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## A Critique of The Biophysical Society's*

## DRAFT

## Comments on

## "Radiation Standards for Hot Particles"**

by


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Thomas B. Cochran


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* Prepared by The Biophysical Society's Science and Technology Advice and Information Service [STAIS] Committee on the "Hot Particle Problem."

** "Radiation Standards for Hot Particles," Arthur R. Tamplin and Thomas B. Cochran, Natural Resources Defense Council, 14 February 1974.

## Introduction

The draft comments prepared by the Biophysical Society contain a summary by Jane and Richard Setlow, the coordinators of the STAIS Committee on the "Hot Particle Problem," followed by the individual comments of the five committee members. The summary and individual comments are reviewed separately below.

## Summary Comments by Jane and Richard Setlow

The summary prepared by Drs. Jane and Richard Setlow indicates the hot particle problem is a valid and serious one. Two of the reviewers felt that the standards should be made more restrictive. There was only one reviewer who stated that there was no reason to change the standard. Except for the latter, most reviewers felt that more information was needed to establish such a standard on a firm basis.

We agree that the available data are not adequate to firmly establish the quantitative parameters in our hypothesis. At the same time, we feel the available data fully support the hypothesis qualitatively. In our report, "Radiation Standards for Hot Particles,"[1] we cited the ICRP and NCRP reservations relative to hot particles. Both this report and "The Hot Particle Issue,"[2] our critique of WASH-1320, present evidence that suggests that hot particles offer a unique carcinogenic risk. This possibility is acknowledged in

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

2/ Tamplin, Arthur R. and Thomas B. Cochran, "The Hot Particle Issue: A Critique of WASH 1320 as it Relates to the Hot Particle Hypothesis," Natural Resources Defense Council, Washington, D. C., (November 1974).

the NCRP and ICRP reservations. In other words, there is evidence that suggests that existing exposure standards are not adequate when hot particles are involved. However, to modify these standards, a quantitative estimate of the risk is required. That was the major purpose of our original hot particle report. We petitioned for a modification of the existing standards because there is a present need to protect the workers in -- and the public from -- a rapidly growing plutonium oxide fuel industry. If plutonium were to be banned, like cyclamates, we could await more definitive data, but right now it appears that the nuclear industry is going ahead with its plans.

In attempting to assess our assignment of quantitative values to the hypothesis, it is unfortunate that two of the reviewers[3] attempt to set aside one hypothesis with another. This can only be done with experimental data. Instead of focusing on whether the available data support or contradict our hypothesis, these reviewers proposed totally different hypotheses and estimated quantitative risks based on these different hypotheses. Even if we assume these alternate hypotheses are developed more rigorously and are equally plausible, they still would be only hypotheses and could not be used to set aside ours. Our hypothesis, for which we find support and no contradictory evidence, at present gives a higher risk per particle than the alternate hypotheses. Confronted with different estimates of risk from two or more hypotheses that cannot be set aside, we feel that it would be worthwhile for the committee to express its opinion as to the approach that should be followed in

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3/ Drs. M. L. Randolph and Arthur Cole.

establishing public health standards in such situations. Should the public and workers assume the risk, should the substance be banned, or should the industry be required to develop the technology to reduce the exposure to a level suggested as prudent by the existing but incomplete data? What principle should apply to the practice of public health and safety in such cases?

Comments by M. L. Randolph

A. Overall Views --

We will comment on the conclusions in this section as we review the related material in the subsequent sections.

B. Major Technical Considerations --

Page 2, ¶ 1: Our conviction is found in other experimental evidence detailed in "Radiation Standards for Hot Particles" and "The Hot Particle Issue," our critique of WASH-1320 which we have submitted to the Biophysical Society committee. Perhaps some confusion could have been avoided had we carefully delineated the experimental evidence that supports the hypothesis qualitatively from the evidence used to quantify the hypothesis in order to establish radiation standards.

Page 2, last ¶, beginning 1) (p. 22-26): Albert observed a nearly constant ratio of tumors per atrophied hair follicle in the range (1/2000 to 1/4000). Geesaman, based on the observations of Albert, et al., but allowing for a more liberal margin for error, used somewhat larger (order of magnitude) limits of uncertainty on the tumor risk probability, i.e., $10^{-3}$ to $10^{-4}$. Since we had to quantify this risk in order to recommend a standard, we selected the median between 0.001 and 0.0001, namely 0.0005, or 1/2000.

On the next page (p. 3) Randolph states,

> "I don't understand how the number of hair follicles damaged by large area electron irradiation relates to the volume irradiated by a hot particle . . . One way to estimate the hazard of one micron hot particle would be to assume induction proportional to the volume irradiated."

It is clear that Randolph does not understand our (actually Geesaman's) hypothesis qualitatively, and therefore does not appreciate why the Albert experiments were used to quantify the hypothesis. We will attempt to rephrase the basic hypothesis avoiding the use of the term "critical architectural unit" which may be the source of some confusion.

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).

There is considerable experimental evidence to support the hypothesis and the corollary qualitatively. However, the only good biological data which quantifies a) the tumor risk per altered tissue structure, is the Albert data. The altered tissue structure

(or "critical architectural unit") in this case is the hair follicle, and the probability of the tumor production once this alteration has taken place is on the order of 1/2000. The same Albert data, and the experiments of Laskin (see discussion on pp. 32-33 of "Radiation Standards for Hot Particles") support the choice of 1000 rem/year to the local tissue as the quantitative value for b) the critical particle activity. The Richmond experiments (see our critique of WASH-1320, pp. 25-29) suggest equivocally that the critical activity may be somewhat higher for particles in the lung. These experiments point out one of the uncertainties in our quantification of the hypothesis.

Randolph's statement on page 3, "one way to estimate the hazard of a one micron hot particle would be to assume tumor induction proportional to the volume irradiated," is a hypothesis clearly distinct from our hypothesis. This "Randolph Hypothesis" is a simplified and probably not a new variation of several tumor production models based on cells at risk. One hypothesis, however, can not set aside another. This can only be done with experimental data and we find no data that are inconsistent with our hypothesis.

In his second major conclusion on page 1 under "A. Overall Views," Randolph questions the relevance of the Albert, et al., comments that no skin tumors were observed with protons, alpha particles, or low energy (0.3 MeV) electrons. These observations simply reflect the fact that these radiation sources did not penetrate the skin sufficiently to disrupt the hair follicle.

Also, on page 1, where Randolph uses the Scottish verdict "not proven," we would substitute "not set aside." This in turn

raises the question: What conservative radiation protection criteria should be adopted to protect the health of worker and the public? We would suggest that the prudent public health principle is to accept the hot particle hypothesis, rather than some less conservative hypothesis, and that our recommended standards provide a reasonable basis for protection.

Page 3, beginning:

2) (p. 25-26): These $^{32}P$ plaque experiments support our hypothesis qualitatively, namely, a high tumor risk is observed when a small volume of tissue is irradiated at a high dose.

3) (p. 27-28): The Lushbaugh observation lends strong support for the hypothesis qualitatively. While the statistics are obviously poor, this observation is consistent with the quantitative assignment of risk derived from the Albert data and suggests that the hot particle tumor risk that we assigned may even be low.

4) (p. 27-28): While Mr. Gleason's case is equivocal it is also consistent with the hypothesis qualitatively.

5) (p. 30): The work of Laskin, et al., supports the hypothesis qualitatively, and supports the quantitative choice of the minimum critical particle activity as that capable of delivering 1000 rem/year to the tissue at risk (see also p. 39 of our critique of WASH-1320 -- on line 10 of page 39 "10 rads" should read $10^6$ rads).

Page 4, beginning:

6) (p. 31-32): With respect to the beagle experiments by Bair, et al., we see no valid basis for assuming "a linear tumor to radioactivity incidence," below 100% incidence at about 0.3 uCi exposure. As we discuss in our hot particle report, the response

in Bair's experiments was saturated and it is impossible to draw any conclusions with respect to lower exposures.

7) (p. 34-37): No one knows the latent period for carcinogenic response to hot particles in human lungs. It could be 20 to 30 years. It is difficult, we submit, to document non-existent information. We did point out (on p. 37 of our hot particle report) however, that in the experiments reported by Park, et al., the beagle with the smallest lung burden (o.2 uCi) developed lung cancer after an 11 year latent period. The highest Rocky Flats worker exposure (9 years ago) is comparable to the lowest beagle exposure.

8) (p. 38-40): We support the suggestion that an attempt be made to reconstruct the Manhattan contamination experiments (sans human lungs) in order to obtain more information about these exposures.

C. Minor Technical Considerations --

1. We find no reference to the activity of a one micron $^{239}PuO_2$ (or $^{238}PuO_2$) particle on page 7. Pu-238 has the 89 year half-life. Langham ["The Problem of Large Area Plutonium Contamination," U. S. Department of HEW, Public Health Services, Seminar Paper No. 002, Dec. 6, 1968, p. 7] lists the activity of $^{238}PuO_2$ and $^{239}PuO_2$ particles as a function of particle diameter. The activity of a one micron $^{238}PuO_2$ particle is given as $8.0 \times 10^{-2}$ nCi. It is not clear whether these values are measured, or calculated. In either event, assuming Langham's value, and 17.47 curies/gm for Pu-238, the density of Pu-238 in a 1 $\mu$ particle of $^{238}PuO_2$ would be slightly less than 10 gm/cm$^3$.

2. AEC and EPA regulations do include and delineate standards

for both workers and the population. Whether they do so clearly is arguable.

3. DF is defined in "Basic Radiation Protection Criteria," NCRP Report No. 39, p. 84.

4. P. 16. We stand corrected. Assuming some particles in the lung are lodged in areas where they see essentially solid tissue out to 45 μ in any direction, we could have used the soft tissue dose rate value instead of a lung model and obtained $(73 \times 10^4) / (3 \times 10^{-4}) = 2 \times 10^9$, or more than 9 orders of magnitude.

5. The correct number is 57,000. The 53,000 was obtained (with one too many significant digits) from $(16 \times 10^{-9}) / (3 \times 10^{-13})$.

6. P. 24-26. As we noted on p. 5 above, one hypothesis can not be used to set aside another, and we find no data that conflicts with ours.

7. The epithelial cell repair time was used in determining the minimum hot particle activity. This is another of the quantitative uncertainties. The discussion on pp. 25-29 of our critique of WASH-1320 is pertinent to this issue.

8. P. 33. Both the Lushbaugh observation and the Richmond experiments involved dose rates from particles considerably higher than 5000 rem/year. The point is the hot particle can cause severe but highly localized tissue disruption. It is this disrupted tissue mass that we suggest carries a high tumor risk. Above a certain value the total dosage is irrelevant.

9. No comment required.

10. Particle retention and movement is discussed on pp. 9-12 of WASH-1320. On p. 20 of our critique of WASH-1320 we note that

while plutonium particles in the lower respiratory region are not static, auto-radiographic evidence demonstrates that such particles are immobilized in scar tissue and possibly in Type I alveolar epithelial cells. The long residence time of plutonium particles in the lung suggests that such immobilization must occur.

D. Appendix. Tentative Estimate of Maximum Permissible Lung Burden --

Here, Randolph makes a first cut at quantifying a hypothesis based on tumor risk as a function of dose averaged over the entire lung. Referring again back to page 5, one hypothesis can not be used to set aside another hypothesis. We see no data that contradicts our hypothesis. It is interesting to note, however, the quantitative results of Randolph's hypothesis are extremely sensitive to differences in specific activity ($^{238}Pu$ vs. $^{239}Pu$). In this regard, had Randolph (at the top of p. 6) noted that a one micron $^{238}PuO_2$ particle gives a dose of $7 \times 10^{-3}$ rad/year (instead of $2.7 \times 10^{-5}$ for $^{239}PuO_2$), he would have obtained 2.5 particles versus our 2 particles, instead of 600.

Comments by Louis Hempelmann

Most of the points raised by Hempelmann are discussed in "The Hot Particle Issue," our critique of WASH-1320.

We had no intention of being misleading, nor do we feel that we were so in the three instances cited by Hempelmann.

1. Our report, "Radiation Standards for Hot Particles," was issued on February 14, 1974. We had no way of knowing that in

November, Bair would author the WASH-1320 report. Moreover, our critique of WASH-1320 indicated that the conclusions reached in WASH-1320 are not justified so far as hot particles are concerned.

2. We stated in our hot particle report that the Gleason case was not clear cut. In Appendix B of that report we included the basis for the conclusion that the strong possibility that Gleason's cancer was caused by plutonium. We see no sound reason for concluding that several days after the incident, Mr. Gleason would surely remember having had a sliver puncture in his hand. This would not have had to be a gaping wound as Hempelmann seems to imply.

3. The discussion of the lesion excised by Lushbaugh and Langham indicates that the plutonium particle produced a lesion that was highly suggestive of an incipient carcinogenic response to a single plutonium particle imbedded in soft tissue.

Concerning the assumptions that Hempelmann can not agree with or understand:

1. and 2. The purpose of our report was to develop radiation protection standards for hot particles. To do this it is essential to develop quantitative risk estimates. This work of Albert supplied the only available data on the risk of tumor development as a function of a disordered tissue mass. Rather than make a completely arbitrary assumption concerning the risk per particle we chose the value derived from this biological observation. We pointed out in our critique of WASH-1320 (see pp. 10 and 25-29) that these quantitative values are uncertain. At the same time, it is impossible to set standards without quantitative values.

So far as the architectural structure goes, the lesion of Lushbaugh and Langham and the lesions observed around microspheres

in the lungs of rats and hamsters (see our critique of WASH-1320, pp. 10 and 25-29) suggest that particles placed at random in tissue are capable of inducing a lesion with neoplastic changes similar to precancerous cytological changes.

3. We feel that our discussion of the Rocky Flats workers is valid. It is possible that, if the sample size were as large as the number of exposed uranium miners, some cancers would have appeared already.

4. As we indicated in our hot particle report, the nature of the contaminating events at Los Alamos were described in an article by Hempelmann. The particles (droplets) were aspirated from solutions. As a consequence for the range of concentrations given by Hempelmann the particle size would have had to exceed 5 μ in diameter for the most concentrated solution in order to constitute hot particles. The so-called sophisticated calculations of Anderson relate to particles above 0.6 μ in diameter or a factor of 10 smaller. The reconstruction of these contaminating events, the measurements of the particle size and activity, and the behavior of the inhaled fraction in animals would be a worthwhile experiment.

We have discussed this "good experimental evidence" in our critique of WASH-1320 and have shown this evidence to be either irrelevant to the hot particle hypothesis or supportive of it on the following pages of our critique:

1. Pages 23-25. This experiment was similar to those of Albert wherein the beads corresponded to his sieve patterns.

2. Pages 29-30. These did not involve hot particles.

3. Pages 10 and 25-29. These experiments are supportive.

4. Pages 30-31. Specifically the $BaSO_4$ did not involve hot particles and induced few tumors. The Sr-90 beads (one per animal) induced 7 malignancies in 23 rats. While the dose from the beads (0.3 mm in diameter, 244 nCi) was from a localized source, it irradiated the entire lung. Nevertheless, if one chooses to call these hot particles, the cancer risk was about 1/3 instead of 1/2000 per particle as we propose.

Comments by Andrew M. Rauth

Page 1, ¶ 2: This discussion presents an inadequate synopsis of our report. The discussion under "B. Modifying Factors" (beginning p. 13) in "Radiation Standards for Hot Particles," was meant to serve as background information, namely, a review of basic definitions of radiation dose and factors used to calculate dose. In subsequent sections of the report we estimate a risk per hot particle and the critical particle activity (p. 32). We then recommended radiation standards in terms of hot particle lung burdens which were comparable in risk to the uniform whole body exposure. It is not necessary to go back and calculate what this implies in terms of the Distribution Factor (DF). Calculating the DF is simply an interesting academic exercise. Note that the factor of 115,000 assumes the lung burden consists of hot particles of minimum activity. The DF would be smaller for hot particles with higher activities. Clearly, the concept of DF is not particularly useful if the risk is defined on a per particle, rather than a per microcurie (or per unit dose) basis.

It is inappropriate to say the "DF is based primarily on the two experimental pieces of information, the work of Albert and

coworkers cited on pages 22-24 on electron irradiation of rat skin and the work of Bair on $Pu^{239}O_2$." The basic qualitative support for the hot particle hypothesis derives from a number of experiments wherein small volumes of tissue have been exposed to high doses and where cancer was the almost inevitable result. The experiments by Albert and Bair (and their coworkers) are but two of many such experiments. On the other hand, the quantitative parameters in our hypothesis (as summarized on p. 5 of our critique of WASH-1320) are derived from the Albert experiments but not those by Bair. The quantitative parameters we assigned are supported by other experimental observations, e.g., Laskin, et al., (Reference 56 in our report), Lushbaugh's observation (pp. 27-28 in our report), and the experiments of Richmond, et al., (pp. 25-29 in our critique of WASH-1320).

¶ 3: It is stated that:

> "The authors [Tamplin and Cochran] make no comments on the Albert data on the facts that
>
> 1) This is a microscopic tissue irradiation (24 $cm^2$) in a single acute dose.
>
> 2) Not only does the tumor incidence go up at 1000 rads, but it also goes down at doses above 2000 rads."

First, it is important to recognize that out of necessity most radiation standards are based on results from acute, as opposed to chronic, exposures. Concerning the second point, at doses above 2000 rads, one is undoubtedly witnessing one or more competing mechanisms. As one moves to higher doses the entire tissue becomes ulcerated and subsequently killed. In the Albert data the ratio of tumor production to atrophied hair follicles persisted to the point where the entire tissue was ablated and there were no hair follicles. It is important to recognize that a single hot particle

can produce this local tissue disruption without being tissue fatal.

The remainder of this paragraph through the first full paragraph on page 2 contains observations with which we agree. We do not share, however, Rauth's conclusions, drawn from what he admits are "superficial considerations."

Comments by Arthur Cole

Concerning Cole's specific points:

> "P. 26. The 'critical architectural unit' is an attractive and simplified hypothesis. However, little evidence is available to support it."

We would suggest there is ample evidence to support this hypothesis qualitatively, although there is much less experimental data from which the hypothesis can be quantified. As demonstrated in our critique of WASH-1320, most of what has been offered as conflicting evidence is not relevant to the hot particle issue. The relevant data support the hypothesis.

> "P. 27-28. The Lushbaugh study of one observed lesion in 1000 puncture wounds provides no statistical basis for estimating a tumor induction probability."

Our hot particle risk estimate was derived from the Albert data. The Lushbaugh observation is consistent with this risk estimate of one tumor per 2000 hot particles. This causal observation by Lushbaugh would suggest that if a comprehensive search had been undertaken other lesions may have been found. While the observed lesion had not progressed into a tumor, the concern that it might was sufficient to have it excised.

> "P. 41. Section VII . . ."

Cole offers two alternative models for estimating the hot particle risk, the first based on Albert's data and the second based on Bair's data. As we have stated previously one hypothesis can not be used to set aside another. This can only be done with experimental data.

It is perhaps worth noting that Cole's first model is similar to the concept of prescribing a significant volume or significant area following NCRP criteria [NCRP Report No. 39, Criteria 206 and 207], as discussed in our critique of WASH-1320 (p. 6).

With respect to the second model Bair's data are not useful for quantifying the hot particle tumor risk, other than establishing a lower limit on the risk per hot particle in the range of $10^{-6}$ to $10^{-7}$. Cole assumed "a reasonable large probability (approaching unity) would still occur for only $10^6$ hot particles per dog . . .". Cole could have assumed $10^5$, $10^4$ . . and calculated a higher risk. We share Cole's opinion that on the basis of Bair's data alone, the permissible exposure levels should be lowered.

Concerning Cole's final comments, while more experimental work is needed, we submit that our more restrictive standards should be quickly promulgated because it is irresponsible to leave the health of the public and workers in jeopardy while awaiting more definitive data.

Comments by Doris J. Dugas

We are in essential agreement with most of Dugas' comments here. However, they exemplify an approach to this problem that we find quite frustrating, as we discussed in our summary remarks. Standards are required to protect workers and the public from

plutonium exposure. To adopt standards, a quantitative estimate of the risk is required. In the absence of complete data, this risk assessment must be made on the basis of available data.

The only biological observations that we were able to find that allowed an estimate of the risk of cancer given a disrupted tissue mass was the rat skin data. Granted this is uncertain, what is a better value? If the use of plutonium were to be banned pending more definitive data, the public and workers would be protected. But this is apparently not the case. So we selected this approach to quantification because it was an observed biological relationship. As we stated in the summary comments, it would be worthwhile for the committee to propose their approach to this dilemma.

With respect to Dugas' comments on Section V-A, p. 22, the above comments would apply. Moreover, the lesion excised by Lushbaugh and Langham and the lesions and cellular changes observed around microspheres in the lungs of rats suggest that any tissue mass may be the equivalent of a critical volume when hot particles are involved. (See our critique of WASH-1320, pp. 9-10 and 25-29).

The above is also relevant to Dugas' comments on V-B, p. 26 and V-C, p. 29.

As Dugas indicates, VI, p. 32, the epithelial repair time is used to determine the hot particle minimum activity. This is one of the quantitative uncertainties. Our discussion on pages 25-29 of the WASH-1320 critique are pertinent to this issue. If the epithelial turnover time is shorter, the particle activity should be higher.

With respect to Dugas' comments on VI-A, p. 42, the lung seems to be the organ at risk, not the lymph nodes. Although the lymph nodes

accumulate particles and receive a much higher dose, no cancers have been observed in these sites.

Comments by Richard P. Spencer

The latent period for the carcinogenic response to hot particle exposures in the Rocky Flats incident may be 15 to 30 years. As we have commented elsewhere, the need to establish adequate radiation protection standards cannot await the results of this "experiment," otherwise we leave the health of the public and workers in jeopardy.