion in the hamsters wherein there is an extension of the bronchiolar epithelium into the alveoli. This is a suggested mechanism for the histogenesis of bronchiolo-alveolar carcinomas.[12] Moreover, the description of the hamster lesions indicated that, in some cases, the alveoli are lined with cubiodal or columnar epithelial cells. Such lining cells are a histological feature of bronchiolo-alveolar carcinoma.[13] We see no reason for being complacent about these lesions.

These experiments strongly support the proposal that a single particle embedded in tissue is capable of eliciting a carcinogenic response. The killing of cells and the development of a lesion surrounding the particle is the suggested mechanism of carcinogenesis (an injury mediated mechanism). It appears reasonable to propose that the mechanism is similar to that involved in the experiments of Brues et al, wherein sarcomas developed in the fibrous capsule that forms adjacent to a film of plastic and other inert materials, several months after they were implanted subcutaneous in rodents.[14]

11/ Richmond, C. R. and Voelz, G. L.,(eds.), Annual Report of the Biomedical and Environmental Research Program of the LASL Health Division for 1971, Los Alamos Scientific Laboratory Report, LA-4923-PR, April 1972, p. 31.

12/ Evans, Winston R., Histological Appearance of Tumors, Second Edition, Williams and Wilkins Company, Baltimore, Maryland, 1966, pp. 1112-1113.

13/ Ibid, p. 1111.

14/ Brues, A. M., Auerbach, H., De Roche, G.M., and Brube, D., "Mechanisms of carcinogenesis," Argonne National Laboratory, Biological and Medical Research Division Annual Report for 1967, ANL-7409, 1967, pp. 151-155.

The association of lung tumor with peripherally situated scars is discussed in cancer textbooks:

> It is known, for example, that scars in lung tissue marking injuries received years before increase susceptibility of the involved cells to cancer development.[15]

It is reasonable to propose that these lesions disrupt the local tissue architecture and thereby interfere with the normal biochemical and physical communication between the cells that control processes such as contact inhibition which are responsible for maintaining tissue stability. They thus create an area with an increased cancer risk.

While we have here stressed the formation of the lesion surrounding the hot particle, it is important to recognize that many of the cells on the periphery of the lesion are the progeny of cells that received radiation damage during the formation of the lesion. This is implied in the Lushbaugh and Langham quotation on page 5 above. This added effect of radiation damage will be of particular importance for reactor fuels. In this case, the plutonium will be contaminated with beta emitting isotopes that, because of the longer range of beta particles in tissue, will subject the cells surrounding the lesion to appreciable radiation dosage.

Although no tumors appeared in association with the microspheres in the animal experiments, the description of the lesions is suggestive of an incipient tumorogenic response. Richmond, et al, state that they could be considered as precursors of peripheral adenomas and their description is consistent with that of developing

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15/ Cowdry, E. V., Etiology and Prevention Of Cancer In Man, Appleton-Century-Crofts, New York, N.Y., 1968, p. 137.

bronchiolo-alveolar carcinoma. It is reasonable to propose that the induction period for a frank tumor by this mechanism is longer than the life span of rats and hamsters. We submit that the lesions observed around these particles are sufficient to indicate that radiation protection standards should limit the exposure of human lungs to very few hot particles.

B. Quantitative Aspects

The hot particle hypothesis as presented above contains two quantitative parameters. The first is the risk of cancer associated with a particle produced lesion and the second is the particle activity that constitutes a hot particle capable of producing such a lesion. We shall discuss each in turn.

1. Cancer risk per particle produced lesion

In our Hot Particle Report we assumed a cancer risk of 1/2,000 per particle produced lesion. This value was derived from the tumor risk per atrophied hair follicle in the experiments of Albert, et al. (see page 4). To our knowledge this is the only biological data that quantitatively relates the radiation induced disruption of a tissue mass to cancer production. As we indicated in our Hot Particle Report, this risk estimate is not necessarily conservative. One could argue that the descriptions of the particle produced lesion cited above suggest a greater risk. We can see no justification for assignment of a lower risk. While we have been criticized for using rat skin data to estimate the risk in human lungs, we have not seen any suggestion for a better approach that is based upon available biological data.

2. The hot particle activity

In our original Hot Particle Report we selected 1,000 rem/year as the local tissue dose for setting the minimum activity for a hot particle. The 1,000 rem was derived from the experiments of Albert, et al, and Laskin, et al., wherein 1,000 rem was the lowest dosage associated with a carcinogenic response. The one year was based upon the apparent epithelial cell turnover time in the lung. This method of defining the minimum activity for a hot particle carried considerable uncertainty and was so criticized.

Since the publication of the Hot Particle Report, three reports have appeared which present experimental data that allow a more direct determination of the minimum particle activity without resorting to tissue dosage or turnover time. We shall discuss these reports beginning with the one that suggests the largest limiting particle activity and ending with the smallest.

a. Richmond and Sullivan.[16] This report is the latest progress report on the microsphere experiments with hamsters at LASL. As the quotation on page 6 above indicates, lesions were observed almost entirely in the activity levels 4 and above. The particles in level 4 contained 4.3 pCi/particle. It is also indicated that lesions were observed in association with particles from level 3 (0.9 pCi/particle). However, this occurred in animals given 60,000 spheres and the lesions may have been associated with clumping on aggregates of particles.

16/ Richmond, E. R. and Sullivan, E. M., op. cit.

This experiment thus suggests a range for the limiting activity of 0.9 - 4.3 pCi/particle with the lower limit somewhat tentative.

These experiments, at this time, represent the only direct observation of particle produced lesion and serve to establish the upper limit for the minimum particle activity. Had the life span of the animals been longer, it is quite possible that lesionswould have developed around particles of lower activity. Thus, the minimum particle activity is most likely below 4.3 pCi/particles. This 4.3 pCi represents a 60 fold increase in the minimum particle activity relative to the 0.07 pCi (based on 1000 rem/year to beal tissue) adopted in the Hot Particle Report.

Nevertheless, a 60 fold increase in activity requires only a 4 fold increase in particle diameter--for Pu-239, a change from 0.6 μ to 2.4 μ; for Pu-238, a change from 0.09 μ to 0.36 μ and for high burn-up nuclear fuel, a change from 0.4 μ to 1.6 μ. These particles are still in the range that permits deposition in the lower respiratory zone. In other words, even when using this upper limit value, the nuclear industry has a potential hot particle problem.

b. McInroy, et al.[17] This report presents a particle size analysis of plutonium particles in a tracheobronchial lymph node of a Los Alamos plutonium worker. Another study of human respiratory exposure to plutonium relates to 25 workers exposed to plutonium at Los Alamos during the Manhattan Project.[18] The

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17/ McInroy, James F., et al., "Studies of Plutonium in Human Tracheobronchial Lymph Nodes," Los Alamos Scientific Laboratory Preprint, LA-UR-741454, 1974.

18/ Hemplemann, L. H., et al, "Manhattan Project Plutonium Workers; A Twenty-Seven Year Follow-Up Study of Selected Cases," Health Physics, Vol. 25, Nov. 1973, pp. 461-479.

latest examination of this group found them to be free of lung cancer although the report states, "The bronchial cells of several subjects showed moderate to marked metaplastic changes, but the significance of these changes is not clear." If these 25 workers combined retained a total of 2,000 hot particles then the chance of none of them developing lung cancer would be about 0.3 (assuming a tumor risk per particle of 1/2,000). Thus, the particle size distribution given by McInroy, et al., can be used to obtain a limiting particle size that would correspond to some 2,000 hot particles retained in the 25 workers.

Healy, et al., estimates that the initial burden in these workers was about 10 μCi.[19] Table I presents the particle size distribution given by McInroy, et al., wherein the incremental activity in a size range was determined by multiplying the incremental activity fraction by the total activity (10^7 pCi). The particle number was then obtained by dividing the incremental activity by the activity per particle.

Inspection of Table I indicates that for these workers to contain only 2,000 particles a minimum activity somewhat larger than 0.8 pCi/particle is required. There is considerable uncertainty attached to this estimate (see discussion in Letter to Mr. Robert B. Minoque attached as Appendix A to this submission). For one thing the autoradiographic sizing technique tends to overestimate the large particle fraction and hence,

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19/ Healy, I. W., et al., "A Review of the Natural Resources Defense Council Petition Concerning Limits for Insoluble Alpha Emitters," Los Alamos Scientific Laboratory Report, LA-5810-MS, Nov. 1974, p.15.

TABLE I

Estimated Particle Size Distribution For
The Manhattan Projects Workers
(Assumes a total lung burden of 10^7 pCi for the 25 workers)

Diameter Particle μ	Incremental Activity Fraction	Incremental Activity	pCi/particle	Number of particles
<0.1	0.12	1.2×10^{6}	3×10^{-4}	4×10^{9}
0.1 - 0.3	0.58	5.8×10^{6}	9×10^{-3}	6.4×10^{8}
0.3 - 0.5	0.23	2.3×10^{6}	4.1×10^{-2}	5.6×10^{7}
0.5 - 0.7	0.056	5.6×10^{5}	1.1×10^{-1}	5×10^{6}
0.7 - 0.9	0.011	1.1×10^{5}	2.4×10^{-1}	4.7×10^{5}
0.9 - 1.1	0.002	2×10^{4}	4.3×10^{-1}	4.7×10^{4}
1.1 - 1.3	0.0009	9×10^{3}	7×10^{-1}	1.3×10^{4}
>1.3	0.0001	1×10^{3}	>1.0	$<10^{3}$

the limiting activity. Another is that this lymph node particle size distribution may not adequately represent the lung burden of the individual from which it was obtained. In this regard, the exposure of this Los Alamos worker may not be representative of the 25 Manhattan Workers. An examination of the corresponding lung tissue is underway and this may be quite helpful. (See letter from McInroy to Cochran attached as Appendix B to this submission). Finally, assuming it is inappropriate to apply this distribution to the Manhattan Workers and instead applying it only to the individual from which it was obtained (see Appendix A) leads to a minimum activity to constitute a hot particle of 0.14 pCi/particle.

c. Rocky Flats Fire.[20] The approach used above can also be applied to the individuals contaminated during the October 1965, fire at Rocky Flats. This will again give an upper estimate of the minimum activity since, as we discussed in the Hot Particle Report, lung cancer may develop in these individuals over the next 15 or so years.

Mann and Kirchner report that the MMD for the particles in this incident was 0.32 μ with a standard deviation of 1.83.[21] The data they present indicates that the combined lung burden of 25 exposed workers was 1.2×10^6 pCi.[22] Table II was constructed using these data and the same approach as used above for the Manhattan Workers.

Inspection of Table II indicates that for the Rocky Flats Workers to contain only 2,000 hot particles, the minimum activity to constitute a hot particle would have to be some 1.6 pCi/particle. If, however, the minimum particle activity were only 1 pCi/particle, Table II would suggest that around 3 lung cancers could be anticipated in the next 15 or so years (using a risk per particle of 1/2,000).

20/ Mann, J. R. and A. R. Kirchner, "Evaluation of Lung Burden Following Acute Inhalation of Highly Insoluble PuO_2," Health Physics, Vol. 13, 1967, pp. 877-882.

21/ Ibid, p. 881.

22/ Ibid, p. 880. (When a range in lung burdens was given, we used the midpoint)

TABLE II

Estimated Particle Size Distribution For
The Rocky Flats Workers
(Uses a total lung burden of 1.2×10^6 pCi)

Diameter μ	Incremental Activity Fraction	Incremental Activity (pCi)	pCi/Particle	Number of Particles
0.6 - 0.7	0.05	6.0×10^4	0.09	6.7×10^5
0.7 - 0.8	0.033	4.0×10^4	0.14	2.9×10^5
0.8 - 0.9	0.022	2.6×10^4	0.20	1.3×10^5
0.9 - 1.0	0.017	2.0×10^4	0.28	7.1×10^4
1.0 - 1.2	0.014	1.7×10^4	0.44	3.9×10^4
1.2 - 1.4	0.007	8.4×10^3	0.72	1.2×10^4
1.4 - 1.6	0.004	4.8×10^3	1.15	4.2×10^3
1.6 - 1.8	0.0016	1.9×10^3	1.62	1.2×10^3
1.8 - 2.0	0.001	1.2×10^3	2.24	5.4×10^2

This possibility cannot be ruled out at the present time.

d. Sanders and Dagle.[23] This report presents preliminary results of a continuation of experiments wherein Sanders induced a large incidence of lung cancer in rats following exposure to low doses of soluble Pu-238. Of particular interest in these new experiments are three exposure groups involving insoluble particles in which no lung cancers have appeared. One of these groups was exposed to $^{238}PuO_2$ and we shall analyze it because it will be the most critical with respect to particle size and activity.

There were 60 rats in this group who were exposed to an average of 160 pCi of $^{238}PuO_2$ as measured one day after inhalation of particles with a CMD ranging between 0.1 and 0.3 μ. The report indicates that 23 of the 60 rats have died so far with no evidence of lung cancer (571 days past exposure).

We shall use the midpoint of the CMD range. A CMD of 0.2 μ corresponds to a MMD of 0.3 μ. The distribution of particle sizes about the median was not given. We shall therefore arbitrarily assume the particle size distribution obtained at Rocky Flats (MMD = 0.32 μ, σ = 1.83). Table III presents the particle distribution on this basis for a total exposure of 9,600 pCi to the 60 rats.

Inspection of Table III suggests that we can draw no inferences from this experiment at this time. Above 0.1 μ there are only 5,000 particles leading to an expectation of only 2 cancers (assuming a risk of 1/2,000 per particle). If no cancers appear this experiment, this would only suggest a minimum particle activity of around 0.6 pCi/particle. We say

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23/ Sanders, C. L., and G. E. Dagle, "Studies of Pulmonary Carcinogenesis In Rodents Following Inhalation of Transuvanic Compounds, Pacific Northwest Laboratories, Biology Dept., Preprint.

TABLE III

Estimated Particle Size Distribution For
Rats Exposed to $^{238}PuO_2$
(Total exposure for 60 rats = 9,600 pCi)

Particle Diameter u	Incremental Activity Fraction	Incremental Activity (pCi)	pCi/Particle	Number of Particles
<0.1	0.02	192	0.08	2,400
0.1 - 0.2	0.20	1,920	0.64	3,000
0.2 - 0.3	0.24	2,300	2.2	1,060
0.3 - 0.4	0.18	1,730	5.1	340
0.4 - 0.5	0.12	1,150	10	115
0.5 - 0.6	0.09	865	18	48
0.6 - 0.7	0.05	480	28	17

only suggests because with only 5,000 particles the chance of no cancers appearing would be 0.08 which is not generally considered statistically significant. Furthermore, as stated above, the particle size distribution is unknown and must be assumed somewhat arbitrarily.

Table IV presents a similar analysis for a group of 60 rats exposed to 12,000 pCi of $^{239}PuO_2$. Inspection of Table IV indicates that if no tumors appear in this group, it would be suggestive of a minimum particle activity of 0.14 pCi/particle (assuming a risk of 1/2,000 per particle).

It must be recognized that the above analysis is quite tentative not only because the particle size distribution is speculative, but also because more than half of the rats were still living when these interim results were reported. Moreover, as with the hamsters, the life span of the rats may compromise the induction period for hot particle mediated carcenogenesis.

Minimum hot particle activity. We are now in a position to summarize estimates of the minimum hot particle activity. As stated earlier, our initial definition of the minimum hot particle activity was based upon the dose to surrounding tissue which was quite uncertain. The experimental results above allow assessment of this parameter without resort to dose calculations. These observations and analysis lead to the following estimates of the minimum activities:

Minimum Activity pCi/particle	Experimental Basis
0.9 - 4.3	Observation of particle produced lesions Rocky Flats Workers
1.6	Manhattan Workers
0.8	$^{238}PuO_2$ in rats
0.6	$^{239}PuO_2$ in rats and (in Appendix) from lymph node
0.14	1,000 rem/year
0.07	

TABLE IV

Estimated Particle Size Distribution For Rats Exposed To $^{239}PuO_2$ (Total exposure For 60 rats = 12,000 pCi)

Particle Diameter μ	Incremental Activity Fraction	Incremental Activity (pCi)	pCi/particle	Number of Particles
0.6-0.7		600	0.09	6650
0.7-0.8		395	0.14	2820
0.8-0.9		263	0.20	1315
0.9-1.0		204	0.28	730
1.0-1.2		163	0.44	37
1.2-1.4		84	0.72	117
1.4-1.6		48	1.15	42

These activity values range over a factor of 60 but the diameter varies by only the cube route, or a factor of 4. Particle produced lesions which could be considered as precursors of peripheral adenomas were observed around the 4.3 pCi particles. Hence, it would be fortuitous if this value did not overestimate the minimum activity.

Until more experiment data becomes available we would choose a conservative approach to selecting the minimum activity. Consequently, we can see little justification for assuming a minimum activity greater than 0.6 pCi/particle and we believe it prudent to select a lower value as we have previously proposed.

III. The Sensitive Tissue

In his statements and questions during the December 10 and 11, 1974, hearings, Dr. Radford implied (and attempted to solicit concurence) that hot particles can only be expected to induce cancer in man in the more proximal bronchi because in man this is the sensitive tissue. We cannot agree with this and as the transcript (pages 2-262 to 2-268) indicates, Dr. Bair did not concur.

While the predominant lung tumor in man is bronchiogenic, bronchiolo-alveolar carcinomas also occur. It would appear that because of genetic factors, influenced by the prevalent carcinogens, the more proximal bronchi are the most sensitive tissue. Nevertheless, we submit that alpha-emitting hot particles represent a new and unique carcinogenic agent. As such, we see no a priori reason for doubting that, as in animals, bronchiolo-alveolar carcinoma will be induced in man by PuO_2 deposited in the peripheral regions of the lungs.

Along with Dr. Little, Dr. Radford has presented evidence demonstrating that Po-210 in cigarette smoke concentrates in the segmental bifurcation.[24] Dr. Edward A. Martell has proposed that the Po-210 is contained in insoluble particulates which accumulate at these bifurcations.[25] As a consequence the dose to the local tissue is several rem/year. This is suggested as the carcinogenic mechanisms related to cigarettes.

24/ Little, J. B. and Radford, E. P., Science, 155, 1967 pp. 606-607.

25/ Martell, Edward A., Nature, 249, May 17, 1974, pp. 215 - 217.

The Po-210 particles involved have 2 orders of magnitude less activity than hot particles. The mechanism involves continuous exposure at "low" dose rates while the hot particle hypothesis involves a significantly higher dose rate that is capable of producing a tissue disruptive lesion around the particle. Because of the particle size distribution, exposure to PuO_2 aerosols could involve both mechanisms. As a consequence, the risk could be larger than that estimated by each hypothesis independently.

IV. PuO_2 Exposure Standards

In our petition and Hot Particle Report, we concluded that, consistent with the whole body exposure standard of 5 rem/year, the alpha-emitting hot particle standard should be 2 particles in the human lung. Using the estimated minimum hot particle activity of 0.07 pCi, this resulted in the suggested reduction of the MPLB by 115,000. However, as we stated in our Hot Particle Report, this factor of 115,000 would apply only when it was not determined that the activity was not on hot particles. Using the particle size distribution determined for the Rocky Flats fire, and allowing only 2 particles above 0.07 pCi would still have required a reduction of the MPLB by a factor 16,000.

Table V presents the particle size distribution (using the Rocky Flats statistics) for high burnup Pu fuel that would be used in Pu recycle in LWR's or in the LMFBR. This table serves to illustrate the nature of the problem associated with hot particle exposure standards in the nuclear reactor industry. As we indicated above, we can see little justification for selecting a

TABLE V

Estimated Particle Size Distribution For High Burnup Pu Fuel (0.2 Ci/g) (Assuming a Lung Burden Of 16,000 pCi)

Particle Diameter μ	Incremental Activity Fraction	Incremental Activity (pCi)	pCi/particles	Number of Particles
0.6-0.7	0.05	800	0.32	2500
0.7-0.8	0.033	530	0.47	1100
0.8-0.9	0.022	350	.66	530
0.9-1.0	0.017	272	0.91	300
1.0-1.2	0.014	224	1.58	142
1.2-1.4	0.007	112	2.49	45
1.4-1.6	0.004	64	4.10	15
1.6-1.8	0.0016	26	5.30	5
1.8-2.0	0.0001	16	7.30	2

minimum hot particle activity greater than 0.6 pCi/particle. Inspection of Table V indicates that a 2 particle limit at 0.6 pCi/particle would still require a reduction of the MPLB by a factor approaching 2000.

A 1000 fold reduction would cause the MPLB for occupational exposure to be only 16 pCi and as such would be far below the limits of detectability. But that appears to be the situation with plutonium. Dr. Morgan, at the December 10th hearings, recommended a reduction in the whole body burden by about a factor of 400 based on other considerations; namely, exposure to the bone. It appears that commensurate with other radiation protection standards, if you can detect Pu in the human body, a significant overexposure has already occurred. This, we propose, is the conclusion to be drawn from the record of the EPA hearings in Washington, D.C. and Denver, Colorado.

Since acceptable levels of Pu in humans are below detectable levels, it is apparent that the exposure standards can be enforced only by enforcing strict compliance to design specifications and operational procedures that have the objective of zero release. We submit that compliance with adequate design specifications and operational procedures is the only way to effectively meet any exposure standard and we suspect that it was quite effective at the Army's bacteriological warfare laboratory where zero release was an objective.

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February 4, 1975

Appendix A

Mr. Robert B. Minogue
Acting Director
Standards Development
Nuclear Regulatory Commission
1717 H Street, N. W.
Washington, D. C.

Dear Mr. Minogue:

We are writing in response to a suggestion at the meeting of January 9, 1975, that it would be useful if we provided written comments on two issues discussed in "A Review of the Natural Resources Defense Council Petition Concerning Limits for Insoluble Alpha Emitters," J. W. Healy, C. R. Richmond and C. E. Anderson, LASL, LA-5810-MS, November, 1974. These issues to be addressed are:

(a) The discussion beginning on page 4, "B. Limitations on the Usefulness of Radiation Dose" with particular emphasis on the statement,

> "It is for these reasons that most scientists have refrained from using dose calculations, such as those given earlier, to arrive at conclusions as to the effect of radioactive particles but have preferred to depend upon experimental evidence which bears more directly on the actual conditions."

(b) The statement on page 15,

"In a recent study McInroy et al., 37 measured the distribution of plutonium particle size in a lymph node of a deceased worker by the autoradiographic technique. Although this individual was exposed at a later time than those discussed above, it is of interest that these estimates also indicated that 15% of the plutonium was in particles larger than 0.07 pCi."

We do not agree with the first part of the statement from page 4. Most scientists who have considered the particle problem have used dose calculations to arrive at the conclusion that particle irradiation is unique and that its consequences may be significantly different from uniform irradiation.

At the same time, we agree that it is preferable to use experimental data that bear directly on the problem when estimating the risk from particle irradiation. In fact, in responding to criticisms of our Hot Particle Report, such as WASH-1320, much of our effort was directed toward demonstrating that most of the cited experiments were not relevant to hot particles.

We would suggest that the most pertinent observations involve the lesion excised from the palm of a mechanic by Lushbaugh and Langham and the microsphere experiments conducted by Richmond, et al. These experiments strongly suggest that a single hot particle embedded in tissue is capable of eliciting a tumorgenic response. Richmond, et al, described the lesions induced in the lung of hamsters as precursors of peripheral adenomas. We submit that these observations alone are sufficient to indicate that every effort should be made to prevent such particles from being deposited in human lungs. They strongly suggest that a single hot particle represents a significant hazard and

that the radiation protection standards should certainly limit the exposures to very few particles.

This, however, leaves us with the problem of what constitutes a hot particle. In the subsequent discussion of the statement on page 15, we address this issue and define the hot particle from experimental data without the use of dose calculations.

With respect to the statement on page 15, the unpublished paper by McInroy, et al., reports new and potentially significant data that were not available when we wrote, "Radiation Standards for Hot Particles." Our analysis of these data and their implication with respect to the proposed hot particle standards is given below.

The following data were presented for Case 7-138, the metal fabrication worker who died of a crushed chest in 1973, twenty six years after his first exposure.

Lymph Node activity (12 nodes)

Mean concentration	770 ± 493 pCi/g Pu-239 80 ± 43 pCi/g Am-241
Maximum concentration (node #11)	1800 pCi/g

Distribution of $^{239}PuO_2$ particles (in node #6):

Mass median diameter	MMD = 0.3 μm
Geometric std. deviation	σ_g = 1.6
Count median diameter	CMD = 0.2 μm

Based on these data (and McInroy, et al.'s, Table 5 and Figure 2) we find that 7 percent (as opposed to 15% reported by Healy, et al.) of the lymph node activity was estimated to be on hot particles. This represents a substantial number of hot particles by our definition (activity $\geq$ 0.07 pCi).

The measured distribution of $^{239}PuO_2$ particles size is given in McInroy, et al.'s Table 5. For particle diameters larger than 0.6 μm (corresponding to 0.07 pCi) the following data are presented:

Dia μm	Midpoint	Incremental Fraction	Activity pCi/particle	Activity pCi/node	Particles per node
0.6					
	0.7	0.056	0.11	37	340
0.8					
	0.9	0.011	0.24	7	29
1.0					
	1.1	0.002	0.43	1	2
1.2					

Total activity in sample (node #6) = 657 pCi.

Assuming the total mass of the tracheobronchial lymph nodes is 15 grams, the total number of hot particles (activity >0.07 pCi) in the lymph nodes is

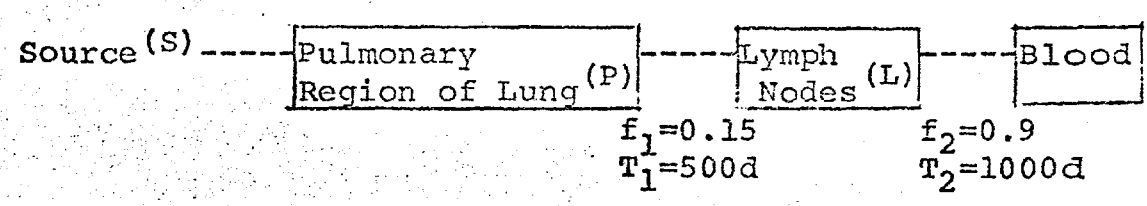
$$(15g)\left(770 \frac{pCi}{g}\right)\left(\frac{340 + 29 + 2}{657\ pCi}\right) \text{ particles} = 6500 \text{ hot particles.}$$

This probably overstates the number of hot particles in the lymph nodes for the following reasons: (a) smaller particles tend to aggregate into larger particles in lymph tissue (See WASH-1320, pp. 10-12), (b) according to McInroy (private communication with TBC, Jan. 20, 1975) aggregates (particularly with respect to the larger particles) were observed and reported as single particles (the experimental design of the particle size measurements, because of aggregation, tended to maximize the estimate of large particles), and (c) because one is looking at a plane view, it is difficult using the audioradiographic technique to distinguish star track coming from two point sources at different depths but along the same line of view. Paul

Morrow pointed out to one of us (TBC private communication, Jan. 20, 1975) that the audiographic technique is not very reliable for particle sizes below about 0.5 μm to 1.0 μm because of the difficulty in distinguishing individual particles. In other words, aggregates of particles would appear as point sources below this size range. In addition, there is a sizable (64 percent) statistical uncertainty in the 770 pCi/g estimate, and the lymph nodes analyzed may not be representative of the total tracheobronchial lymph node mass.

It is possible to make a crude estimate of the lung burden based on the lymph node concentration, or burden at death. We have done this using the ICRP lung model (ICRP Publication 19, p.6) for lack of better data.

In our case the ICRP model is simplified to



where f and T are the regional fraction and biological half-life, respectively, for Class Y compounds.

The rate equations are

$$\frac{dP}{dt} = S(t) - \lambda_1 P \qquad \text{pulmonary region}$$

$$\frac{dL}{dt} = f_1\lambda_1 P - f_2\lambda_2 L \qquad \text{tracheobronchial lymph nodes}$$

where

$$\lambda_1 = \frac{0.693}{(500/365)} = 0.5 \qquad f_1 = 0.15$$

$$\lambda_2 = \frac{0.693}{(1000/365)} = 0.25 \qquad f_2 = 0.9$$

We have assumed the rate at deposition of activity in the pulmonary region, is constant throughout the 26 year exposure period to simplify the calculation, i.e. $S(t) = R$. This yields

$$P = \frac{R}{\lambda_1}(1-e^{-\lambda_1 t}) ,$$

$$L = \frac{f_1 R}{f_2 \lambda_2} \left[1 + \frac{e^{-\lambda_1 t}}{\frac{1}{f_2 \lambda_2} - \lambda_1} - \frac{e^{-f_2 \lambda_2 t}}{\frac{1}{f_2 \lambda_2} - \frac{1}{\lambda_1}} \right]$$

For t = 26 yr, the time of death

$$L(26) = 12 \text{ nCi} \approx \frac{2}{3} R$$

$$R = 17 \text{ nCi/yr}$$
$$P(26) \approx 2R \approx 34 \text{ nCi}$$

There is considerable uncertainty in these values for a number of reasons reviewed on pp.5-9 of ICRP Publication 19. The parameters are for a class of compounds as opposed to PuO_2. Retention may be a strong function of particle size. The biological half-lives are not known within a factor of 5; $T_{1/2}$ = 500d may represent anything between 100d and 10,000d. The ICRP model parameters are not consistent with uranium miner exposure data. It should also be noted that the calculated pulmonary and lymph node burdens are higher than the 33 nCi of ^{239}Pu based on urine assay (McInroy, et al., p.5) and that the exposure was surely not uniform over the 26 year period, but probably highest "during the early years of laboratory operation (1945 - 1955) before improved industrial hygiene and health physics requirements reduced significantly the air levels of plutonium in the laboratories and the workers were provided with more efficient personal respiratory protection" (McInroy, et al., p.5.).

Nevertheless, assuming a pulmonary burden of 34 nCi and the particle size distribution in the lung is the same as the measured distribution in the lymph node, the number of particles greater than 0.07 pCi (0.6 μm dia) is

$$(34 \text{ nCi})\left(\frac{371 \text{ particles}}{657 \text{ pCi}}\right)(10^3 \text{ pCi/nCi}) = 20{,}000 \text{ hot particles}$$

The probability of cancer induction at a risk of 1/2000 per particle would be essentially unity.

Assuming a minimum activity to constitute a hot particle is 0.14 pCi, corresponding to a 0.8 μm diameter $^{239}PuO_2$ particle, the number of hot particles in the pulmonary region would be

$$\frac{(34)(31)}{657} \times 10^3 = 1600 \text{ particles.}$$

The tumor risk would be about 0.5.

There is an obvious need for a careful particle size analysis of the lung tissue available from Case 7-138, and a pathological examination to determine whether lesions are associated with the larger particles. Dr. McInroy has informed one of us that an examination of the lung tissue is underway.

It can be argued that it is premature to modify the proposed hot particle standard ["Radiation Standards for Hot Particles"] by shifting the minimum hot particle activity until the lung data is available. However, our original choice of the minimum hot particle activity carried considerable uncertainty (See "A Critique of the Biophysical Society's DRAFT Comments on "Radiation Standards for Hot Particles," pp.4-6). The choice of 1000 rem/year to the local tissue as the cut off defining a hot particle was based on the choice of (a) 1000 rem supported by the experiments by Albert, et al., and Laskin, et al., (b) one year as the tissue repair

time in the lung, and (c) the Geesaman lung model assuming the lung was inflated to 1/2 maximum.

The combined uncertainty associated with these assumptions is more than a factor of two. Had the lymph node data been available to us at the time we prepared our report we would have used these data in establishing the minimum (or critical) hot particle activity. We therefore propose increasing the minimum hot particle activity by a factor of two to 0.14 pCi. This new value should of course be re-examined as in light of any new data, particularly the Case 7-138 lung data when it becomes available.

One of the criticisms of our report raised by Dr. Gamertsfelder, and others, is the arbitrariness or uncertainty in the choice of 1000 rem/yr to the local tissue as the definition of the critical particle activity. We can avoid the use of dose or dose rate altogether in defining the critical particle activity by basing the cut off on the observations by Lushbaugh, et al., the hamster experiments of Richmond, et al., and the lymph node study by McInroy, et al. Lushbaugh, et al. reported a lesion in palmer tissue that developed around a particle containing 0.08 μg (5nCi) of Pu-239. Richmond, et al. observed lesions in the lungs of hamsters around particles containing 4.3 pCi. Moving down further in activity, we postulate on the basis of the study of McInroy, et al. that lesions probably did not occur around particles less than about 0.14 pCi, otherwise Case 7-138 probably should have developed cancer according to the hot particle hypothesis. On the basis of these data it seems logical to select a critical particle activity between 0.14 pCi/particle and 4.3 pCi/particle. We would suggest a value close to 0.14 pCi/particles to be conservative and because of the limitations of the Richmond, et al. experiments set forth on pp.25-28 of our critique of WASH-1320 namely, that had these experiments been performed with animals that have longer life spans, it is quite possible that lesions would have developed around particles of lower

activity. Notice we have avoided the use of dose altogether.

Finally, as we stated earlier, the observations of Lushbaugh and Langham along with those of Richmond, et al., strongly suggest that a single hot particle represents a significant hazard and that the standards should limit exposures to very few particles. Moreover, the direct observation by Richmond, et al. of lesions induced by particles containing 4.3 pCi clearly demonstrates that there is a hot particle problem associated with the nuclear industry. Particles with this activity are within the size range that can be deposited in the deep respiratory tissue. In other words, there is experimental evidence that bears directly on this problem and that evidence indicates the need for more restrictive standards when hot particles are involved.

If you wish to discuss these, or other issues further, don't hesitate to call us.

Sincerely,

Thomas B. Cochran
Arthur R. Tamplin

cc: Dr. William A. Mills
Dr. W. D. Rowe

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IN REPLY
REFER TO: H-5-75-165
MAIL STOP: 486

Appendix B

February 10, 1975

Thomas Cochran, Ph.D.
National Resources Defense Council
1710 Nth Street, N.W.
Washington, D. C. 20036

Dear Dr. Cochran:

In reference to our recent telephone conversation concerning the particle size distribution of PuO_2 in the tracheobronchial lymph nodes of a former employee of Los Alamos Scientific Laboratory ("Studies of Plutonium in Human Tracheobronchial Lymph Nodes", LA-UR-74-1454), I checked with the person that had counted the tracks associated with the "stars" in our autoradiographs about the possible presence of clusters of particles. He did not find many stars in which he was able to distinguish more than one center from which the tracks originated. However, it is my feeling that there is no way in which we could identify whether the tracks were formed from the decay of plutonium in a single particle or a cluster of small particles. The best we can say is that if a group of small particles was counted as a single particle, the size estimate was of this larger, composite diameter. This means that our estimate of the activity median diameter of 0.32 μm may be on the high side as counting any aggregate of particles as a single particle tends to maximize the estimate of the size distribution.

I am very interested in your calculation of the lung burden from the lymph node concentrations. My estimate of plutonium in the lung, based upon the average concentration of ^{239}Pu in eight transverse sections, taken from the superior lobe of the right lung, was 36 ± 19 nCi. The variance is quite large due to the variation in the distribution of the particles throughout the lung. The estimate, however, is remarkably close to your calculated value of 34 nCi. This may be fortuitous but I will be able to improve our estimation as we continue to analyze sections from this lung.

As regards our plans for continued study of this autopsy case, I have discussed with our pathologist the possibility of examining sections of lung tissue for lesions that could be associated with the presence of plutonium and, at the same time, attempt to measure the particle size distribution within the lung, using the same techniques used with the lymph nodes. We have decided to attempt this, although there are several serious problems that are evident, For example, our lung specimen was inflated with dry nitrogen, shortly after the autopsy, to a configuration approximating the natural shape it would have in the thoracic cavity. This was frozen in this form and has since been used in studies with our lung counter to compare the in vivo and in vitro measurements of plutonium and americium present The sectioning, mounting and staining of tissue that has been frozen presents some

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problems when attempting a histological examination due to the disruption of structure by freezing and to the dehydration that has occurred during storage

I will be happy to keep you informed as to our progress. If you have additional questions and/or suggestions, please write or call me at 505-667-4709.

Sincerely,

James F. McInroy

James F. McInroy
Tissue Section Leader
Industrial Hygiene Group

mlg