

# **The Cancer Hazard from Inhaled Plutonium**

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## Foreword

The calculations presented here, and in the other reports of this CNR series, represent a first approximation of the biological hazards from plutonium exposure.

In essence, these are studies of the dosimetry of plutonium exposure. There are certain critical voids in mankind's knowledge of the physical and physiological parameters which determine the dosimetry, and thus we have made necessary assumptions which are all clearly identified.

It is anticipated that as additional data become available, the calculations herein will be updated to take them into account.

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## Summary of Conclusions

- (1) The lung cancer potential in humans from inhaled insoluble compounds of plutonium (such as  $\text{PuO}_2$  particles) has been grossly underestimated by such authoritative bodies as the International Commission on Radiological Protection and the British Medical Research Council.
  
- (2) The term "lung cancer dose", used freely in this report, has a specific scientific definition, namely, the reciprocal of the lifetime lung cancer risk per unit of radiation, whatever be the units under discussion. In more popular terms, one "lung cancer dose" of a carcinogen such as plutonium introduced into a population will assure one extra lung cancer death.
  
- (3) The lung cancer hazard of plutonium inhalation is much higher for cigarette-smoking humans than for non-smokers. The calculations presented here suggest the following values for inhalation of insoluble plutonium particulates.

### For Cigarette-Smokers:

$\text{Pu}^{239}$

- (a) 0.058 micrograms deposited  $\text{Pu}^{239}$  represents one "lung cancer dose".
- (b) 7,830,000,000 "lung cancer doses" per pound of  $\text{Pu}^{239}$ .

Reactor-Pu

- (a) 0.011 micrograms deposited reactor-Pu represents one "lung cancer dose"
- (b) 42,300,000,000 "lung cancer doses" per pound of reactor-Pu.

### For Non-Smokers:

$\text{Pu}^{239}$

- (a) 7.3 micrograms deposited  $\text{Pu}^{239}$  represents one "lung cancer dose".
- (b) 62,600,000 "lung cancer doses" per pound  $\text{Pu}^{239}$ .

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Reactor-Pu

- (a) 1.4 micrograms deposited reactor-Pu represents one "lung cancer dose".
- (b) 338,000,000 "lung cancer doses" per pound of reactor-Pu.

(4) While the estimated hazard is about 127 times lower for non-smokers than for smokers, the hazard for non-smokers for reactor-Pu, which is what nuclear energy provides, is indeed severe. Clearly, there would be no source of comfort available even if no one in the population smoked cigarettes.

(5) The reason for the gross underestimate by ICRP or BMRC is their use of a totally unrealistic, "idealized" model for the clearance of deposited plutonium from the lungs and bronchi, plus their non-recognition of the bronchi as the true site for most human lung cancers. The erroneous model used by such organizations fails totally to take into account the effect of cigarette-smoking upon the physiological function of human lungs.

(6) Plutonium nuclides, or other alpha particle-emitting nuclides, in an insoluble form, represent an inhalation hazard in a class some five orders of magnitude more potent, weight for weight, than the potent chemical carcinogens.

(7) The beagle dog data on lung cancer production from inhaled plutonium already are in good general accord with the human estimates of this report, even though it is widely realized that the current beagle data must be overestimating the lung cancer dose. When the beagle data become available at lower dosages, it is virtually certain that they will not be significantly different from the human estimates.

(8) None of the calculations presented in this report make any use of "hot particle" theories and are in no way dependent upon such theories. Unfortunately, so much effort has been expended, for example, by the British Medical Research Council, in countering "hot particle" theories that they overlooked the real cancer hazard derivable from straightforward dosimetry, as presented here. It turns out that dosimetry provides cancer risk estimates well within order of magnitude agreement with those predicted by Geesaman-Tamplin-Cochran.

(9) The lung cancer potential of insoluble particles of plutonium compounds should result in worldwide rejection of nuclear fission energy involving any kind of plutonium handling or recycling. No meaningful mitigation of this problem would be achieved even if cigarette smoking stopped totally.



## THE CANCER HAZARD FROM INHALED PLUTONIUM

John W. Gofman\*

### Introduction

At this critical juncture for societal choices of energy supply for the future, one possible choice is a nuclear fission economy based upon the element plutonium (element 94). Tamplin and Cochran <sup>(1)</sup> have pointed out that the U.S. AEC projected that over 4 million megawatts of nuclear capacity will be installed between 1970 and 2020. Based upon this estimate, Tamplin and Cochran pointed out that over the lifetime of these plants this installed capacity could result in a cumulative flow of approximately 200 million kilograms (440 million pounds) of plutonium through the nuclear fuel cycle. Putting this much plutonium "through the nuclear fuel cycle" means plutonium becomes a commonplace article of commerce, being handled by thousands of workers and being transported on highways, railways, and airways in numerous shipments per day.

Plutonium is widely recognized as a potent carcinogen, and is of particular concern in the form of insoluble particles of plutonium dioxide ( $\text{PuO}_2$ ) as a very potent agent for the production of lung cancer in man. Estimates have been made by several individuals and groups of the number of human lung cancers to be expected for the inhalation of specified quantities of  $\text{PuO}_2$  particles. Such estimates range over several orders of magnitude, with Cohen <sup>(2)</sup> providing the lowest estimate, Tamplin-Cochran <sup>(1)</sup> providing the highest estimate, and the British Medical Research Council <sup>(3)</sup> providing evidence suggesting an intermediate value. Unfortunately, the problem has been clouded by needless polemic discussion of whether or not the "hot particle" hypothesis (Geesaman) <sup>(4)</sup>

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is correct. The issue of  $\text{PuO}_2$  particle carcinogenicity can be approached in a straightforward manner with no reference whatever to "hot particle" theories.

It is our purpose here to present such a straightforward analysis leading to some reasonable limits for the expected numbers of human lung cancers for the inhalation of plutonium particulates. There are certain crucial voids in our knowledge of the behavior and disposition of  $\text{PuO}_2$ , once deposited in the lung. As a result, the estimate of the number of cancers becomes dependent upon the assumptions used where evidence is lacking. Cohen, in his analysis, simply overlooked the important problems of behavior of the  $\text{PuO}_2$  in the lung. The British Medical Research Council paid lip service to certain of the problems, but then neglected to indicate how failure to address the problems might provide a falsely low estimate of lung cancer hazard from plutonium inhalation.

#### Detailed Analysis of Lung Cancer Induction by Plutonium

The analysis of the lung cancer-producing properties of inhaled plutonium particulates (usually, but by no means necessarily, insoluble particles of  $\text{PuO}_2$ ) proceeds by several steps.

Step 1: Analysis based upon the known carcinogenicity of x-rays, gamma rays, and neutrons for human lung tissue, followed by analysis of the dose to be delivered to lung tissue by inhaled particulates of plutonium, assuming the plutonium delivers its radiation to the entire mass of broncho-pulmonary tissue. Since the nuclear power industry will provide mixtures of plutonium nuclides, rather than the predominant nuclide,  $\text{Pu}^{239}$ , the analysis will consider effects of  $\text{Pu}^{239}$  and effects of Pu mixtures from nuclear power reactors, to be designated simply as "reactor-Pu".

Step 2: Analysis of the nature of the problem of non-uniform distribution of plutonium within the lung and the crucial problem of which cells in the broncho-pulmonary system are involved in human lung cancer production.

Step 3: Final estimates of the probable limits to be placed upon the lung cancer expectations per pound of plutonium deposited in lung tissue of human populations.

Step 1. Analysis based upon the known carcinogenicity of x-rays, gamma rays and neutrons for human lung tissue.

There has been, for several years, conclusive evidence that human population groups exposed to x-rays, or to combinations of x-rays, gamma rays, and neutrons have developed an excess of lung cancers that must be attributed to radiation exposure. Gofman and Tamplin<sup>(5-23)</sup> have presented comprehensive analysis of the quantitative aspects of such lung cancer production. More recently the BEIR Committee presented its analysis of the same evidence.<sup>(24)</sup> We shall discuss the differences (minor, at best) in the conclusions to be derived from both analyses. There is abundant additional proof that broncho-pulmonary irradiation produces lung cancer in man from the tragic experience of uranium (and other) miners exposed to radon gas and daughter products of radon. However, we shall refrain from using these latter data for quantitative purposes because virtually everyone realizes that dose estimation in rads or rems is exceedingly tenuous at best for the miners.

The analysis of Gofman-Tamplin led to the conclusion that, for diffuse lung irradiation, 1 rem means 2% increase over the spontaneous lung cancer death rate each year in an exposed population, once the latent period of some 10-15 years is passed.<sup>(25)</sup> Precisely how long this 2% per year increase (in lung cancer death rate) persists is not known from direct evidence. A modestly conservative estimate (agreed to by many observers) is a persistence of 30 years, but persistence for the remainder of the life span of the exposed population cannot be ruled out. The BEIR Committee recognized this uncertainty in its report. The value of 2% increase over spontaneous lung cancer death rate, according to Gofman-Tamplin, applies for young adults of the 20-30 year age range.

Some workers have analyzed lung (and other cancer) production by radiation in terms of the absolute number of cancers produced per rem exposure of a population, with no reference to a percent increase over the spontaneous occurrence rate. Cohen has chosen this approach, with the strange statement that:

"It may be noted that our calculations employed the "absolute risk" model of Reference 5 (the BEIR report) rather than the "relative risk" model. Primarily this is because the age-dependent risk of each type of cancer is not readily available, and the calculations are more complex. In ref. 5, the relative risk model gives a two times larger effect. However, the available evidence tends to support the absolute risk model and it seems to be preferred by most experts in the field, so its use is justified by our aim to determine the most probable effects."

The available evidence, in the opinion of the present author, is very much in favor of the opposite conclusion - namely, that the relative risk method has very sound foundation indeed. A variety of pertinent sources of evidence points strongly to radiation action as a multiplier of other carcinogenic influences (e.g., radiation multiplies the effect of cigarette smoking in the uranium miners). If radiation acts as a multiplier, then the best approach is the relative risk method, with a specified percent increase over the spontaneous cancer fatality rate per rem of exposure. The BEIR Committee was unable to choose between the two approaches, commenting as follows: (p.99, BEIR Report)

"Absolute risk estimates are generally more useful for purposes of radiation protection than are relative risk estimates, because they specify directly the number of persons affected. On the other hand, if the risk due to radiation were found to increase in proportion to the natural risk, then the relative risk would provide the more appropriate estimate. Since the existing knowledge of radiation carcinogenesis is not always sufficient to indicate which type of estimate applies best in a given situation, both the absolute risk (where possible) and the relative risk are given in this report."

Since the present author considers the scientific evidence overwhelmingly in favor of the relative risk method, that method (including BEIR's relative risk estimates)

will be used in all calculations here. It is a very simple matter, as will be noted, to convert the relative risk estimates, scientifically sound, into absolute numbers of lung cancer fatalities. Moreover, in periods of rapidly changing lung cancer death rates (such as the 1940-1975 period in the USA), the relative risk method can avoid serious errors of under-estimation. The absolute risk method, using data for populations exposed in or before 1945, may be truly irrelevant in making estimates for the real world of 1975.

The most recent datum from the American Cancer Society provides the estimated value, 63,500 lung cancer deaths per year (1975) for men in the USA. <sup>(26)</sup> Virtually all these lung cancer deaths are in men over 25 years of age, so they may be taken to occur in a population of approximately 50 million men (those over 25 years of age).

The spontaneous (or as BEIR calls it, the "natural") lung cancer death rate, therefore, is

$\frac{63500}{5 \times 10^7}$ , or  $1.27 \times 10^{-3}$ /year. Expressed otherwise, this means 1.27 fatal lung cancers per 1000 persons per year, spontaneously occurring in men over 25 years of age.

If we now utilize the Gofman-Tamplin figure above of a 2% increase over the spontaneous rate per rem of exposure, we arrive, per rem, at the following:

$(0.02) (1.27 \times 10^{-3})$ , or  $2.54 \times 10^{-5}$ /year as the expected increase in lung cancer fatalities per year per rem of exposure. Henceforth in this discussion, we shall refer to estimates arrived at in this manner as "Gofman-Tamplin" estimates.

The BEIR Committee arrived at a somewhat lower percentage increase per rem of exposure. However, BEIR realized that the exposed subjects had not been followed long enough to be sure they were on the "plateau" of observed effects. We may quote BEIR Report (p. 156) as follows:

"It is possible, therefore, that in the final analysis the absolute risk in these groups will approach  $2/10^6$ /year/rem and the relative risk will reach 0.5% or higher. For the three groups (miners and Japanese

survivors) in which up-to-date information is available, it is significant that many new cases have been added during the past few years."

This is a powerful admission by the BEIR Committee. They are admitting that their estimate is only four-fold lower than Gofman-Tamplin and admitting that when all the evidence is in, they may be even closer to Gofman-Tamplin estimates.

Let us not anticipate the future, and simply proceed utilizing the BEIR figure of 0.5% increase in relative risk per year per rem, realizing that it is not a most conservative public health estimate. \*

Since 0.5% is 1/4 of 2%, we would say that BEIR should conclude that the risk of fatal lung cancer, for USA subjects in 1975, is

$$1/4 \times 2.54 \times 10^{-5} / \text{year/rem}, \text{ or } 6.3 \times 10^{-6} / \text{year/rem}.$$

Henceforth in this discussion, we shall refer to estimates based upon this number as "BEIR" estimates.

Cohen, in his analysis, quotes BEIR as giving "The cancer risk of radiation to the lung as  $1.3 \times 10^{-6} / \text{year-rem}$  for adults". This low figure, based upon absolute data from 1945, may be truly irrelevant for exposure of populations today.

Henceforth in this discussion, we shall refer to Cohen's analysis based upon the  $1.3 \times 10^{-6}$  lung cancer deaths/year-rem as the "Cohen" estimate.

It was stated above that most observers (including BEIR Committee) consider the "plateau" effect may persist for 30 years, or even longer. And while not truly conservative (in the absence of positive knowledge), we shall, for present purposes, utilize the potential underestimate of 30 years on the "plateau".

This leads to the following total lung cancer production per rem as follows:

"Gofman-Tamplin"  $30 \times 2.54 \times 10^{-5} = 7.62 \times 10^{-4}$  lung cancer deaths per lifetime-man-rem.

"BEIR"  $30 \times 6.3 \times 10^{-6} = 1.89 \times 10^{-4}$  lung cancer deaths per lifetime-man-rem.

"Cohen"  $30 \times 1.3 \times 10^{-6} = 3.9 \times 10^{-5}$  lung cancer deaths per lifetime-man-rem.

\*See Note 1 in "Supplemental Notes".

The Concept of the "Lung Cancer Dose"

It has become commonplace recently to alter such presentations of risk into another format, namely, that which describes "the lung cancer dose". This is a simple and useful way to present the estimates. If the lifetime risk is x per man-rem, then the "lung cancer dose" is (1/x) man-rems.

Thus, for illustration, if the lifetime risk is 1 out of 10, which means 0.1 per man-rem, then the "lung cancer dose" is 1/0.1, or 10 man-rem.

Applying this relationship to the estimates above, we derive the following:

"Lung Cancer Dose", in man-rem

"Gofman-Tamplin"	$\frac{1}{7.62 \times 10^{-4}}$ , or 1310 man-rem.
"BEIR"	$\frac{1}{1.89 \times 10^{-4}}$ , or 5290 man-rem.
"Cohen"	$\frac{1}{3.9 \times 10^{-5}}$ , or 25,600 man-rem.

Calculation (Step 1 level) of "Lung Cancer Dose" for Insoluble Inhaled Plutonium Particles

The Cohen approach (which we shall here term Step 1 level calculations) is to calculate plutonium dosage as though the dose were distributed throughout the entire mass of lung tissue. While it will be shown below (Step 2 calculation) why this is not reasonable, it will suffice for Step 1 calculations. Cohen has used the reasonable value of 570 grams as the lung mass for average man (exclusive of blood). Further, Cohen has applied a factor of 10 for conversion of rad to rem for the alpha-particle radiation of plutonium. The British Medical Research Council Report suggests (p.10) a value of 10-20 for this conversion. Again, even though possibly not conservative enough, we shall use the Cohen value of 10 for conversion of rads to rems.

To convert microcuries of plutonium deposited to dose in rems, Cohen has used the equation:

$$\text{Dose in rems/day} = 51 \text{ EQ/M rems/day-microcurie}$$

where E = energy deposited by alpha radiation in MEV

M = mass of organ in grams

Q = quality factor (the ratio of rems to rads, or the ratio of carcinogenic damage of the Pu alpha particles to that of gamma rays of the same energy).

(E for Pu<sup>239</sup> = 5.1 MEV; Q = 10; M = 570 grams)

We shall accept all this for Step 1 calculation purposes, except to re-iterate that using M = 570 grams assumes distribution of the dose to the whole lung tissue mass. In Step 2 calculations below, this crucial issue will be treated in detail.

Using the equation above, Cohen arrives at 2000 rems (for that portion of the plutonium presumed to be retained in the lung with a 500 day half-time for removal) per microcurie of deposited plutonium (Pu<sup>239</sup>). We shall return later to this "500 day half-time for removal", but for Step 1 calculation, the 2000 rems per microcurie will be accepted. Incidentally, since the other Pu nuclides in "reactor-Pu" will have E values not very different from the 5.1 MEV for Pu<sup>239</sup>, the same calculation will apply per microcurie of other Pu nuclides.

Since we have, above, assigned for the "Cohen" estimate, a value of 25,600 man-rem as the "lung cancer dose", it follows that 1 microcurie of Pu<sup>239</sup> delivers  $\frac{2000}{25600}$ , or 0.08 "lung cancer doses".

Expressed otherwise, 1/0.08, or 12.5 microcuries Pu<sup>239</sup> (For "Cohen" estimates) deposited provide one "lung cancer dose".

In Cohen's paper, he used a risk of "about 4.7 percent" per microcurie instead 8% per microcurie by including the risk for children (erroneously, we believe) and the

risk for adults well beyond 30 years of age. Since we are comparing all estimates for adults 20-30 years of age, we have made the minor adjustment in Cohen's estimate back to 8% per microcurie (as per his Figure 2).

Cohen stated, additionally, that of all the plutonium particulates inhaled, only 25% is retained for potential deposition, and he therefore multiplies his "lung cancer dose" by a factor of 4. Since all these discussions relate to deposited plutonium, rather than inhaled plutonium, it is inappropriate to utilize this particular factor of 4. Thus, we shall leave the "Cohen" estimate at 12.5 microcuries deposited Pu<sup>239</sup> per "lung cancer dose" or per "lung cancer death".

There are 16.3 micrograms of Pu<sup>239</sup> required to provide 1 microcurie of Pu<sup>239</sup> alpha radiation. (This is directly calculable from the 24,000 year half-life of Pu<sup>239</sup>).

Therefore, the "Cohen" estimate becomes

$(12.5)(16.3)$ , or 204 micrograms of Pu<sup>239</sup> deposited per "lung cancer dose".

For "BEIR" estimate, with 5290 man-rem per "lung cancer dose", we calculate

$\frac{5290}{2000}$ , or 2.65 microcuries Pu<sup>239</sup> per "lung cancer dose".

Converting to micrograms,  $2.65 \times 16.3 =$  43.2 micrograms Pu<sup>239</sup> deposited per "lung cancer dose".

For "Gofman-Tamplin" estimate, with 1310 man-rem per "lung cancer dose", we calculate  $\frac{1310}{2000}$ , or 0.66 microcuries Pu<sup>239</sup> deposited per "lung cancer dose".

Converting to micrograms,  $(0.66 \times 16.3) =$  10.8 micrograms Pu<sup>239</sup> deposited per "lung cancer dose".

All these data are summarized in Table 1.

Table 1

Step 1 Calculation

(assuming distribution of plutonium-239 throughout entire lung mass)

<u>Estimate</u>	<u>Man-Rem per "Lung Cancer Dose"</u>	<u>Micrograms Pu<sup>239</sup> deposited per "Lung Cancer Dose"</u>
"Gofman-Tamplin"	1,310	10.8
"BEIR"	5,290	43.2
"Cohen"	25,600	204

Cohen has pointed out, correctly, that the mixture of plutonium nuclides from power reactors contains, in addition to Pu<sup>239</sup>, several shorter-lived nuclides. Therefore, he states, correctly, that reactor-grade Pu is some 5.4 times as hazardous by weight as pure Pu<sup>239</sup> (as high as 10 times in high burn-up light water-reactor fuel). Taking this 5.4-fold hazard factor into account, we arrive at the estimates in Table 2.

Table 2

Step 1 Calculation

(assuming "reactor-Pu" distributed throughout entire lung mass)

<u>Estimate</u>	<u>Micrograms Reactor Grade Pu per "Lung Cancer Dose"</u>
"Gofman-Tamplin"	2.0
"BEIR"	8.0
"Cohen"	37.8

We are now in a position to make a Step 1 estimate of the "lung cancer doses" per pound of Pu<sup>239</sup> or per pound of reactor-grade Pu. The reader may well ask "Why calculate per pound of plutonium?" The answer is simply this. For considerations of the hazard posed by a plutonium-based nuclear fission energy economy, we know the number of pounds expected to be in daily commerce, and thus it is well to know the number of "lung cancer doses" involved in such an economy. \*

\*See Note 2 in "Supplemental Notes"

The calculation itself simply involves the number of micrograms per pound and the number of micrograms per "lung cancer dose".

$$1 \text{ pound} = 454 \text{ grams}$$

$$\text{or, } 1 \text{ pound} = 4.54 \times 10^2 \times 10^6 = 4.54 \times 10^8 \text{ micrograms.}$$

Illustratively, we may calculate the number of "lung cancer doses" per pound of Pu<sup>239</sup> in the form of insoluble PuO<sub>2</sub> particles or other finely dispersed insoluble Pu compounds.

From Table 1, for "Gofman-Tamplin" estimates, we have 10.8 micrograms Pu<sup>239</sup> deposited per "lung cancer dose".

Therefore, "Lung Cancer Doses" per pound of Pu<sup>239</sup> =  $\frac{4.54 \times 10^8}{10.8}$ , or 42,000,000 "lung cancer doses".

Similar calculations, for all three estimates, both for Pu<sup>239</sup> and "reactor-Pu" are presented in Table 3.

Table 3

Step 1 Calculation

"Lung Cancer Doses" per pound of Plutonium

<u>Estimate</u>	<u>"Lung Cancer Doses" per pound Pu<sup>239</sup></u>	<u>"Lung Cancer Doses" per pound Reactor-Pu</u>
"Gofman-Tamplin"	42,000,000	227,000,000
"BEIR"	10,500,000	56,800,000
"Cohen"	2,225,000	12,000,000

It must be re-iterated here that all calculations of Step 1 type assume that the plutonium is distributed throughout the entire lung tissue mass. It does not assume uniformity of dose, but rather that the entire lung mass is the distribution region for the plutonium. As will be shown in Step 2 below, this may mean that the estimates of Table 3

represent minimum, rather than probable, estimates of the "lung cancer doses" per pound of plutonium.

Step 2: Analysis of the Nature of the Problem of Non-Uniform Distribution of Plutonium Within the Lung and the Crucial Problem of Which Cells in the Broncho-pulmonary System are Involved in Human Lung Cancer Production.

When a population is irradiated by x-rays, gamma-rays, or neutrons, and a dose is properly estimated for lung, we can expect, correctly, that the dose in rems to all segments of the lung-bronchus system is, to a good first approximation, everywhere identical. Under these circumstances it is reasonable to state that 570 grams of lung tissue have been irradiated. Even if some of the tissue (e.g. cartilage, smooth muscle, fibro-elastic support tissue) is not at all involved in cancer production, the dose estimate to the critical tissue susceptible to cancer production is still correct.

For inhaled particulate matter, estimation of the radiation dose as though the particles are distributed into 570 grams of lung tissue can be totally absurd. For example, it is extremely unlikely that any significant part of the inhaled particulates lodges in such tissues as bronchial cartilage, bronchial smooth muscle, walls of pulmonary arterio-venous network, or in fibro-elastic tissue. Therefore, the deposited particulates are distributed into some mass of tissue (including the critical cells for development of lung cancer) much less than 570 grams in mass. How much less? A reasonable first approximation, eliminating cartilage, fibro-elastic support tissue, arterial and venous walls, smooth muscles, and nerves, is that the relevant mass of tissue for distribution of the inhaled plutonium particulates cannot be more than 1/2 of 570 grams. Though this is just a beginning of Step 2 considerations, it immediately permits revision of Table 3 estimates upward by a factor of two. The revised results are presented in Table 4.

Table 4

(Preliminary Step 2 Calculation, based upon 0.5x570, or 285 grams as the Lung Tissue Mass)

"Lung Cancer Doses" per pound of Plutonium

<u>Estimate</u>	<u>"Lung Cancer Doses" per pound Pu<sup>239</sup></u>	<u>"Lung Cancer Doses" per pound Reactor-Pu</u>
"Gofman-Tamplin"	84,000,000	454,000,000
"BEIR"	21,000,000	113,600,000
"Cohen"	4,450,000	24,000,000

The Relevant Tissue for Lung Cancer Production

It is well known that the large preponderance of "lung" cancers arise in the bronchi rather than in the parenchymal lung tissue. Indeed it is this preponderance that accounts for lung cancer generally being referred to as bronchiogenic cancer. The BEIR report recognizes this, as does the British Medical Research Council Report. McCallum (27) states that such cancers are rare in the trachea or the two main-stem bronchi. The cancers are also relatively rare in the bronchioles. So the crucial tissue at risk must be the segmental bronchi, and, within these, the epithelial layer of the bronchi. What is really required is an estimate of the dose delivered by insoluble plutonium particles to this critical tissue, where almost all of the bronchiogenic cancers arise. The British Medical Research Council Report recognized this requirement, but in an apparent zeal for a pejorative analysis of the Geesaman-Tamplin-Cochran "hot particle" thesis, the B.M.R.C. report simply failed to address the most crucial problem of all.

The very fate of human societies may well rest upon this issue, considering the the proposed handling of some 440 million pounds of plutonium (and reactor-grade at that) in the next 50 years in a plutonium-based nuclear fission energy economy.

It is strange indeed that virtually all workers (Cohen, British Medical Research Council, ICRP, and others) have seemed fascinated by the 25% of inhaled plutonium deposited in the tissues beyond the bronchi, when virtually all the cancers arise in the bronchi. It almost seems as though the prevailing mood is that if a serious problem is simply neglected, it may disappear.

### The Dose to Relevant Tissue

As will become evident below, it is no simple matter, in the current state of our ignorance, to calculate the true dose from insoluble  $\text{PuO}_2$  particles to the relevant bronchial tissue.

All the above-mentioned groups or individuals have made use of a model for lung dynamics developed by a Task Group of the ICRP.<sup>(28)</sup> This model may be totally irrelevant for the question of exposure of the relevant bronchial cells. What does this model suggest, and where may it fail seriously in the real-life situation?

The model suggests that when  $\text{PuO}_2$  particles are inhaled that some 8% deposits in the "tracheo-bronchial" region and some 25% deposits in the deep respiratory tissue ("pulmonary tissue"). It further assumes that the  $\text{PuO}_2$  deposited in the tracheo-bronchial region is rapidly cleared into the intestine via the naso-pharynx, with 99% being cleared in less than a day. For the "pulmonary tissue" (tissue beyond the terminal bronchioles), the model suggests that 40% of the deposited  $\text{PuO}_2$  is cleared in a day and 40% is cleared with a half-time of some 500 days. The remaining 20% is presumed, in the model, to be cleared via lymph and blood. The 80% (including the 40% rapidly cleared plus the 40% slowly cleared) are presumed to go back up through the tracheo-bronchial system to nasopharynx and thence to intestine.

This model is totally based upon the assumption of normally functioning epithelium of the bronchial system, particularly of normally functioning cilia<sup>\*</sup> to propel the particles

\*Cilia are specialized hair-like structures arising from the surface of lining cells, with the function of propelling material.

back up the tracheo-bronchial tree. If that ciliary function is impaired, then all the assumptions concerning clearance rate can be vastly in error, if applicable at all.

While the Task Group of ICRP was quite happy that the model seemed in reasonable accord with experimental animal data on a variety of particulate materials, the model may be irrelevant for humans in real-life circumstances.

Let us recall that most lung cancers (bronchiogenic cancers in man) occur in smokers of cigarettes. Roughly such cancers are 10x as likely in cigarette smokers than in non-smokers. This being the case, we really need to know what the circumstances of  $\text{PuO}_2$  deposition and retention will be in cigarette smokers in the population, since this will overwhelmingly determine the bronchiogenic lung cancer effects.

In the extensive studies of lung cancer reported by the Surgeon General, (29) one outstanding set of facts was pointed out, based upon the work of Auerbach et al (30).

- (a) There is considerable alteration of bronchial epithelium in cigarette smokers.
- (b) There is a serious loss of ciliary presence in cigarette smokers (to say nothing of function of what cilia remain).

If our cigarette smokers have a serious loss of ciliary presence and function, of what use is a model that predicts clearances based upon intact ciliary function? We must face the possibility that, as a result of impairment or loss of ciliary function,  $\text{PuO}_2$  deposited in the tracheo-bronchial epithelial region of man may be cleared extremely slowly. Further, the  $\text{PuO}_2$  coming back up from the deep pulmonary tissue may also be hung up in the bronchial region, since it is assumed that the ciliary function is what propels it on, ultimately to the intestine.

It will indeed be no easy task to ascertain, for cigarette smoking humans, precisely what the clearance rates are for  $\text{PuO}_2$  in human bronchial tissue. But it would

represent the height of public health irresponsibility either (a) to assume that an invalid, irrelevant model provides answers or (b) to neglect the problem simply because it is difficult.

An approach to Estimation of the Plutonium Dose to Relevant Bronchial Cells

There are two parts to this estimate:

(a) Estimation of the fraction of tracheo-bronchial region that is relevant for bronchiogenic cancer.

(b) Estimation of the clearance of  $\text{PuO}_2$  particles by bronchial epithelium with impaired ciliary function, as in cigarette smoking humans.

(a) Estimation of the Relevant Part of the Tracheo-Bronchial Region

In the Task Group publication <sup>(28)</sup> it is estimated that the air volume of nasopharynx plus tracheo-bronchial region down through terminal bronchioles is  $133 \text{ cm}^3$ , of which  $50 \text{ cm}^3$  is assigned to the nasopharyngeal volume. This leaves  $83 \text{ cm}^3$  for the entire tracheo-bronchial region. Since virtually no cancers arise in the trachea, we can subtract approximately  $33 \text{ cm}^3$  for the tracheal volume, leaving  $50 \text{ cm}^3$ . The right and left main-stem bronchi (also rarely involved in cancer) represent a volume of approximately  $11 \text{ cm}^3$ , so this leaves  $39 \text{ cm}^3$  for the bronchial region, including the terminal bronchioles. As a reasonable first approximation,  $1/2$  of this volume will be assigned to the relevant bronchi, and  $1/2$  to the volume of smaller bronchial branches plus bronchioles. Therefore, we have, finally, approximately  $20 \text{ cm}^3$  for the volume in relevant bronchi. From Gray's Anatomy <sup>(31)</sup>, the diameter of such intrapulmonary bronchi can be estimated as approximately  $0.23 \text{ cm}$ . (or radius =  $0.115 \text{ cm}$ ).

Treating these bronchi as cylindrical tubes,

Volume =  $\pi r^2 h$ , where  $h$  = equivalent length of total bronchi of this class

$$20 = 3.14 (0.115)^2 h$$

$$\text{or, } h = \frac{20}{(3.14)(0.013)} = \frac{20}{0.04} = 500 \text{ cm.}$$

To calculate the surface area of such bronchi, we use:

$$\begin{aligned}\text{Area} &= 2\pi r h \\ &= 2\pi (0.115) 500 \\ &= (6.28)(0.115) (500) \\ &= 361 \text{ cm}^2\end{aligned}$$

A reasonable approximation for average height of the stratified columnar epithelium of these bronchi is 30 microns, or  $3 \times 10^{-3}$  cm.

$$\begin{aligned}\text{Therefore, Volume of Epithelial Tissue} &= \text{Area} \times \text{cell layer height} \\ &= 361 \times 3 \times 10^{-3} = 1083 \times 10^{-3} \\ &\approx 1 \text{ cm}^3.\end{aligned}$$

Since the density of soft tissue is  $\approx 1$  gram/cm<sup>3</sup>, it follows that the mass of relevant bronchial tissue is  $\approx 1$  gram.

(b) Estimation of the Clearance of PuO<sub>2</sub> Particles by Bronchial Epithelium with Impaired Ciliary Function

The work of Auerbach et al (cited in the Surgeon General's Report on Smoking) shows the following severe losses of cilia in cigarette smokers (Table 5). These were controlled studies in which the pathologist did not know the smoking habits for the cases studied.

The Surgeon General's report comments as follows on loss of ciliary function (Ref. 29, pp 269-270:

"Inhibition of ciliary motility following exposure to tobacco tars, cigarette smoke, or its constituents has been demonstrated frequently with experimental use of respiratory epithelium from a wide variety of animal species." (17 references quoted).

"Similar results have been obtained with ciliated human respiratory epithelium." (2 references). "Although all investigations have been conducted in vitro, the uniformity of the inhibitory effects in a number of different experimental models is impressive."

Table 5 (Data of Auerbach et al)

Loss of Cilia and Epithelial Cell Abnormality

<u>Group</u>	<u># Cases</u>	<u># Slides studied</u>	<u>Percent of slides with cilia absent and averaging 4 or more cell rows in depth.</u>
Never Smoked regularly	65	3324	1.1%
Ex-Cigarette Smokers	72	3436	4.1%
Cigarettes - 1/2 pk/day	36	1824	4.7%
Cigarettes - 1/2-1 pk/day	59	3016	7.9%
Cigarettes - 1-2 pks/day	143	7062	16.9%
Cigarettes - 2+ pks/day	36	1787	37.5%

As noted in Table 5, over and above the loss of cilia there is marked abnormality in the epithelial layer of the bronchi.\* Whether these altered epithelial cells may more avidly engulf PuO<sub>2</sub> particles than do normal epithelial cells, either by phagocytosis or endocytosis, is totally unknown. It is possible that the failure of clearance of PuO<sub>2</sub> by such regions may be seriously enhanced over and above the failure of clearance due to the absence of cilia. The Auerbach data reveal the absurdity of the model used by ICRP, by Cohen, and by BMRC for evaluation of PuO<sub>2</sub> clearance by the real population expected to be exposed to PuO<sub>2</sub> inhalation. In the heavy smokers, who will contribute most of the lung cancers, 37.5% of the cells have lost their cilia entirely. We can, therefore, with sound reason, presume that such regions of absent ciliary function will clear PuO<sub>2</sub> particles very slowly, if at all. It would not be at all conservative, for such regions, to assume that the half-time for clearance is 500 days for PuO<sub>2</sub> particles.

\*Normal epithelium would show one or two cell rows in depth. Note that Table 5 describes the slides showing four or more cell rows in depth.

Quantitative Treatment of Smokers and Non-Smokers For Plutonium Lung Cancer Hazard

Inasmuch as the strong evidence indicates a different physiological handling of PuO<sub>2</sub> particulates for smokers versus non-smokers (henceforth, smokers will be considered to mean cigarette smokers), it is essential to consider these as separate sub-populations. The first step in such separate handling is to re-estimate the risks of lung cancer for smokers versus non-smokers.

For the overall male population (USA), the spontaneous lung cancer rate =  $1.27 \times 10^{-3}$ /year. (P.5, this report). Two subpopulations will be considered as a very reasonable approximation:

1/2 the men as non-smokers

1/2 the men as smokers (all cigarette smokers combined).

Let  $x$  = lung cancer rate for non-smokers

and  $10x$  = lung cancer rate for smokers (P.15, this report).

Then, overall rate =  $(1/2)(x) + 1/2(10x) = 1.27 \times 10^{-3}$

$$\text{or, } \frac{11x}{2} = 1.27 \times 10^{-3}$$

$$x = 0.23 \times 10^{-3}/\text{year}$$

$$10x = 2.3 \times 10^{-3}/\text{year}$$

With these evaluations of  $(x)$  and  $(10x)$ , it is possible to convert all tables presented above into separate tables for smokers and for non-smokers. Wherever risks are involved, values for smokers (compared with overall population) must be multiplied by  $\frac{2.3 \times 10^{-3}}{1.27 \times 10^{-3}}$  or a factor of 1.81.

Values for non-smokers (compared with overall population) must be multiplied by

$$\frac{0.23 \times 10^{-3}}{1.27 \times 10^{-3}} \text{ or a factor of } \underline{0.181}.$$

Table 3 can now be converted to one which treats smokers and non-smokers separately. These converted data, utilizing the factors above (1.81 and 0.181), are presented in Table 6.

Table 6

Step 1 Calculation: Separate Data for Smokers and Non-Smokers

Lung Cancer Doses per Pound of Plutonium\*

For Cigarette Smokers:

<u>Estimate</u>	<u>"Lung Cancer Doses" per pound Pu<sup>239</sup></u>	<u>"Lung Cancer Doses" per pound Reactor-Pu</u>
"Gofman-Tamplin"	76,000,000	411,000,000
"BEIR"	19,000,000	103,000,000
"Cohen:	4,030,000	21,700,000

For Non-Smokers:

"Gofman-Tamplin"	7,600,000	41,100,000
"BEIR"	1,900,000	10,300,000
"Cohen"	403,000	2,170,000

\*Note: This is still a Step 1 calculation assuming plutonium distributed into the entire 570 grams of (bloodless) lung tissue mass.

Step 3 Calculations of Lung Cancer Hazard from PuO<sub>2</sub> for Smokers and Non-Smokers

(a) The Cigarette Smokers:

As a result of the presence of large regions of cilia-free bronchi, coupled with potentially impaired ciliary function in additional regions, it is highly reasonable to estimate that clearance from cilia-free bronchial regions will be comparable with that estimated for cilia-free pulmonary regions. This leads to  $T_{1/2} = 500$  days for clearance for such cilia-free regions. From Table 5, cigarette-smokers of more than 1 pkg. per day average ~25% cilia-free regions.

Therefore, if we assume 25% of bronchi will show impaired clearance, we can hardly be overestimating the effect. It may not be conservative enough.

In the ICRP Task Group Model it is assumed that

25% of inhaled  $\text{PuO}_2$  deposits in pulmonary tissue

8% of inhaled  $\text{PuO}_2$  deposits in tracheobronchial region.

It is further assumed by ICRP that only 60% of the  $\text{PuO}_2$  deposited in pulmonary tissue is retained for long-term clearance and that none of the  $\text{PuO}_2$  deposited in the tracheobronchial tree is retained for long-term clearance.

With impaired ciliary clearance for 25% of the bronchial region, we shall assume

(a) that 25% of that deposited in tracheobronchial tree is subject to retention.

25% of 8% = 2% of total. Moreover, we shall use ICRP's estimate that 40% of this clears within a few days, leaving  $0.6 \times 2 = 1.2\%$  for long-term retention.

(b) Further, of the 40% coming up rapidly (as per ICRP) from the pulmonary region that 25% of this 40% is retained in the bronchial region.

25% of (40% of 25%) = 2.5% is retained, additionally, of which 60% is retained long-term. Long term, therefore = 1.5%. Therefore, total retained for long-term clearance becomes

$$1.2 + 1.5 = 2.7\% \text{ in bronchial region.}$$

The ICRP Model allows 60% of 25%, or 15%, of total to be retained in pulmonary region, providing dose to this region.

Since we have just calculated 2.7% to be retained in the bronchial region, it follows that the bronchial region has a radiation source =  $\frac{2.7}{15}$ , or 0.18 as strong as the pulmonary region.

But to estimate dose to bronchial region, we must also incorporate the estimated tissue mass (bronchial) irradiated. This was shown above to be one gram.

Therefore, the overall radiation dose to bronchial region

$$= (0.18) \times \frac{(570)}{1} \times (\text{Dose to pulmonary region})$$

$$= (103) \times (\text{Dose to pulmonary region}).$$

This dose, in the cigarette smokers, will completely dominate the additional dose received by the pulmonary region.

It is now possible to estimate the lung cancer doses per pound of PuO<sub>2</sub> by applying this factor of 103 as a multiplier for all the values for smokers in Table 6. The results of this calculation are presented in Table 7.

Table 7

Step 3 Calculation: Final Estimate of PuO<sub>2</sub>-induced Lung Cancers in Cigarette Smokers

<u>Estimate</u>	<u>"Lung Cancer Doses" per pound Pu<sup>239</sup></u>	<u>"Lung Cancer Doses" per pound Reactor-Pu</u>
"Gofman-Tamplin"	7,830,000,000	42,300,000,000
"BEIR"	1,960,000,000	10,600,000,000
"Cohen"	415,000,000	2,240,000,000

The number of micrograms Pu per lung cancer dose is now readily estimated for the cigarette smokers. For example, from Table 7, the Gofman-Tamplin estimate is 7,830,000,000 lung cancer doses per pound Pu<sup>239</sup>.

$$1 \text{ pound} = 4.54 \times 10^8 \text{ micrograms}$$

$$\text{Therefore, } \frac{7.83 \times 10^9}{4.54 \times 10^8} = \text{lung cancer doses per microgram.}$$

The micrograms per lung cancer dose is the reciprocal, or  $\frac{4.54 \times 10^8}{7.83 \times 10^9} = 0.058$  micrograms.

In a similar fashion all the values of Table 7 can be treated to provide the estimates of Table 8.

Table 8

Final Step 3 Estimates of Micrograms Pu per Lung Cancer Dose in Cigarette Smokers

<u>Estimate</u>	<u>Micrograms Pu<sup>239</sup> per lung cancer dose</u>	<u>Micrograms Reactor-Pu per lung cancer dose</u>
"Gofman-Tamplin"	0.058	0.011
"BEIR"	0.23	0.043
"Cohen"	1.10	0.203

(b) The Non-Smokers

For this population sub-group, the Auerbach data (Table 5) show the following:

Never Smoked Regularly: 1.1% of bronchial regions show cilia absent.

Ex-Cigarette Smokers: 4.1% of bronchial regions show cilia absent.

We shall weight the "never smoked" twice as heavily as the ex-cigarette smokers and arrive at a value of 2% as an average for bronchial regions showing cilia absent in a cross-section of non-smokers.

For the cigarette smokers, a value of 25% was used above for the bronchial regions showing ciliary absence. Therefore, we arrive at the estimate that, whatever dosage of the relevant bronchi is taken for cigarette smokers, the appropriate value for non-smokers is 2/25, or (0.08) of that dosage. The number of expected lung cancers from plutonium inhalation in non-smokers will therefore be  $(0.008) \times (\text{lung cancers expected in smokers})$ . (0.08 for source strength and 0.1 for cigarette-lung cancer risk.)

Accordingly, Table 9, providing lung cancer doses per pound of Pu for non-smokers is derived from Table 7 by multiplying all values by (0.008).

Table 10, providing micrograms Pu per lung cancer dose, is derived from Table 8 by dividing all values by (0.008).

Table 9

Final Step 3 Estimates of PuO<sub>2</sub> Induced Lung Cancers per Pound in Non-Smokers

<u>Estimate</u>	<u>Lung Cancer Doses per pound Pu<sup>239</sup></u>	<u>Lung Cancer Doses per pound Reactor-Pu</u>
"Gofman-Tamplin"	62,600,000	338,000,000
"BEIR"	15,700,000	85,000,000
"Cohen"	3,300,000	17,900,000

Table 10

Final Step 3 Estimates of Micrograms Pu per Lung Cancer Dose in Non-Smokers

<u>Estimate</u>	<u>Micrograms Pu<sup>239</sup> per lung cancer dose</u>	<u>Micrograms Reactor-Pu per lung cancer dose</u>
"Gofman-Tamplin"	7.3	1.4
"BEIR"	28.8	5.4
"Cohen"	138.0	25.4

In the treatment here, both for smokers and non-smokers, no crediting was given to diminished ciliary function over and above ciliary absence. It is quite possible that we have underestimated the hazard of plutonium inhalation as a result. Nevertheless, the preference is to understate the hazard wherever data are not absolutely firm, provided all concerned realize that there may well be an understatement.

GENERAL DISCUSSION

Are the Estimates Too High or Too Low?

It is evident from all the discussion up to this point that certain key parameters of physiological function are not available through direct experimental evidence for humans. One fact, however, is outstanding--that is the failure of authoritative bodies such as ICRP or BMRC to come to grips with the real-life problem of bronchopulmonary retention of PuO<sub>2</sub> particles in cigarette-smoking humans. This failure has led them to the use of a totally unrealistic and probably irrelevant model which drastically underestimates the lung cancer hazard of PuO<sub>2</sub> inhalation. One may ask whether the retention in bronchial tissue, secondary to loss of ciliary function, will really lead to a 500-day half-time for clearance of PuO<sub>2</sub> particles. We simply don't know, but it is just as reasonable to expect an even longer retention time as it is to hope for a shorter retention time. Since ciliary function is the mechanism counted upon for differentiating rapid clearance in the bronchi versus slow clearance in the pulmonary region, the absence of effective ciliary function makes it reasonable, as a first approximation, to expect clearance times to become identical.

If there be any intrinsic more rapid clearance mechanism (aside from cilia) for bronchial cells than for pulmonary cells, such mechanism is totally hypothetical. Indeed, the effect can be such as to worsen the estimates.

One may ask whether the metaplastic and hyperplastic epithelium of the bronchi of cigarette-smoking humans is more or less active in the engulfing of  $\text{PuO}_2$  particles than is the normal epithelium. We simply don't know, but it is, a priori, equally probable that such epithelium can be less, equally or more active in engulfing  $\text{PuO}_2$  particles. The burden of proof that metaplastic and/or hyperplastic epithelium is less active in engulfing  $\text{PuO}_2$  particles would rest upon those who think it may be less active. From what we know about the general physiology of injured or inflammatory tissue, the expectation, if anything, is for greater phagocytic activity, not less. And this would make the  $\text{PuO}_2$  carcinogenicity worse than calculated, not better.

#### The Hazard of Dispersal of Plutonium Oxide Aerosols

Cohen endeavored to show that plutonium dispersal was not as bad as general opinion has held it to be. The seriousness of his under-estimate of the cancer hazard of inhaled  $\text{PuO}_2$  aerosols is evident in this report. Thus, comparison of Cohen's 2,225,000 lung cancer doses per pound of  $\text{Pu}^{239}$  (Table 3) with the final "Gofman-Tamplin" estimate of 7,830,000,000 for cigarette-smoking humans, shows that Cohen is low by a factor of  $\frac{7,830,000,000}{2,225,000}$ , or 3520 times too low. Even for the non-smokers, his estimate is some 30 times too low.

In view of these serious under-estimates of the lung cancer hazard from inhaled Pu, most of his estimates of the hazard of plutonium dispersal will require scaling up by a factor of 3520 times.

Cohen, in his general thesis that plutonium, while very toxic, is not as toxic as many have thought, presented a calculation that insoluble reactor grade Pu is roughly

60 times more carcinogenic than benzpyrene. Benzpyrene is a now-famous substance, being one of the most potent chemical hydrocarbon carcinogens known. If we correct Cohen's estimate by the 3520 fold factor required, his estimate would then be that reactor grade Pu is roughly 211,000 times as carcinogenic as benzpyrene for smokers. It would seem that this revision would materially enhance the carcinogenic stature of plutonium for Cohen.

In consideration of "lung cancer doses" per pound of plutonium it must be recalled that this reflects the expected number of fatal lung cancers per pound of deposited plutonium. The question of how much of dispersed PuO<sub>2</sub> actually gets deposited is a wholly separate issue, based largely upon meteorology and dispersal conditions. Thus, if plutonium is dispersed and falls out over the ocean, there are few humans around to inhale it, so very few of the cancers can occur. On the other hand, dispersal with fallout in a city can lead to very drastic consequences in lung cancer fatalities.

It has been estimated that the nuclear weapons testing of the 1950s and 1960s has resulted in the worldwide fallout of some 11,500 pounds of plutonium-239 equivalent.<sup>(35)</sup> Some have suggested that if plutonium is so virulent a carcinogen as it appears to be, why haven't more cases of lung cancer occurred as a result of this fallout? The author has calculated the consequences of this plutonium fallout, and these consequences will be presented in a separate report.<sup>(32)</sup> Huntington has repeatedly raised the question of whether the increasing epidemic of lung cancer may be, in part, due to plutonium fallout.<sup>(33)</sup> Huntington may well have raised one of the most crucial public health issues of our time.

#### Comparison of Human Data with Experimental Beagle Data

The British Medical Research Council Report has reviewed the beagle dog studies of Bair and Thompson.<sup>(34)</sup> The initial depositions were between 3 nanocuries

and 50 nanocuries of Pu-239 per gram of bloodless lung. Even at the lowest level (3 nanocuries per gram of lung), essentially 100% of the dogs died of lung cancer. We know, therefore, that 3 nanocuries per gram of bloodless dog lung is at least one "lung cancer dose". As BMRC pointed out, the true "lung cancer dose" could be much lower, and on-going experiments at lower doses will be required to test this issue.

But, there are sufficient data already to compare the beagle evidence with the human calculations presented in this report.

$$3 \text{ nanocuries per gram} = 3 \times 10^{-3} \text{ microcuries per gram.}$$

To scale to human, with a 570 gram bloodless lung we have

$3 \times 10^{-3} \times 570$ , or  $1710 \times 10^{-3}$ , or 1.7 microcuries of Pu-239 is at least one "lung cancer dose".

Conversion to micrograms,  $1.7 \times 16.3 = 27.1$  micrograms of Pu-239 is at least one "lung cancer dose".

In Table 8, "Gofman-Tamplin" estimates are that 0.058 micrograms is the lung cancer dose for cigarette smoking humans, and in Table 10, the similar estimates are that 7.3 micrograms of Pu<sup>239</sup> is the lung cancer dose for non-smoking humans.

Curiously enough it has been overlooked that beagle dogs raised in laboratories are not in the habit of smoking cigarettes. If a relevant comparison is to be made with humans, the appropriate treatment would be to compare the beagle data with the estimates for non-smoking humans.

Let us compare these values directly:

For the beagle dog (a non-smoker): 27.1 micrograms Pu<sup>239</sup> is at least one lung cancer dose.

For the human (non-smoker): 7.3 micrograms Pu<sup>239</sup> is one lung cancer dose.

As the BMRC report pointed out, virtually 100% of the beagles developed lung cancer at 3 nanocuries per gram of bloodless lung. It would be in the realm of miracles that the 3 nanocuries/gram happened to coincide with one lung cancer dose. In all likelihood, the true lung cancer dose for non-smoking beagle dogs is lower than 3 nanocuries per gram, and quite possibly considerably lower, just as was pointed out by the British Medical Research Council Report. Since the beagle data are even now so close to the estimates calculated here, it seems virtually certain that the newer beagle data will not be significantly different from the human estimates.

The Standards for "Permissible" Exposure to Plutonium, Occupational and for the Public-at-Large

The existing guidelines for "permissible" exposures to plutonium particulates permit:

- (a) Occupational workers: Maximum lung burden = 0.016 microcuries.
- (b) Public-at-Large: Permissible burden for the average person = 0.0005 microcuries.

Tamplin and Cochran<sup>(1)</sup>, at the time of releasing their report, stated that the current guidelines make it extremely likely, indeed almost certain, that exposed individuals (occupationally-exposed) would develop fatal lung cancers.

It is of interest to test this prediction of Tamplin and Cochran against the calculations of this report, calculations that in no way depend upon the hot particle approach utilized by Tamplin and Cochran.

Predictions for Occupational Exposure

Since 16.3 micrograms represent 1 microcurie of Pu<sup>239</sup>, the occupational permissible burden of 0.016 microcuries represents 0.26 micrograms of Pu<sup>239</sup> equivalent.

For Cigarette-Smoking Workers:

1 lung cancer dose = 0.058 micrograms (Table 8). Therefore, each worker is permitted to acquire a lung burden of  $\frac{0.26}{0.058}$ , or 4.5 lung cancer doses. Since it only takes one lung cancer to kill a human, it is something of an overkill to guarantee 4.5 fatal lung cancers per worker. For these workers, therefore, we not only agree with Tamplin-Cochran, but we believe they understated the hazard.

For Non-Smoking Workers:

1 lung cancer dose = 7.3 micrograms (Table 10). Therefore, each worker is permitted to acquire a lung burden of  $\frac{0.26}{7.3}$ , or 0.036 lung cancer doses. Therefore, the expectation is that approximately one such worker out of thirty would develop fatal lung cancer at the permissible dose.

Predictions For the Public-at-Large

The implications of this report's calculations for the public-at-large are much more startling. The permissible average burden of 0.0005 microcuries of Pu<sup>239</sup> corresponds to 0.0082 micrograms of Pu<sup>239</sup> equivalent.

The population of the USA is roughly 1/2 non-smokers, 1/2 cigarette smokers. Since there are some 10<sup>8</sup> males per generation, at the current US population size, there are 5x10<sup>7</sup> cigarette smokers and 5x10<sup>7</sup> non-smokers.

Total lung cancer doses, for cigarette smokers,

$$5 \times 10^7 \times \frac{0.0082}{0.058} = 5 \times 10^7 \times 0.14 = 7 \times 10^6 \text{ lung cancer doses.}$$

Total lung cancer doses, for non-smokers,

$$5 \times 10^7 \times \frac{0.0082}{7.3} = 5 \times 10^7 \times 0.0011 = 0.06 \times 10^6 \text{ lung cancer doses.}$$

Combining these, we have 7,060,000 extra fatal lung cancers that can be expected in USA males per generation if the population exposure to plutonium approached that which regulations now permit.

Since these lung cancers would occur over a 30-year period, the expectation would be for  $\frac{7,060,000}{30}$ , or 235,000 extra fatal cancers per year in men.

Since the current lung cancer fatality rate, from all causes combined, is 63,500 per year in men, the conclusion must be drawn that governmental regulatory bodies are not disturbed over causing an additional four times as many lung cancer deaths as are now occurring.

Many serious public health experts consider 63,500 lung cancer fatalities per year to represent a most serious epidemic. How should they view the burgeoning plutonium-based nuclear fission energy economy, proceeding under regulatory standards that would permit a four-fold increase supplementary to this epidemic?

### Supplemental Notes

Note 1: The BEIR relative risk percentage refers to adults. If it were restricted to 20-30 year old adults, the BEIR value might have to be increased even further than the 0.5% value used in this report (for BEIR). This entire present report, for consistency, compares all estimates for males in the 20-30 year age range (see p.3, this report).

Note 2: Calculation of fatal doses per pound of a toxic material of commerce may, at first glance, appear to represent an effort to exaggerate toxicity. This is incorrect. Indeed, it will be quite relevant, in the future, to describe all industrial pollutants in a similar manner. For substances handled in commerce in pound or ton quantities, a rational reference framework will be to require toxic or fatal doses per pound.

Some observers have pointed out that society has handled many highly toxic non-radioactive pollutants in pound or ton quantities. Since, in general, no careful followup studies have ever been made for most such pollutants, it may well be that a societal reappraisal of such non-radioactive pollutants is urgently indicated.

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