ENVIRONMENTAL IMPACT STATEMENT

CLEANUP, REHABILITATION, RESETTLEMENT OF ENEWETAK ATOLL — MARSHALL ISLANDS

APRIL 1975

DEFENSE NUCLEAR AGENCY
Washington, D.C. 20305

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Volume II A of IV

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A Resource Sciences company

Advanced Technology/Engineering/Construction/Management/Maintenance & Operations

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ENEWETOK ATOLL

Early Return Program

Operational Plan

Japtan Island

Marshall Islands District

Trust Territory of the Pacific Islands

ENEWETOK EARLY RETURN
Operational Plan
Japtan Island

This plan is predicated on the return during the first quarter of 1975 of approximately 50 Dri-Enewetok to Japtan Island, as an advance party of the total return of the Enewetok people to their home atoll following cleanup and rehabilitation.

The physical plan for this temporary community makes certain assumptions based on the joint return agreements between the Defense Nuclear Agency, Department of Interior, and the Trust Territory Government. Following are these assumptions.

1. The 50 returning people will be broken into family groups and it is assumed that natural population appreciation will be accepted.

2. The District Administrator's Representative and family will be in addition to the original 50 people and he will require housing and an office within the temporary camp.

3. Based on the above, 10 living units will be required and will be accommodated in 2 and 4 room apartments in buildings #2191 and #2106.

4. The Trust Territory Government will supply all regular Governmental supplies and field trip service, but all required public facility personnel will be included in the original 50 returnees.

5. Employment for some of the adult males will be available in Enewetok Atoll by various agencies with the initial employment linked, through the Trust Territory of the Pacific Islands, with the Atomic Energy Commission's (AEC) test planting program.

6. Self-employment by fish drying and seafood collection will be stimulated by mutual assistance from all agencies within the parameters of the Enewetok Council's resolution on return.

7. Development costs for the camp would be kept at a minimum, in recognition of its temporary nature, while accommodating the needs of the early returnees.

8. The majority of the materials and collateral equipment for the early return are available within the atoll (see attached building breakdown).

9. The returnees will be utilized in the construction of the temporary camp, by their request. The T. T. P. I. will furnish the required supervisory personnel, equipment and building materials.

HOUSING:

Housing will be accommodated in buildings #2191 and #2106 as shown on the Holmes & Narver Engineering study for cleanup. Building #2191 will be remodeled into six 2-room units, and building #2106 into four 4-room units. Limited remodeling of the existing interior spaces would be required, consisting mainly of the removal of existing walls, walling of the existing central hallway, and repair of the existing structure. Exterior doors would be required on both sides of each of the two buildings. Construction of an exterior wash area with adjacent crushed coral porch plus a bathing area, will be required. (See attached plan.)

Costs are estimated to include transportation, material acquisition, wages and supervisory personnel, with overtime and per diem for T. T. P. I. district center personnel.

COMMUNITY FACILITIES:

The school, meeting hall and church will be located in building #2103. Minimal remodeling is required to accommodate these functions. Furniture and fixtures for the school, including benches and tables, can be made from scrap materials available on the islands.

A warehouse/storage space is projected for approximately 1/2 of building #2190, with the remaining 1/2 utilized as a radio room, Distad Representative's Office, and a dispensary. The latter facility is to be operated as an office for minor consultation and treatment in the similar manner to all outer island dispensaries. Major emergency medical needs will be accommodated at the dispensary on Enewetok or by air lifting to the T. T. P. I. field hospital on Ebeye. Emergency costs incurred by DNAFC will be reimbursable as per the mutual support document.

Standard radio equipment will be required for the Distad Representative's Office. A radio antenna can be accommodated utilizing existing poles and aluminum poles adjacent to the radio area, although antenna wire will be required. The generator for the radio will be housed in an abandoned container which is on site.

UTILITIES/COMMUNICATIONS:

The only major utility required will be additional water catchment tanks and the digging of 2 surface wells. Based on a consumption of

catchment water of 20 gallons per person per day and assuming a maximum of 20 days dry spell, eight 5000-gallon water tanks will be required. The rubber bladder utilized during the September, 1974 field trip will be maintained as reserve storage.

The sole electrical requirement will be a standard 1.5-kw generator to operate the radio which will be housed as noted above. All other community lighting and cooking requirements will be met through the use of kerosene lamps and stoves.

Single pit toilet facilities (benjo's) will be supplied and constructed for each family with siting done to reduce potential ground water contamination. A garbage pit will be dug as shown on the attached plan.

TRANSPORTATION:

Japtan Island will become a regular Trust Territory field trip stop. Service will be covered within the regular northern island run and is expected to average one stop per month.

Use of the existing weekly "Capitol" flight will be available only for emergency service, administrative visits and transportation of limited goods to Ebeye for sale. The latter item is subject to approval by M.A.C.

Inter-atoll transportation will be by private boat, with the possible exception of a 65' boat now under study to be supplied by the T.T.P.I. Its main use will be on the run from Enewetok to Ujelang and as intra-atoll transportation of the labor force.

ECONOMIC DEVELOPMENT:

The following sources of income are anticipated for the community.

1. Direct employment of Enewetok people by T.T.P.I./A.E.C., and possibly DNAFC.

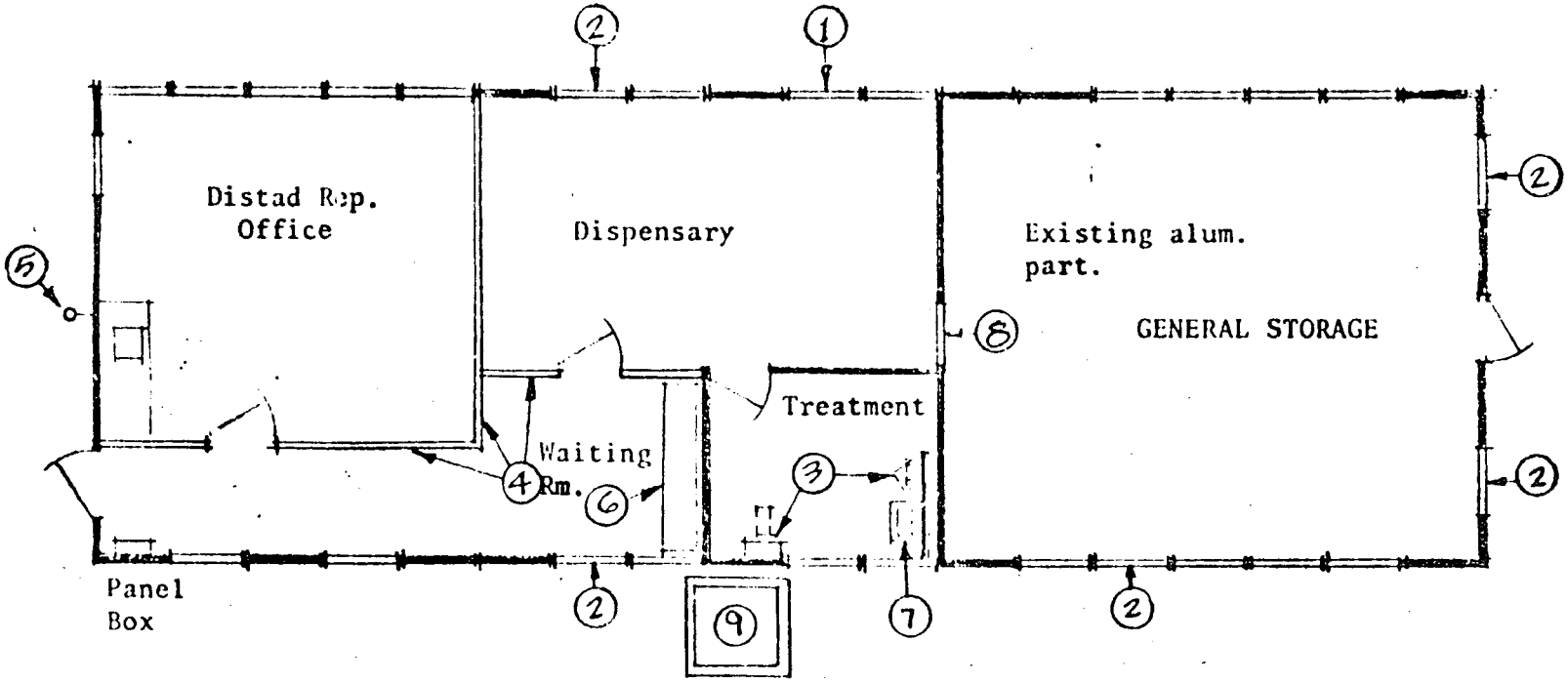
2. Self-employment and sale of dried fish.

3. Self-employment and sale of scrap metals.

Certain of the above items will require mutual cooperation between Defense Nuclear Agency, the Trust Territory of the Pacific Islands and the Atomic Energy Commission, but it is anticipated this will cause no hardships in the period prior to actual cleanup and rehabilitation.

Repairs and Alterations

Scale: 4' Sheet 1



To Do:

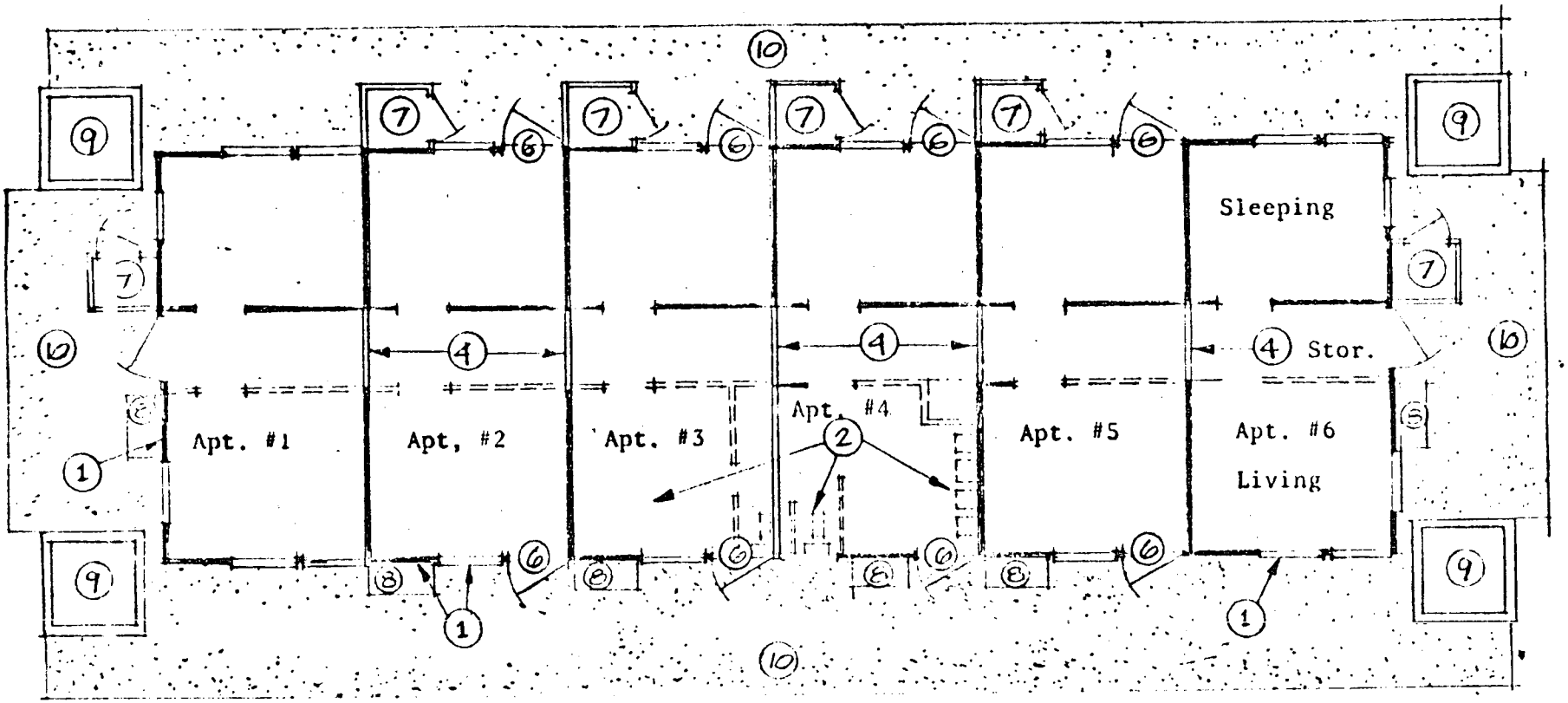
1. Repair wall sections
2. Repair windows
3. Remove toilet W.C. and urinal
4. Install alum. partitions
5. Install radio antenna
6. Install bench
7. Hookup lav. to water cistern
8. Seal door
9. Install cistern and guttering

Equipment and Furniture Req.:

1. Distad Rep office
   a. Desk
   b. 2 chairs
   c. Filing cab.
   d. Table
   e. Radio and Ant. *
   f. Book cabinet
2. Dispensary
   a. Treatment table *
   b. Desk
   c. 2 chairs
   d. Cabinet and counter Medicine storange LKR.
3. Storage
   a. Asst'd storage racks

Repairs & Alterations

Scale: 4' Sheet 2



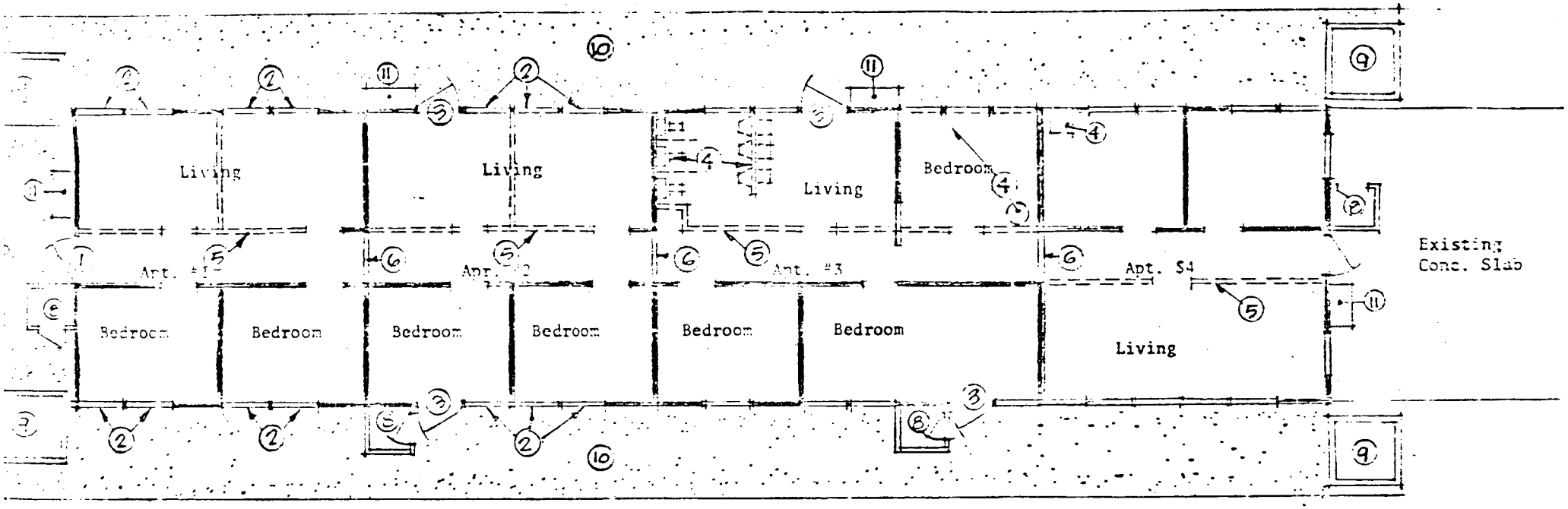
To Do:

1. Repair wall sections
2. Remove sinks toilets, showers, H-W.H.T.R. and all piping; plug drains
3. Remove partitions (dotted lines)
4. Add partitions
5. Fill space between flr. and bot. of partition w/aluminum sheathing (typical of all partitions)
6. Make doorways and plywood drs.
7. Construct 4'x4 shower rm.(alum. roof and siding,coral aggr.flr.)
8. Construct wash stand
9. Install cisterns and guttering
10. Place coral aggregate apron

Alterations

JAPTAN EARLY REVIEW PROJECT

Scale: 4' Sheet 3



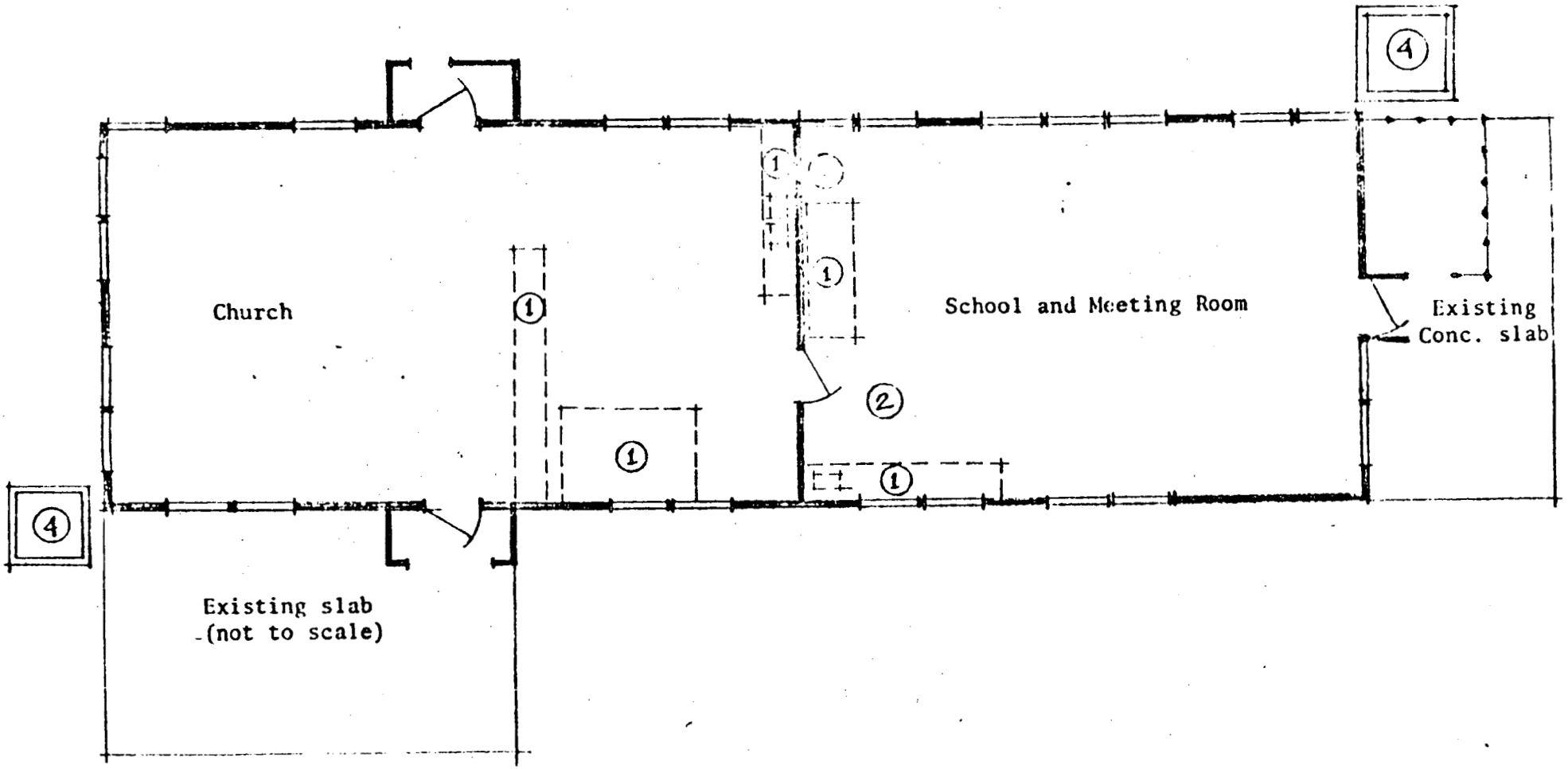
To Do:

1. Repair Door
2. Remove present window, replace with aluminum flaps up and down
3. Remove window, make door frame and install door
4. Remove sinks, toilets, showers, H-W Htr and all piping, plug drains
5. Remove partitions (dotted lines)
6. Add partitions
7. Fill space between flr. and partition bottom as needed
8. Construct 4'x4' shower room (aluminum rfg. and siding, coral agg. flr.)
9. Install cisterns and guttering
10. Place coral aggregate apron
11. Construct wash stand.

12/11/74

Repairs and Alterations

Scale: 4' Sheet 4



To Do:

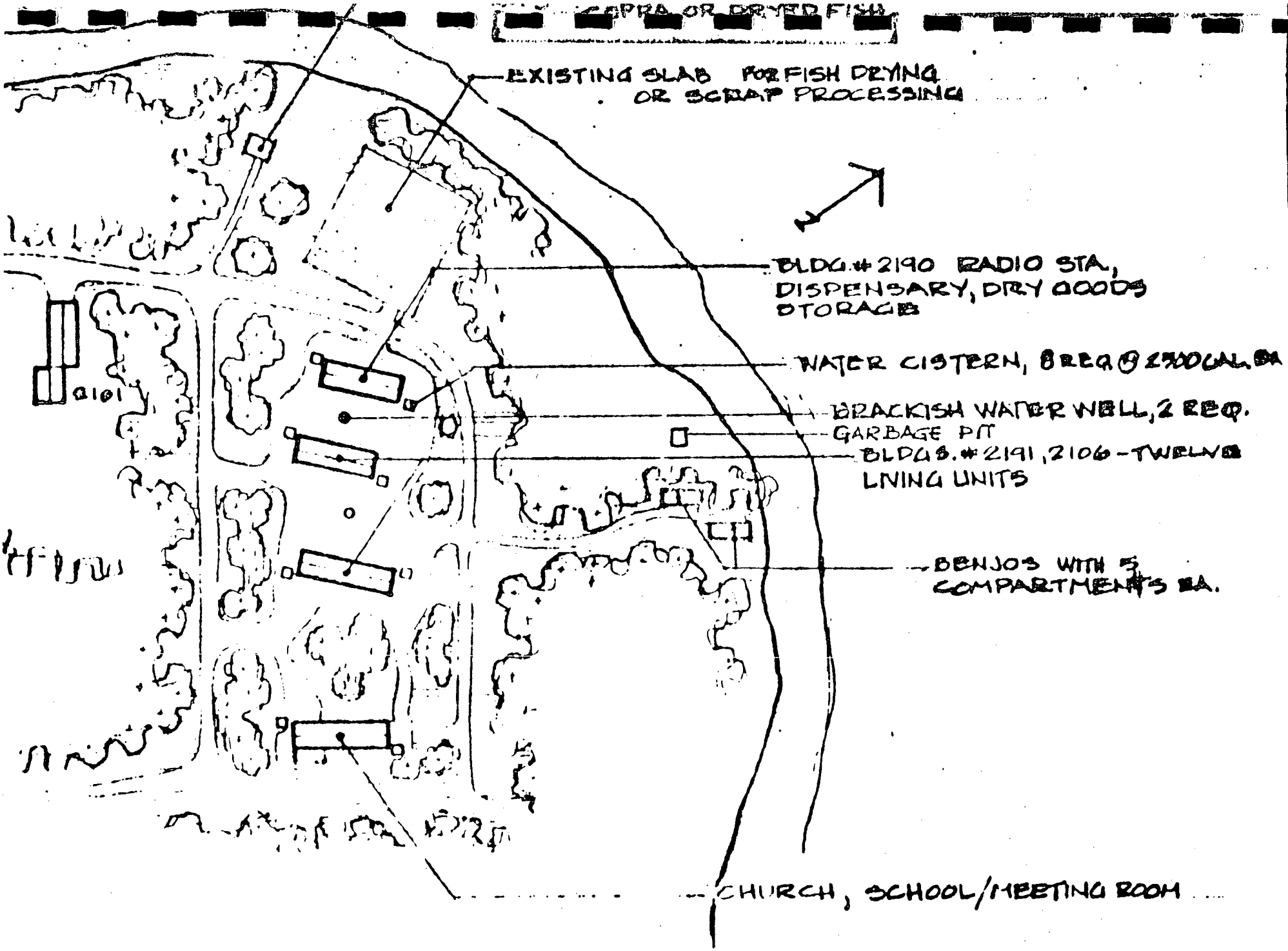
1. Remove all permanent fixtures including sinks, washer, oven hood, counter, H-W HTR, reefer

2. Fill in space to ceiling above partition
3. Clean thoroughly and paint all interior
4. Install cistern and guttering

Equipment and Furniture Needed:

1. Church
   a. PEWS (lumber from power house annes.)
   b. Alter (Medren)

2. School
   a. Desk
   b. Chair
   c. Shelves
   d. Storage lockers
   e. Desks



JAPTAN ISLAND

PRELIMINARY CAMP DESIGN.

UNIVERSITY OF MINNESOTA
TWIN CITIES

Department of Anthropology
215 Ford Hall
Minneapolis, Minnesota 55455

September 16, 1974

MEMORANDUM

TO: Mr. Jack Woolfenden
Systems Sciences Division
Holmes and Narver, Inc.
400 East Orangethrope Avenue
Anaheim, California 92801

FROM: Dr. Robert C. Kiste

SUBJECT: Eniwetok Resettlement Project: Opinions Concerning the Eniwetok People's Reactions to ACE's Conclusion that Northern Islands of Eniwetok Atoll May Not Be Resettled

In our phone conversation of August 22, 1974, you asked me to provide some projections/opinions about how the Eniwetok people would react to the news that the islands from Bokoluo (Alice) to Runit (Yvonne) in the northern part of Eniwetok Atoll will be denied to them for resettlement--at least for several decades. I indicated at the time that I was somewhat reluctant to comment on this because there are people such as Tobin who know the situation and are in contact with the people. My main reservation stemmed from the fact that my main research with the people was conducted 10 years ago and subsequent contacts with some of them in 1969 and 1973 were brief. Nonetheless, you indicated an interest in my own reactions to the situation.

After we discussed the matter, the three volumes of the Draft Environmental Impact Statement dated September, 1974 arrived. I read it rather carefully to

determine just what the situation is and reread relevant portions of Volume 1 of the Eniwetok Atoll Master Plan. I then went back to the data I collected on land tenure--particularly the materials relating to land rights and the history of the inheritance of rights to the three islands which apparently will be/can be resettled: Japtan (Muti, David), Medren (Parry, Elmer) and Eniwetok (Fred). Some of the opinions I list below are based on general Marshallese attitudes toward land and others are derived from specific data I collected among the Eniwetok people. From the article that appeared in the September 9, 1974 issue of the Honolulu Advertiser, I realize that the Eniwetok people have already given their initial response to the situation, and I would predict that it was something like the first item below.

1) Briefly and first of all, the people of the Enjebi will be greatly disappointed. And it is not a simple matter of not being able to return to what they think of as home. Marshallese attitudes regarding land, particularly ancestral homelands are difficult for Westerns to appreciate. There is almost a sacred quality about an islander's emotional attachment to his home atoll--and more specifically--those parcels of land within that atoll to which he has rights. While the majority of the islanders living today were born after the 1947 reloaction, such attitudes have been instilled in them by those who knew Eniwetok well. Further, there is the memory that life was indeed better in the past at Eniwetok; indeed, this was true in fact, and the people have tended to idealize the past and believe that it was actually a better state of affairs than it actually was.

2) The proposed resettlement of the entire population on Japtan and Eniwetok has yet other potential implications for the Enjebi people. Authority over land is tantamount to real social and political power. The men and women

who were the senior members or elders of extended family groupings which held rights to the same land had very substantial power and influence over their kinsmen. They were important members of their society--they were people who counted and were significant personages in the community's social life. For the people of Enjebi who would now hold such social positions, the current situation--not being resettled on the land to which they would possess traditional rights--may reduce their status in atoll affairs.

3) Related to point 2 above is the fact that islanders have already been very reluctant to reside on land to which they have no traditional claim. People who are on the land of other islanders have felt insecure and threatened because their status with regard to any right to the land is very uncertain. The Bikinians have had such an experience on Jaluit Atoll when an attempt was made to establish a colony of Bikinians from Kili on Jaluit--this is covered in my book which you know about and the relevant sections are indicated in the index. The Bikini case differs from the current one in that the peoples involved came from separate atolls and not the same one. Nevertheless, the same kind of sentiments about not transgressing on the land of others can and often is manifest in the same atoll population. So, I would anticipate some potential problems along this line. This issue has in fact already come up--see W. Carleton Hawpe's "Status Report on Ujelang--Eniwetok Survey Trip, July-August 1973" dated August 17, 1973 in Eniwetok Master Plan, Volume 2, pages 7-8. In the case Hawpe cites, some of the people of the Eniwetok community felt insecure about their right to reside on Medren (Parry) when it was proposed that all the Eniwetok Island be settled on Medren. Not all members of the Eniwetok community possessed rights on Medren even though that island was within the domain of the Eniwetok Island chief. The situation would be even worse if the Enjebi community were to be settled on Medren. As noted

below, some of them possessed rights to Medren--but far from all of them did and Medren isn't within the Enjebi chiefs domain. In short, it is very probable that many Enjebi people would not at all be pleased with the prospect of settling on Medren for all the reasons indicated.

4) As for the question: Who actually has rights to Medren? This is an extremely complex question for a variety of reasons. The island was at one time held by two brothers who were both chiefs of the Eniwetok Island community (the younger brother succeeded his elder brother upon the latter's death). The two brothers died during the German colonial era (1885-1914)--probably early in that era--and they divided the land among some of their numerous children. The island was not developed at the time, and the children of the two chiefs more or less lost control of the island early in the Japanese period which began in 1914. A Japanese trader established himself on the atoll (a fact reported by Tobin and which appears someplace in the Master Plan or DEIS), and he planted Medren in coconuts for the copra trade. Apparently, the trader led the islanders to believe that he had full right to the copra (claimed he was backed by the Japanese colonial government). So, the islanders did not actually exploit the island's resources from some point in time beginning about the 1920's until their relocation in 1947. Since the islanders had lost control of the island, the normal processes which would have occurred--i.e., people working the land, being allocated rights to the land--did not occur. When I say "being allocated rights to the land," I am making reference to the fact that, in contrast to the matrilineal land tenure system which prevailed in the rest of the Marshalls, the land tenure system at Eniwetok Atoll was bilateral. What this means, and as I noted in my August 30, 1973 memo to Stan Kaplan (see Eniwetok Atoll Master Plan, Volume 2) is: "In most cases, a married couple divided the land they had each inherited among their

children, and a child usually received some land from both his father and mother. As younger islanders matured, they worked the land with their parents. As the parental generation died and as members of the next generation married and produced children, the process was repeated with parents allocating land among their offspring." The point is, all of these processes of dividing and allocating land to younger generations did not actually occur because of the trader's intervention. Today, any islander who is descended from the children of the two chiefs could claim some right to Medren. To complicate issues even more, a good number of the children of the two chiefs were females who produced a great number of children. The grandchildren and great-grandchildren of those females are alive today and can make some claim to Medren. Among these individuals are members of both the Enjebi and Eniwetok communities. Obviously, the situation on rights to Medren is exceedingly complex. The fact that the island was divided into a number of wato makes it even more complicated--it isn't just a matter of who has, or can claim, some right to the island--it is a matter of claims to particular parcels of the island. Some living individuals will now have claim to more than one of the wato because they can now trace descent from more than one of the children of the two chiefs.

5) There are also some problems with regard to Japtan. I received conflicting accounts as to how rights to the island were inherited. One account indicated that the island was inherited by the Enjebi chief and some of his relatives. The other account indicated that the island was inherited by the Eniwetok chiefs and his relatives. The issue/conflict was not resolved prior to the people's relocation in 1947 because the same Japanese trader mentioned above had turned the island into a copra plantation for his own illegal profit and the islanders were not actually working the land themselves. If my information is

correct and if I understand the situation correctly, I think there could be a sizable hassle about who has rights to what on Japtan.

6) With regard to Eniwetok, I think the island represents a problem that will be general to the issue of land rights that will arise as resettlement occurs. As you know, the island is divided into a fairly large number of wato. Certain ones such as Kabnene on the west is covered with the airplane hanger and I forget what else. At the east end, the wato Jabinbok (Jabonbok) is the site of the Coast Guard Station (see Master Plan, Plate No. 21). As people are resettled and if Eniwetok Island becomes a residential island, those who have rights to wato which are covered with concrete, buildings, or other things, will want, in fact demand, that some reallocation of land occur. Others who have land that is relatively free from such liabilities will oppose such a proposal.

This is a general problem for the entire atoll. People who have lost land, either because land has been destroyed (as in the case of the two islands which were blasted out of existence), or the land which cannot be used because of radiation dangers (as in the case of Runit), will want to have some redistribution of land occur. Those who lost will desire redistribution; those who have lost nothing or little will resist.

This also is reflected in Hawpe's report to Gilmore. Look at page 3 of the report. Hawpe reports that there was an argument which caused a split ". . . between the reformers--those wishing a new land reapportionment, and the traditionalists who backed the status quo."

8) In Volume 1 of the DEIS, it is noted that there is ". . . a demise of traditional system" and some indication that ". . . the old division between Enjebi and Eniwetok peoples has lost much of its meaning." (section 3, page 51). This is from the memo I wrote for Kaplan and has been true on Ujelang because

the people have been residing on the same island and have formed a common council. I would not be at all surprised if hassles over land at Eniwetok Atoll today will lead to some divisions of the population, and one potential line of division may be based on the traditional split of the population between the two communities as the members of each emerge as separate interest groups with regard to land.

9) Obviously, I am suggesting that there will be some hassles over land rights. At the same time, I am rather certain that it is an area that outsiders should not get involved in. The British colonial government in the Gilbert and Ellice Island Crown Colony attempted to survey, mark, and register land parcels in the atolls of the Gilberts. It appeared to administrators to be a relatively simple affair. In contrast, it took 50 years of court cases over disputed land rights, land boundaries, etc. The recent attempt to do something similar for the entire Marshalls has been abandoned as far as I know.

The business of land and rights to it is something that is best left for the people to work out for themselves, as painful as the process might be. My own discussions with people about land rights and the histories of land parcels always brought up and rekindled old disputes as the above mentioned case of Japtan may suggest.

As a practical consequence for the rehabilitation program, disagreements over land among the Eniwetok people could result in delays in planning or implementation of a facet of the program, But, in the last analysis, I believe that the best course of action is to spell out in detail what can in fact be done in the way of rehabilitation, describe the implications, and then let them decide what they'll do about land rights. The best way to generate some animosity would be for an outsider to get involved in their land affairs.

10) For many of the reasons outlined above, I doubt that the Eniwetok Island community would ever be willing to give up Eniwetok Island for the collective ownership of the entire atoll population for the purpose of establishing the Eniwetok Corporation--or whatever it is or may be called.

11) I have previously stressed that in light of the increased size of the total population, the matter of allowing the people to keep Ujelang as well as having Eniwetok returned to them should be seriously explored. Considering the fact that so much of Eniwetok is now not available to the people, it seems all the more important to explore this possibility. Such a move would probably cushion the impact of the loss of the northern portion of the atoll.

The above are my reactions. I will certainly be interested in following the course of events. Aside from land, an item that should be considered: What will the extensive use of outhouses do to the fresh water lens of each of the inhabited islands?

I hope the above is of some use and outlines the basic problems and issues that are potentially involved.

SANITARY PLAN FOR ENEWETAK ATOLL

by

E. R. QUAM
Chief Civil Engineer

March 18, 1975

HOLMES & NARVER, INC.

A Resource Sciences company

Advanced Technology/Engineering/Construction/Management/Maintenance & Operations

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1. INTRODUCTION

This study has been performed for the purposes of determining the material and equipment requirements for waste water treatment and disposal and also for comparing the costs of the several methods of waste water disposal. Since Enewetak Atoll was activated as a nuclear test site 28 years ago there has been no waste water treatment installed. Sewage effluents have been pumped into the lagoon or ocean through outfalls located away from the shore. This is currently the practice on the one occupied island, Enewetak. This study investigates methods of treating waste water through the various phases of cleanup, rehabilitation and resettlement of the atoll.

The waste water disposal methods compared are:

Case 1. 400-man camp, Enewetak Island.

a. Rehabilitation of existing sewers, lift stations and lagoon outfalls. (No treatment).

b. Rehabilitation of existing sewers, installation of five new lift stations and 60,000 gpd sewage treatment plant.

Case 2. Temporary quarters, Japtan Island.

a. Rehabilitation of existing collection system and outfall.

b. Installation of 17,500 gpd sewage treatment and collection system.

Case 3. Permanent housing, Enewetak Island.

a. Connection to sewage treatment system (Case 1b) if installed for 400-man camp.

b. Installation of septic tank systems for housing clusters.

Case 4. Permanent housing, Medren Island.

a. Installation of new septic tank systems for housing clusters.

b. Connection to 17,500 gpd sewage treatment plant (Case 2b) relocated from Japtan temporary camp.

Case 5. Permanent housing, Japtan Island.

a. Installation of new septic tank system for housing clusters.

2. 400-MAN CAMP, ENEWETAK ISLAND (CASE 1)

2.1 WASTE WATER ANALYSIS

Fresh water use - cooking, bathing, laundry	=	70 gpcd
Salt water use - flushing	=	30 gpcd
Total	=	100 gpcd

(gpcd = gallons per capita per day)

Chlorides from 30% salt water = 18,000 x .30 = 5,400 ppm

This concentration will require at least a 50 to 75 percent larger "extended aeration" plant than a plant using only fresh water.

2.2 REHABILITATE EXISTING SANITARY SEWER SYSTEM - ENEWETAK ISLAND (CASE 1a)

This plan would include the complete rehabilitation of the existing sanitary sewer system on Enewetak Island. The present installation is a collection system which deposits untreated effluent into the lagoon from seven outfalls, and into the ocean from one outfall located in the vicinity of the airfield.

This plan would involve the following:

a. Inspection and cleaning of 120 l.f. cast iron pipe.

b. Inspection and cleaning of 390 l.f. steel force main.

c. Inspection and cleaning of 12,600 l.f. vitrified clay pipe, 4", 6" and 8" diameters.

d. Inspection and repair of 32 sanitary manholes.

e. Inspection, repair and replacement of 8 outfall lines.

f. Replacement of two duplex sewage lift pumps.

(The foregoing scope from "Engineering Study for a Cleanup Plan" HN-1348.1.)

Estimated peak flow from 400-man camp, using a peak flow factor of 5:

$$400 \times 100 \text{ gpcd} = \frac{40,000}{960} = 42 \text{ gpm} \times 5 = 210 \text{ gpm (for 16 hours/day).}$$

This flow rate would be within the capabilities of the present system after proper rehabilitation.

2.3 SEWAGE TREATMENT PLANT (CASE 1b)

2.3.1 Size of Plant

The sewage treatment plant would provide primary and secondary treatment and chlorination before dumping the effluent into the lagoon.

400 persons @ 100 gpd = 40,000 gpd (gallons per day)

40,000 gallon plant @ 150 percent* = 60,000 gpd

*For effluent reduction of BOD of 85 to 90 percent.

Since the chlorides are slightly over 5,000 ppm in lieu of 7,000 ppm, the 60,000 gpd plant should provide an effluent with a BOD and suspended solid reduction of 85 to 90 percent. Chlorination of this effluent with a dosage of 25 ppm will provide a safe waste water discharge into the lagoon. A 60,000 gpd unit will require approximately 10 hp for operation.

2.3.2 Lift Stations

It will be necessary to rehabilitate the existing collection system to transport the sewage from its sources to the treatment plant. Rehabilitation will begin at the Coast Guard Station N 35875 E 124080 at the north end of the island and five new lift stations will be required at the existing lagoon outfalls. The new treatment plant will be located south of the main camp area, approximately at coordinates N 32700 E 121350 (see Drawing G-1). The plant will require a new outfall from the site to the lagoon.

2.3.2.1 Lift Station and Pump Computations. The new lift station characteristics and pump requirements are listed in Table G-1. These values were determined by means of the following calculations, using Lift Station 1 as an example.

Data:
- Peak flow = 150 gpm
- Length of force main = 1,950 ft
- Static head requirement = 8 ft
- Head loss coefficient, C = 130
- Friction head loss, h_f = 16.2 ft/1000 ft

Calculations:

$$\text{Total friction head loss} = \frac{1,950}{1,000} \times 16.2 = 31.6 \text{ ft}$$

$$\text{Static head} = \underline{8.0 \text{ ft}}$$

$$\text{Total head} = 39.6 \text{ ft}$$

The pump selected for this application would be able to raise 150 gpm through 41 ft, using a 3-hp motor. The pumps are duplex pumps, installed in pairs, one of which is kept inoperative as a spare.

2.4 ESTIMATED COSTS - 400-MAN CAMP, ENEWETAK

2.4.1	Rehabilitate existing sewers, 2 new lift stations and outfalls (no treatment). (No electricity incl'd)	$ 70,000.00
2.4.2	Rehabilitate existing sewers (including Coast Guard lift station), install five new lift stations, force mains and sewage treatment plant. (No electricity incl'd)	$223,950.00

3. TEMPORARY HABITATION DURING EARLY RETURN AND CLEANUP PROGRAMS, JAPTAN ISLAND (CASE 2)

3.1 BASIC DATA

Population approximately 100 persons @ 100 gpd = 10,000 gallons. Increase due to use of brackish water = 75 percent. (Dwg. No. G-2)

3.2 REHABILITATE EXISTING SANITARY DISPOSAL SYSTEM - JAPTAN ISLAND (CASE 2a)

This operation would consist of the rehabilitation of the existing disposal system on Japtan Island. The present installation is a collection system (capable of serving approximately 500 inhabitants) which deposits untreated effluent into the lagoon. It would include the inspection, cleaning and repair of the existing facilities with the approximate cost of $11,000.00.

3.3 TREATMENT PLANT (CASE 2b)

3.3.1 Size of Plant

17,500 gpd
5 hp required for plant operation.

3.3.2 Lift Stations

Plant will require one lift station and a collection system. The collection system will consist of 1,050 ft of 8" PVC pipe and three manholes.

TABLE G-1: NEW LIFT STATION CHARACTERISTICS AND PUMP REQUIREMENTS - ENEWETAK ISLAND SEWAGE SYSTEM (CASE 1b)

Lift Station No.	Lift Station Location	Peak Flow gpm	Line Segment ft	Pump Head Requirements			Pump Characteristics			
				Friction ft	Static ft	Total ft	Capacity gpm	Speed rpm	Horse-power	Head ft
1	N34620 E122940	150	1950	31.5	8	39.5	150	1750	3	41
2	N33160 E121680	200	650	17.5	18	35.5	200	1750	5	36
3	N30845 E118110	40	710	1.6	10	11.6	40	1750	1/2	14.2
4	N31160 E118740	60	1880	8.9	10	18.9	60	1750	3/4	19.8
5	N31960 E120400	60	1280	6.05	10	16.1	60	1750	3/4	19.8

Note: Coast Guard Lift Station is existing but should be rehabilitated making total to be (6).

Lift Station = $\frac{10,000}{750}$ = 13.5 gpm

Peak load = 13.5 x 5 = 67 gpm
Use 80 gpm each, duplex pumps with

1150 rpm
3/4 hp each
18.7' head

Equipment and materials -

300'-4" PVC force main
1050'-8" PVC pipe
3 - manholes
1 - duplex lift station

3.4 ESTIMATED COSTS - TEMPORARY HABITATION, JAPTAN

3.4.1	Rehabilitate existing sanitary facilities	$ 11,000.00
3.4.2	Install new collection system, manholes, lift station and treatment plant (No electricity incl'd)	$ 27,662.00

4. PERMANENT HOUSING, ENEWETAK ISLAND (CASE 3)

4.1 HOUSING CONNECTED TO SEWAGE TEATMENT PLANT REMAINING FROM CLEANUP OPERATION (CASE 3a)

4.1.1 Sewage Treatment Plant

The sewage treatment plant installed for the 400-man camp is more than adequate for the demand that would be contributed by the permanent residents.

400-man camp treatment plant = 40,000 gpd
Housing demand - 66 homes @ 4/house = 264 persons
264 x 80 gpcd = 21,120 gpd
Size of Treatment Plant = 60,000 gpd (@ 150% - see para. 2.3.1)

This low demand on the 60,000 gallons (@ 50%) plant will produce an excellent effluent provided that the plant is properly operated and maintained.

4.1.2 Collection System

The collection system from the housing clusters will require the installation of 8" PVC pipe with manholes every 300 ft on center. The sewer line slope would be approximately 0.4%. Lift stations will be required at approximately 1200-ft intervals each with 300 ft of force main. (Dwg. G-3)

4.1.3 Lift Station Requirements (beginning at the South End of the Island)

Kabnene Wato to Mwillimor Wato

21 homes @ 4 persons = 84 x 80 = 6720 gpd

12 hour base $\frac{6720}{720}$ = 9.3 gpm x 5 = 46.5 gpm peak

Lift Station No. 1

$\frac{6720}{40}$ = 168 min/day = 2.80 hr/day

300 ft. force main @ 2.5'/1000	=	0.75'
Static head	=	9.0'
Use		10.0'

Duplex pump 40 gpm

1150 rpm
1/2 hp motor
Head = 11.1 ft

Sewer line = 1200' of 8" PVC and 4 manholes

1 lift station 300'-4" PVC force main

The characteristics and pump requirements of the other line sections are shown in Table G-2.

4.2 SEPTIC TANKS AND LEACH FIELDS (CASE 3b)

4.2.1 Requirements

Fresh water, bathing and cooling	=	60 gpcd
Brackish water flushing	=	20 gpcd
Total contribution	=	80 gpcd

TABLE G-2: LIFT STATION CHARACTERISTICS AND PUMP REQUIREMENTS FOR PERMANENT HOUSING ON ENEWETAK ISLAND, (CASE 3a)

Lift Station No.	Watos	Homes in Section	Peak Flow gpm	Line Segment ft	Pump Characteristics			
					Capacity gpm	Speed rpm	Horse-power	Head ft
1	Kabnene to Mwillimar	21	47	300'-4" 1200'-8" 4 manholes	40	1150	1/2	11.1
2	Larej to Bukinam	7	15.5	300'-4" 1200'-8" 4 manholes	40	1150	1/2	11.1
3	Kabinbet to Mokoni	11	24.6	300'-4" 1200'-8" 4 manholes	40	1150	1/2	11.1
4	Lositak to Tuon	17	38	300'-4" 1200'-8" 4 manholes	60	1150	1/2	12.9
5	Mwonjini to Loksbar	4	9	400'-4" 1200'-8" 4 manholes	60	1150	3/4	19.8
6	Kilorok to Lisimlok	4	13.5	150'-4" 1200'-8" 4 manholes	40	1150	3/4	21

Septic Tank

24-hr retention + 75% increase for brackish water + 25% sludge Storage = 100% increase for design purposes.

Single house - 4 persons @ 80 gpd = 320 gpd

320 + (100% x 320) = 640 gpd

$$\frac{640 \text{ gpd}}{7.48 \text{ g/cu ft}} = 86 \text{ cu ft tank} = 3'W \times 8'\text{-}3''L \times 3'\text{-}6''D.$$

(See Table G-3 Housing Cluster for 2, 3, 4 & 5 houses)

The placement of the septic tanks and the flow of water is illustrated in Sketch A.

4.3 ESTIMATED COSTS - PERMANENT HOUSING, ENEWETAK

4.3.1 Housing connected to existing treatment plant installation of 6 lift stations, force mains and collection sewers and manholes (Case 3a) (No electricity incl'd)	$161,197.00
4.3.2 Installation of septic tanks and leach fields for housing clusters (Case 3b)	$ 62,857.00

5. PERMANENT HOUSING, MEDREN ISLAND (CASE 4)

Due to the long period of disuse and the deteriorated condition of the existing collection and outfall system on Medren, no attempt is made in this study to estimate rehabilitation of the system.

5.1 SEPTIC TANKS AND LEACH FIELDS (CASE 4a)

5.1.1 Requirements

Fresh water bathing & cooking	= 60 gpcd
Brackish water flushing	= 20 gpcd
Total	= 80 gpcd

Septic tank

24-hour retention + 75% increase for brackish water + 25% sludge storage or 100% increase

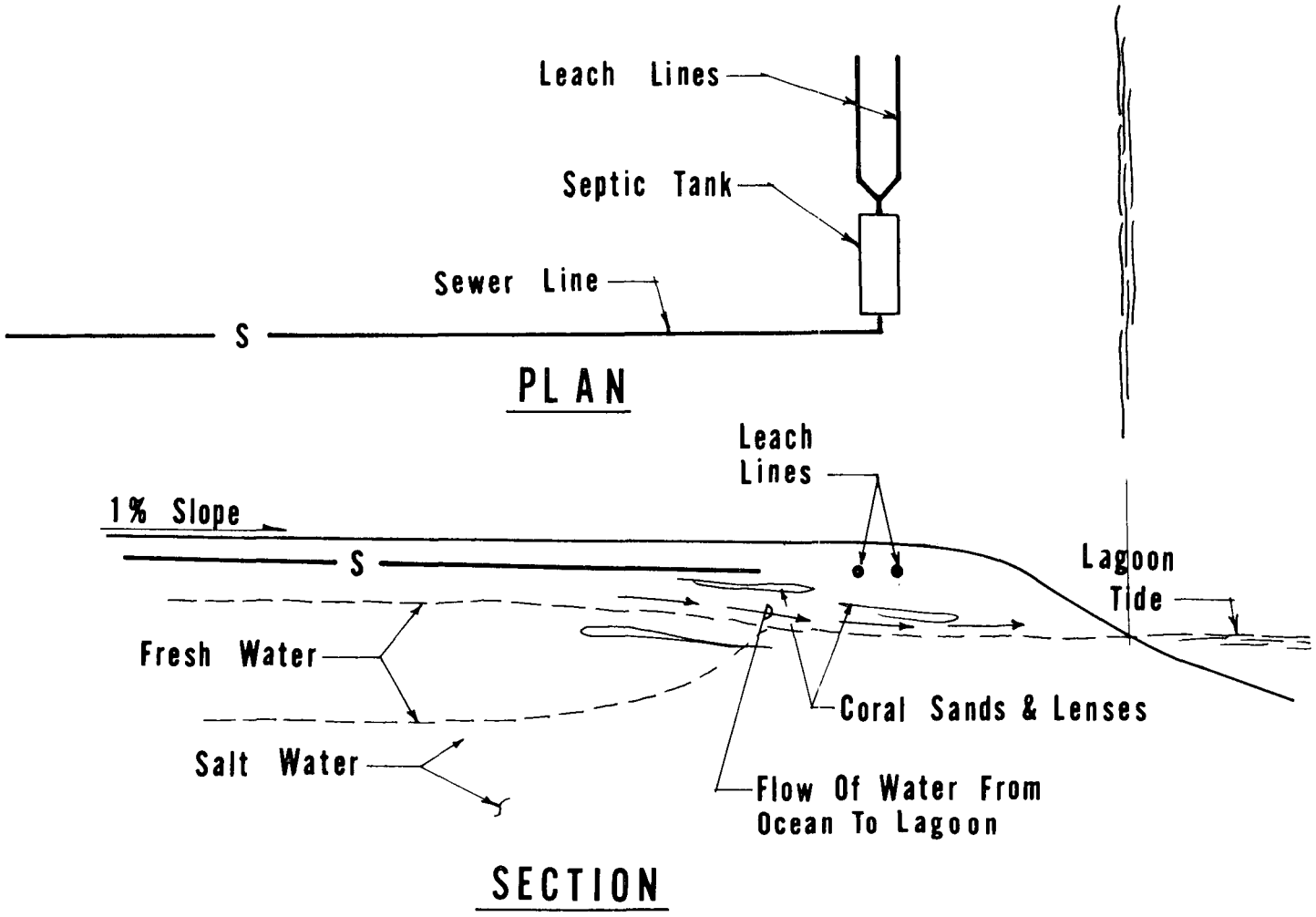
TABLE G-3: LEACH FIELDS AND LINES REQUIRED FOR PERMANENT HOUSING ON ENEWETAK ISLAND - CASE 3b

Houses Per Group	Waste Water/ Group gpd	Leach Field* Area Required sq. ft.	Leach Line** Length Required ft.	Septic Tank			Estimated Cost per Cluster $
				Length ft. -in.	Width ft. -in.	Depth ft. -in.	
1	320	80	20	8-3	3-0	3-6	1250
2	640	160	40	11-0	4-0	4	1670
3	960	240	60	14-6	4-6	4	3030
4	1280	320	80	17-3	5-0	4	3450
5	1600	400	100	22-2	5-0	4	4620

*Fine sand and coral - 4 gal/sq. ft. = daily absorption capacity.

**4 sq. ft. = leach area per foot of pipe. Leach line diameter = 4 in.

SKETCH A - SEPTIC SYSTEM INSTALLATION



The placement of the septic tanks and leach lines near the lagoon and above high tide and ground water will provide good leaching areas. The effluent from the septic tanks will leach through the coral sands and lenses thereby purifying the effluent as it enters the salt water. As the flow is toward the lagoon, the fresh water will not be contaminated. The salt water in the sands and lagoon will soon destroy any coliform that may be present.

5-house group

5 x 4 = 20 persons @ 80 gpd = 1600 gpd
1600 gpd + (100% x 1600) = 3200 gpd

$$\frac{3200 \text{ gal}}{7.48 \text{ gal/cu ft}} = 428 \text{ cu ft}$$

∴ size: 5'W x 22'-2"L x 4'D

The leach field and septic tank requirements of other housing groups are shown in Table G-4.

5.2 HOUSING CLUSTERS CONNECTED TO SEWAGE TREATMENT PLANT - MEDREN ISLAND (CASE 4b)

5.2.1 Sewage Treatment Plant

Sewage treatment plant relocated from Japtan after cleanup camp is removed. Treatment plant for 17,500 gpd fresh and brackish water. (Dwg. G-4)

Medren Population

47 houses @ 4 = 188 @ 80 gpd = 15,000 gpd

Added chlorides of approximately 4,500 ppm added to a 17,500 gpd plant should produce an effluent with 90 to 95% reduction of BOD and suspended solids, provided the plant is properly operated and maintained.

5.2.2 Lift Stations

Jitoenmwenelap Wato to Lomake Wato

18 houses @ 4 = 72 x 80 = 5760 gpd

12-hour base $\frac{5760}{720}$ = 8.0 gpm x 5 = 40 gpm peak

Lift Station No. 1

$\frac{5760}{40}$ = 144 min = 2.4 hrs per day

Force main 300'-4" H_f = 2.5 x 0.3 = .75'
Static = 9.0'
Use = 10.0'

TABLE G-4: LEACH FIELDS AND LINES REQUIRED FOR PERMANENT HOUSING ON MEDREN ISLAND (CASE 4a)

Houses per Group	Waste Water/ Group gpd	Leach Field* Area Rqd sq ft	Leach Line** Length sq ft	Septic Tanks				Estimated Cost/ Cluster $
				Volume gal	Length ft. -in.	Width ft. -in.	Depth ft	
1	640	160	40	1280	11-0	4-0	4	1250
2	960	240	60	1920	14-6	4-6	4	1670
3	1280	320	80	2660	17-3	5-0	4	3030
4	1600	400	100	3200	22-2	5-0	4	3450

*Fine sand and coral 4 gal/sq ft = daily absorption capacity.
**4 sq ft = leach area per foot of pipe leach line diameter = 4 in.

Use 40 gpm duplex pump

1150 rpm
1/2 hp motor
Head = 11.0 ft

Use 1200'-8" PVC sewer pipe - 4 manholes
300'-4" PVC force main

Other lift station and pump characteristics are shown in Table G-5.

5.3 ESTIMATED COSTS, PERMANENT HOUSING, MEDREN

5.3.1	Installation of septic tank and leach field for housing clusters	$ 42,438.00
5.3.2	Installation of sewage treatment plant (from Japtan temporary housing usage) and collection systems for housing clusters	$127,267.00

6. PERMANENT HOUSING, JAPTAN ISLAND (CASE 5)

Inasmuch as only four families have elected to settle permanently on Japtan, the sewage treatment plant recommended for the temporary housing, Case 2, is of much greater capacity than needed. Therefore, a septic tank system is recommended for this situation.

6.1 SEPTIC TANK SYSTEM

6.1.1 Housing Area

4 residences @ 4 persons = 4 x 4 = 16

16 @ 80 gpd = 1280 gallons

6.1.2 Septic Tank

1280 + (100% x 1280) = 2560 gal capacity
2560/7.48 = 342 cu ft
Use 5'W x 17'-3"L x 4'D

6.1.3 Leach Line

80 lineal feet required.

TABLE G-5: LIFT STATION CHARACTERISTICS AND PUMP REQUIREMENTS FOR PERMANENT RESIDENCE ON MEDREN ISLAND - CASE 4b

Lift Station Number	Watos	Homes in Section	Peak Flow gpm	Total Flow gpd	Force Main ft.	Pump Characteristics			
						Capacity gpm	Speed rpm	Horse-power	Head ft.
1	Jitoenmwenelap to Lomake	18	40	5,760	300	40	1150	1/2	11.0
2	Lowit	2	44.9	6,400	300	40	1150	1/2	11.1
3	Lonen to Wotto	16	35.6	11,520	300	40	1150	1/2	11.1
4	Mwenelap to Lobet	9	20	14,400	300	40	1150	1/2	11.0
5	Jabonbok	2	22.5	15,040	300	40	1150	3/4	17.8

6.2 ESTIMATED COSTS, PERMANENT HOUSING, JAPTAN

6.2.1 Installation of Septic Tank System $ 3,449.00

7. CONCLUSION

7.1 WASTE WATER DISPOSAL SYSTEM

7.1.1 400-Man Camp - Enewetak Island (Case 1)

Over the last 28 years Enewetak Atoll has been occupied by personnel whose numbers have ranged from approximately twenty to several thousands. Past practice has included periodic inspections of sanitary outfall conditions in the lagoon by medical personnel. During this period there were no known instances of harmful effects from the use of the existing sanitary waste systems. On this basis it does not appear necessary or feasible to install a sewage treatment system for the 400-man camp.

Although a sewage treatment system for this application would appear to be desirable from the aspect of eliminating the discharge of raw sewage into the lagoon, the cost factor, the scheduled duration of operations, and past experience at Enewetak do not favor this disposal method.

The cost differential between rehabilitating the existing collection system and installing a new treatment system is approximately $150,000. This is exclusive of maintenance and operation costs. Both systems include some electrically driven mechanical equipment. The existing system has two duplex lift stations while the treatment system would have five plus the treatment plant. It can be assumed that the treatment system would be somewhat more expensive to operate and maintain.

The 400-man camp is scheduled to be operational for a 24-month period, after which all facilities will be disposed of in accordance with governing regulations. It is understood that the necessary technical skills and knowledge required for operation and maintenance of a sewage treatment system would not be available from the TTPI or from the atoll residents. In view of the short duration of camp operation and the lack of expertise among the permanent population it would not be feasible or practical to install a sewage treatment system on Enewetak Island.

7.1.2 Temporary Quarters - Japtan Island (Case 2)

For the reasons stated in 7.1.1 above, it would appear feasible to rehabilitate the existing collection system and outfall on Japtan for use by the Enewetak people during their temporary occupancy of the island. However, since the TTPI has planned to use benjo over open pits for the

50 to 60 people in temporary residence, rehabilitating the existing system would not be economically feasible. The benjos and garbage pits are planned to be located near the shore, away from the central part of the underground fresh water lens. This arrangement appears to be suitable for the small size of the population and would involve a minimum cost.

7.1.3 Permanent Housing - Enewetak, Medren and Japtan Islands (Cases 3, 4 and 5)

Considering the immediate and long-range requirements of the Enewetak people, sanitary waste disposal could best be handled by the installation of septic tank systems. Sewage treatment systems of any size would create problems in operation and maintenance, and would also require electrical power for operation. Since there would be little likelihood of operational and maintenance skills being available and no power would be available to operate a treatment system, the installation of such a plant would be unfeasible. In addition, assuming these were available the costs involved would probably be beyond the people's ability to sustain.

The septic tank systems, coupled with water seal toilets, would represent an upgrading in sanitary waste handling as compared to current use of open pit benjos. The tanks and leach fields would be located adjacent to the lagoon shore where effluent would filter through the coral before entering the lagoon. These lagoon-side locations would provide assurance that the islands' fresh water lens would not be polluted as the underground water tends to migrate through the coral from the ocean toward the lagoon (see page 11). Also the septic tank systems requirements are minimal as no fuel or electrical power would be required, no manpower for operation would be needed and the systems would be dependable.

7.1.4 Recommendations

- Rehabilitate the existing waste water disposal system to serve the 400-man camp on Enewetak.
- Utilize open pit benjos for the temporary residents on Japtan in accordance with the Master Plan.
- Install septic tank and leach field systems to serve the housing clusters for the permanent residents of Enewetak, Medren, and Japtan Islands in accordance with the Master Plan.

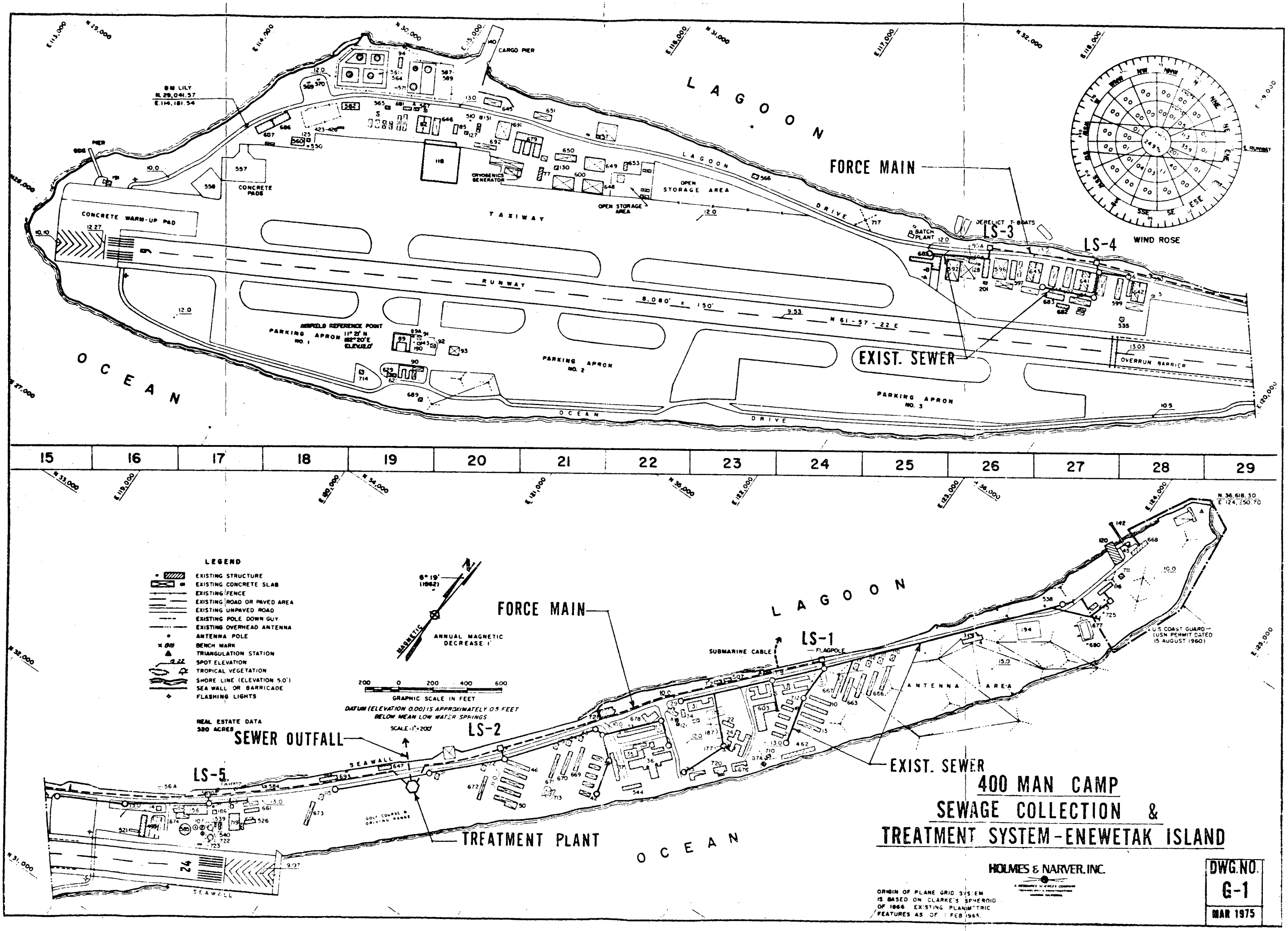
TABLE G-6

WASTE WATER DISPOSAL METHOD

COST/SYSTEM

Case No.		Rehabilitation of Existing System	New Sewage Treatment System	New Septic Tank System
1	400-Man Camp	$70,000.00	$223,950.00	N/A
2	Temp. /Japtan	$11,000.00	$ 27,662.00	N/A
	Permanent			
3	a. Enewetak	N/A	$161,197.00	$62,857.00
4	b. Medren	N/A	$128,935.00	$42,438.00
5	c. Japtan	N/A	$ 27,662.00	$ 3,449.00

Note: All electrical facilities for the 400-Man - Camp and Temporary Services for Japtan for cleanup and early inhabitants would be serviced from existing facilities, but when the islands are available for permanent inhabitants all new electrical services would have to be installed.


LAGOON
OCEAN
CARGO PIER
BM LILY
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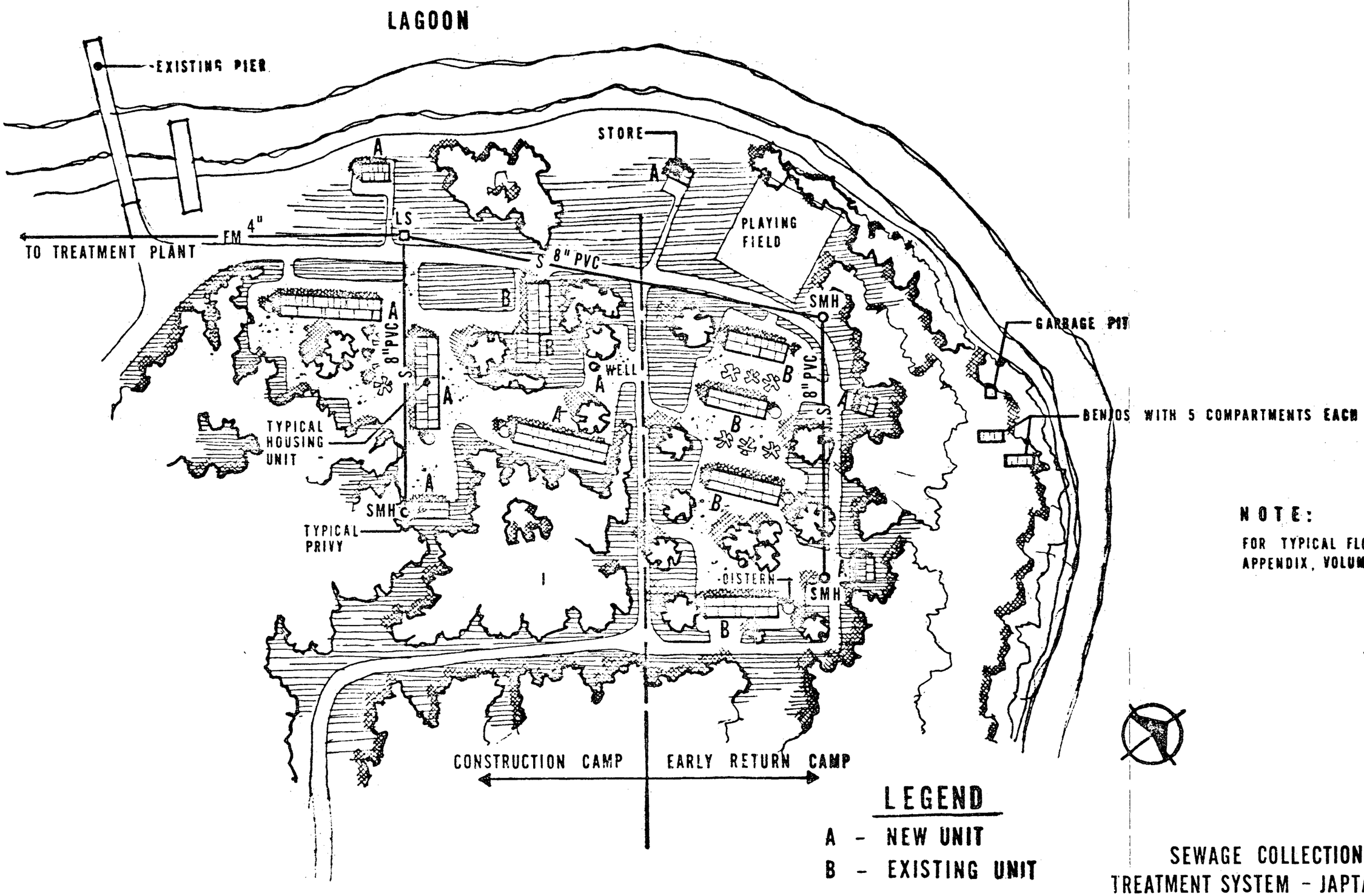
E 114,181.54
PIER
CONCRETE PADS
CONCRETE WARM-UP PAD
TAXIWAY
CRYOGENICS GENERATOR
OPEN STORAGE AREA
OPEN STORAGE AREA
LAGOON DRIVE
FORCE MAIN
DERELICT T-BOATS
BATCH PLANT
LS-3
LS-4
WIND ROSE
RUNWAY
8,080' x 150'
N 61-57-22 E
AIRFIELD REFERENCE POINT
PARKING APRON NO. 1
PARKING APRON NO. 2
PARKING APRON NO. 3
EXIST. SEWER
OVERRUN BARRIER
OCEAN DRIVE
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
LEGEND
EXISTING STRUCTURE
EXISTING CONCRETE SLAB
EXISTING FENCE
EXISTING ROAD OR PAVED AREA
EXISTING UNPAVED ROAD
EXISTING POLE DOWN GUY
EXISTING OVERHEAD ANTENNA
ANTENNA POLE
BENCH MARK
TRIANGULATION STATION
SPOT ELEVATION
TROPICAL VEGETATION
SHORE LINE (ELEVATION 5.0')
SEA WALL OR BARRICADE
FLASHING LIGHTS
6° 19' (1962)
MAGNETIC
ANNUAL MAGNETIC DECREASE 1'
GRAPHIC SCALE IN FEET
DATUM (ELEVATION 0.00) IS APPROXIMATELY 0.5 FEET BELOW MEAN LOW WATER SPRINGS.
SCALE - 1" = 200'
REAL ESTATE DATA
320 ACRES
SEWER OUTFALL
LS-2
LS-5
LS-1
FLAGPOLE
SUBMARINE CABLE
FORCE MAIN
ANTENNA AREA
U.S. COAST GUARD (USN PERMIT DATED 15 AUGUST 1960)
N 36,618.30
E 124,250.70
SEAWALL
GOLF COURSE & DRIVING RANGE
TREATMENT PLANT
EXIST. SEWER
400 MAN CAMP
SEWAGE COLLECTION &
TREATMENT SYSTEM-ENEWETAK ISLAND
HOLMES & NARVER, INC.
ORIGIN OF PLANE GRID SYSTEM IS BASED ON CLARKE'S SPHEROID OF 1866. EXISTING PLANIMETRIC FEATURES AS OF 1 FEB 1964.
DWG. NO.
G-1
MAR 1975



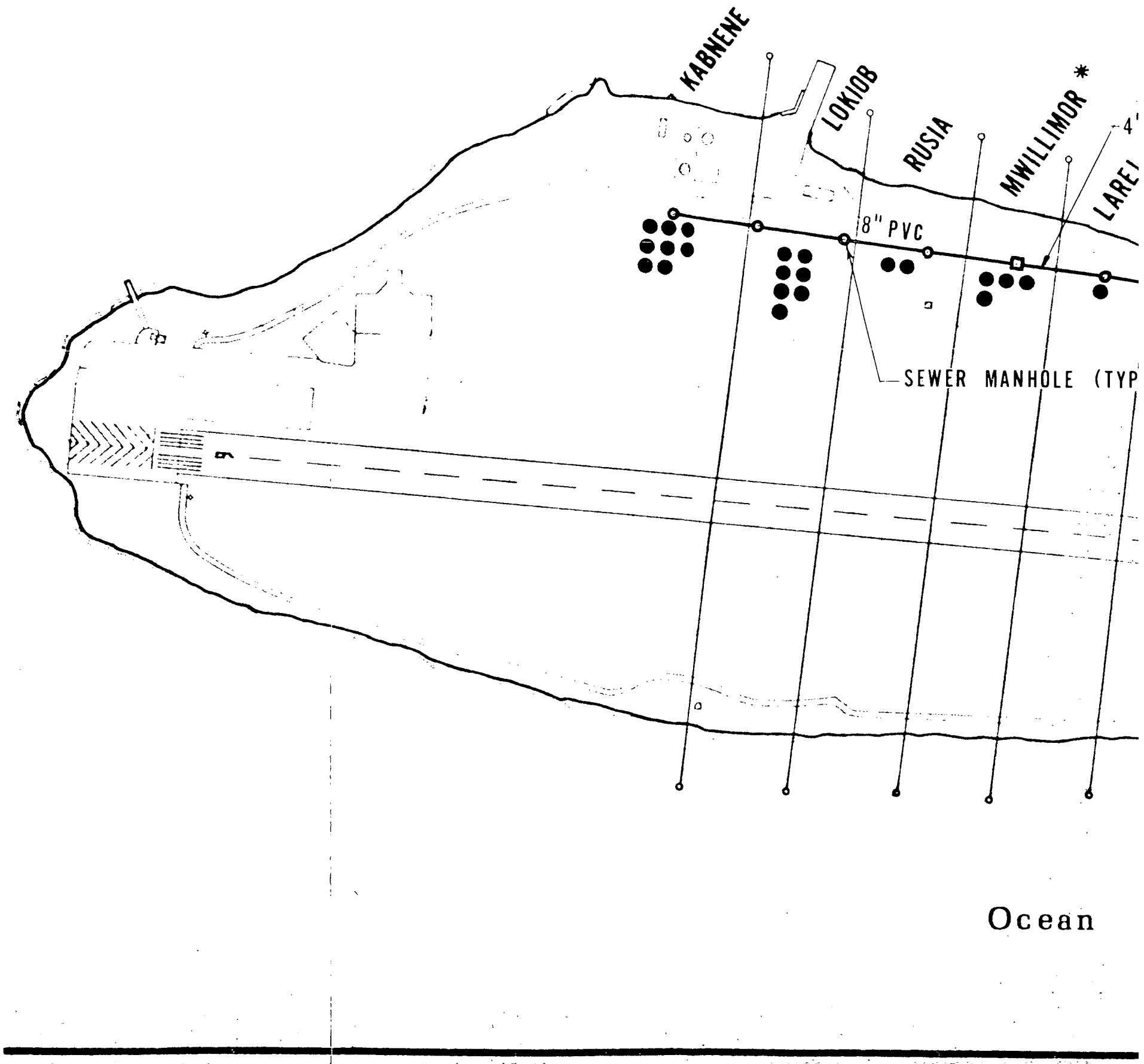
NOTE:

FOR TYPICAL FLOOR PLANS SEE APPENDIX, VOLUME 2

SEWAGE COLLECTION & TREATMENT SYSTEM - JAPTAN ISLAND

HOLMES & NARVER, INC.

DWG NO G-2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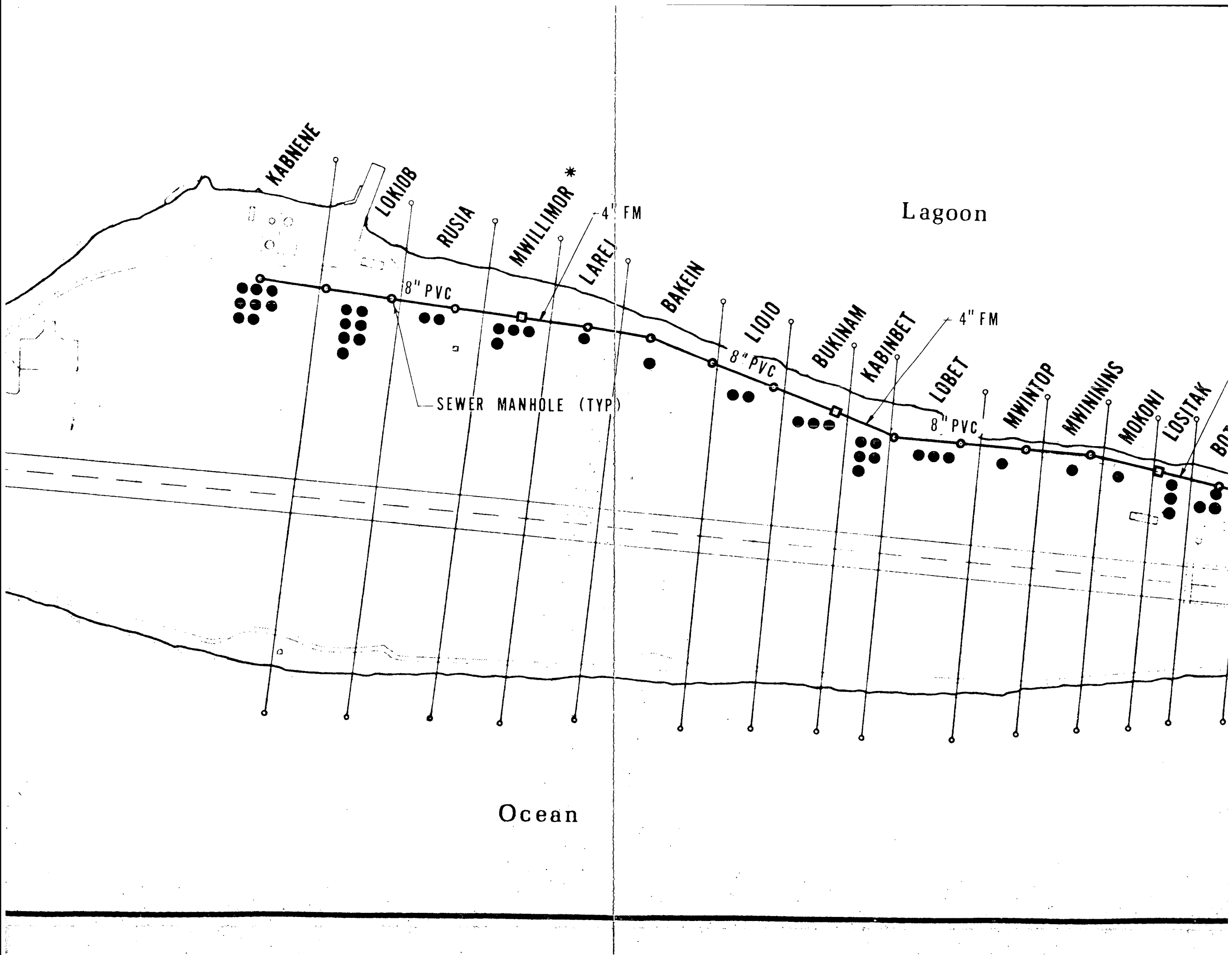
RUSIA
MWILLIMOR *
LAREI
8" PVC
SEWER MANHOLE (TYP
Ocean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MWILLIMOR *
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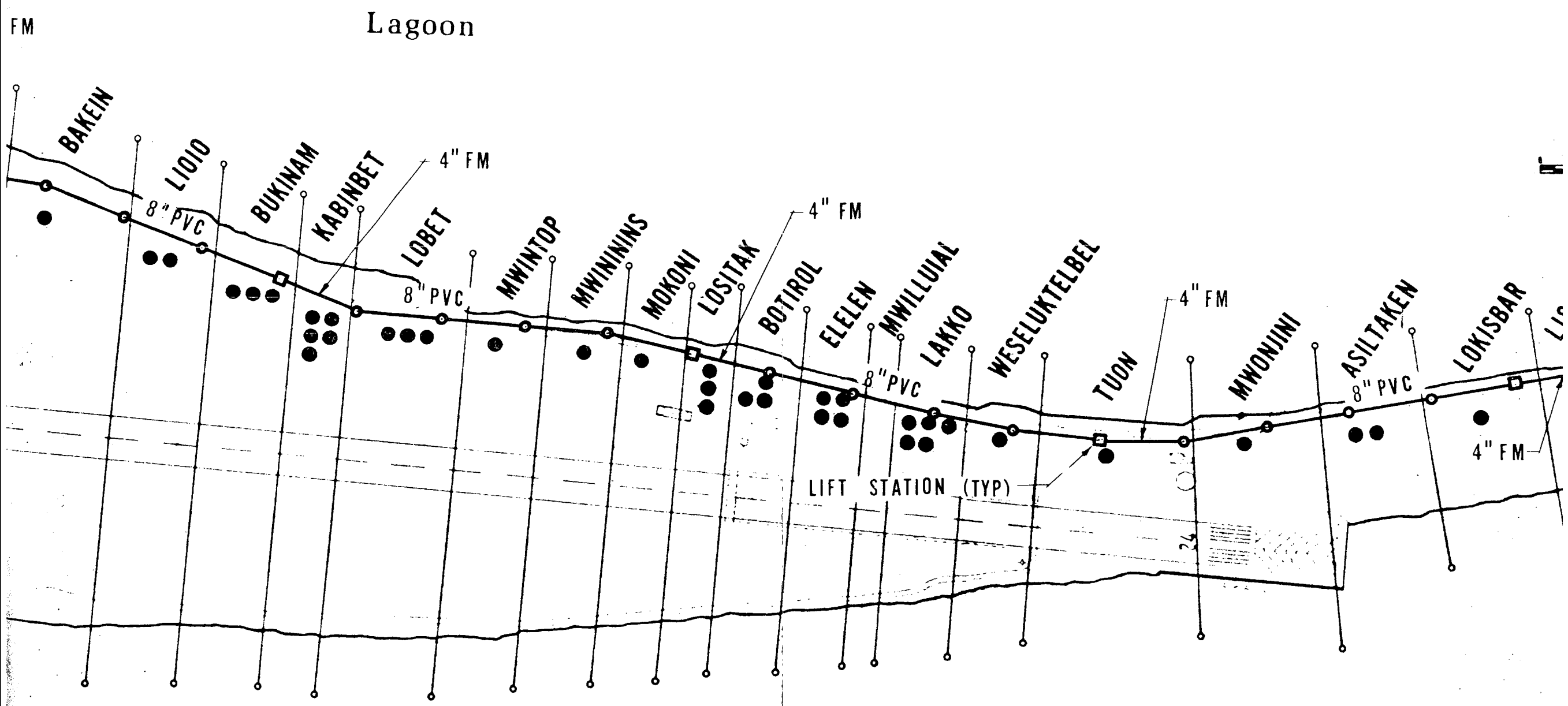
8" PVC
SEWER MANHOLE (TYP)
Lagoon
Ocean


FM
Lagoon
BAKEIN
LIOIO
BUKINAM
KABINBET
LOBET
MWINTOP
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MOKONI
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BOTIROL
ELELEN
MWILLUIAL
LAKKO
WESELUKTELBEL
TUON
MWONJINI
ASILTAKEN
LOKISBAR
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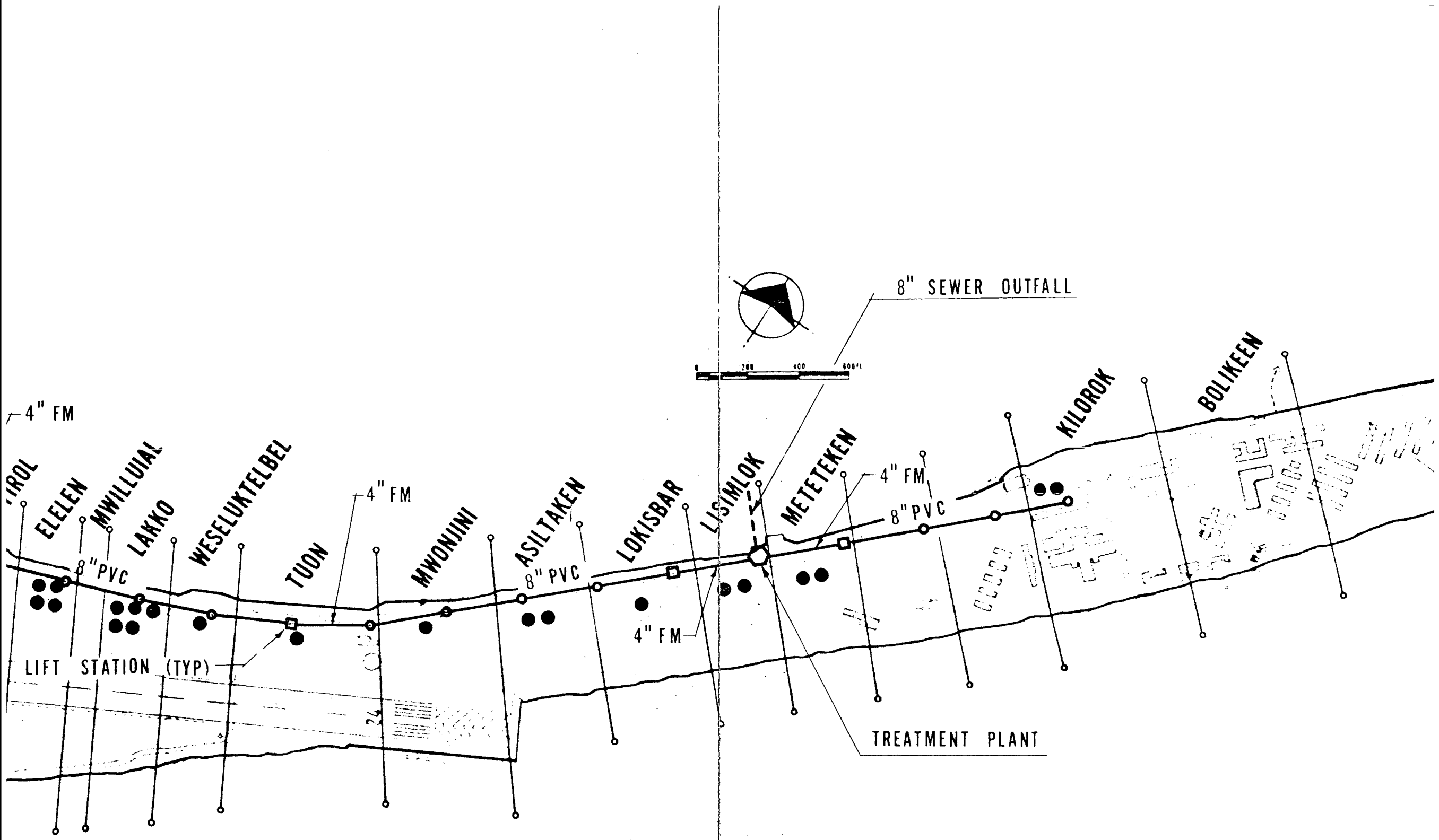
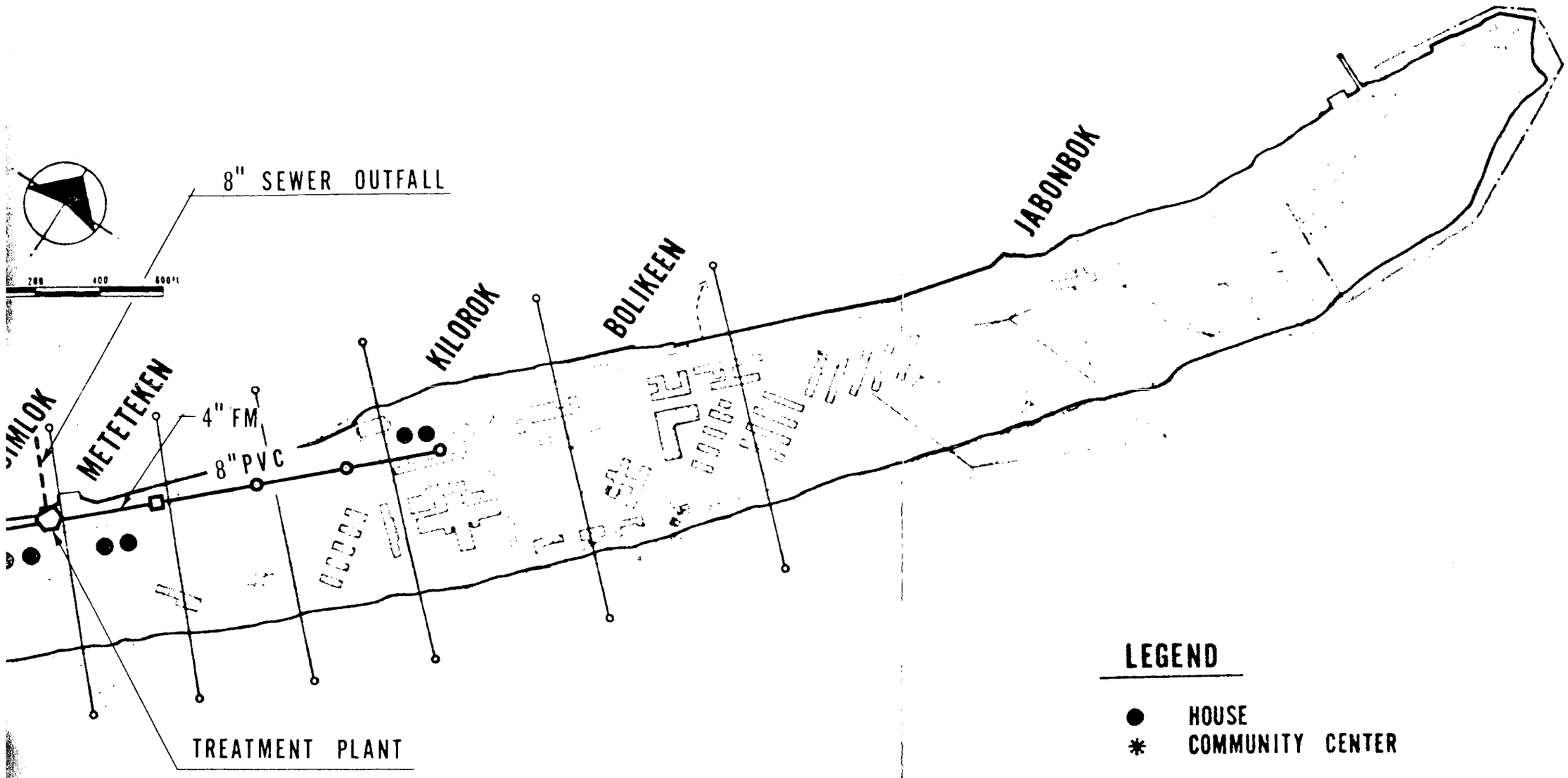
8" PVC
8" PVC
8" PVC
4" FM
4" FM
4" FM
4" FM
LIFT STATION (TYP)


8" SEWER OUTFALL
4" FM
ELELEN
MWILLUIAL
LAKKO
WESELUKTELBEL
TUON
MWONJINI
ASILTAKEN
LOKISBAR
LISIMLOK
METETEKEN
KILOROK
BOLIKEEN
8" PVC
LIFT STATION (TYP)
TREATMENT PLANT



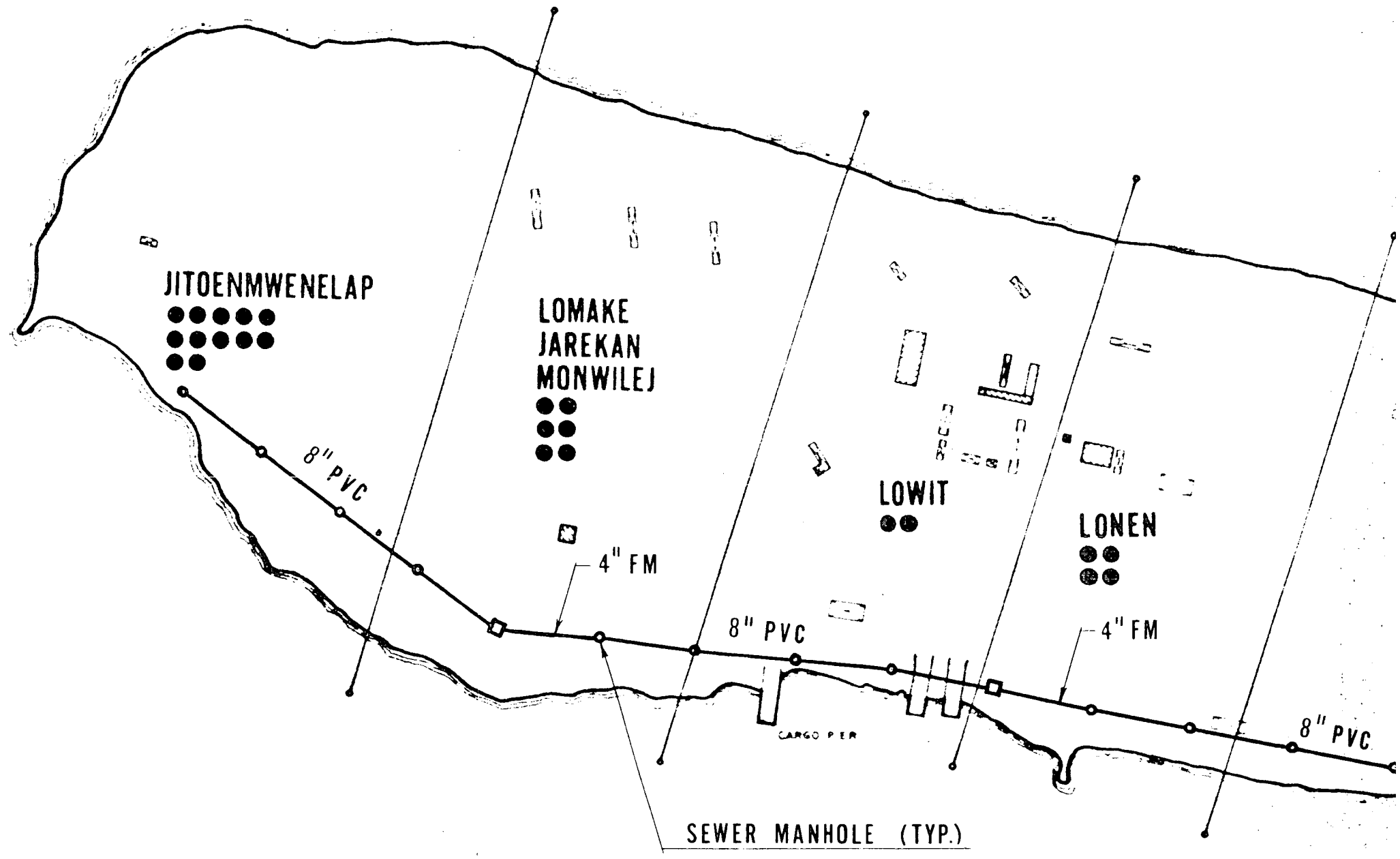
LEGEND

- ● HOUSE
- ✱ COMMUNITY CENTER

SEWAGE COLLECTION & TREATMENT SYSTEM- ENEWETAK ISLAND

HOLMES & NARVER, INC.

DWG NO
G-3
MAR 1975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LOMAKE
JAREKAN
MONWILEJ
LOWIT
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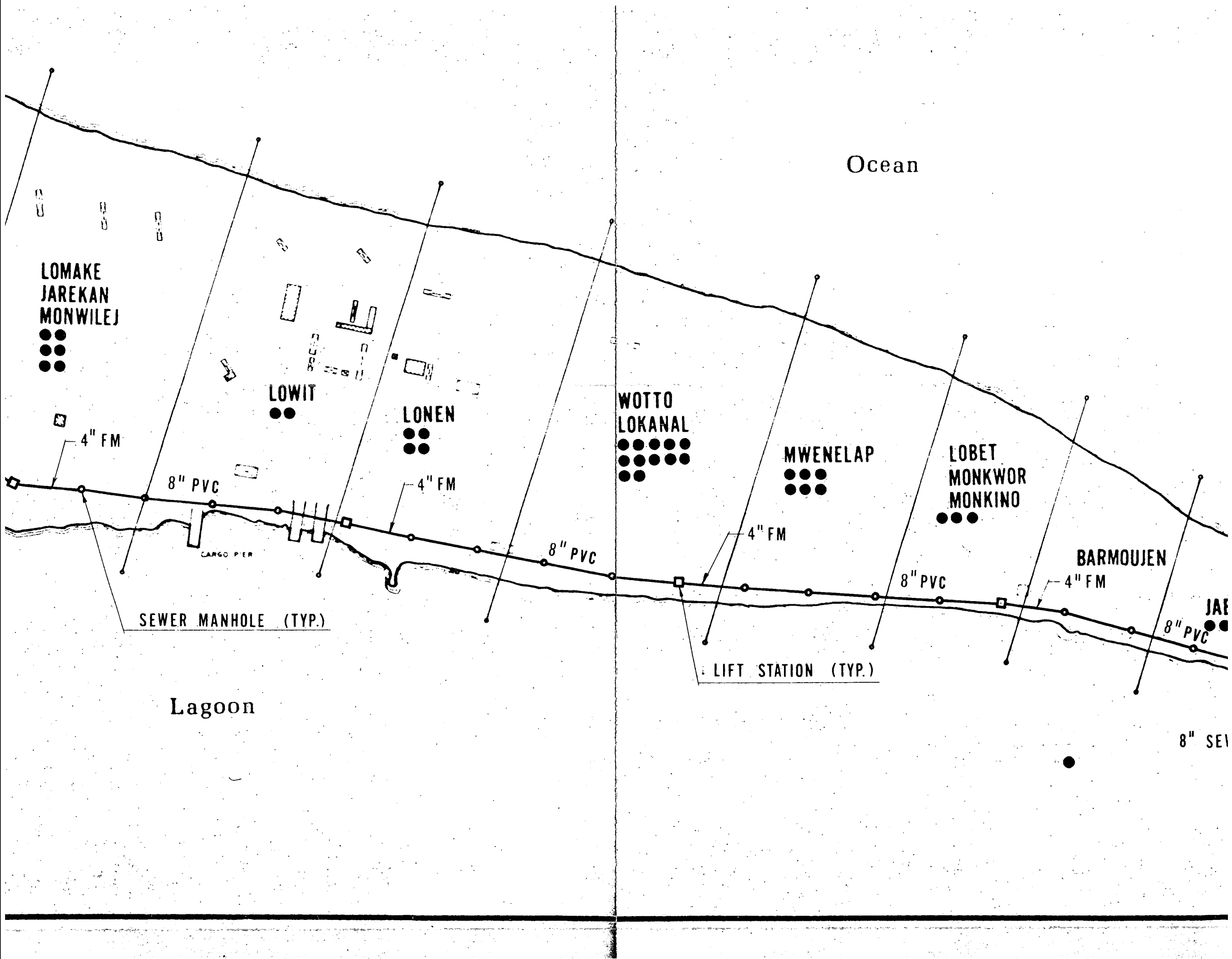
4" FM
8" PVC
CARGO PIER
SEWER MANHOLE (TYP.)

Lagoon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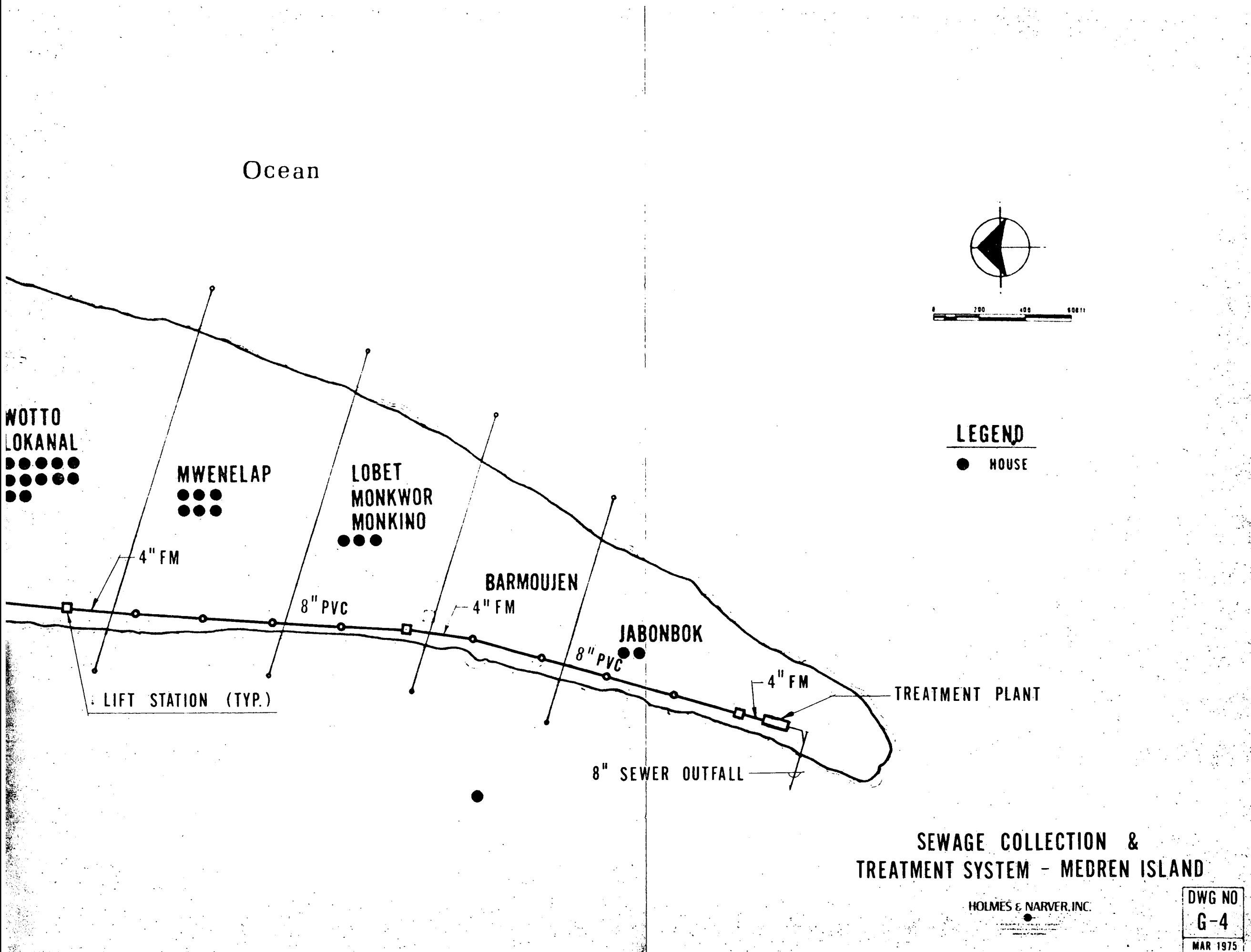
JAREKAN
MONWILEJ
LOWIT
LONEN
WOTTO
LOKANAL
MWENELAP
LOBET
MONKWOR
MONKINO
BARMOUJEN
4" FM
8" PVC
4" FM
8" PVC
4" FM
8" PVC
4" FM
8" PVC
CARGO PIER
SEWER MANHOLE (TYP.)
LIFT STATION (TYP.)
Lagoon



SEWAGE COLLECTION &
TREATMENT SYSTEM - MEDREN ISLAND

HOLMES & NARVER, INC.

DWG NO
G-4
MAR 1975

FEASIBILITY STUDY FOR CRATER CONTAINMENT OF CONTAMINATED MATERIAL AT ENEWETAK

PREPARED BY:
U.S. ARMY ENGINEER DIVISION, PACIFIC OCEAN
CORPS OF ENGINEERS

21 MARCH 1975

FEASIBILITY STUDY FOR CRATER CONTAINMENT OF CONTAMINATED MATERIAL AT ENEWETAK

SUMMARY

Four methods studied for accomplishing the crater containment of contaminated materials vary in cost from 9.3 million dollars to 36 million dollars. The recommendation to proceed without a liner to the crater is not for reason of economy alone, but is because the added efforts will achieve no significantly higher degree of protection. The omission of a liner in the crater may result in a slightly greater degree of permeability of the resultant mass. However, the degree of leaching or solution movements of contaminants from the resultant matrix would be orders of magnitude less than the continued movement of remaining contaminants from the islands. The resulting increment of contamination from such leaching would be infinitesimal and would be far below the background level of these contaminants in the present lagoon sediments.

FEASIBILITY STUDY FOR CRATER CONTAINMENT OF CONTAMINATED MATERIAL AT ENEWETAK

A. AUTHORITY.

1. Message DNA/OALG 2021Z 7 Feb 75, subject: "Feasibility Study for Crater Containment of Contaminated Material," requested the Corps of Engineers to undertake the subject study.

2. Message DNA/OALG 1825Z 27 Feb 75, same subject, provided additional instruction and criteria for the conduct of the requested feasibility study.

B. GENERAL CRITERIA AND DISCUSSION.

1. POD has studied four methods for accomplishing the semi-permanent containment of contaminated material in a crater or craters at Runit island. The technical problems involved are primarily associated with the location, removal and containment of the plutonium contaminated soil. Only the latter problem -- the containment of the contaminated materials in the craters -- is addressed in this study. When these problems are solved the disposal of the contaminated debris (metal and concrete) will pose no significant difficulties.

2. The study is based upon accomplishing the objectives outlined in paragraph 4, DNA/OALG message 1825 27 Feb 75, which is quoted in its entirety:

> "4. The concept for entombment of the material in the craters described in the DEIS was intended to accomplish the following:

"A. Reduce the transport potential of plutonium by placing it in the crater(s) in such manner that erosive water velocities are held to the lowest practivable level.

"B. Reduce the availability of small contaminated particles and contaminated scrap by binding them in a cementatious matrix.

"C. Provide a coating for the sand and PU particles to shield and reduce the hazards of Alpha emissions.

"D. Disperse the radioactive material within disposal criteria in a relatively uniform manner within the larger mass of material available.

"E. Place the material in a semi-permanent location where it would be least available to man but where it could be observed and retrieved if necessary or desirable. (Note: Leak proof containment is not required or intended)."

It is noted that ERDA was not an information addressee for this message.

3. The study assumes that the quantities established for Case 3 in the DEIS are approximately correct, and presupposes that a feasible method for locating and removal of the plutonium contaminated soil will be devised.

4. Existing condition of the craters: The two craters are water filled and are open to tidal flushing. Lacrosse Crater is located further seaward on the reef flat. The remnants of the lip of this crater is discontinuous on all sides leaving only four small islets, the largest of which extends to a height of +12 feet. Cactus Crater takes a bite out of the northern end of Runit island. Its lip is

continuous for 80% of the perimeter and hence is open to the tide for only about 200 feet of the northern sector. The lip on the island side reaches a height of +25 feet. The general location is shown on Plate I. The dimensions and volumes of the craters are shown on Plate II. The water in the craters is non-contaminated. See schematic section Plate III. The bottoms of the craters are covered with a layer of clean coral sand sediments which has accumulated since the test programs. It should be noted that since the publication of the DEIS, information has become available of two exploratory drill holes within Cactus Crater. These were made in connection with the EXPOE drilling program. These two holes reveal the presence of an extensive contaminated zone extending to more than twice the depth of the apparent bottom of the crater. In this zone the gamma count is up to 4400 CPS. The normal background counts in holes adjacent to the crater ranged from 20 to 120 CPS. If one were to extrapolate the information from these two holes, one might surmise that this zone might approximate the true crater at the time of detonation. This information reduces the apparent advantage of providing a high strength liner in the crater to a moot point, since the volume of contaminated material below the liner would probably exceed the volume of that contained within it.

5. The four methods considered in this study vary widely in cost and sophistication. In recommending the least expensive solution, POD does so, not to achieve economies at the expense of the Enewetak people, but because the added costs will achieve no significantly higher degree of protection.

6. POD staff members have previously commented to the effect that dewatering of the craters as described in the DEIS paragraph 6.2.3 was not economically feasible because of the extremely high permeability of the crater substrate and the natural formations extending to great depth. Scheme IV of this study addressed directly this problem of dewatering, and developed the highly complex grouting methods that would be required to successfully accomplish the dewatering.

7. One of the methods considered (Scheme II) involves precasting of the contaminated soil into soil-cement blocks which would then be dunked or deposited in the water filled craters. Two of the methods involve the underwater placement of a soil-cement slurry. The most commonly used method for the placement of large volumes of concrete underwater is the tremie method which is described below.

8. Tremie method of concrete placement under water: Tremie pipes are used to place fresh concrete or cement slurry under water. The tremie pipes are filled with concrete with a plug end and lowered into the water. The plug is removed from the bottom of the pipe and concrete or cement slurry flows out at the end of the pipes. From this time on the ends of the tremie pipes must be kept continually immersed in concrete. Concrete or cement slurry is continually fed to the barge mounted hopper from batch plant via concrete pumps on shore. This seal between the bottom of tremie pipes immersed in fresh concrete and cement slurry must not be lost. See Plate IV. Tremie concrete normally sets in about 2½ to 4 hours. Note Plate IV shows the barge to tremie.

C. DESCRIPTION OF METHOD.

1. Scheme I: No Crater Liner. This method provides no liner for the crater. A semi-permanent dike is provided around Cactus Crater. The contaminated soil is mixed to form a soil-cement slurry, which is pumped to a tremie hopper mounted on a small barge from which it is fed to tremies for placement under water. The contaminated debris (scrap) will be placed during the tremie placement operation resulting in its being completely encased in the soil-cement matrix. The solidified mass will be covered with an 18-inch thick concrete cap at elevation of about +8 feet. (See Plate V.)

2. An alternative to the tremie placement of the soil-cement slurry in Scheme I involves eliminating the tremies and pumping the slurry directly into prefabricated bags. These bags will be made from plastic impregnated nylon fabric similar to those marketed under the trade name "Fabriform". See Plate VI. This alternate would eliminate many of the problems or hazards associated with tremie placement of the contaminated slurry (see further comment in the section headed, Advantages and Disadvantages).

D. ADVANTAGES AND DISADVANTAGES.

1. Scheme I. This is the most economical and quickest solution. It provides for secure storage and meets the general objectives outlined in paragraph 4, DNA/OALG message 1825Z, 27 Feb 75. This solution reduces the respiratory hazard from the surface of the land and places the material in a known location which can be avoided, but can still be observed or monitored. The possibility of minor losses of contaminated soil during transportation to Runit

is slightly greater than that for Scheme II. It does not provide a liner for the crater as described in the DEIS. Hence the degree of permeability of the resultant mass may be slightly greater than the other methods. In this regard it must be pointed out that the concept of containing these contaminated materials in a completely impermeable vessel is quite unrealistic in the context of the environment of the northern islands of the Enewetak atoll. Remaining contaminants on the islands continue to exist in the highly pervious environment of the natural soils. By contrast the solid matrix of the soil-cement mass of Scheme I is less permeable by at least an order of magnitude in addition, the plutonium bearing particles will be coated with a film of cement paste. These facts coupled with the more recent information of zone of contaminated materials below the crater, make further consideration of lining the crater redundant.

2. One of the disadvantages of tremie placement of the contaminated slurry in sea water is controlling and/or removing laitance. Laitance is caused by the washing (a partial dispersion) of the wet concrete at the interface of the water and the advancing concrete mass. The problem is usually worse in a sea water environment than is the case with fresh water. The resulting laitance material is in two forms:

a. 1st the heavier aggregate from which most of the cement paste has been washed out. This settles on the top of the concrete mass.

b. 2nd is the lighter fluffy gel of hydrated cement and finely suspended matter. The latter tends to accumulate and remains in suspension for longer periods.

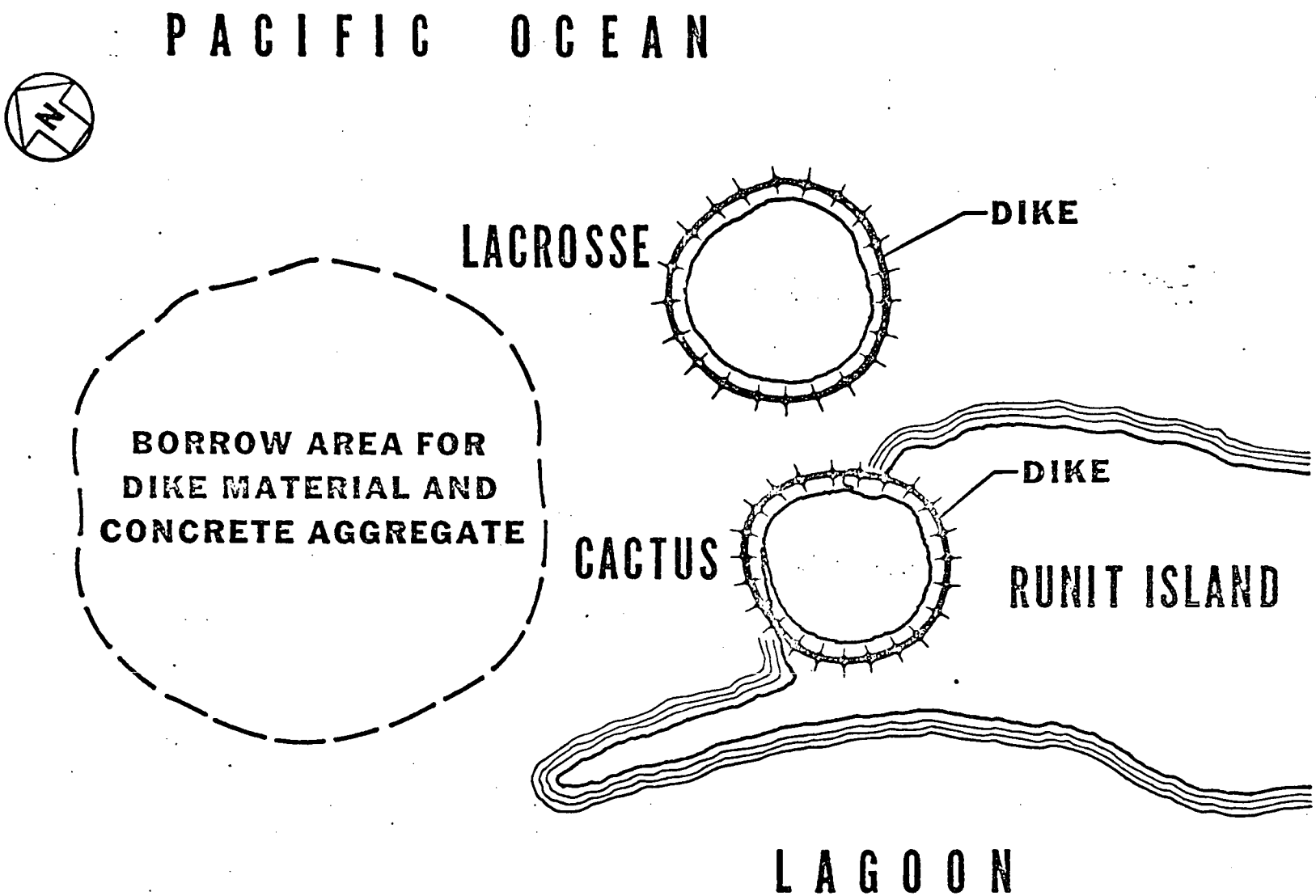
The unconsolidated aggregate (1st portion above) would be covered by subsequent lifts. The cumulative floc or gel (2nd portion) will be contaminated. In order to assure that it will set up, it is planned to recirculate this material through the mixer for the final lifts of the slurry above elevation zero.

Another method of resolving the laitance problem is the variation of Scheme I using plastic impregnated nylon bags (Plate VI). It is anticipated that the cost of manufacturing these bags will be offset by savings from eliminating the tremie operation.

E. CONCLUSION.

Plate VII shows a summary of cost and construction time. Consideration of feasibility included constructability, logistics, construction time, cost, and satisfactory achievement of the containment objectives. Scheme I involving placement of a soil-cement slurry without a crater liner is the most feasible solution.

PLATES



PLAN

0 200 400 600

SCALE IN FEET

PLATE I

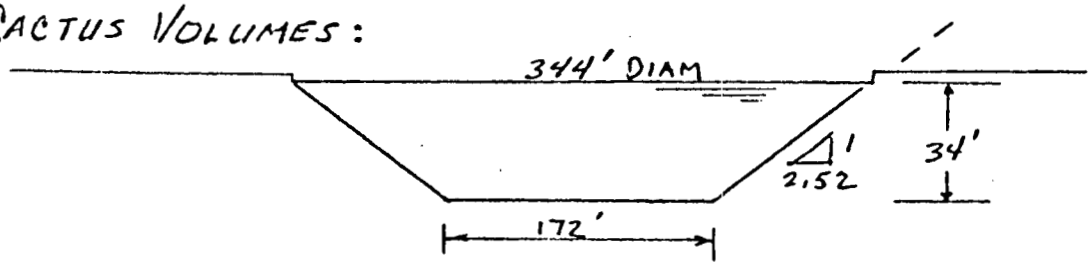
U.S. ARMY ENGINEER DIVISION, PACIFIC OCEAN
CORPS OF ENGINEERS

PROJECT TITLE ENEWETAK CLEANUP SH NO. ____ OF ____ SHS
~~LOCATION~~ ASSUMED QUANTITIES FOR CRATER STUDY SECTION ____
DRAWING(S) NO. ____
COMPUTED BY W.U.M DATE 13 MAR CHECKED BY ____ DATE ____

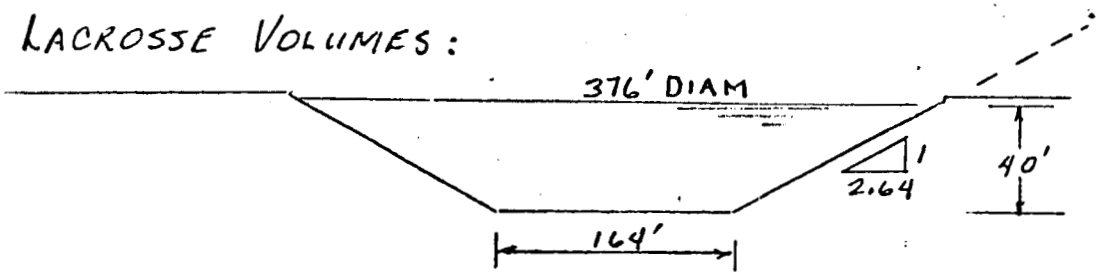
DESIGN ANALYSIS

Ref Data: 1. TOPO MAP HN1348.2
2 SEISMIC PROFILES, General Oceanographics Inc 5-30-74

CACTUS VOLUMES:



LACROSSE VOLUMES:



Weighted average side slopes from seismic profiles
Surface area planimetered from topo. map, and average diameter computed from measured area.
Volumes by average end area, for averaged truncated cone.

Water surface = 0'	CACTUS	LACROSSE
@ elev 0	73 000 CY	98,000 CY
@ elev +3'	84 000 CY	111,000 CY
@ elev +6'	96 000 CY	125,000 CY
@ elev +9'	108 000 CY	

PLATE II

POD Form 115
1 Jul 70

LACROSSE CRATER

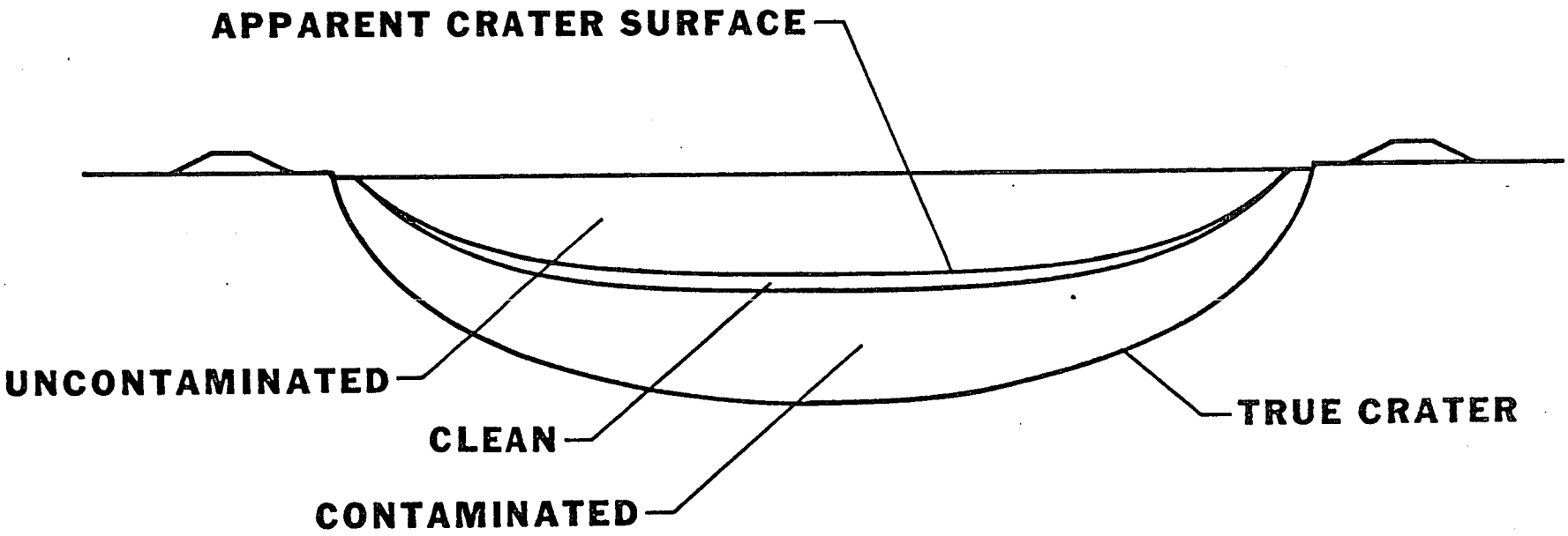


PLATE III

TREMIE METHOD OF CONCRETE PLACEMENT UNDER WATER

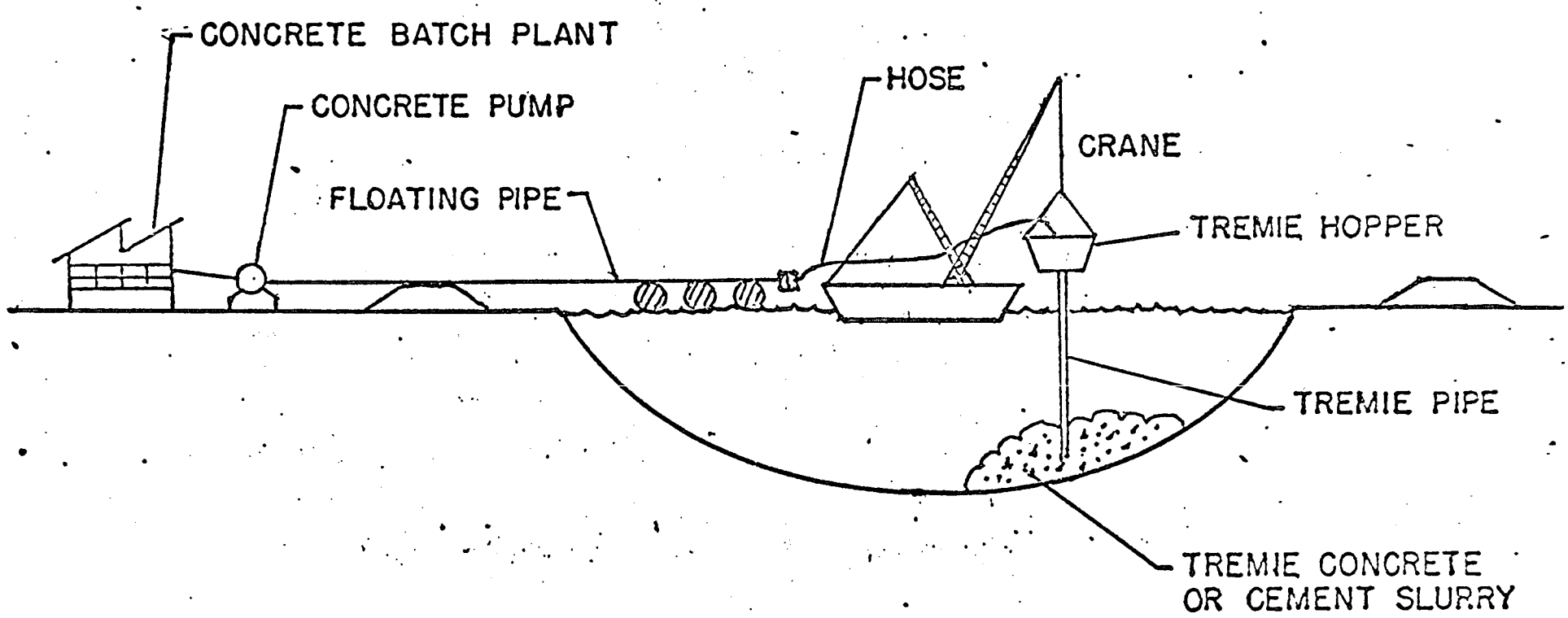
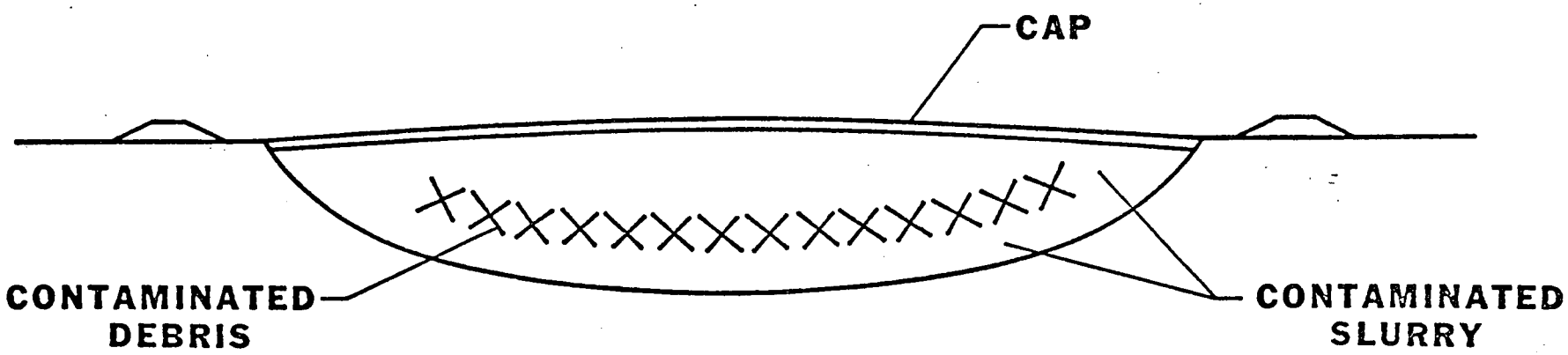


PLATE IV



PHASE I PLACE CONTAM SOIL CEMENT SLURRY

PHASE II PLACE CONTAM DEBRIS IN SLURRY

PHASE III CONTINUE SLURRY PLACEMENT

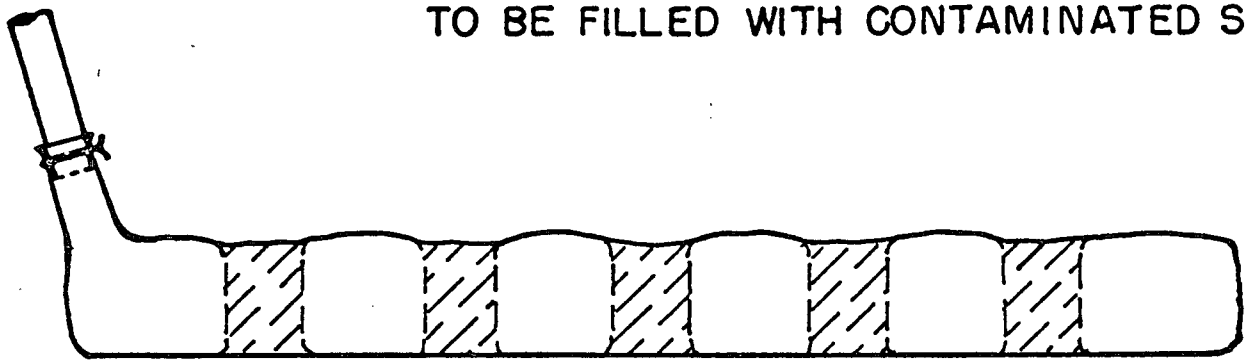
PHASE IV PLACE CAP

SCHEME I NO LINER

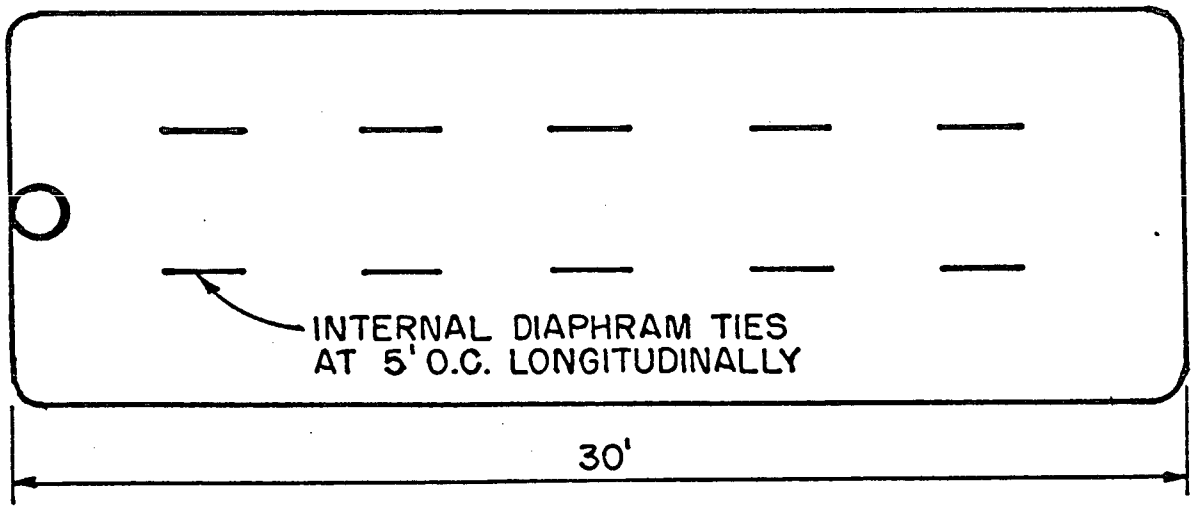
PLATE V

10'x30' NYLON BAGS 33 CUBIC YARDS EACH

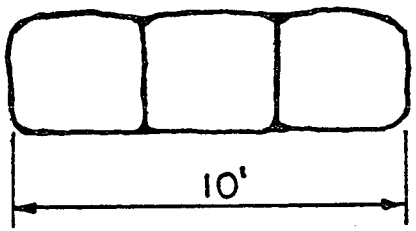
TO BE FILLED WITH CONTAMINATED SLURRY



ELEVATION



PLAN



SECTION

2500 BAGS REQUIRED

PLATE VI

CRATER ENCRYPTMENT

SCHEME	ESTIMATED CONSTRUCTION COST (CWE)	ESTIMATED CONSTRUCTION PERIOD
I	$9.3 MILLION	18 MONTHS
II	$17.2 MILLION	21 MONTHS
III	$11.3 MILLION	20 MONTHS
IV	$36.0 MILLION	42 MONTHS

PLATE VII

UNITED STATES
ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION
WASHINGTON, D.C. 20545

January 29, 1975

Major General W. E. Shedd, USA
Deputy Director for Operations
and Administration
Defense Nuclear Agency
Washington, D. C. 20305

Dear General Shedd:

Your letters of October 9 and November 26, 1974, raise the issue of the impact of the Natural Resources Defense Council (NRDC) petition to the Atomic Energy Commission (AEC) and the Environmental Protection Agency (EPA) based upon their report "Radiation Standards for Hot Particles," for the lowering of plutonium standards upon the Draft Environmental Impact Statement of the Enewetak Atoll.

The issues raised by the NRDC are identical to those they have raised concerning the LMFBR and the GESMO statements. The question is one of the probability of a unique hazard to the respiratory tissues for a given amount of inhaled radioactive material (particularly plutonium) distributed in the form of small, discrete, radioactive particles or aggregates as compared with a more homogeneous distribution of the material.

It is premature at this time to engage in a comprehensive analytical discussion of the potential consequences should the standards proposed by the NRDC petition and report be adopted. It would be more appropriate to resolve the issue generically rather than address each application of it independently.

Because of the importance of this question and because of its widespread ramification, some time ago I requested of those most familiar with the data bearing upon the relative significance of uniform vs. non-uniform exposure of the lungs to inhaled plutonium that an analysis and report be prepared which addressed and summarized the scientific evidence to date. This report (WASH-1320) was published in September 1974, and a copy is enclosed. I would call your attention to page one, particularly, where the summary and conclusions are stated. The National Radiological Protection Board of England reaches similar conclusions.

(Recently the NRDC published a critique of this document, which you included with your second request.)

The Los Alamos Scientific Laboratory has recently published a review of the NRDC petition (LA-5810-MS), a copy of which is also enclosed. I would direct your attention to the abstract of the document.

The National Council on Radiation Protection and Measurements (NCRP) has been asked for an opinion on this subject. The NCRP report has been prepared and should be released in the near future.

Both the AEC and EPA requested the National Academy of Sciences to appoint a committee of experts to study the subject. This committee, an ad hoc committee of the Academy's Committee on the Biological Effects of Ionizing Radiation, has met and is functioning. A report is not expected for at least 6-12 months, however.

Directly related to this issue were EPA public hearings held December 10 and 11, 1974, the purpose of which was to evaluate the environmental impact of plutonium and the other transuranium elements and to consider whether new guidelines or standards are needed to assure adequate protection of the general ambient environment and of the public health from potential contamination of the environment by radionuclides of these elements. The AEC offered extensive testimony and was questioned by the Hearing Panel. The NRDC presented their viewpoint and was similarly questioned by the Hearing Panel. While at this time we do not have copies of the transcript of these hearings, you might find the NRDC testimony and response to questioning to be of interest vis-a-vis the "hot particle" issue. Copies should be available from the EPA at their public document room.

The Nuclear Regulatory Commission is formulating a response to the NRDC petition to lower plutonium standards. This response, as well as the opinions of the NRDC and the National Academy of Sciences, will determine the extent to which various operations are affected.

In summary, until the primary issue is resolved it appears inappropriate to address each specific application separately. You might wish to include the NRDC papers in the Final Statement. Should this be your

decision, I would recommend that the enclosed documents also be appended. This would maintain a balanced perspective and it provides the reader with the material in WASH-1320, without which the NRDC critique of WASH-1320 would be somewhat meaningless.

Sincerely,

James L. Liverman
Acting Deputy Assistant Administrator
for Environment and Safety

Enclosures:
1. WASH-1320
2. LA-5810-MS

WASH-1320

A Radiobiological Assessment of the Spatial Distribution of Radiation Dose from Inhaled Plutonium

by W. J. Bair, C. R. Richmond,
and B. W. Wachholz

United States Atomic Energy Commission

SEPTEMBER 1974

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C., 20402 - Price $1.10

Erratum Sheet For

"A Radiobiological Assessment of the Spatial Distribution of Radiation Dose from Inhaled Plutonium"
(WASH-1320)

Please note that there is an error in the second sentence in column 2 on page 12.

The sentence now reads:

In experimental however, it is not known whether the plutonium can be found in the circulating blood; however, it is not know whether the plutonium has been absorbed from the lung directly or reabsorbed from liver or bone to which the plutonium had Been translocated previously from the lung.

The sentence should read as follows:

In experimental animals at long times after exposure, plutonium can be found in the circulating blood; however, it is not known whether the plutonium has been absorbed from the lung directly or reabsorbed from liver or bone to which the plutonium had been translocated previously from the lung.

PREFACE

This report was prepared at the request of the Division of Biomedical and Environmental Research, U.S. Atomic Energy Commission. The authors have attempted to assemble and review the data currently available which bears upon the problem of uniform versus nonuniform dose distribution in the lung. This problem has been termed the "hot particle" question. Because the quantity of material available from laboratories and individuals in the United States and foreign countries far exceeds the space limitations of this document, the more peripheral work, as judged by the authors, was omitted. While a compendium of all information relative to the subject would be useful, the authors elected to prepare a report of less voluminous dimensions, directed specifically to a radiobiological assessment of the spacial distribution of plutonium in the lung.

The authors requested and received assistance from numerous individuals and/or laboratories throughout the country in an effort to include additional general and specific expertise in various disciplines, as well as to consider as broad a sampling of expert opinions as possible.

Grateful acknowledgment is extended to:

Roy Albert, M.D., New York University
Battelle Memorial Institute, Pacific Northwest Laboratory
George W. Casarett, Ph.D., University of Rochester
Marvin Goldman, Ph.D., University of California at Davis
Los Alamos Scientific Laboratory
Clarence C. Lushbaugh, M.D., Oak Ridge Associated Universities
Roger O. McClellan, D.V.M., and the staff of the Inhalation Toxicology Research Institute, The Lovelace Foundation
Harald Rossi, Ph.D., Columbia University

Their assistance in reviewing drafts of this report, as well as their initial contributions, is most appreciated; however, the authors accept sole responsibility for the content of the report and for the opinions and the conclusions expressed herein.

It is hoped that the report will serve as an informative scientific document which will provide the reader with an overview of the applicable human, experimental and theoretical evidence to date. For additional information the reader is referred to the specific references provided.

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SUMMARY AND CONCLUSIONS

1. Recognition of the importance of spatial distribution of dose to radiation protection practices by national and international standards setting organizations and the scientific community predates the discovery of plutonium. Continued examination of the radiobiological aspects of the spatial distribution of dose, especially as regards alpha-emitting particles, has not led to major changes in radiation protection standards. However, the problem is and should be continually reassessed.

2. Experimental animal studies clearly indicate that inhaled radioactive particles move from the lung to other organs and may be excreted from the body by several mechanisms. The experimental data also show that truly uniform distributions of inhaled radionuclides in lung seldom, if ever, occur. However, because of the mobility of plutonium within lung, there is some biological justification for averaging the radiation dose to the total tissue.

3. Although particles deposited in lung are dynamic and mobile unless trapped, i.e., in scar tissue, experiments have simulated the static plutonium particle to study the biological effects of truly "hot spots" of radioactivity in lung. These and other comparative experiments of uniform and nonuniform distributions of absorbed energy from radioactive particles suggest a biological sparing effect for both acute and late responses to the nonuniform distribution. Available experimental data indicate that averaging the absorbed alpha radiation dose from plutonium particles in lung is radiobiologically sound.

4. Dosimetric models used to predict lung tumor probability in animals and in human beings are biologically deficient, primarily because of the lack of the required biological information. Also, most models are based on studies of tumor induction in irradiated rat skin and on the assumed validity of extrapolating to lung tissue. This practice is questionable for several reasons including the fact that the results of studies with rats, i.e., tumor type, vary with rat strains and that the results of comparable studies of irradiated mouse skin have not given results identical to the rat experiments. Thus, use of these models can lead to erroneous predictions of tumor probabilities.

5. Consideration of mechanisms of radiation carcinogenesis suggests that there has been no change in direction or strength of data which would compel departure from the concept that average lung dose for alpha particles provides a reasonable and conservative base for protection.

6. After thirty years experience with plutonium in laboratory and production facilities, there is no evidence that the mean dose lung model on which occupational radiation protection standards for plutonium are based is grossly in error or leads to hazardous practices. Currently available data from occupationally exposed persons indicate that the nonhomogeneous dose distribution from inhaled plutonium does not result in demonstrably greater risk than that assumed for a uniform dose distribution. Thus, empirical considerations lead to the conclusion that the nonuniform dose distribution of plutonium particles in the lung is not more hazardous and may be less hazardous than if the plutonium were uniformly distributed and that the mean dose lung model is a radiobiologically sound basis for establishment of plutonium standards.

I. STATEMENT OF THE PROBLEM

The nonuniform distribution of radionuclides and the attendant biological response of tissues at risk relative to the spatial distribution of the absorbed energy have been of interest for many decades to the scientific community, particularly those individuals and groups charged with the responsibility for derivation of exposure standards. Permissible limits for the respiratory intake of radioactive materials are commonly calculated on the assumption of complete absorption of the radiation energy by the critical organ. Further, it is implicitly assumed that there is a uniform distribution of the energy per gram of tissue throughout the critical organ. This particular situation raises the interesting question as to the probability of a unique hazard to the respiratory tissues for a given amount of inhaled radioactive material distributed in the form of small, discrete, radioactive particles or aggregates as compared with a more homogeneous distribution. Stated in another way: for the same amount of radioactive material, is the biological harm to the lung greater or less when the energy is concentrated into very small tissue volumes than when the energy is absorbed by the entire organ? For alpha and some other radiations, the distribution of energy will be nonuniform and consequently concentrated about the particles, thereby producing intense radiation doses to the nearby cells. For the case of nonuniform distribution of alpha-emitting materials in the lung, the initial biological interaction is that of an extremely large energy deposition in a very small tissue volume. For such situations, the use of the organ-mean dose concept for radiation protection has been seriously questioned.

At present the recommended dose limit (occupational exposure) for lung is 15 rem/year; the quantity of ^{239}Pu required to deliver this dose equivalent rate, if one uses the currently accepted method of assuming homogeneous absorption of energy throughout the entire lung, is 0.016 μCi. However, as shown in Table I, the number of cells which absorb the energy is a function of the size of the particles comprising the 0.016 μCi. As the particle size increases there are fewer particles and, therefore, fewer cells are irradiated but at progressively increasing dose rates.

The theoretical aspects of dosimetry and oncogenesis, results of animal experiments, and 30 years experience with humar beings occupationally exposed to plutonium will be examined to assess the relative hazards of nonuniform and uniform distribution of alpha radiation in lung and other tissue. This assessment will be applied to an evaluation of the currently accepted practice of averaging the radiation dose throughout the lung, or other organs as appropriate, for purposes of quantitating the biological effects of inhaled plutoninum and for establishing radiation protection standards.

Table I

RELATIONSHIP OF PARTICLE SIZE TO NUMBER OF CELLS AT RISK FOR A STATIC LUNG BURDEN OF 0.016 μCi $^{239}PuO_2$*

Particle diameter	Number of particles	Activity per particle	Cells at risk	Fraction of lung
(μm)		(pCi)		(%)
0.1	5.4×10^{7}	3×10^{-4}	3×10^{11}	30
0.3	2.0×10^{6}	0.01	1.3×10^{10}	1
0.7	1.8×10^{5}	0.08	1.2×10^{9}	0.1
1.0	5.4×10^{4}	0.3	3.6×10^{8}	0.03

* Assuming static particles in a structureless human lung of uniform density 0.2 g cm^{-3} with an average cell volume of 10^{3} μm^{3}. Cells at risk are taken to be those in a sphere of radius equal to the alpha range (200 μm at the assumed density).

II. BACKGROUND

The nonuniform distribution of radiation dose within the body and within tissues of the body has been of long standing interest to those concerned with the potential exposure of persons to radiation, especially from radionuclides. Almost every kind of radiation exposure, whether it be for diagnostic or therapeutic purposes, from accidental occupational exposures, from fallout radionuclides, or from natural background radiations, results in nonuniform absorption of energy within the body. In 1969, an International Commission on Radiological Protection Task Group (ICRP, 1969) identified three classes of nonuniformity of dose:

> "(i) Partial irradiation of an organ or tissue, where the part irradiated is representative of the whole organ or tissue, as in external irradiation of skin or bone marrow."
>
> "(ii) Partial irradiation, where the part irradiated is not representative of the whole. This often occurs with internal emitters, such as bone-seeking radioactive materials in bone, where certain locations and cell types are preferentially irradiated. A special case of this class is irradiation by short-range emitters metabolically localized in structures which are biologically very important, for instance, tritiated thymidine in DNA."
>
> "(iii) Irradiation from radioactive materials in particulate form."

This report will deal with the third class, which is the common situation following the deposition of radioactive materials in the respiratory tract.

The decision to use the average dose to the lung* (and other organs) has been consistently maintained over three decades by numerous organizations and individuals. The bodies responsible for such recommendations have not ignored the subject during these decades, but, rather, have periodically reviewed the relevant human and experimental data and have maintained their position that nonhomogeneous dose distribution does not result in a demonstrably greater risk than does uniform dose distribution. Thus, there has been recognition, if not complete resolution, of this problem since the 1940's. In the early days of the Manhattan Project, the concern for the problem of nonuniform dose distribution led to studies of radionuclides inhaled or deposited on skin. In fact, interest in nonuniform dose distribution in animals and man predates the discovery of plutonium in 1941 because of the occupational and medical exposures to ^{226}Ra.

At the Chalk River Tri-Partite Conference attended by scientists from the United States, the United Kingdom, and Canada (McMurtrie, 1950), Dr. Hamilton pointed out, in relation to the possible pathological effects of radioactive particulates in the lungs, that cells in the immediate neighborhood of a dust particle containing 1 or 2 percent of plutonium would be subjected to a dose of about 400 r/day. The general opinion which emerged from the discussion was that the carcinogenic effect per unit volume is probably considerably less for the irradiation of small masses of tissue than for large.

The National Academy of Sciences-National Research Council considered the question of nonuniform dose distribution in Publication 848, Effects of Inhaled Radioactive Particles (NAS-NRC, 1961a). This publication pointed out that lung exposures are often expressed as mean dose to the lung by calculating the dose assuming uniform distribution of radioactive material throughout the lung, although uniform distribution of inhaled particles is not observed in practice. The report also stated that because local concentration of particles results in nonuniform distribution of energy, the dose

* The average radiation dose is calculated by assuming the complete and homogenous absorption of energy throughout the entire organ. An exception to this approach is the calculation of dose resulting from the inhalation of radon daughters.

delivered to small volumes of lung tissue could vary by several orders of magnitude above and below the mean value and, therefore, the calculated mean dose to the lung should be used with caution in estimating biological effects.

Report 848 also contains specific discussions of point sources and tumor production and the then current status of the radioactive particle hazard evaluation. It also recognized as unresolved the effect of the spatial distribution of the radiation on pulmonary tumorigenesis. It was not known whether differences in tumor production were due to the particular tissue in which the deposition occurs or to the localization and resulting strong irradiation of the tissue. The skin experiments, cited in Report 848, using radioactive point sources as compared with flat plates indicated that, in the range where extremely large doses are given, with consequent killing of cells, tumor production was considerably lessened for localized sources. The report, however, states that these experiments shed no light on the localization of smaller quantities of materials where the dose rate is not adequate to definitely kill the cells within a given range of the radioactive material.

The subject of energy distribution also was considered in the National Academy of Sciences-National Research Council Report of the Subcommittee on Internal Emitters of the Committee on Pathological Effects of Atomic Radiation (NAS-NRC, 1961b). In chapter IV, entitled Special Problems, the report states that there are good reasons to believe that, when radiation is uniformly delivered to tissues, the biological effects may differ from those observed when the radiation arises from focal aggregations of radioactive material (point sources) (Marshall and Finkel, 1959, 1960). In the latter case, dose rates close to the point source would be different from those near the end of the range of the particles with an extremely high dose rate found near the origin. The report notes that spatial differences in dose may have considerable importance if the relationship between biological injury and energy absorbed is not linear.

The NAS-NRC report (1961b) pointed out that spatial distribution of dose is of significance when particular tissue elements are selectively irradiated, and insofar as the relation between dose and the degree or probability of any type of injury is not linear. The report states that the available information is not adequate to define differences in hazard between focal and diffuse radiation.

The question of nonuniform dose distribution was addressed also in the BEIR Report (NAS-NRC, 1972). A statement is made that an important issue is whether local or "hot spot" radiation doses are more effective in producing cancer of the respiratory tract as compared with uniform radiation exposure to the entire respiratory epithelium. The report cites the work of Grossman *et al.* (1971), in which ^{210}Po chloride was given intratracheally either alone or with hematite particles, as being pertinent to the issue. Because polonium solution alone was as effective as polonium given with hematite, the authors of the BEIR Report thought that it may be inferred that a higher localized dose from alpha particles was not more carcinogenic than the same mean tissue dose delivered more uniformly to critical cells.

The 1971 report of the National Council on Radiation Protection and Measurements, entitled Basic Radiation Protection Criteria (NCRP, 1971), contains a concept of "significant volume" over which radiation dose should be averaged. The report states:

> "Simplifications in practice hinge largely on reporting a single representative protection dose for a limiting organ system even when the actual irradiation is grossly non-uniform. The representative dose is taken as the highest that can be obtained by averaging over a prescribed significant volume. The implication of this concept, or at least the convention that is followed, is that any redistribution of a given dose within such a volume does not materially alter the radiation response. It is usually assumed that the 'significant volume' should be of the order of one cubic centimeter. This will be grossly conservative under most circumstances, and in special situations use of a larger volume is justified."

As indicated in the NCRP report, there are some cases in which choice of significant volumes or areas are virtually meaningless. For example, the averaging of dose over the entire lung or over one cubic centimeter may have little meaning if a single radioactive particle in the lung or lymph node can be carcinogenic.

The ICRP periodically has addressed this subject of nonuniform dose distribution, usually by special groups commissioned by the ICRP to study the question. In its Publication 9 (ICRP, 1966), the ICRP pointed out that for the case of nonhomogeneous distribution of absorbed dose in the lung, an estimate of the

Dose Equivalent to the whole lung as determined merely by the product of QF and the mean absorbed dose might be greatly in error but full understanding of this problem must await further experimental evidence. The report indicated that there was no clear evidence to show whether, for a given mean absorbed dose, the biological risk associated with a nonhomogeneous distribution is greater or less than the risk resulting from a more diffuse distribution of that dose in the lung.

The authors of the ICRP report point out that the problems of high local concentration of dose are most severe for radioactive particles, especially alpha-emitters, in tissue where the local dose can reach very high levels even though the mean tissue dose may be very low. They state that one cannot assume that linearity of radiation dose and effect will hold at these high doses and dose rates yet there may be a great deal of cell death, particularly for the short well-defined range of alpha particle irradiation, and the number of affected but viable cells may be small as compared with the number of killed cells.

The report (ICRP, 1966) states:

> "On the basis of general considerations and of some experimental data and clinical experience the Task Group were of the opinion that, for late effects, the same radiation energy absorption might well be less effective when distributed as a series of 'hot spots' than when uniformly distributed. Thus, with particulate radioactive sources within a tissue, a mean tissue dose would probably introduce a factor of safety. However, a severe practical problem has now been recognized in connection with the inhalation of plutonium particulates, and is now being considered in detail by a Task Group of Committee 1 of ICRP."

Current radiation protection standards for limiting radiation dose to the lung from internally deposited radioactive materials continue to be based upon our collecting knowledge of the effects of radiation on the lung. Calculations of the average dose to lung tissue as a correlative step between biological effects and a quantity of radionuclides have been based on the assumption that the absorption of energy is uniform throughout the mass of tissue. It is well known that this situation does not exist for "insoluble" radionuclides which can produce focal spots of high levels of radiation close to the particle, with the level decreasing with distance in a pattern depending upon the quality and energy of the radiation. Also well known is the fact that postulated cases of uniform distribution of energy for "soluble" radioactive materials seldom, if ever, occur.

Since the opinions of the standard setting bodies were expressed, additional data have accumulated which bear on the problem and will be discussed in the sections to follow. While the question of nonuniformity of dose cannot be answered unequivocally, these new data tend to support the conclusion expressed by the ICRP Task Group (ICRP, 1969) that for radioactive particles "a mean tissue dose would probably introduce a factor of safety."

Thus, it is clear that nonuniform distribution of radiation dose has been examined continually by national and international standard setting bodies. The fact that these organizations have not changed or recommended changes in the procedures used for calculating dose to the lung as the result of their deliberations is an indication of implicit guidance on this particular problem.

III. ANIMAL STUDIES

The disposition and biological effects of inhaled plutonium and other radionuclides have been reviewed recently (Buldakov *et al.*, 1969; Sanders *et al.*, 1970; Bair *et al.*, 1973; Bair, 1974; Healy, 1974). Therefore, attention will be given only to those experimental data relevant to spatial distribution of radiation dose from inhaled radionuclides.

A. Retention of Plutonium in Lung

Airborne radioactive particles are similar to most other particles when they are inhaled in that deposition in the respiratory tract is primarily dependent upon the physical properties of the particles and the respiratory characteristics of the individual inhaling the particles. The ICRP Task Group on Lung Dynamics (Morrow *et al.*, 1966) dealt with the deposition of particles in the respiratory tract in considerable detail.

Within the first week after exposure, a fraction of the deposited plutonium is cleared from the respiratory tract and excreted. The amount of plutonium cleared depends upon the fraction of readily solubilized material present and the distribution of the plutonium within the respiratory tract. Plutonium deposited upon the ciliated epithelium of the upper respiratory tract may be trapped in mucus and transported to the esophagus and swallowed. Plutonium deposited in the lower regions of the lung is not readily available for clearance and may be incorporated into the cellular structures of the lung and retained for a long time.

The kinetics of the clearance of plutonium from lung are complicated and difficult to quantitate. Because the clearance of plutonium from the lower lung appears to be exponential with time over a reasonably long period after exposure, retention half-times are estimated. Animal experiments and limited human data provide a range of values for the retention half-times of several plutonium compounds, Figure III–1. The retention half-times for organic complexes of plutonium, plutonium nitrate and plutonium fluoride range from less than 100 days to about 300 days in rats and dogs. The retention half-times for PuO_2 are substantially longer, ranging from 200 to 500 days in rats, 300 to 1000 days in dogs and 250 to 300 days in human beings. The wide range of values for dogs is largely due to extensive experimentation with a variety of plutonium oxides with different physical characteristics. For example, PuO_2 calcined at high temperatures is cleared more slowly than air oxidized plutonium; PuO_2 comprised of large particles ($\sim$ 3 μm AMAD) tend to be cleared more slowly than aerosols of small particles ($\sim$ 0.1 μm AMAD); and $^{238}PuO_2$ has a much shorter lung retention time than $^{239}PuO_2$. The relatively low value for human beings, compared with dogs, suggests either that man clears plutonium particles from his lung faster than dogs do or that the materials inhaled in the human

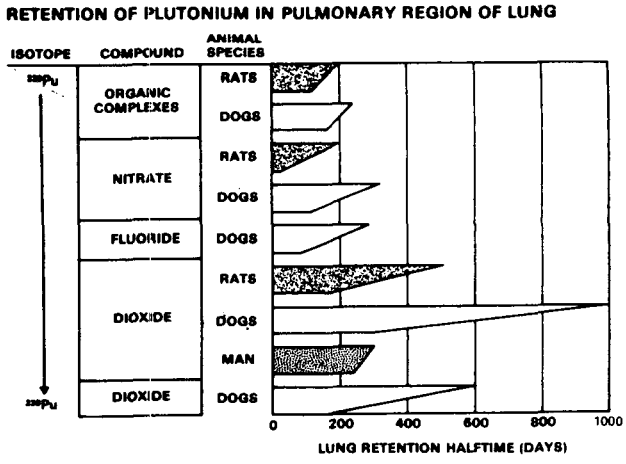

Figure III–1.—Retention of Plutonium in Pulmonary Region of Lung. Ranges of published values for retention half-times are indicated for each animal species and plutonium compound (Bair, in press).

accident cases, from which these data were obtained, were more soluble than plutonium dioxide.

Plutonium appears to be retained in the lower respiratory tract longer than most other materials that have been studied. Thorium dioxide and ruthenium dioxide show retention half-times comparable to those observed for plutonium. Uranium-oxide, cerium oxide and other metal oxides are retained at half-times of less than 200 days, some less than 100 days. The reason for the relatively long retention time of plutonium is not known, but may be due to its low solubility in tissue fluids, chemical binding with proteins and other constituents of lung, and the cytotoxic action of the emitted alpha radiation.

B. Spatial Distribution of Plutonium Within Lung

From the moment plutonium is deposited in the respiratory tract, biological and physical forces are at work to cause the removal of the plutonium. That these forces are not as effective for plutonium as for other inhaled material is indicated by the relatively long retention half-times observed for plutonium. Particles deposited in alveolar spaces may be cleared via the lymphatic system, mucociliary pathway of the tracheobronchial tree, or by dissolution and absorption into blood. With all of these processes at work removing plutonium from lung, although at low rates, it is difficult to visualize plutonium remaining static throughout its residence time in the lung. Techniques have not been developed to document the course of individual particles and aggregates of plutonium in lung. However, the temporal and spatial characteristics of plutonium within tissues can be inferred from autoradiographs of tissue sections prepared from animals exposed to plutonium aerosols.

The first observation is that plutonium and especially insoluble plutonium compounds are nonuniformly deposited throughout lung. Further, plutonium may deposit unequally among the lung lobes or among portions of lung lobes. Deposition of plutonium following inhalation, however, is more uniform than after intratracheal injection—an experimental technique often used when exposure of animals to plutonium aerosols is not feasible. Studies of inhaled plutonium nitrate in both rats and dogs show that immediately following the inhalation exposure, plutonium is present in both particulate and nonparticulate forms (Koshurnikova *et al.*, 1971; Sanders *et al.*, 1971; Ballou and Park, 1972; Lafuma, 1974), as evidenced by the presence of alpha stars and single tracks in autoradiographs, Figure III–2. Autoradiographs from dogs exposed to inhaled $^{239}PuO_2$ show an initial relatively diffuse distribution of plutonium throughout the entire lung (Clarke *et al.*, 1966).

Plutonium not rapidly removed from the respiratory tract by the mucociliary pathway or by absorption into the blood, may be engulfed by macrophages. Phagocytosis of particles deposited on the non-ciliated epithelium distal to the terminal bronchioles and in the alveoli usually occurs very rapidly (Sanders, 1969). The alveoli of the lung contain reticuloendothelial cells derived in part from circulating monocytes. These reticuloendothelial cells consist of mononuclear cells and histiocytes within the septal walls and alveolar macrophages in the air spaces, all of which are capable of phagocytizing plutonium.

Phagocytized plutonium particles are rapidly localized in the phagolysosomes of reticuloendothelial cells (Sanders and Adee, 1970). While the mechanism is not known (Casarett and Milley, 1964), the alveolar macrophage appears to be capable of transporting plutonium from the alveoli to the ciliated epithelium of the bronchioles. These phagocytic cells containing plutonium particles and aggregates can then be removed from the lung in the mucous blanket which is propelled up the respiratory passage by ciliary action. This mechanism of clearing plutonium from the lung is important early after an inhalation exposure and apparently continues to function long afterward, as evidenced by the appearance of macrophages containing plutonium in lung lavage fluid at long times after exposure (Sanders and Adee, 1968), and by the continued appearance of plutonium in feces, although the latter is only circumstantial evidence.

Both soluble and insoluble plutonium not immediately cleared from the lung tend to become further aggregated. This mobility and aggregation of plutonium may have large effects on the temporal and spatial distribution of the alpha radiation dose. A few days after inhalation of plutonium nitrate, single tracks in autoradiographs decrease, Figure III–3,

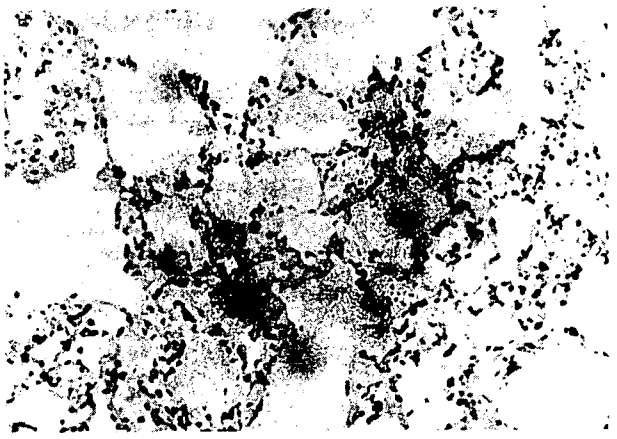

Figure III–2.—Autoradiograph of lung section from dog 1 day after inhalation of $^{239}Pu(NO_3)_4$. 320X. (Provided by J. E. Ballou, Battelle-Northwest).

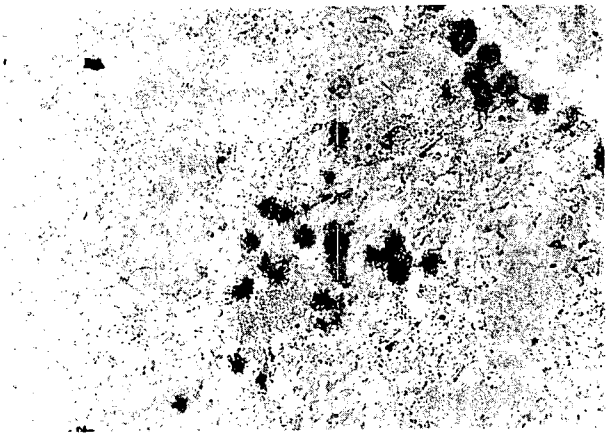

Figure III–4.—Autoradiograph of lung section from dog several weeks after inhaling $^{239}Pu(NO_3)_4$. 120X. (Provided by J. E. Ballou, Battelle-Northwest).

Figure III–3.—Autoradiograph of lung from dog 14 days after inhalation of $^{239}Pu(NO_3)_4$. 320X. (Provided by J. E. Ballou, Battelle-Northwest).

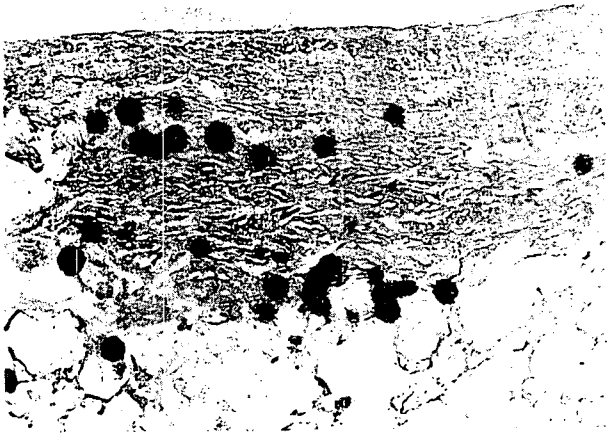

Figure III–5.—Autoradiograph of lung section from dog several months after inhalation of $^{239}PuO_2$, showing subpleural concentration of plutonium particles. 320X. (Provided by G. E. Dagle, Battelle-Northwest).

and after several weeks nearly all of the plutonium appears to be aggregated, Figure III–4. It is not known whether this represents continued aggregation, perhaps by chemical binding, of the plutonium in the lung or whether aggregation only appears to be increased as the non-aggregated plutonium is absorbed into the blood and thus disappears from the lung leaving only the aggregates.

Plutonium particles, and to a lesser extent aggregates of soluble plutonium, are transported to thoracic lymph nodes. Clearance of particles to lymph nodes occurs *via* lymphatic vessels in the thorax that drain interstitial spaces. Particles either penetrate the interstitium directly or gain access by transport in phagocytic cells (Morrow and Casarett, 1961; Casarett and Milley, 1964). Autoradiographs

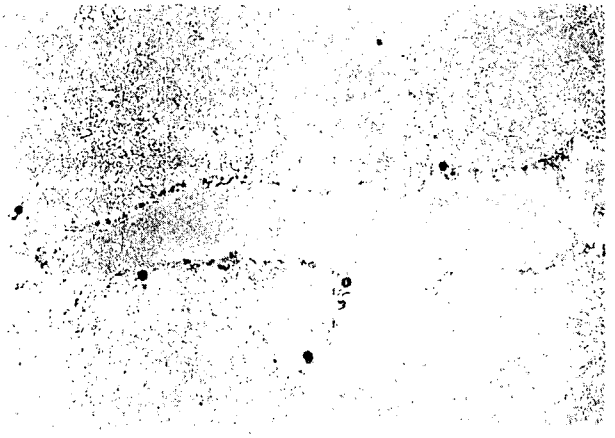

Figure III–6.—Autoradiograph of lung section from dog several months after inhalation of $^{239}PuO_2$, showing peribronchiolar accumulation of plutonium particles. 50X. (Provided by G. E. Dagle, Battelle-Northwest).

of lung tissues taken from dogs several weeks and months after inhalation of PuO_2 show alpha stars concentrated in subpleural areas, apparently in lymphatic vessels, Figure III–5. Autoradiographs also suggest that some plutonium particles become immobilized in scar tissue in subpleural areas. Plutonium particles transported to lymph nodes are deposited in lymphatic sinuses of subcapsular and medullary areas. The particles eventually appear sequestered in "hot spots" of scar tissue and do not appear to be mobile. The residence time for plutonium in lymph nodes appears to be very long; there is no direct evidence for clearance of inhaled plutonium particles from thoracic lymph nodes although clearance of plutonium from cervical lymph nodes of dogs after subcutaneous injection (Lebel *et al.*, 1972) and from mesenteric lymph nodes of rats after intraperitoneal injection (Sanders, 1974) has been reported.

Plutonium particles not phagocytized by alveolar macrophages and removed by the mucociliary pathway or transported to the lymphatics can be found in Type I alveolar epithelial cells and in peribronchiolar vascular areas, Figure III–6. There is autoradiographic evidence of particles being immobilized in scar tissue in the alveolar and peribronchiolar areas. Although Type I alveolar epithelial cells phagocytize plutonium particles rapidly—within a few hours after deposition (Sanders and Adee, 1970), the fate of particles phagocytized by these cells is not known. The Type I cells do appear to be relatively radioresistant to alpha irradiation (Sanders *et al.*, 1971). It is possible that plutonium particles, other than those in lymphatics or trapped in scar tissue, retained in the lung for long periods, are cycled through generations of Type I or other cells.

Type II alveolar epithelial cells, or the so-called "granular pneumonocytes," do not phagocytize plutonium particles (Sanders *et al.*, 1971) and, thus, do not appear to be directly involved in clearance of plutonium from lung.

The intracellular localization of plutonium particles within pulmonary macrophages has been demonstrated by autoradiography of smears from pulmonary lavage fluid and of lung sections (Sanders, 1969). Lesions in macrophages have been observed as early as one hour after phagocytosis of large amounts of plutonium.

There is much experimental evidence for the absorption of plutonium into the blood almost immediately after deposition of soluble and even "insoluble" plutonium compounds in the respiratory tract (Bair and McClanahan, 1961; Bair and Willard, 1961). In experimental however, it is not known whether the plutonium can be found in the circulating blood; however, it is not know whether the plutonium has been absorbed from the lung directly or reabsorbed from liver or bone to which the plutonium had been translocated previously from the lung. Plutonium is also continuously excreted in urine after an inhalation exposure. Again it is not known whether the origin is the lung directly or the secondary liver and bone pools. Mercer (1967) suggested that dissolution of plutonium particles deposited in the deep alveolar lung region was the major pathway for clearence and that dissolution rates were directly proportional to the surface area of the particles and their chemical composition. It seems certain that dissolution of plutonium particles and aggregates does occur in the lung, although at low rates, and accounts for at least some of the mobility of plutonium in the lung as well as clearance from the lung.

Although the kinetics are unknown and even a qualitative description is still rather primitive, there is ample evidence that plutonium deposited in lung is subjected to biological and physical forces. This argues against either particles or aggregates of plutonium remaining static indefinitely, except for the plutonium that becomes immobilized in scar tissue. To the contrary, while the rates may be low, movement of plutonium within lung tissues, by several mechanisms, certainly occurs, as the lung attempts to expel the plutonium and other foreign material. The migration of deposited plutonium particles in lung is recognized in the USSR as at least partially compensating for the nonuniformity of the radiation exposure from plutonium particles and justifying acceptance of the concept of averaging the radiation dose over the entire lung mass (Zalmanzon and Chutkin, 1971).

C. Pulmonary Neoplasia

High doses of inhaled plutonium in experimental animals have been shown to cause severe radiation pneumonitis and fibrosis resulting in early death due to respiratory in-

sufficiency (Bair *et al.*, 1973). Lymphopenia is the earliest response seen in animals after inhalation of PuO_2 and has been observed in dogs with total lung deposition of 0.08 μCi (Park *et al.*, 1974). Cancer is a potential long-term response to plutonium in the body and has been observed in experimental animals to occur in lung, bone and liver, all of which are major repositories of plutonium deposited in the respiratory tract (Bair, 1974). However, lung cancer is the biological response of most relevance to this discussion of the spatial distribution of radiation dose from inhaled plutonium.

Experimental data on plutonium-induced lung cancer are summarized in Table III–A. In rats exposed to ammonium plutonium pentacarbonate or plutonium citrate, the incidence of pulmonary neoplasia was about 10% at doses of the order of 0.01 μCi/g of lung, and above 30% at 0.015 to 0.026 μCi/g lung. The lung tumors were squamous cell carcinomas, adenocarcinomas, and hemangiosarcomas. Sixty to 100% of the animals in the range of doses studied (40 to 7320 rads) developed pulmonary sclerosis. The maximum incidence of malignant neoplasms in the lungs (30–47%) was observed at an absorbed dose of 500–1000 rads. Studies with soluble plutonium in dogs have been concerned with acute effects and no tumors have been reported. Plutonium-239 oxide caused pulmonary neoplasia in mice given doses by intratracheal injection ranging from 0.02 to 1.0 μCi/gram lung (Wager *et al.*, 1956; Temple *et al.*, 1959, 1960). One tumor was seen in a mouse that inhaled about 0.25μCi $^{239}PuO_2$ per gram lung (Bair, 1960). In a larger study with nearly 800 mice that inhaled about 0.1 to 2 nCi per gram (Bair *et al.*, 1962), there was no shortening of life-span and no evidence of pulmonary neoplasia in the animals available for histopathological examination. Rats showed a 50% tumor incidence at inhaled (through a glass tube inserted into the trachea) $^{239}PuO_2$ doses of about 0.2 μCi/gram lung (Lisco, 1959). These tumors were epidermoid carcinomas, adenocarcinomas, and hemangioendotheliomas. No primary tumors of thoracic lymph nodes were seen in any of the rodent experiments.

In beagle dogs given a 10–30 minute exposure to $^{239}PuO_2$, deposition of more than 0.1 μCi/g lung caused death within about a year due to respiratory insufficiency (Park *et al.*, 1972). Thirty dogs died between 55 and 412 days postexposure due to plutonium-induced pulmonary edema, fibrosis, and bronchiolar and alveolar epithelial hyperplasia and metaplasia. The subsequent severe respiratory insufficiency was characterized by progressive hypercapnia and hypoxia. In another experiment with 40 dogs, 32 died or were sacrificed when death was imminent. Five were sacrificed for study of plutonium distribution in tissues. Of the 32 deaths, 30 were due to plutonium-induced pulmonary fibrosis and/or neoplasia. The three remaining dogs have died and all grossly showed lung tumors; however, the histopathology and radiochemistry results are incomplete (Park and Bair, 1974). Twenty-four dogs had pulmonary neoplasia in addition to fibrotic and metaplastic lesions, Figure III–7. The survival times of these dogs are plotted as a function of the estimated amount of plutonium initially deposited in the alveolar regions of the lungs of the dogs, expressed as nCi/g of blood-free lung. The curve was fitted to all the data by least squares analyses to describe the relationship between quantity of plutonium deposited and the time of death due to pulmonary neoplasia and/or pulmonary fibrosis-induced respiratory insufficiency. Another curve was fitted to just the pulmonary neoplasia data points by least squares analyses. In these dogs the development and growth of the pulmonary neoplasms were followed radiographically. In all cases tumors appeared to originate in the periphery of the lung, the location of most of the plutonium. This observation is consistent with the histopathology which showed that the predominant tumor type was bronchiolar-alveolar carcinoma. Epidermoid tumors similar to those generally attributed to cigarette smoking and/or exposure to radon daughters as in uranium miners, were incidental findings in a few dogs which also had bronchiolar-alveolar carcinoma (Howard, 1970). The estimated initial alveolar deposition in the dogs with plutonium-induced pulmonary neoplasia was 0.2 to 3.3 μCi or 3 to 45 μCi/gram of bloodless lung. Metastasis occurred to thoracic lymph nodes and to many systemic organs.

In addition to bronchiolar-alveolar carcinomas, other types of tumors were incidental findings in several dogs. Two dogs developed benign-appearing tumors of endothelial origin which were classified as hemangiomas. Thoracic lymph nodes, as well as a few hepatic

Table III–A
PLUTONIUM-INDUCED LUNG CANCER IN EXPERIMENTAL ANIMALS

Compound	Animal species	No. of animals	Exposure method*	Deposited in lungs (μCi)	Deposited in lungs (μCi/g)	Dose to lungs** (rads)	Mean survival time (days)	Lung tumor incidence No.	Lung tumor incidence %	Tumor type	Reference
^{239}Pu	Rat	258	Control	—	—	—	570 ± 8	1	0.39	Squamous cell	Koshurnikova,
Citrate	Rat	157	Inhal.	0.008	0.0026	47	635 ± 3	11	7.1	cancer, adeno-	Lemberg, and
	Rat	124	Inhal.	0.02	0.0067	117	585 ± 12	3	2.5	carcinoma, and	Lyubchansky,
	Rat	203	Inhal.	0.04	0.013	234	545 ± 11	17	8.4	hemangiosarcoma	1971
	Rat	31	Inhal.	0.08	0.026	467	546 ± 22	11	35.5		
	Rat	105	Inhal.	0.15	0.050	852	464 ± 12	27	25.7		
	Rat	113	Inhal.	0.25	0.08	1390	416 ± 12	27	24		
	Rat	39	Inhal.	0.36	0.12	1740	221 ± 13	3	7.7		
	Rat	90	Inhal.	0.51	0.17	2370	124 ± 9	2	2.2		
	Rat	12	Inhal.	0.80	0.26	3090	69 ± 5	0	0		
	Rat	20	Inhal.	1.03	0.34	3820	64 ± 2	0	0		
^{239}Pu	Rat	48	Inhal.	0.004	0.0013	41	571 ± 21	2	4.2	Squamous cell	Koshurnikova,
Ammonium	Rat	101	Inhal.	0.007	0.0023	80	571 ± 16	7	7	cancer, adeno-	Lemberg, and
Plutonium	Rat	91	Inhal.	0.017	0.0057	186	584 ± 12	12	13.2	carcinoma, and	Lyubchansky,
Penta-	Rat	126	Inhal.	0.045	0.015	497	582 ± 11	48	38	hemangiosarcoma	1971
carbonate	Rat	83	Inhal.	0.15	0.05	1065	484 ± 14	38	45.9		
	Rat	126	Inhal.	0.25	0.08	1615	361 ± 11	31	24.6		
	Rat	22	Inhal.	0.35	0.12	2140	247 ± 21	2	9.0		
	Rat	65	Inhal.	0.46	0.15	2780	139 ± 10	3	4.6		
	Rat	23	Inhal.	0.77	0.26	3900	78 ± 7	0	0		
	Rat	11	Inhal.	1.46	0.48	7320	77 ± 6	0	0		
^{239}Pu	Rat	42	I.T.(HNO_3)	—	—	—	586 ± 20			Squamous cell	Erokhin,
$Pu(NO_3)_4$	Rat	80	I.T.	0.00042	0.00014	2.7	541	2	2.5	cancer, adeno-	Koshurnikova,
	Rat	17	I.T.	0.0042	0.0014	28	755	1	5.9	carcinoma, and	Lemberg,
	Rat	22	I.T.	0.01	0.003	62.5	793	2	9.9	hemangiosarcoma	Nifatov, and
	Rat	88	I.T.	0.031	0.01	205	592	4	8.16		Puzyrev, 1971
	Rat	59	I.T.	0.048	0.016	318	704	7	17.5	(Incidence calcu-	
	Rat	62	I.T.	0.1	0.03	622	589	12	18.9	lated on animals	
	Rat	108	I.T.	0.42	0.14	2760	426	33	33	at risk)	
	Rat	86	I.T.	1.0	0.3	5960	330	19	24.2		
^{239}Pu Plutonyl Triacetate	Rat	48	I.T.	1.0	0.3	1580	405	19	39.6	Squamous cell cancer, adeno-carcinoma, and hemangiosarcoma	Erokhin, Koshurnikova, Lemberg, Nifatov, and Puzyrev, 1971
^{239}Pu	Rabbit	8	Inhal.	—	0	0	1431.5 ± 201	—	—	Malignant	Koshurnikova,
Ammonium	Rabbit	13+	Inhal.	—	0.02	120	926.4 ± 96.8	—	—		Lemberg, and
Plutonium-	Rabbit	18+	Inhal.	—	0.17	1010	673.9 ± 74.8	?	18.7		Lyubchansky,
Penta-	Rabbit	20+	Inhal.	—	0.50	2960	631.5 ± 61.5	1	5.0		1971
carbonate											
^{239}Pu	Rabbit	12	I.T.	—	0.65	3840	665.7 ± 53.6	7	58.3	Malignant	Koshurnikova,
$Pu(NO_3)_4$	Rabbit	13	I.T.	—	2.38	13950	428.2 ± 31.2	3	23.0		Lemberg, and Lyubchansky, 1971
$^{239}PuO_2$	Mouse	21	I.T.	0.003	0.008	115	500	1	5	Fibrosarcoma	Temple *et al.*, 1959
	Mouse	17	I.T.	0.06	0.15	2300	400	2	12	Squamous cell carcinoma	Wager *et al.*, 1956
	Mouse	41	I.T.	0.16	0.4	4000	100	1	2.5	Bronchiolar carcinoma	Temple *et al.*, 1959
	Mouse	73	Inhal.	0.1	0.25	—	500 +	1	1.4	Bronchiolar carcinoma	Bair, 1960
$^{239}PuO_2$	Rat	—	I.T.	0.2-1	—	—	>250	—	50-100	Epidermoid adenocarcinoma	Lisco, 1959
$^{239}PuO_2$	Dog	8	Inhal.	0.6	.0071 ± .0026	1230	2922 ± 732	7	87.5	Bronchiolar-	Park and Bair,
	Dog	13	Inhal.	1.3	.0147 ± .0029	2086	1992 ± 437	11	84	alveolar	1972
	Dog	6	Inhal.	2	.0229 ± .0021	2498	1539 ± 388	4	67	carcinoma	
	Dog	5	Inhal.	3.1	.0392 ± .0032	4094	1094 ± 236	2	40		
$^{239}PuO_2$	Rat	92	Inhal.	0	0	0	825	1	1.1	Dose calculated	Sanders, 1973
	Rat	30	Inhal.	0.005	0.002	9	650	2	6.6	to 700 days after	
	Rat	30	Inhal.	0.018	0.0072	32	675	7	23.3	exposure	
	Rat	32	Inhal.	0.2	0.092	375	550	8	25.0		

* Inhal. = Inhaled: I.T. = intratracheal injection.
** Calculated to time of death unless otherwise noted. Mean organ dose.

nodes, showed sclerotic lesions associated with accumulated plutonium. Three dogs had thoracic lymph node lesions of endothelial origin classified as hemangiosarcoma, lymphangiosarcoma and endothelioma. Another dog had a possible malignant lymphoma involving the mesenteric and mandibular lymph nodes. Autoradiographs of these nodes showed no radioactivity. This isolated case is not considered to be associated with the plutonium exposure.

In contrast to the results with $^{239}PuO_2$, preliminary data from a study of inhaled $^{238}PuO_2$ in dogs show a high incidence of osteosarcoma, although pulmonary neoplasia also occurred (Park *et al.*, 1974). This is consistent with the observed translocation of ^{238}Pu to bone following inhalation of $^{238}PuO_2$ in both dogs and rats.

Sanders (1973) has recently reported on the carcinogenicity of inhaled ^{238}Pu in rats. Three groups of 35 animals each inhaled an aerosol of ^{238}Pu in saline which gave initial lung burdens of 0.005 μCi, 0.018 μCi, and 0.2 μCi with associated cumulative radiation doses to lung of 9 rads, 32 rads and 375 rads, respectively, at 700 days postexposure. However, because of the rapid clearance of ^{238}Pu from lung, nearly all of the radiation dose was delivered to lung within 30 days after the inhalation exposure. The lung tumor incidence within the 0.005 μCi group was not significantly different from the control group. Groups receiving the two higher levels showed a statistically significant increased incidence of tumors but no increased mortality rate.

Osteosarcomas were observed in $^{238}PuO_2$ treated animals at the highest dose level only (i.e., greater than 50 rads accumulated dose to skeleton) which correlated with the translocation of plutonium to bone. The aerosol (crushed $^{238}PuO_2$ microspheres) was 72% ultrafilterable and was considered "soluble." Of the 19 pulmonary tumors found, there were 14 bronchiolar-alveolar tumors, two mixed carcinomas, one epidermoid carcinoma, one undifferentiated carcinoma and one malignant lymphoma.

There are limited data available on plutonium inhalation by nonhuman primates. Metivier *et al.* (1972) reported studies in which 19 baboons (Papio papio) were exposed at 2–3 years of age to an aerosol of $^{239}PuO_2$ with a count median diameter of 0.5 μm. The total lung burden at the time of death ranged from 0.01 to 0.1 μCi per gram of fresh

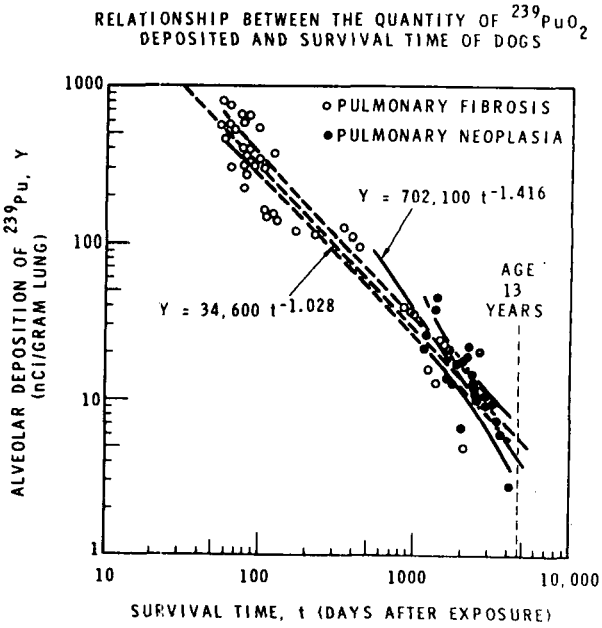

Figure III–7.—Relationship between quantity of $^{239}PuO_2$ deposited and survival time of dogs, Park *et al.*, 1972.

lung. Translocation was largely to tracheobronchial lymph nodes. All of the baboons had radiation pneumonitis. In addition, two epidermoid carcinomas of about 1.0 cm diameter were found after 80 days and two mucous-secreting adenocarcinomas of the same size were found after 180 days. Animals living past 80 days postexposure showed extensive areas of squamous metaplasia or nests of small "tumorlets." The authors concluded that baboons may be more sensitive than dogs to acute internal alpha irradiation.

Figure III–8 shows the incidence of lung cancer in the animal experiments described above as a function of the calculated total mean radiation dose to the lung. These data show an increased incidence of rat lung cancer occurring with doses as low as 10 rads. In rats and mice, the peak incidence probably occurs at doses between 200 and 1000 rads. The results from the only dog experiment show higher incidences than have been observed in rats.

The marked histopathologic changes in tracheobronchial and mediastinal lymph nodes of dogs that have inhaled plutonium (Clarke and Bair, 1964), and those occurring is superficial cervical and axillary lymph nodes of dogs given plutonium implants in the subcutaneous fascia over the dorsal metacarpus (Lebel *et al.*, 1972) were not observed to have been detri-

mental to the dogs. The only possible exception is one dog given a 5.8 μCi implant of air-oxidized plutonium in the dorsal metacarpus. This dog showed a generalized lymphadenopathy after four months and died of lymphosarcoma. However, because of the early development of this lesion the authors were hesitant to attribute it to the plutonium (Lebel *et al.*, 1970; Watters and Lebel, 1972). The calculated radiation dose to the superficial cervical lymph nodes was about 7000 rads. No other neoplasms were observed in these dogs, but they had been at risk for less than three years. In the plutonium inhalation studies at Battelle-Northwest, over 50 dogs have been at risk five to 11 years (Park *et al.*, 1972). Metastases of primary pulmonary tumors to tracheobronchial and mediastinal lymph nodes and lymphatics were common. However, as previously mentioned, only one dog had a possible malignant lymphoma, which was confined to the mesenteric and mandibular lymph nodes. It can be concluded from the relatively numerous rodent and dog experiments with ^{238}Pu and ^{239}Pu in which many lymph nodes have been exposed to a wide range of doses and dose rates from background

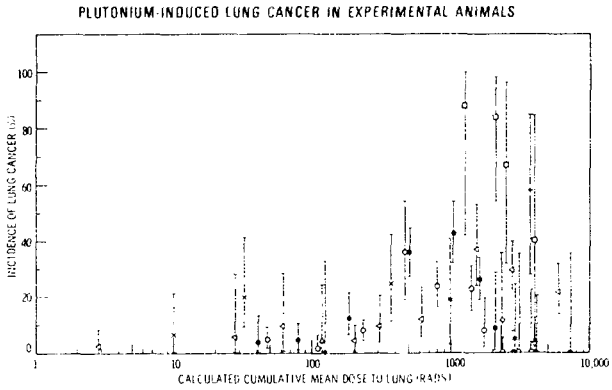

Figure III-8.—Plutonium-induced Lung Cancer in Experimental Animals. Mean incidence and radiation dose values are those reported in the literature. Binomial confidence limits were calculated from data included in the referenced literature.

- □ $^{239}PuO_2$—Dogs (from Park and Bair, 1972)
- ▽ $^{239}PuO_2$—Mice (from Temple *et al.*, 1959, 1960)
- △ $^{239}PuO_2$—Mice (from Temple *et al.*, 1959, 1960)
- ◇ $^{239}PuO_2$—Mice (from Wager *et al.*,1956)
- ○ ^{239}Pu Citrate—Rats (from Koshurnikova *et al.*, 1971)
- ● ^{239}Pu Ammonium plutonium pentacarbonate—Rats (from Koshurnikova *et al.*, 1971)
- × ^{238}Pu—Rats (from C. L. Sanders, 1973)
- ◁ ^{239}Pu—Rats—$Pu(NO_3)_4$ (from Erokhin *et al.*, 1971)
- + ^{239}Pu—Rabbits—$Pu(NO_3)_4$ (from Koshurnikova *et al.*, 1971)
- * ^{239}Pu—Rabbits—Ammonium plutonium pentacarbonate (from Koshurnikova *et al.*, 1971)

to thousands of rads, that lymph nodes are much less susceptible than lung tissue to the oncogenic action of alpha radiation from plutonium.

D. Experiments of Special Relevance to Nonuniform Dose Distribution

A number of factors influence the biological effects that may be produced by radionuclides. If, for example, the material is readily translocated from the lung to other organs, the eventual damage to these other organs may well appear earlier than lung lesions. Thus, in considering lung dose we are focusing primarily on those materials that will be retained in the lung for reasonably long periods of time and possibly causing low dose effects such as cancer which may occur late in life. Increased incidences of pulmonary neoplasia have been observed in experimental animals when there was no statistically significant shortening of life-span.

In most of the experiments there appears to be a relation between the radiation dose and the time or occurrence of malignancies in animals. In general, the higher the dose rate, the shorter time required for cancer induction. However, when the lung dose rate is too high, the animal will die from other causes such as respiratory insufficiency before there is time for cancer to occur. The data plotted in Figure III-8 suggest there is an optimal dose for the production of malignancies.

The production of early death by causes other than cancer can be regarded as a result of "wasted radiation" in interpretations which consider oncogenesis to be the most sensitive end point. From this standpoint, doses which lead to death before cancer appears can be considered to be overkill of the organism since the full expression of the oncogenic effects is not attained. For a single radioactive particle of $^{239}PuO_2$ in the lung (or other tissue), the dose rate near the particle can be high enough to cause the death of all cells within a given radius even if the residence time of the particle is short. Such cells will not be able to reproduce and subsequently result in cancer.* Radiation from particles which led to such overkill

* The presence of dead cells, cellular products or fibrosis may be required before a cellular transformation can express itself as a cancer. However, this concept has not been generally accepted.

should be less hazardous than equivalent radiation energy distributed over a large tissue volume. In fact, such a concept would lead immediately to the conclusion that the larger the particle (in terms of activity) the less effective the radiation emitted would be in producing cancer because of the increased fraction of radiation energy wasted on dead cells. An experiment showing this effect was done by Passonneau *et al.*, (1952) using glass beads containing ^{90}Sr on rat skin. The same amount of activity was used for the same area of skin but the activity was distributed either in a uniform flat plate, in 50 beads, in 20 beads or in 10 beads. The results given in Table III–B indicate clearly a decrease in the tumor production efficiency as the radioactivity was concentrated in fewer sources irradiating a smaller total area of tissue. However, the beads with the most radioactivity produced the largest number of tumors per bead and the smallest number of tumors per microcurie. The relevant parameter is tumors per microcurie because the basic question is how the risk from hot particles compares with the risk from uniformly distributed radiation doses.

Dean and Langham (1969), using data derived by Albert (1967a) on the production of tumors in rat skin, predicted on an absolute basis the probability of tumor production from various sizes of plutonium particles. The results of this calculation predict a very high probability of tumor production from most particle sizes relative to a 0.016 μCi lung burden. The experiment of Albert on rat skin is not really applicable to radioactive particles deposited in lung because it did not deal with particles, while Passonneau's is applicable to the extent that it deals with particulate radioactive sources, yet it still requires extrapolation from skin to lung.

The recent Natural Resources Defense Council (NRDC) petition (Tamplin and Cochran, 1974) uses mainly the results obtained in radiation skin experiments (Albert *et al.*, 1967a, 1967b, 1967c) to infer alpha-particle risks in the lung. Hence, a critical test of their hypothesis is whether a hot particle pattern of alpha irradiation of the skin can produce tumors.

Two approaches have been used in skin experiments. The first was to determine whether isolated small areas of irradiated skin gave the same yield of tumors per unit as large-area skin irradiations. The focal irradiation pattern with low LET radiation, electrons (Albert *et al.*, 1967b), was less efficient than the large area exposure in producing tumors. However, with high LET radiation (protons) there was no difference (Burns *et al.*, 1972). If these results can be extrapolated to alpha radiation, they suggest that the risk from particulate sources is no greater than from uniformly distributed sources.

The second approach involved the irradiation of different depths in skin. In studies of electron radiation with varying energies and penetrating power, the occurrence of tumors and atrophic follicles suggested the existence of target cells at a depth of about 0.3 mm in the skin corresponding to the lower end of the resting hair follicle (Albert *et al.*, 1967a). This critical depth remained constant even when the skin was irradiated with the hair in the growing phase, i.e., when the follicles extend to a depth of 0.8 mm (Burns *et al.*, 1973a). There was a quantitative association between the incidence of tumors and atrophic follicles for various types of ionizing radiation, various spatial distributions of dose within the skin and for different phases of hair growth (Albert *et al.*, 1967c). A plausible explanation for the experimental results is that each follicle has a population of stem cells at a depth of 0.3 mm that are concerned with the production of sebaceous cells and hair. These stem cells apparently constitute the most sensitive potential oncogenic cell population to ionizing radiation in the rat skin since all the tumors were mainly of hair follicle origin (Albert *et al.*, 1969). Neoplastic transformation of a significant number of these target cells required

Table III–B

TUMOR PRODUCTION IN RAT SKIN FOLLOWING EXPOSURE TO FLAT PLATE AND POINT SOURCES OF $^{90}Sr/^{90}Y$*

Source	Activity	Number of rats	Number of tumors: Total	Number of tumors: Per bead	Number of tumors: Per μCi	Relative efficiency
Flat Plate (1000 μCi)	28.6 μCi/cm²	71	89	—	0.00049	1.59
Flat Plate (1500 μCi)	42.9 μCi/cm²	73				
50 Beads	30 μCi/bead	58	27	0.009	0.00031	1.00
20 Beads	75 μCi/bead	77	24	0.016	0.00021	0.671
10 Beads	150 μCi/bead	74	16	0.022	0.00014	0.464

* Modified from Passonneau *et al.* (1952) by information given in NAS-NRC Publication 848 (NAS-NRC, 1961a).

large radiation doses which in turn killed most of the target cells and thus caused follicle atrophy.

Similar studies were reported (Albert *et al.*, 1972) in which the dorsal skin of mice was irradiated with electrons in single exposures at varying dose levels. Comparison of these data with the rat skin experiments showed that the radiation sensitivity of the mouse skin for hair follicle destruction was at least twice that of the rat, that the incidence of atrophic follicle formation in the mouse was considerably less than in the rat, and that as a consequence the incidence of epithelial skin tumors (adnexal tumors) is "markedly lower in mice than in rats." Thus the hair follicles in the mouse skin exhibit a lesser ability to form atrophic hair follicles and a greater sensitivity to the lethal action of the radiation. Furthermore, there are striking differences between strains of rats in the incidence of adnexal tumors resulting from similar doses of electron skin irradiation (Albert *et al.*, 1961).

Because alpha radiation from a plutonium particle has a range in unit density tissue of only about 40 microns, the effect of focal irradiation at different levels of the hair follicle is a crucial test of the recent NRDC proposal (Tamplin and Cochran, 1974). Alpha irradiation of the skin from the surface to a depth of about 0.15 mm did not produce tumors (Heimbach *et al.*, 1969). This result, however, is consistent with the existence of a target cell population at a depth of about 0.3 mm. However, selective irradiation of the lower end of the hair follicle at a depth of 0.3 mm by use of the Bragg peak from an alpha beam did not produce tumors or atrophic follicles unless there was substantial irradiation of the entire follicle. This observation suggests that even though the critical cell population is located at 0.3 mm, there are recovery mechanisms that block oncogenesis when only part of the "critical architectural unit of tissue" is irradiated. What these recovery processes might be is not understood. Nevertheless, this result does not support the contention that a single plutonium particle irradiating a "critical architectural unit" such as the hair follicle, will produce a tumorigenic risk of the magnitude assumed by Tamplin and Cochran (1974).

Richmond *et al.* (1970) investigated the effects of ^{238}Pu dioxide particles lodged in the rodent lung vasculature following intravenous injections. These particles averaged about 180 μm in diameter and gave average dose rates to the entire lung of about 3.5 rems per hour with the alpha particle dose rate at the surface of the particle on the order of 10^8 rads per hour. The longest exposure until sacrifice was a group of 6 rats which lived to 600 days. Examination of the lung following these exposures indicated the presence of a microlesion with complete degeneration of the cells close to the particle. However, the evidence indicated that this was not simply a stable type of scar tissue but rather that the lesion was in a dynamic state in which the collagen was renewed constantly with subsequent liquification. Within this time period there were no tumors produced nor were there any indications of effects that would be deleterious to the animal's overall well being. It is noteworthy that the energy delivered to the lung, if averaged over the entire lung, would be on the order of 2,000,000 rads in 600 days. This dose, if uniformly distributed, is much greater than that shown to cause deaths in relatively short times and is considerably above doses shown to produce lung cancers.

In the experiment of Richmond *et al.* (1970), the particles appeared to be firmly fixed in the blood vessels, and therefore were not representative of particles actually deposited in the alveoli. Although movement of such particles is known to occur, compared with inhaled plutonium they are relatively static. Cells located at the periphery of the zone of cellular destruction caused by the radiation may receive radiation doses ranging from just sublethal to essentially zero.

Experiments in which $^{238}PuO_2$ microspheres, similar to those used in the rodent studies, and $^{239}PuO_2$ microspheres were surgically implanted into the lung of beagle dogs yielded results that were qualitatively similar to those observed in rodents. The implanted plutonium particles produced small discrete microlesions but no lung malignancies were observed (Richmond *et al.*, 1974). It should be recognized that relatively few animals were used and that the times of exposure were not long. However, one dog was sacrificed at 4 years and 2 are still alive 7 years past implant. That lung malignancies have not been observed even though the local radiation doses were extremely intense is of considerable radiobiological interest.

Any repopulation of the volumes of destroyed tissue could result in rapid proliferation of damaged cells which have received sublethal doses of radiation. This situation would appear to have a high potential for producing cancer but is difficult to investigate experimentally without an understanding of the basic mechanism of cancer production and of the response of such damaged cells to an otherwise normal environment. Information on this possibility is limited but some indication that it is not a predominant problem can be obtained from the experiments of Passonneau (1952) and Richmond *et al.* (1970, 1974) which did involve just such conditions in several types of tissue.

Current work uses a similar experimental design but with 10 μm diameter zirconium oxide microspheres containing PuO_2 at specific activities corresponding to respirable particles of PuO_2. These experiments are directly applicable to the hot particle problem (Richmond and Voelz, 1972, 1973; Richmond and Sullivan, 1974). In these experiments every animal received 2000 plutonium-containing particles. Eight exposure levels and two control groups were used with particle specific activities ranging from 0.07 to about 60 picocuries. Of the 713 hamsters used in this experiment only two control animals and one injected animal are alive at present. Table III–C shows the radiation doses calculated by three dosimetric models and the number of expected tumors per group as calculated from a lung model (Coleman and Perez, 1969) based on Albert's skin data. This model is basically similar to those developed by Geesaman (1968) and Dean and Langham (1969) as the dose response function assumed in the calculation is based upon the Albert rat skin data. About 1% of the lung mass of the animals shown in Table III–C was irradiated, and the median dose rate to those cells within alpha range of a microsphere was estimated to be 20–1800 rad/day.

No aberrant clinical signs have been observed in any of the animals that have died or have been sacrificed to date. Blood samples have revealed no abnormalities even after long exposures and there have been no regional lymph node effects. Occasionally, small accumulations of macrophages are seen around spheres but the fibrous encapsulation previously described for the larger more radioactive (about 180 micron diameter) spheres (Richmond *et al.*, 1970, 1974) are not seen. Two rarely occurring tumors were observed among animals included in Table III–C. One hamster developed an angiosarcoma of the lung after 9.5 months exposure to 2000 microspheres each containing 0.42 picocurie alpha activity (level 2A). Another animal developed a lung sarcoma at the same exposure level after 12 months. Table III–C shows a predicted tumor incidence of 40 tumors for this group (level 2A). No other lung tumors have been observed in this experiment. Every animal in the experiment should have developed two lung tumors if the tumor probability is 10^{-3} per particle as speculated by Geesaman (1968).

Table III–C

EXPOSURE CONDITIONS FOR PRELIMINARY EXPERIMENT (2000 SPHERES/ANIMAL, ABOUT 70 ANIMALS/GROUP)

(Richmond and Voelz, 1972)

Isotope	Level Number	nCi/Animal	Specific Activity pCi/sphere	Equivalent Diameter Pure $^{238}PuO_2$ (μm)	Local Dose Rate at "Averaged Dose Rate"[b] (rads/yr)	Local Dose Rate at Surface of Sphere (rads/hr)	Local Dose Rate at 40 μm from center (rads/hr)	Expected Tumor Incidence[a] (tumors/group)
^{239}Pu	1	0.14	0.07	0.09	13	4.2×10^{1}	6.8×10^{-1}	2
	2	0.44	0.22	0.13	42	1.2×10^{2}	2.2×10^{0}	10
	2A	0.84	0.42	0.16	81	2.5×10^{2}	4.1×10^{0}	40
	3	1.82	0.91	0.21	175	5.5×10^{2}	1.0×10^{1}	60
	3A	3.2	1.6	0.26	310	1.0×10^{3}	1.7×10^{1}	40
^{238}Pu	4	8.6	4.3	0.36	875	2.5×10^{3}	4.2×10^{1}	10
	5	26.6	13.3	0.52	2710	8.4×10^{3}	1.3×10^{2}	0
	6	119.0	59.4	0.86	12100	3.6×10^{4}	5.8×10^{2}	0

[a] Using NUS structure lung, with a lung density of 0.19 g/cm³. (Coleman and Perez, 1969.)
[b] Assuming 1 g of lung irradiated.

An additional 485 animals were injected with larger numbers of spheres, 6000–1,000,000 per animal, to irradiate over 98% of the lung. Lower specific activity spheres were used, and median dose rates ranged from 6–25 rad/day. One of these animals developed a primary lung tumor. Other animals have been injected with 50,000–900,000 spheres to extend the range of sphere specific activity down to 0.015 pCi/sphere. Lung burdens were 0.86–177 nCi, and median dose rates were 1.3–320 rad/day. There are about 2000 animals in this study.

Approximately 1150 animals have lived their full life spans or have been sacrificed to date as part of this experiment. About 5.7×10^6 spheres with specific activities in excess of 0.07 pCi each were injected into these animals. The observation of three primary lung tumors suggests a tumor risk of roughly 10^{-7} per particle as a preliminary estimate. These results are particularly significant in view of the demonstration by Little *et al.* (1970a, 1970b, 1973) that the Syrian hamster develops pulmonary neoplasms with high efficiency and short induction time following exposure to soluble ^{210}Po.

The distribution of all exposure conditions is summarized in Figure III–9 in which the ordinate is the number of spheres per animal (scale on left) or fraction of lung irradiated (scale on right), and the abscissa is sphere specific activity. The diagonal lines are loci of constant plutonium dose and are labeled with the lung burden in nCi. The special interest in burdens between 10 and 100 nCi is occasioned

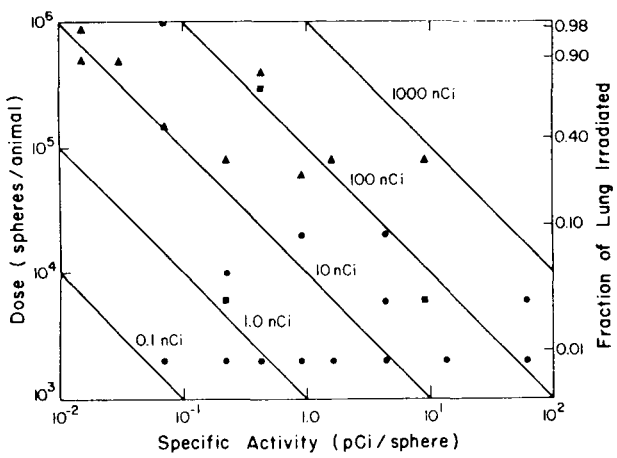

Figure III–9.—Distribution of exposure groups with respect to number of spheres per animal (ordinate) and specific activity of spheres (abscissa). The lines are loci of constant lung burden and are labeled with nCi of plutonium per animal. Symbols indicate year of injection: (●) 1971; (■) 1972; and (▲) 1973 (Richmond and Sullivan, 1974).

by the report of Little *et al.* (1970a) that a high tumor incidence develops rapidly in hamsters exposed to these levels of soluble ^{210}Po.

In a study of $^{239}PuO_2$ particles administered by intraperitoneal injection in rats, about 2% of the plutonium was found in the vasculature of the lung 300–500 days post-injection (Sanders, in press). The mean lung doses from these plutonium particles of > 0.3 μm diameter ranged from 10 to 600 rads for three treatment levels: 0.072, 0.360 and 2.900 μCi. Of 106 rats that survived longer than 200 days (life shortening occurred in the highest dose groups and was due to irradiation of the peritoneal cavity), one rat in the lowest dose group died with a bronchiolar-alveolar adenocarcinoma after 823 days. There was no other primary pulmonary neoplasia and little evidence of cellular reaction to the plutonium particles in the lung, even among those cells adjacent to the particles. Inflammation, fibrosis, and epithelial hyperplasia and metaplasia were not observed. In general these findings agree with the results from the current plutonium microsphere studies at Los Alamos (Richmond and Voelz, 1972, 1973; Richmond and Sullivan, 1974).

The liver has been used to determine the effectiveness of $^{239}PuO_2$ particles in producing chromosome damage relative to the amount produced by ^{239}Pu citrate in the ionic or monomeric form (Schubert *et al.*, 1961). Brooks *et al.* (1974) injected monodisperse $^{239}PuO_2$ particles (0.17, 0.30, 0.44 and 0.84 μm) intravenously into Chinese hamsters. About 90% were deposited and retained with a long effective half life in the liver. Using these four particle sizes and ^{239}Pu citrate, two cytogenetic studies were conducted. In the first, a constant total activity, 1×10^{-3} μCi/gm body weight, was injected using the three sizes of PuO_2 particles. Constant activity and variable particle size produced a constant average radiation dose to the liver with a varied local radiation dose and percent of the liver irradiated. In the second study, a constant particle size, 0.30 μm, was injected with activity ranging from 6×10^{-3} to 6×10^{-5} μCi/g body weight. The local radiation dose rate around each particle was constant in this case and the average radiation dose and number of particles were variable. Unexposed animals and animals administered ^{239}Pu citrate at a concentration of 6×10^{-4} μCi/g body weight were used for comparison purposes.

When the average dose was related to the aberration frequency for the ^{239}Pu citrate (Figure III–10), there was a linear increase according to the equation $Y=0.02+4.8\times10^{-3}D$ where Y is aberrations per cell and D is dose in rads. This relationship implies that approximately 200 rads of irradiation from uniformly distributed ^{239}Pu were required to produce an average of 1 aberration per cell. Because cells with radiation-induced chromosome aberrations have poor reproductive potential, these cells can be considered as reproductively dead (Carrano and Heddle, 1974). Abnormalities observed following injection of the particles increased in an approximately linear manner over an average dose range up to about 200 rads, then plateaued at higher doses. The slope of the ascending portion of the dose-response curve for the particles was less than that observed following injection of ^{239}Pu citrate. The relationship between aberration frequency and average dose to a sphere of tissue within the range of alpha radiation from plutonium particles indicates that the efficiency of producing aberrations decreased as the particle size increased. At the smallest particle size, 0.1 μm, the response was close to that seen in animals exposed to ^{239}Pu citrate suggesting that the dose distributions in the liver were similar.

In addition to determining the aberration frequency per cell, the distribution of damage throughout the cell population was also determined. The distribution of damage among liver cells exposed to plutonium particles was non-Poisson, indicating that the damage was limited to relatively few cells, some of which were severely injured. The damage in cells exposed to ^{239}Pu citrate (Brooks *et al.*, 1974) was described by a Poisson distribution, indicating a large number of less severely damaged cells; similar results were observed in experiments with ^{241}Am (McKay *et al.*, 1972) and ^{252}Cf (Brooks *et al.*, 1972). This implies that a larger fraction of the irradiated cells were reproductively dead after nonuniform irradiation than after uniform irradiation, and perhaps also indicates a smaller risk for tumor induction.

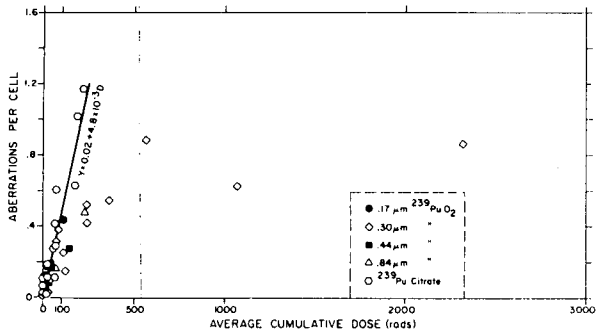

Figure III–10.—Chromosome aberration frequency in the liver of the Chinese hamster following intravenous injections of $^{239}PuO_2$ particles or ^{239}Pu citrate relative to average tissue dose in rads.

Little and co-workers (Little *et al.*, 1970a, 1970b; Grossman *et al.*, 1971; Little *et al.*, 1973) studied the effects of ^{210}Po chloride adsorbed onto hematite (ferric oxide) particles in Syrian golden hamsters following intratracheal instillation. Animals were given 15 weekly injections of 3 mg of hematite containing either 0, 0.01 or 0.2 μCi of ^{210}Po; the mean radiation doses calculated for the entire lung were 225 and 4500 rads, respectively, at the end of one year (Little *et al.*, 1970a). The earliest and highest incidence of pulmonary neoplasia occurred in those hamsters receiving the larger dose of ^{210}Po; the first lung cancer appeared in an animal sacrificed 15 weeks after administration. This experiment showed that lung cancer could be produced in hamsters by alpha radiation, but it did not consider the relative effectiveness of uniform versus nonuniform dose distribution.

In an experiment designed to consider uniform and nonuniform dose distributions (Grossman *et al.*, 1971), four groups of 50 hamsters each were given separate intratracheal instillations twice per week for seven weeks of either 3 mg hematite followed by 0.2 μCi ^{210}Po in saline, saline followed by 0.2 μCi ^{210}Po, saline followed by 0.2 μCi ^{210}Po adsorbed onto 3 mg hematite, or saline followed by 0.2 μCi ^{210}Po adsorbed onto 0.3 mg hematite. In an additional experiment (Little *et al.*, 1973) hamsters were given seven weekly injections of 0.2 μCi ^{210}Po alone in saline. The cumulative radiation dose to the lung was about 800 rads as compared with about 2000 rads when the same amount of activity was given adsorbed on either 3 or 0.3 mg hematite particles. The mean tumor induction time was considerably shorter for the group given ^{210}Po in saline, and the tumor incidence was lowest for the group with the most nonuniform distribution of ^{210}Po.

The major differences among the groups in these experiments was in the microscopic distribution of the ^{210}Po as shown by autoradiog-

raphy. Distribution throughout the lung was distinctly nonuniform for the ^{210}Po contained on hematite. Reduction of the mass of hematite particles from 3 to 0.3 mg should have had the effect of further increasing the nonuniformity of the ^{210}Po in the lung as there were 1/10 as many particles administered and each one contained 10 times as much activity. Preliminary results suggested that an equal amount of ^{210}Po adsorbed on 0.3 mg hematite was even less effective for lung tumor induction than when adsorbed on a larger number of carrier particles of lower specific activity (Table III–D and Fig. III–11).

Little *et al.* (1973) tentatively concluded that ". . . in the dose range studied, alpha radiation is more carcinogenic when a lower but relatively uniform dose is delivered to a large volume of lung tissue than when a similar amount of radioactivity is distributed nonuniformly such that the primary effect is to deliver much higher radiation doses to relatively small tissue volumes."

Studies of a beta-gamma emitter failed to confirm the existence of a unique carcinogenic hazard due to intense irradiation of tissue surrounding radiation particles in lung (Cember and Watson, 1958a, 1958b; Cember *et al.*, 1959; Cember, 1963; Cember, 1964a, 1964b; Cember and Stemmer, 1964). In a series of experiments with intratracheally administered $^{144}CeF_3$ and $^{144}CeCl_3$ in rats, the incidences of pulmonary neoplasia were similar to those observed at comparable radiation doses in experiments where ^{90}Sr containing glass beads were implanted in rat lungs.

Table III-D

INFLUENCE OF DOSE DISTRIBUTION ON ^{210}Po CARCINOGENESIS

Treatment Schedule* Mon	Wed	Radiation Dose**	Number of Animals Autopsied 58th Week	Number Still Alive	Number with Lung Tumors	Tumor Incidence
3 mg heme	^{210}Po alone	800 rads	37	0	22	60%
Saline	^{210}Po–3 mg heme	2000 rads	31	6	18	58%
Saline	^{210}Po–0.3 mg heme	—	25	12	9	36%

* Animals received two instillations each week for 7 weeks. Polonium-210 (0.2 μCi) given either *alone in saline or bound to* hematite particles in amounts indicated.

** Cumulative radiation dose averaged over whole lungs for period up to 1 week after last instillation. These doses tentatively assigned, *based on preliminary radiochemical data.*

When Cember gave 0, 4.5, 45 or 4500 microcuries of $Ba^{35}SO_4$ as a single intratracheal injection to rats, no lung cancer or any other lesion suggesting that cancer might develop was observed in any of the experimental animals during a nine-month observation period (Cember *et al.*, 1955). When the $Ba^{35}SO_4$ was given as 10 weekly doses of 375 microcuries each, 2 of the 16 rats which survived the injection regime died at 312 and 319 days later with extensive squamous cell carcinomas of the lung (Cember and Watson, 1958b). Calculated radiation doses were on the order of 12,000 rads.

Cember and Watson (1958a) implanted ^{90}Sr containing glass beads in the lungs of rats. The beads contained from 1.09 to 59.3 μCi ^{90}Sr and were 320 ± 110 μm diameter. Seven of the 23 rats (30%) developed primary pulmonary neoplasms: 4 had squamous cell carcinomas and 3 had lymphoid neoplasms. The earliest death in a tumor bearing animal occurred at 169 days following implant. The total radiation dose in these animals, calculated for a sphere of tissue with a radius equal to the range of the beta radiation, ranged from 47,000 to 260,000 rads. Murine pneumonia was a problem with the experimental animals. No acute deaths were due to radiation effects and no life-shortening was observed.

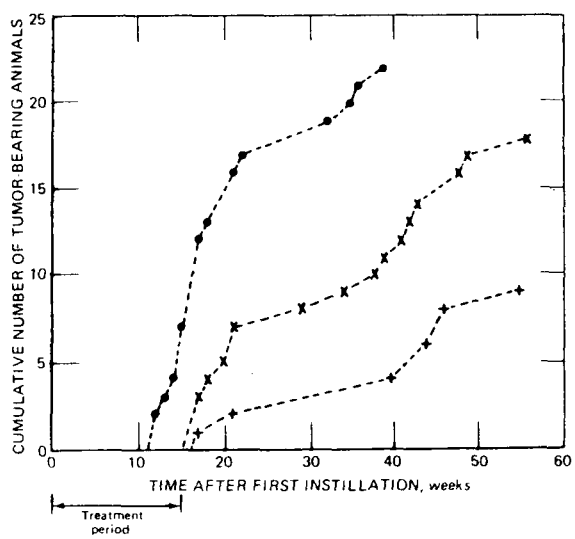

Figure III–11.—Influence of dose distribution on the induction time of lung tumors. Hamsters were given seven weekly intratracheal injections of 0.2 μCi of ^{210}Po and hematite particles by different treatment plans: ●- - -●, ^{210}Po in saline and 3 mg of hematite given on different days each week. x- - -x, ^{210}Po adsorbed onto 3 mg of hematite particles. +- - -+, ^{210}Po adsorbed onto 0.3 mg of hematite particles (see Table III-D).

The experiments of Cember are of considerable relevance to the problem of nonuniform dose distribution. Cember (1964a) stated that the question of the unique carcinogenic hazard associated with the high absorbed dose gradient around a single radioactive particle deposited in the lung seemed to be answered by the results of the acute $Ba^{35}SO_4$ exposures together with the ^{144}Ce experiments. He also pointed out that the negative results of the long term retention of several $Ba^{35}SO_4$ particles, under conditions suitable for testing the hypothesis that such focal radiation presents a unique carcinogenic hazard to the lung, imply the absence of such a hazard associated with one or a very small number of loci. His review also emphasized that, for a given total amount of absorbed energy, low-level, continuous exposure of the total lung may be more carcinogenic than the same amount of energy delivered acutely to a restricted volume of tissue.

Furthermore, Cember (1964a) realized that the quantitative relationship among total absorbed dose, the temporal and spatial distribution of the dose, and probability of developing radiogenic lung cancer had not been established at that time. However, the similarity of the lung tumor dose response curves for soluble $^{144}CeCl_3$ and insoluble $^{144}CeF_3$, suggested the absence of a hot particle effect. He states "should this be true, then it follows that radiation dose to the lung from inhaled radioactive dusts may be calculated, for purposes of estimating radiological risk, by assuming uniform absorption of energy throughout the lung." However, the ^{144}Ce experiments should be interpreted with caution since Cember (1964b) noted that the $^{144}CeCl_3$, which is soluble in solution, produced discrete focal areas of radioactivity in the lung following injection.

In the summary of his review Cember (1964a) states, "Experiments with rats have shown that radioactive substances deposited in the lung can lead to pulmonary neoplasia. Radiations from ^{35}S, ^{90}Sr–^{90}Y, and ^{144}Ce elicited bronchogenic carcinoma and alveolar cell carcinoma in addition to several other tumor types. These experiments did not confirm the existence of a unique carcinogenic hazard due to the intense concentration of absorbed energy in the lung tissue immediately surrounding an inhaled radioactive particle."

Studies reviewed by Moskalev (1972) with inhaled ^{239}Pu citrate or ammonium ^{239}plutonium pentacarbonate have shown a significant increase in the incidence of lung tumors in rats at cumulative absorbed radiation doses to the lung of about 50 rads. Studies in rats reported by Sanders (1973) indicated increased lung tumor formation at 9 and 32 rads following inhalation of ^{238}Pu although the number of tumors in the 9 rad dose group were not statistically significant as compared with unirradiated controls. According to Koshurnikova *et al.* (1968) the microdistribution of ^{239}Pu in the lungs and regional lymph nodes at long times after exposure is characterized by nonuniformity. This has also been observed in dogs, Figure III–3. Therefore, it is likely the radiation dose from the ^{238}Pu in Sanders' study was more distributed in lung tissue than the ^{239}Pu in the studies reviewed by Moskalev, thus irradiating a relatively larger number of sensitive cells. This could account for Sanders finding lung cancer occurring at lower radiation doses from ^{238}Pu than has been associated with ^{239}Pu. However, dose rate cannot be excluded as a contributing factor because the ^{238}Pu in Sanders' experiment was cleared very rapidly from the lungs; nearly all of the radiation exposure occurred within 100 days after inhalation of the ^{238}Pu aerosol.

Preliminary results from studies by Lafuma (1974) and his colleagues with compounds of ^{238}Pu, ^{239}Pu, ^{241}Am and ^{244}Cm in rats indicate that the toxicity increases with the dispersion of the inhaled radionuclide in lung. Curium-244 nitrate was the most highly dispersed and the most toxic at equivalent radiation doses. Curium-244 was also cleared from lung more rapidly than the other radionuclides with a pulmonary retention half-time of only eight days.

The conclusion which results from a careful consideration of these experimental animal studies is clear. None of the results unequivocally prove that plutonium distributed in lung tissue as particles is more hazardous than the same amount of plutonium distributed uniformly. To the contrary, experimental results lead to the conclusion that the hazard of plutonium increases with the dispersion of plutonium within the lung. Although inhaled plutonium is seldom if ever uniformly distributed in lung but is aggregated, a model based on uniform distribution is probably the conservative approach for radiation protection purposes.

IV. HUMAN EXPERIENCE

There has been no recorded incidence of cancer in man resulting from the internal deposition of any plutonium isotope in the more than three decades that plutonium has been used. This excellent record has resulted from extremely effective control methods. The absence of tumors is also significant evidence concerning the tumorigenic potential of plutonium in the lung because a number of wartime accidental exposures occurred three decades ago—a time comparable with probable tumor induction times. Data from occupationally exposed Pu workers, limited as it is, constitutes human experience of the most relevant kind for establishing value judgments where experimental data are not always conclusive for formulating risk evaluations.

During late 1944 and 1945, at what is now the Los Alamos Scientific Laboratory, 29 men associated with the Manhattan Project as plutonium workers were identified on the basis of nose swipes or urine radioassay as having received plutonium exposures (Hempelmann *et al.*, 1973b). Of these, 3 were later dropped from the series as the result of improved assay techniques which indicated lower plutonium burdens than estimated earlier, and 1 died of coronary heart disease. These individuals were all young men involved in four basic operations related to the development of the first nuclear weapons: plutonium purification (wet chemistry); fluorination (dry chemistry); reduction to metal; and recovery.

Clinical and laboratory data from this group of men have been collected periodically since 1953. These data consisted of medical histories, physical examinations, blood counts and chemistry, urine radiochemistry, routine urinalysis, and roentgenograms (Hempelmann *et al.*, 1973b). Studies of sputum cytology, lymphocyte karyology, and chest counting for uranium L x-rays were begun in 1970. Table IV–A shows information on estimated date of exposure and estimates of the body burden as determined by urine radiochemistry measurements made in 1953 and 1972 (Hempelmann *et al.*, 1973a). In all cases, the values represent estimates of the body burden based on a urine excretion model obtained from human data (Langham, 1957). In all cases but two, the 1972 estimates are higher than those for 1953, usually by a factor of 2–3 and occasionally by a factor of 5–6. The 1972 estimates are considered to be more relevant as they are based

Table IV–A

PLUTONIUM BODY BURDEN ESTIMATES FOR MANHATTAN PROJECT PLUTONIUM WORKERS

Subject Number†	Average Date of Exposure	ESTIMATED SYSTEMIC BODY BURDEN* 1953	1972
1	Late 1944	0.03–0.06	0.206
2	Late 1944	0.006–0.032	0.03
3	May 1945	0.08	0.42
4	June 1945	0.08	0.26
5	June 1945	0.08	0.18
6	June 1945	0.06	0.14
7	June 1945	0.06	0.15
8	June 1945	0.04	0.11
9	July 1945	0.06	0.11
10	July 1945	0.05	0.10
11	July 1945	0.03	0.05
12	July 1945	0.03	0.12
13	July 1945	0.02	0.005
16	July 1945	0.006	0.03
17	August 1945	0.04	0.13
18	August 1945	0.04	0.10
19	August 1945	0.03	0.02
20	August 1945	0.02	0.05
21	August 1945	0.02	0.04
22	August 1945	0.02	0.05
23	September 1945	0.02	0.04
24	September 1945	0.006	0.03
25	September 1945	0.006	0.01
26	October 1945	0.02	0.006
27	October 1945	0.02	0.05

* Microcurie ± approximately 50% at the year indicated.

† Subjects #14 and #15 were dropped because of the death of one subject from coronary heart disease and the low body burden of the other as determined by modern assay techniques. Two others, not shown, were dropped from the original 29.

upon more excretion data and improved analytical techniques. High plutonium levels of nose swabs at the time of exposure suggested that most of the subjects received their exposure via inhalation.

Based on data shown in the last column of Table IV–A, the 25 men shared a total systemic plutonium burden of approximately 2.5 μCi in 1972. If one assumes, as a rough approximation, that 25% of the initial lung burden was translocated from the lung to the systemic circulation and then to organs such as the liver and bone, it follows that the total initial lung burden for this group of men was approximately 10 μCi.

During the most recent examinations performed at Los Alamos (Hempelmann *et al.*, 1973a) estimates were made of the amount of plutonium in the chest (lung and respiratory lymph nodes) of each man using *in vivo* chest counting techniques. At 27 years following contamination, 14 of the 21 men measured had calculated chest burdens ranging from 0.003 to about 0.010 μCi. This observation indicates that some of the plutonium was inhaled or retained in a relatively insoluble form, which is consistent with the fact that some of the individuals were known to have been exposed to $^{239}PuO_2$ because of the work they performed. Studies of these and other men are continuing.

Except for the ailments one would expect in a group of men mostly in their early fifties, all of the Manhattan Project workers are in remarkably good health. This is additional information that tends to support the general argument that the radiation protection guides for plutonium have not been grossly in error. Although the study group is relatively small (25 men), the magnitude of the plutonium burdens, the long time since exposure, and the cooperativeness of the men make it unique and extremely valuable. However, because something like 16 to 20% of all deaths annually in the United States are from cancer, one might be concerned about the size of the group, as 4 or 5 might be expected to die from "naturally occurring" cancer had they never been exposed to plutonium. However, evidence obtained from experimental animal studies indicates that plutonium induces specific kinds of cancer, primarily lung carcinomas, bone sarcomas, and to a lesser extent bile duct tumors, depending on the route of exposure.

Although the particle size distribution of the inhaled material is unknown, an estimate can be made on the basis of aerosols produced by somewhat similar incidents. The value of 0.32 μm for the mass median diameter was measured for an incident involving a fire at the Rocky Flats facility in 1965 (Mann and Kirchner, 1967) and is similar to values found in a glovebox at a fuel fabrication plant by Raabe (in preparation) and by Moss *et al.* (1961) for plutonium aerosols in plant and laboratory operations. Ettinger *et al.* (1973) report various particle sizes for several operations. For a recovery operation, a submicron aerosol had a typical activity median aerodynamic diameter of 0.3 μm.

If one assumes a log-normal particle size distribution with a mass median diameter of 0.32 μm, standard geometric deviation (σ_g) of 1.83, and a density of about 10 g/cm^3, the number of particles above a given size can be calculated. In this case, about 15% of the mass can be shown to be associated with particles larger than 0.6 μm real diameter (about 2 μm aerodynamic equivalent diameter). One can then calculate that each person in the group of 25 men might have retained about 4×10^5 particles above 0.6 μm diameter (0.07 pCi or more per particle) from the orginal 10 μCi. If the cancer risk for such "hot particles" were 5×10^{-4} per particle, as postulated by the Natural Resources Defense Council report (Tamplin and Cochran, 1974), the 4×10^5 particles should yield about 200 cancers per man or about 5000 for the group. Even the residual plutonium (average of 6 nCi per man) measured in 14 of the original Manhattan Project plutonium workers should yield 3 cancers per person. One could also argue that the number of cancers predicted from such a risk estimate might be ten times larger as the product of 10^8 particles (10 μCi ÷ 0.07 pCi), each 0.6 μm real diameter, and the risk estimate of 5×10^{-4} per particle yields 5×10^4 tumors for the group. The observed lung cancer incidence after almost 30 years since exposure is zero.

Because of observations of chronic lymphopenia in dogs exposed to plutonium oxide aerosols, one might expect to observe chromosome damage in lymphocytes of exposed plutonium workers. This observation led Dolphin (1971) to investigate the possibility of chromosomal aberrations in lymphocyte cultures obtained from workers in England known to have been

exposed to plutonium. He compared the findings in eight plutonium workers who had been exposed to plutonium plus 14 rad of external irradiation over a 7-year period with workers who had received external irradiation only and found that the dicentric yield of lymphocytes of the plutonium workers could be accounted for by the external radiation dose received by the workers. Dolphin (1971) also cites another case in which a plutonium worker was found, by chest-counting, to have 10 to 20 times the permissible level of plutonium in the lung about three years after an inhalation accident. Chromosome analysis indicated minimal radiation exposure to the lymphocyte series even at a high level of exposure of the subject.

Brandon *et al.* (1973) reported an increased incidence of chromosomal aberrations in plutonium production workers at the Dow Rocky Flats plant. These investigators contrasted chromosomal aberrations observed in lymphocyte cultures from six unexposed controls, seven workers exposed to penetrating radiation, and 27 men thought to have internal deposition of plutonium. Although the workers with lung burdens of plutonium had levels of chromosome aberrations greater than those observed for controls, the highest incidences of chromosomal aberrations were observed in plutonium workers who were thought to have primarily liver and bone burdens rather than significant lung burdens. Because some of these individuals worked around hot cells, the contribution to the total radiation dose (plutonium plus penetrating radiations) from the penetrating radiation is uncertain and complicates the analyses.

The most recent physical examinations were performed on 24 of the 25 Manhattan Project workers during the past several years (Hempelmann *et al.*, 1973a). In addition to the usual hematological procedures, blood samples were obtained from these men for chromosomal studies. Utilizing established cytogenetic techniques for cultured lymphocytes, no chromosomal abnormalities were found in any of the subjects. However, it is planned that recently developed chromosomal banding techniques will be utilized in the future in evaluating the presence or absence of lymphocyte chromosomal aberrations.

Despite their relative rarity, much useful information has been obtained from accident cases. Information obtained from the AEC's Division of Operational Safety indicates that, during the period 1957–1970, there have been on the order of 200 contractor personnel exposed to 25% or more of the maximum permissible body burden (MPBB) for plutonium. These data also indicate that inhalation is the major portal of entry and that more than half of the cases are below 50% of the MPBB (0.04 μCi).

It may be instructive to look at a specific instance of an industrial accident which was reported by Mann and Kirchner (1967). On 15 October 1965, a fire in a plutonium fabrication plant resulted in a large-scale spread of plutonium oxide. The Rocky Flats body counter was used to measure the plutonium in the lungs of all employees working in the area and, of approximately the 400 employees counted, 25 were found to have enough plutonium in their lungs to deliver a dose of 15 rem per year or greater (i.e., at least 0.016 μCi). Data from each employee were obtained with a pair of scintillation detectors in contact with the subject's chest; the 60 keV photon peak of ^{241}Am was used in the measurements. The ^{241}Am content of the plutonium released in the fire was determined, and the plutonium quantity was then estimated from calibrations using a chest phantom with similar ^{241}Am/^{239}Pu ratios. The plutonium consisted of "high-fired" PuO_2; particle size measurements of air samples collected after the fire indicated a 0.32 μm mass median diameter (MMD) with a geometric deviation (σ_g) of 1.83. Lung counting data to date show a slow clearance of plutonium, confirming the high degree of insolubility of the inhaled material. On the average, 30% of material initially deposited in the lung was cleared in 2 to 3 months, with the remaining material clearing slowly with little or no measurable absorption into the bloodstream.

Of the 25 people who were involved in the Rocky Flats incident, two had burdens as high as 0.16 μCi, a factor of 10 above the current maximum permissible lung burden. Of those available for follow-up, most are measured for retained activity several times each year. Information from these cases should ultimately be included in the U.S. Transuranium Registry (USTR).

By using the same assumptions employed above for the Manhattan Project workers, one can estimate the number of "hot particles" [e.g., more than 0.07 pCi per particle as de-

fined by Tamplin and Cochran (1974)] retained in the deep lung of each of the involved Rocky Flats personnel to be about 10^4 to 10^5. Again, if the cancer risk were 5×10^{-4} per particle, as postulated by the Natural Resources Defense Council report (Tamplin and Cochran, 1974), these particles should yield 5–50 lung cancers per person. To date, none of these workers has shown detrimental effects associated with his inhalation exposure of "insoluble" plutonium oxide in 1965. In this regard, an increased incidence of lung cancer has been reported as early as 5 to 9 years after uranium miners were exposed to radon decay products and other biological stressing agents such as tobacco smoke and diesel fumes (Lundin *et al.*, 1971).

The local dose to tissue from each of the approximately 10^4 to 10^5 "hot particles" retained in the lungs of the Rocky Flats workers, assuming a sphere of lung tissue at risk (180 μm radius) around each particle, is about 1200 rad/yr. Assuming an effective half-life for lung clearance of 500 days, the cumulative local dose to some cells over the 8.5 years for each particle might be 2400 rad. This calculation assumes a static particle irradiating a fixed group of cells. Calculations based upon other models (e.g., moving particles) would result in smaller doses. Based on this information, one might expect detectable biological effects in the lung to have occurred in some of these exposed workers, yet none has been reported to date.

One case of plutonium contamination resulting from a puncture wound is extremely interesting, as it has been interpreted by some as resulting in a "precancerous lesion" (Tamplin and Cochran, 1974). In this reference, the following statement is made: "This precancerous lesion indicates that a single plutonium-239 particle irradiates a significant (critical) volume of tissue and is capable of inducing cancer." Information on this case was originally published in 1962 (Lushbaugh and Langham, 1962) and appeared again with additional information in 1967 (Lushbaugh *et al.*, 1967).

The radiation dose around the plutonium implanted in the palmar skin was estimated to be 75,000,000 rad for the 4.25 year period between contamination and excision. However, this kind of estimate may be meaningless, as we do not know which cells were exposed or for what time periods. The entire lesion was small, being of the order of 2.8×10^{-5} cm^3.

The authors (Lushbaugh and Langham, 1962) stated:

> "Although the lesion was minute, the changes in it were severe. Their similarity to known precancerous epidermal cytological changes, of course, raised the question of the ultimate fate of such a lesion should it be allowed to exist without surgical intervention. Although no malignancies of the skin of man have ever been shown autoradiographically to be associated with such alpha-emitting foreign bodies, the changes here would seem to indicate that the development of such a lesion is possible."

This particular case has been referred to as representing a "precancerous" condition resulting from plutonium (Tamplin and Cochran, 1974) and might have been the basis of a recent statement (Gillette, 1974) which reads as follows: "Only one human cancer case is clearly linked to plutonium exposure." Actually, no human cancer case has ever been "clearly linked" to plutonium exposure. The U.S. Transuranium Registry (Norcross and Newton, 1972) continues to attempt to correlate postmortem findings with body plutonium measurements.

Cytologic changes have been described in cells in the vicinity of embedded plutonium particles in man. However, the malignant cellular transformation required for the diagnosis of actual cancer has never been found next to "hot particles" in human tissue (Lushbaugh and Langham, 1962; Lushbaugh *et al.*, 1967). Similar results have been reported for several animal experiments designed to study the biological effects of hot particles (Richmond *et al.*, 1970, 1974). On the other hand, under certain exposure conditions, plutonium is an efficient cancer-producing agent in experimental animals.

For many years, several AEC contractor laboratories have conducted tissue analysis programs to determine plutonium levels in various tissues of both occupationally exposed personnel and members of the general population (Lagerquist *et al.*, 1972; Nelson *et al.*, 1972; Campbell *et al.*, 1973). For example, as shown in Table IV–B, plutonium concentrations have been determined for lung, liver, lymph nodes, kidney, and bone for the period 1959–1971 for nonoccupationally exposed persons from several regions of the United States and for occupationally exposed persons. Similar data have been obtained from nonoccupationally exposed persons for the period 1972–1973, as shown in

Table IV–C (Richmond and Sullivan, 1974). The average lung concentration for the latter period is about 0.3 pCi for the 1000 g lung, and the lymph node concentration (per kilogram) is about 11 pCi. The increase in lymph node concentration is due to greater care in lymph node excision; the mass of relevant tissue excised was reduced 5–7 fold, with consequent apparent increase in Pu concentration.

Plutonium is present in extremely small quantities in various organs of contemporary adult humans. Although most of the plutonium was produced from atmospheric testing of nuclear weapons prior to the 1963 limited test ban, some material from contemporary atmospheric weapons testing by China and France adds to the total human burden. The current lung burden estimate for persons in the United States is about 0.3 pCi $^{239,240}Pu$, and an estimate of the total amount in the body is about 3.2 pCi (Bennett, 1974).

The AEC's Health and Safety Laboratory (HASL) recently has used information obtained from the International Commission on Radiological Protection to model the intake and body burden from fallout plutonium and to estimate the radiation dose to man from this source (Bennett, 1974). The cumulative lung and bone dose estimated from the period 1954–2000 is 16 and 34 mrem, respectively. Bennett (1974) also compared the body burden based on their model with that actually obtained from the tissue sampling programs. The agreement between the Colorado-New Mexico tissue data and the model predictions for 1970 and 1971 was good.

Table IV–B

50th Percentile Distribution of Plutonium in Human Tissue (1959-1971)

	Plutonium Disintegrations per Minute per Kilogram				
	Lung	Liver	Lymph Node	Kidney	Bone
Nonoccupationally Exposed:					
Los Alamos	1.3 (57)*	1.1 (58)	5.0 (52)	0.1 (54)	0.4 (35)
New Mexico and U.S.	1.0 (76)	0.9 (73)	4.0 (66)	0.2 (66)	0.5 (41)
Colorado	0.5 (66)	1.7 (60)	2.0 (46)	1.4 (45)	0.9 (65)
New York	0.4 (26)	1.7 (26)	†	†	2.0 (25)
All Populations	0.8 (217)	1.4 (217)	3.0 (164)	0.6 (163)	0.6 (166)
Occupationally Exposed: ‡					
Potential	4.0 (44)	1.0 (41)	15.0 (42)	0.1 (42)	0.3 (25)
High Potential	100.0 (15)	100.0 (15)	700.0 (14)	10.0 (13)	50.0 (11)

* Number of samples (in parentheses).
† Samples not requested.
‡ Data cannot be compared as a group because of differences in type and duration of exposure.

Table IV–C

50th Percentile Distribution of Plutonium in Human Tissue (1972-1973)

	Plutonium Disintegrations per Minute per Kilogram					
	Lung	Liver	Lymph Node	Kidney	Vertebrae	Gonad**
Nonoccupationally Exposed:						
Los Alamos	0.8 (8)*	1.6 (5)	35 (4)	0.2 (5)	1.6 (5)	
New Mexico and U.S.	0.4 (17)	0.7 (10)	20 (15)	1.2 (10)	0.4 (16)	
Colorado	0.7 (29)	1.8 (25)	15 (22)	3.0 (25)	1.1 (25)	
Savannah River	0.4 (20)	1.2 (14)	40 (6)	2.2 (11)	0.7 (12)	
All Populations	0.6 (74)	1.5 (54)	25 (47)	1.5 (51)	0.7 (58)	0.4 (30)

* Number of samples (in parentheses).
** 7 samples from Savannah River
9 samples from New Mexico and U.S.
14 samples from Colorado

V. THEORETICAL CONSIDERATIONS

A. Dosimetry

The distributions and interactions of the absorbed energy from alpha-emitting plutonium particles among the cellular elements in lung tissue are difficult to examine experimentally and, therefore, have to be considered on a theoretical basis. This requires integrating our knowledge of the properties of alpha radiation with our understanding of the dynamic characteristics of lung, the cell types which populate lung tissue and the interactions which occur between cellular constituents and plutonium particles.

1. Alpha Particle Irradiation of Cells and Tissues

The two plutonium isotopes of primary concern are ^{238}Pu and ^{239}Pu which emit alpha particles of average energy 5.5 MeV and 5.15 MeV, respectively. In passing through a medium such as tissue or air, alpha particles lose energy by collisions with electrons of atoms, producing charged atoms and free electrons or delta rays. The delta rays cause further ionization events. Alpha particles from plutonium have a range of about 40 μm in soft tissue of unit density. The energy of the alpha particle drops to zero at the end of its range. The average loss of energy per unit of path (Linear Energy Transfer, LET) is about 140 keV/μm. However, the loss of energy per unit of path length and the number of ionizing events it produces actually increase along the path of the alpha particle as the energy of the particle approaches zero (the Bragg effect). Ninety percent of the ionization events occur within a cylindrical volume of about 0.01 μm radius around the alpha particle track; most of the remaining 10% occur out to about 0.2 μm.

This pattern of energy dissipation differs greatly from that of electrons (beta radiation or secondary to x and gamma radiation) which are characterized by values of LET that are two or three orders of magnitude smaller. Consequently equal absorbed doses of alpha and electron radiation, although by definition are depositions of equal energy per unit mass of irradiated material, produce drastically different energy distributions at the microscopic level which can be numerically expressed in terms of the quantities of microdosimetry.

The *specific energy*, z, is the energy imparted to the matter in a specified volume divided by its mass. The average or expectation value of specific energy, $\bar{z}$, is equal to the absorbed dose but z may fluctuate greatly around this value (ICRU Report 19, 1971). If a region in tissue is traversed by a particle, the resulting increment of z depends on the LET of the particle and on the length of track within the sphere but a mean always can be specified for a given set of conditions. Thus, for the alpha particles under consideration, and 2.5 μm diameter nuclei (within essentially spherical "cells"), the mean z deposited in such a nucleus is about 500 rads and this value is independent of the absorbed dose, $\bar{z}$. At absorbed doses that are much less than 500 rads most nuclei experience no traversals; the number of nuclei that are traversed is proportional to the absorbed dose and the mean value of z in these nuclei is independent of dose. When absorbed doses are comparable to 500 rads, the probability for multiple traversals becomes appreciable and higher average values of z in traversed cells result (Rossi, 1967).

The same considerations apply to electrons but the numerical values are quite different. Thus, an electron having an LET of 0.3 keV/μm will in traversing the 2.5μm diameter volume impart an average increment of z that is about 1 rad. Hence, at an absorbed dose, $\bar{z}$, of 50 rads where one in 10 nuclei is traversed by an alpha particle delivering an average z (dose to the nucleus) of 500 rads, electrons will traverse almost all nuclei and z will differ little from 50 rads.

2. Biological Factors in Alpha Radiation Dosimetry

In Part III of this report it was pointed out that all inhaled particles, including plutonium and aggregates of plutonium, are subjected to numerous physical and biological forces which tend to remove the particle from the respiratory tract. Therefore, plutonium does not remain static in lung tissue unless the plutonium becomes immobilized in scar tissue, bound to biochemical moieties, or otherwise trapped. However, as evidenced by the relatively long retention time of plutonium in lung, much of the plutonium deposited is made inaccessible for ready clearance by some mechanism such as immobilization or recycling through generations of the several types of cells capable of phagocytizing particles. All of this contributes to the complexity of the spatial and temporal distribution of the absorbed radiation dose from plutonium in lung.

Lung tissue surrounding particles will be irradiated at relatively constant rates, assuming the particles are fixed intracellularly, extracellularly or trapped in alveoli blocked by cellular products or debris. The amount of radionuclide and solubility of the particles will influence the biological damage to the cells. However, relatively soluble plutonium may be chemically bound in cellular material and be retained in lung for a long time, e.g., studies with inhaled $Pu(NO_3)_4$ (Ballou and Park, 1972).

The degree of isolation of particles by cellular debris, fibrosis, and similar changes consequent to biological damage caused by irradiation or physical and chemical irritation of the surrounding tissue is an important consideration. Because alpha emissions from ^{238}Pu and ^{239}Pu have a range of approximately 40 μm in unit density tissue, the degree of this walling-off effect will be a major factor in dosimetric considerations. Complete "walling-off" of the particle might reduce the risk from the alpha emissions to lung epithelial cells greater than 40 μm from the particle boundary, but the risk from the delta rays, X, and gamma radiation accompanying the ^{238}Pu and ^{239}Pu will not be reduced proportionally. Work at Los Alamos (Richmond *et al.*, 1970) and studies at Battelle (Sanders and Park, 1972) indicate this "walling-off effect" is present but variable in thickness. This "walling-off" effect has not been observed in recent studies in which lower specific activity alpha-emitting particles are used (Richmond and Sullivan, 1974).

Another factor is cell turnover. With any given radiation dose rate, the total radiation dose to a given cell will be determined by the time interval between cell divisions. The consequence of a cell being irradiated will be expressed at each cell division by selection against badly damaged cells (i.e., cell death) and by replication of surviving damaged and transformed cells. Thus, to some extent the frequency of cell division will have a bearing on the cellular response to radiation from internally deposited radionuclides. Values for turnover time for the various lung cell types are 5 to 80 days for epithelial cells and a few hundred days for endothelial and mesothelial cells (Shorter, 1970). Of equal importance is the relative radiation sensitivities of the cells. There are little or no useful data available to establish a quantitative relationship between the radiation dose to specific cell types in lung tissues and subsequent biological effects of a health risk nature. It is inevitable that knowledge of the relationship between the dose rate, the probability of sublethal "hits" by alpha particles, the identity of the cells sensitive to the carcinogenic action of radiation and the cell turnover time could lead to a more accurate assessment of the health risks from inhaled alpha-emitting radionuclides.

Consideration of air absorption in the small sphere of lung tissue irradiated by a radioactive particle can be ignored because of the small amounts of air in that volume and the relatively low energy loss in air. The average range of a 5.1 MeV alpha particle in lung tissue with a specific gravity of 0.22 is on the order of 180 μm, and the fraction of the alpha particle energy deposited in air is 4×10^{-3}. An alpha particle can travel about 4 cm in a long, straight airway such as a bronchus. Thus, a small portion of tissue interactions with alpha emissions from plutonium particles can occur at some distance from the source. For example, about 2% of alpha particles penetrate beyond 400 μm from their source (Richmond and Voelz, 1973) and about 40% penetrate beyond 180 μm. About 50% of the alpha energy is absorbed within the confines of one alveolus or within 100 μm of the source (Sanders and Dionne, 1970). Interactions of these long-range alpha particles tend towards dispersal of the absorbed radiation energy in lung tissue.

A minor factor in dosimetric considerations of radioactive particles in the lung is movement during the respiratory cycle of tissue relative to a deposited radioactive particle. For the most part, tissue movement would be such as to increase or decrease the radius of the exposure field concentric with the particle. While the volume would change somewhat during these movements, the mean volume would apply for dosimetry calculations as they relate to possible biologic effects. During a respiratory excursion, particles will tend to move with the tissue in which they are contained. The same cells will be at risk, regardless of the variability of the volume of the tissue sphere.

These biological considerations emphasize the importance of the dynamic characteristics of lung tissue and of particles deposited in this tissue. Although the kinetics of the interactions of plutonium particles and their alpha emissions with cells in lung are not known, they are certainly more complicated than a fixed source of plutonium particles irradiating a static population of cells within a 40–50 μm range.

3. Models for Dosimetry and Tumor Probability

There have been a number of attempts to understand the spatial distribution of energy from alpha emitters deposited in lung by development of models using computer technology applied to various representations of lung architecture. From the preceding discussion it will be obvious that all of these models are deficient in respect to biological considerations.

Scientists at Los Alamos (Richmond and Voelz, 1973) developed a model to determine the number of cells which receive given radiation doses as a function of distance from plutonium microspheres. A first objective of this model was the identification of the effect of lung structure on radial distribution ("radial interaction" function) of encounters between alpha tracks and cells for calculation of dose. Photomicrographs of thin sections of hamster lungs were scanned by a high resolution densitometer, and the digitized images were stored on magnetic tape. Numerical evaluation of the radial interaction function was accomplished by a Monte Carlo technique operating on the digitized images. Mean intercept lengths of alpha tracks in air and tissue were varied by digital manipulation of the images to determine the effects of such parameters as lung density, alveolar size, and wall thickness. These investigators found that lung density could be eliminated as a parameter by appropriate normalization (e.g., expressing "distance" as mass per unit area) but that the scale factor of lung structure (ratio of characteristic dimensions to the range of alphas in tissue) had a profound effect on the radial distribution of energy deposition.

Dean and Langham (1969) developed a theoretical approach to estimating tumorigenic risk from exposure of skin and lung to high specific-activity particles of ^{235}U, ^{238}Pu, and ^{239}Pu. The radiation dose from discrete sources was treated in such a manner that an estimate of the individual cellular response can be made. Dose averaging was not used in the model. Particle movement within the lung was taken into consideration (500-day half-time) and lung density of 0.26 g/cm^3 was assumed. The tumor probability versus dose-response curves, which are the basic ingredients of the model, were taken from the rat skin tumor data (Albert *et al.*, 1967a, 1967b, 1967c). Dean and Langham (1969) point out that the rat is sensitive to skin tumor development and that sensitivity may be different for the human lung. In their model, calculations of the lung tumor probability per particle as a function of particle size show peak responses at about 10^{-1} for a 1 μm diameter ^{238}Pu particle and about 10^{-1} for a 5 μm diameter ^{239}Pu particle.

At the 1 μm diameter size, the tumor probability for ^{239}Pu is three orders of magnitude lower (10^{-4}) as compared with ^{238}Pu (10^{-1}). Dean and Langham (1969) compared the lung dose from 0.016 μCi of ^{239}Pu for 720 days following an acute exposure using the dose averaging technique (3.2 rad) and their model (1.6×10^6 rad absorbed by 3×10^5 cells). This model, like others, makes no allowance for cell repair, turnover and replacement; it does provide for "wasted radiation" and assumes that the Albert data for rat skin (Albert *et al.*, 1961; Albert, 1962; Albert *et al.*, 1967a, 1967b, 1967c) can be applied to lung.

Geesaman (1968) proposed a cubical lattice model to represent clusters of alveoli with elastic walls of uniform thickness. The geometrical representation was a honeycomb-like structure comprised of truncated spheres (the alveoli) wrapped around a duct (the bronchioles). The volume of "tissue" irradiated by a 1 μm $^{238}PuO_2$

particle embedded in the lattice was calculated by considering the angular dependence of the geometrical range of alpha emission in the cubical lattice. Alpha radiation emitted along the lattice axes, in the lattice, and in a sphere about the particle would penetrate about 100 alveoli, according to this model, and irradiate about 10^5 endothelial and epithelial cells. Using published values for turnover times of lung cells and observation of the response of lung cells to a high dose of x-rays, of cultured kidney cells to alpha particle radiation, and of cell cytoplasm to protons, Geesaman estimated that, unless the $^{238}PuO_2$ particle is less than about 0.25 μm diameter, the yearly alpha flux will be lethal for all epithelial cells in the exposed volume of tissue. The equivalent "critical" size for a $^{239}PuO_2$ particle was 1.75 μm. The calculations are for a static source. A moving source will expose a larger volume of tissue, but, according to Geesaman (1968), if the distance traversed is only to an adjacent ciliated bronchiole, the irradiated volume would probably not increase by an order of magnitude. However, one can calculate the distance from an alveolus to the ciliated epithelium to be about 8000 μm (Weibel, 1963) or about 45 times larger than the 180 μm range of a 5.1 MeV alpha particle in lung tissue of density 0.22 g/cm^3. Therefore, the irradiated volume would increase by several orders of magnitude, but the duration of exposure would be drastically shortened as the particle would be removed from the lung after reaching the ciliated epithelium. On the basis of his model, Geesaman concluded that the carcinogenic risk does not scale with the total energy from a plutonium particle.

Using Davies' (1961) model of the alveolar region of the lung, Coleman and Perez (1969) developed a cylindrical model of the nonciliated region of the lung comprised of the respiratory bronchi, alveolar ducts, atria, alveolar sac, and the alveoli. The structure of the lung was assumed to consist of parallel, cylindrical air ducts arranged in such a way that the minimum distances between any adjacent ducts are equal and with maximum ratio of air volume to total volume. The space between air ducts is the tissue volume. This model was deemed adequate for calculation of "smeared" doses but was refined for "local" dose considerations to include "cellular" structures lining the alveoli and a coordinate system. Dose rates in rads per second were calculated for tissue surrounding a static particle from point sources of ^{238}Pu and from volume sources.

Plutonium particles do not reside for long periods of time in the tracheobronchial region of the lung. However, the possibility for exposure of these tissues occurs during inhalation of plutonium and during transport of particles cleared from the lung on the ciliated epithelium. Animal experiments have shown the bronchiolar-alveolar region of the lung rather than the bronchial epithelium to be the primary site of particle retention and the major site of damage induced by inhaled plutonium. However, in addition to tumors of bronchiolar-alveolar origin, a few epidermoid carcinomas were incidental findings at necropsy in beagle dogs at long times after the inhalation exposures (Howard, 1970). To compare the relative radiation doses to the bronchiolar, bronchial and tracheal epithelium from inhaled plutonium, Harley and Pasternack (in press) derived dose curves for 0.06 μm and 2 μm $^{239}PuO_2$ particles from which the dose in rads per minute at any depth in the epithelium of the trachea and terminal bronchioles could be computed. The difference in the dose rates for the largest airway (trachea) and the smallest airway (terminal bronchioles) was small and, therefore, dose rates for intermediate airways were inferred to be about the same. For continuous exposure to the ICRP maximum permissible concentration of 10^{-11} μCi/cm^3 air, the maximum annual dose from 0.06 μm diameter $^{239}PuO_2$ particles is 0.014 rad at a depth of 22 μm in the epithelium of terminal and subsegmental bronchioles. The maximum annual dose from 2 μm particles was similarly calculated to be 1.2×10^6 rad, delivered to the segmental bronchioles.

Recently Mayneord and Clarke (1974) completed a mathematical study of the carcinogenic risks associated with radioactive particles using a nonlinear peaked cellular dose-response function, a power law response. Assuming that all cells of a tissue are equally at risk, it was concluded that beta radiation from a point source of ^{86}Rb or ^{35}S is more hazardous at low source strengths than the same activity uniformly distributed; however, the opposite is true at high source strengths. The mean dose at which the transition occurs increases with the beta energy emitted by the particles and with increasing organ mass and

power law cellular response. However, if the tumorigenic response is a linear function of dose, the uniform tissue irradiation rather than the point source gives the greatest expectation. Under the most pessimistic conditions of numbers of hot particles of both high and low beta energy, the authors conclude that the carcinogenic risk is not more than about a factor of 10 greater than predicted by a linear hypothesis. With alpha radiation the expectation of events which might lead to cancer from a point source is greater than that from uniform irradiation of the same amount of energy for point source strengths up to that at which cell killing predominates. However, because of the small number of particles emitted the authors question the application of this macroscopic method and suggest that the stochastic methods of microdosimetry might be a better approach. The authors conclude, that in the light of present knowledge of cellular response, spatial distribution of cells at risk and localization of particles within tissue, the use of mean organ doses and the assumption of a linear relationship between dose and effect is a reasonable guide to estimating the carcinogenic risks from radioactive particles.

These dosimetric models can be useful in understanding how a given biological effect such as cancer occurs following deposition of plutonium in lung and might even lead to identification of possible mechanisms for cancer induction. However, because these models are deficient with respect to the biological aspects of plutonium in lung (in most cases for the simple reason that the biology is not adequately known), the models are not dependable for predicting the health consequences of plutonium. In fact these models can be used to yield almost any answer desired.

B. Radiation Carcinogenesis Relative to Spatial Distribution of Dose

The calculated radiation doses around hot particles are an unreliable base for the calculation of biological effects because of the lack of adequate biological models for carcinogenesis. Experimental data, meager as it is in some instances, is more valuable than models based upon *calculated* radiation doses, which in themselves may be very uncertain, and upon inferences from other organ systems that may have no relevance to the organ system in question. This latter point is particularly true for the use of dose-effect models derived from rat skin data as the basic input for models of human lung carcinogenesis arising from radiation.

The importance of understanding wasted radiation before trying to solve the "hot particle" problem cannot be overemphasized. Because of the pattern of alpha energy deposition in a tissue volume around a given plutonium particle, the nearest cells are virtually all killed while those more distant are either exposed to very low radiation doses or are not irradiated. Because of the short range of the alpha particle, most of the deposited energy is absorbed within extremely small tissue volumes. Depending on the number of particles and their dispersion and mobility, much of the lung may be unaffected.

These observations lead one to a hypothesis to explain the relative sparing effects on tissue of alpha particle radiation associated with plutonium particles as compared with a more uniform distribution of energy. The following discussion considers primarily those cells that are affected in some manner but not killed by the alpha irradiation (Richmond *et al.*, 1970). A large variety of cellular changes can result from alpha irradiation, yet only a small percentage of these changes can lead to carcinogenesis. Because of the many possible alterations, the chance of the specific change or combination of changes required to produce an oncogenic response is extremely unlikely to occur in any single cell. There is a large probability that death of a cell would precede the occurrence of the critical random events that would result in an oncogenic response; however, if one administers sublethal radiation doses to a sufficiently large number of cells, it becomes more probable that oncogenic changes would occur, depending upon the cell number and the radiation dose. This idea has been mentioned by numerous authors, including Archer and Lundin (1967).

A common hypothesis is that a direct linear relationship exists between radiation-induced neoplasms and ionizing events per cell multiplied by the number of cells irradiated. However, for nonuniformly distributed alpha radiation the "wasted radiation" must be considered. Although the quantification may not be clear, it is obvious that the amount of

tissue irradiated is an important factor in the production of cancer. Cember (1964a) stated:

> ". . . , the likelihood of inducing lung cancer seems to increase as the volume of irradiated lung tissue increases—that is, as the number of radiation foci increase and overlap. Furthermore, the experimental results imply that the carcinogenicity of a given amount of absorbed radiation energy increases, up to a point, as the absorption of energy is spread out both time- and space-wise. From a practical point of view this means that, for a given amount of absorbed energy, low-level, continuous exposure of the total lung may be more carcinogenic than the same amount of energy delivered acutely to a restricted volume of tissue."

Others have postulated models for cancer induction in which a "threshold" volume or minimal mass of tissue must be damaged before the carcinogenic process of unlimited cellular proliferation overrides the inhibitory mechanisms regulating growth processes (Rashevsky, 1948). There is evidence that transformed cells in physical contact with normal unaffected cells are prevented from dividing (Sivak and Van Duuren, 1970). Widespread tissue damage, such as could occur with a more uniform distribution of the same amount of energy, could release transformed cells from this growth restraint. As Mayneord (1968) points out, "Radiation must be much more effective in killing cells or in interfering with their ability to multiply than in causing the alleged specific malignant transformation of individual cells or of small foci of cells."

Mechanisms for preventing or mitigating errors in replication which can produce somatic mutations must exist, because there are probably on the order of 10^{12} to 10^{13} mitoses every day in the human body (Burnet, 1964). Therefore, even for those cells damaged by radiation in such a way as to be transformed there are processes that prevent the development of a malignant growth. Each change does not produce a malignant growth. Thus, a carcinogenic agent may induce an event in a single cell or a group of cells which is followed by the development of clones of cells which gradually but rarely free themselves from growth controls exerted by the entire organism (Mayneord, 1968). In some tissues these controls may result from the autoimmune response or from cellular contact inhibition of division (Burrows and Horning, 1953). It is suggested that normal cells can act as mitotic inhibitors; thus, one cell bearing a malignant potential might be prevented from dividing by the influence of surrounding normal cells. Uncontrolled mitosis would be prevented unless the inhibition were removed in some way.

The free movement of transformed cells in culture stops when they are in contact with normal cells, suggesting that the transformed cells are responsive to inhibitory signals from normal cells (Stoker, 1964, 1967). Although transformed cells may be inhibited by contact with normal cells, they can continue to grow and move when in contact with other transformed cells. The requirement of cell-to-cell contact for transfer of materials between cells is known, and the presence of growth inhibitors in normal cells has been postulated, but this mechanism is apparently deficient in transformed cells (Burk, 1966).

Thus, both acute and late effects of the same quantities of plutonium in the lung might reasonably be predicted to be less hazardous when the plutonium is nonuniformly distributed as compared with a more uniform distribution for the following reasons. For nonuniformly distributed plutonium, the volume of irradiated tissue is much less, much of the radiation dose is wasted, in most cases cells are either killed or not irradiated, many fewer cells are irradiated but not killed, and the ratio of damaged (transformed) cells to normal cells is much smaller than for uniformly distributed plutonium. All the above factors are important, yet the last may prove to be the most important, especially for extremely nonuniform dose distribution patterns.

One can also consider the mechanisms of carcinogenesis from the standpoint of pathological changes in tissue irradiated both by uniform and by nonuniform distributions of energy. The following is a discussion of carcinogenic mechanisms that may be applicable to irradiation of skin and lung (Casarett, 1965, 1973a, 1973b). The mechanisms of most, if not all, types of cancer appear to be multi-event, multi-stage processes including cellular initiating events which confer cancer potential upon cells and promotional events or conditions which stimulate or permit proliferation of the tissue in which the cancer originates (including the cancer-potentiated cells) and/or permit proliferative advantage or autonomy of the cancer-potentiated cells.

In the development of some cancers, for example those of lung or skin, the promotional as

well as the cellular initiating events appear to be closely associated at the sites of origin of the cancers and to be largely independent of extraordinary influence of remote factors generated in other organs. In such cancers, the promoting events or conditions appear to consist of tissue damage and disorganization (cell degeneration and necrosis, vascular degeneration, fibrosis, compensatory cellular proliferation, and metaplasia) the so-called "precancerous lesion."

Radiation in sufficient doses to a large enough volume can cause both the cellular initiating events and the promotional events. The most likely candidates for cellular initiating events are certain types of mutations or chromosomal aberrations. High frequencies of such changes can be caused by relatively modest doses of radiation, and also by other mutagenic agents. However, increasing the radiation dose increases the incidence of reproductive sterility among cells, even in cell types that are relatively resistant to destruction. Such permanently sterilized cells cannot be the source of cancer. Thus, a maximum in the dose response curve is to be expected.

On the other hand, the so-called precancerous lesions, if they are to be caused largely by the radiation and not by other pathologic conditions or aging, require large doses of radiation; that is, doses capable of inducing the progressive vascular changes and connective tissue reactions sufficient to reach a degree and extent of tissue disorganization that is cancer-promoting prior to the time when such lesions might have developed if radiation had not been involved. Such large doses sterilize many cells and eventually lead indirectly to non-selective cell necrosis secondary to the vasculoconnective-tissue-circulatory degeneration, with persistent and abortive attempts by some of the nearby and less affected cells, even in normally low-turnover tissues, to proliferate in compensatory fashion, often atypically. The probability that damage will overwhelm restorative mechanisms and produce gross local tissue breakdown increases with the size of the area exposed, in particular, when the linear scale exceeds the size of the sensitive structure or target. This critical size might be determined by the ability of the local restorative mechanisms to compensate for such injury.

The character of the precancerous lesions in this type of mechanism is such that they progress to a particular degree of severity faster after higher doses than after lower doses, thereby accounting at least in part for the shorter latent period after the higher doses. If, however, the promotional condition is supplied by means other than the radiation dose in question, the size of the radiation dose required to assure the development of a particular cancer within the remaining life expectancy, if that expectancy is long enough to accommodate at least the minimal latent period, is the size of the dose required to cause or to complete the cellular initiating events in sufficient incidence.

For this type of mechanism, if the promotional condition is to be supplied largely by the radiation exposure, the optimum carcinogenic dose is likely to be that which provides a net optimum balance between effective promotional tissue damage and incidence of reproductively capable cancer-potentiated or transformed cells. Larger doses sterilize and/or kill excessive numbers of cells and reduce or even abolish induction effectiveness. The volume of irradiated tissue, with respect to numbers of reproductively capable cancer-potentiated cells and amount or critical volumes of tissue involved in the promotional precancerous lesions, is likely to be an important factor influencing the probability of development of cancer.

For cancer induced by local exposure of the tissue of origin there is, in general, an increase in incidence and reduced latent period with increasing radiation dose within a certain dose range. With further increase in dose, there tends to be a decline in the rate of increase in incidence per unit dose. This decline at high dose levels is represented first by a plateau in the dose-incidence curve at peak incidence level, and then by a fall in the curve at still higher dose levels. The fall in the incidence curve at the highest dose levels has been attributed to degrees of tissue destruction, including cell reproductive sterilization, that reduce or eliminate cancer induction.

Although the germinal cells of the hair follicles in the dermis are rapidly renewing cells relatively sensitive to the direct necrotizing actions of ionizing radiation, the epithelial cells of the lung are slowly renewing cells relatively resistant to the direct necrotizing actions of ionizing radiation. Both of these epithelial cell types can be reproductively

sterilized by irradiation and both can be depleted indirectly by interference with their microcirculatory support as a consequence of substantial progressive vasculoconnective tissue changes. Such changes increase the histohematic connective tissue diffusion barrier and reduce effective blood circulation in the processes of widespread fibrosis.

Radiation-induced lung cancer or skin cancer apparently is preceded by a considerable degree and extent of local tissue damage, disorganization, and fibrosis, that is, the so-called precancerous lesion. The experimental induction of cancer in either of these organs by irradiation of the normal organ apparently requires large radiation doses. That is, there seems to be a large minimal or "threshold" dose, but the required doses are reduced if the promotional local tissue damage and disorganization is caused by means other than the radiation. As discussed earlier, the dosimetric models used to predict lung tumor response to alpha particle radiation (see section V.B) are based upon dose response data obtained from experiments using rat skin.

In the experiments by Albert *et al.* (1961, 1967a, 1967b, 1967c, 1969) and Burns *et al.* (1968, 1973a, 1973b) involving induction of cancer in rat skin by intense electron irradiation, most of the cancers were said to be similar to hair follicle epithelium, and the promoting condition was apparently the tissue damage and disorganization in the dermis, including the tissue of hair follicles. The field of irradiation was large, relative to the follicle size, and in one experiment was 24 cm^2. The fact that there was a relationship between the incidence of cancer and the number of atrophied hair follicles in the large field of dermis irradiated and damaged at or about the level of hair follicles, and elsewhere to some extent, may be related only incidentally, in part or wholly, to the achievement of the required degree and volume of disorganized dermis. The required volume may be considerably larger and qualitatively broader than the volume of a single hair follicle and the structures contained within the hair follicle. The geometrical effect of exposure with sieve patterns observed in Albert's experiments, notably the suppression of cancer induction at 1700 R but not at 2300 R, may be a suggestive indication of the importance of distinguishing between effects on hair follicles as individual structural units and the more general effects on volumes of dermis and its vasculature as promoting conditions.

At present there is no compelling reason to believe that the critical structure or volume required for radiation-induced promotion of cancer arising from cancer-potentiated cells of hair follicles is limited to the hair follicle. There is also no cogent evidence that the lung has analagous discrete susceptible architectural units with critical tissue volume as small as the sphere of alpha particle range from an isolated "hot particle."

Increase in the risk of lung cancer with increase in the number of inhaled particles (for example, insoluble PuO_2 particles) retained in deep lung tissue may not be simply a function of increasing numbers of retained particles that are widely separated from one another in location and tissue effect, but possibly a function of the frequency with which certain minimal numbers of particles become lodged within sufficient proximity of one another to cause relatively confluent tissue disorganization throughout a promotionally effective tissue volume that is larger than the sphere of effect of a single particle (or sub-minimal number of closely associated particles), and at the same time, to increase substantially the number of cancer-potentiated, reproductively capable cells near and within the volume of disorganized tissue.

With protracted, nonuniform exposure of tissue to alpha particles, there is uncertainty not only as to the tissue component dose relevant to carcinogenesis, but also as to the portion of the total accumulated dose that effectively contributes to the induction of the cancer. In cases of intense irradiation, some of the total accumulated dose is "wasted" and irrelevant, as regards the induction of a cancer. Some of the dose in excess of the minimal induction dose conceivably may shorten the latent period to some extent by substituting for other contributing factors that would have occurred eventually but later.

Considering the amount of human data available for carcinogenic risk estimates, and the variability and uncertainty concerning dosimetric factors (e.g., relevant doses, differences in spatial and temporal dose distribution, etc.), it has thus far been regarded as necessary to select single values of quantities that

characterize the exposure of an organ or that organ in a group of individuals. Mean accumulated tissue dose is the only criterion that can be used practically at present until adequate knowledge of more relevant criteria becomes available. Furthermore, when the energy is deposited nonuniformly and its influence in the exposed organ or a group of individuals is not known, the nonuniformity cannot be dealt with until more adequate data are available. The linear (proportional) hypothesis is the only one that normally permits the use of mean dose as the significant dose factor for conditions of nonuniform exposure and exposure rate in an organ or among individuals, for purposes of estimating risk or setting dose limits in the absence of adequate data on distribution of dose and dose rates.

It is highly questionable that the ratio of induced cancers to atrophied hair follicles in Albert's experiments with large volume external irradiation of rat skin can be taken as the basis for the risk of cancer induction from a radioactive particle in or near a hair follicle in skin or isolated in deep respiratory tissue. It is also highly questionable that the existing standards for uniform radiation exposure of the whole body or lung can be used as the basis for establishing particle exposure standards by simply equating the risk of cancer induction between the two types of exposures, that is, uniform vs. grossly nonuniform. The risk for uniform irradiation of man as represented in the NAS-NRC BEIR report (1972) is based on the linear hypothesis as applied to data from uniform low LET irradiation of all cells in the lung over a dose range associated with a rising dose-incidence relationship. This dose range did not involve doses so large as to greatly reduce the carcinogenic effectiveness by excessive cell sterilization and killing, but was capable of contributing to tissue disorganization anywhere in the irradiated lung. As indicated earlier, there are many more cells at risk in the case of uniform distribution of dose than with nonuniform distribution, for the same amount of radiation dose. Also, the bulk of the available evidence suggests that in the radioactive particle situation the great majority of cells surrounding a single isolated particle within its sphere of irradiation are likely to be reproductively sterilized if not destroyed.

C. Assessment of Experimental Animal Data

The question of whether the practice of expressing the radiation exposure to lungs from inhaled plutonium as an average dose is reasonable can be considered empirically by examining the results from experimental animal studies in which the late effects, such as lung cancer, were observed in several animal species.

In reports of the carcinogenic response of experimental animals to inhaled radionuclides the authors generally calculated mean radiation doses to the total lung. To avoid hand drawing the "best" line through the data, a logarithmic probit curve was selected from among possible transforms and was fitted to data from a number of experiments in which there were several dose groups showing a progressive increase of cancer incidence or a single dose group if the lifespan was not substantially reduced compared with the controls (Thomas and Bair, submitted for publication). Binomial confidence limits were also calculated. Results from studies of beta-gamma emitting radionuclides are plotted in Figure V–1. The heavy line is the curve fitted to the composite data. The thin lines were fitted to individual multidose experiments and provide a kind of experimental error band. No statistical validity is ascribed to this procedure; however, it is a useful expedient by which to summarize the nature and magnitude of the dose effect curve. A similar treatment of data from experiments with plutonium is shown in Figure V–2.

The composite curves for the experiments with beta-gamma emitters and for alpha emitters are redrawn in Figure V–3. At all doses the incidence of lung cancer was greater for alpha emitters (plutonium) than for the beta-gamma emitters; however, the differences between the two curves were greater with increasing dose. At a mid-point tumor incidence of 20 percent, the corresponding doses are 300 rads for alpha emitters and 3500 rads for beta-gamma emitters. Thus, based on calculated mean lung doses, alpha emitters were about 10 times more efficient for lung tumor induction than were beta-gamma emitters. At 10 and 30 percent incidences, the alpha emitters were about 5 and 20 times more efficient, respectively, than beta-gamma emitters. Since the RBE for alpha particles ranges from 1 to 20, depending upon the biological system and

response studied (NCRP, 1971), and is often given as 10, this greater efficiency of alpha radiation in producing lung cancer in experimental animals appears reasonable.

Consider now the dose to the lungs of the animals that inhaled the alpha emitter, plutonium, calculated on the basis of a "critical volume" of lung tissue, that fraction of lung tissue actually irradiated by static dispersed or aggregated particles in the lung. It was pointed out in the discussion of experimental animal studies that nearly all plutonium compounds deposited in lung tend to form aggregates and are never uniformly distributed. Table I gives the calculated fractions of lung irradiated by a lung burden of 0.016 μCi $^{239}PuO_2$ of different particle diameters. For purposes of this discussion it will be assumed that 0.1 percent of the lung is irradiated. On this basis the calculated alpha doses for the experimental animal data would be increased by a factor of 1000 and the lung cancer incidence curve is transposed to the right of the beta-gamma dose effect curve, Figure V–3. Now it would appear that alpha radiation from particulate sources in lung is about 100 times less efficient than beta-gamma radiation in causing lung cancer in experimental animals. This factor of 100 would become 10 if one assumed an irradiated lung volume of 1 percent. The curve would still be to the right of the beta-gamma curve, which is radiobiologically unrealistic, i.e., it implies an RBE for alpha particles of less than 1.

One can conclude from these considerations that the mean dose to lung from plutonium

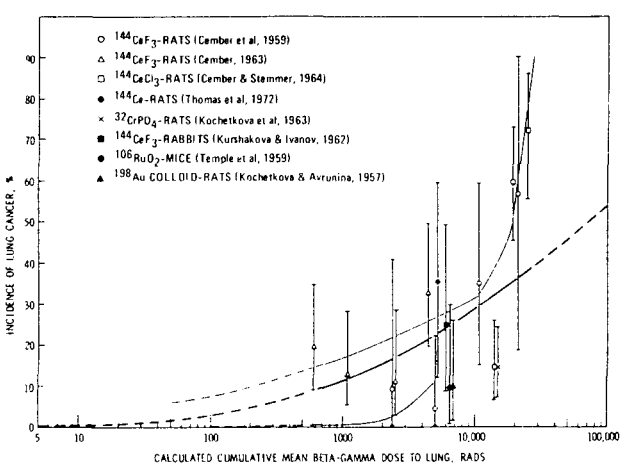

Figure V–1.—Relationship between incidence of lung cancer and radiation dose to lung from inhaled beta-gamma emitting radionuclides in experimental animals.

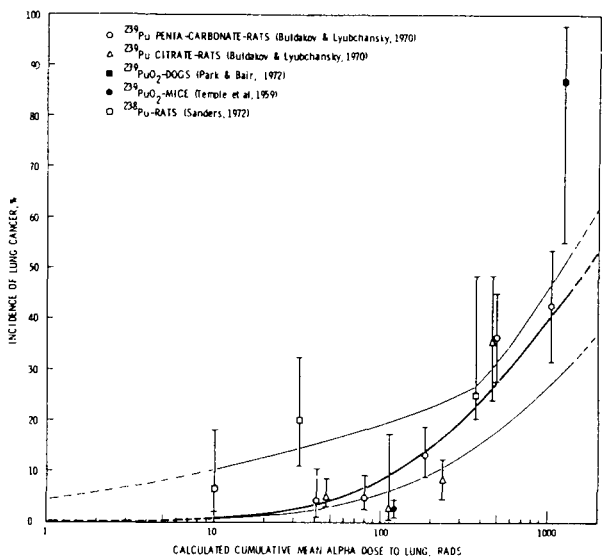

Figure V–2.—Relationship between incidence of lung cancer and alpha radiation dose to lung from inhaled plutonium in experimental animals.

particles is a biologically reasonable basis for expressing the quantitative relationship between tumor incidence and alpha radiation dose. Also, one can conclude that the mean dose concept represents a conservative approach to the establishment of permissible limits for plutonium provided the radiation protection criteria for lung exposure is based on a limiting rad dose.

It is significant that the dose-effect curves for beta-gamma emitters and alpha emitters

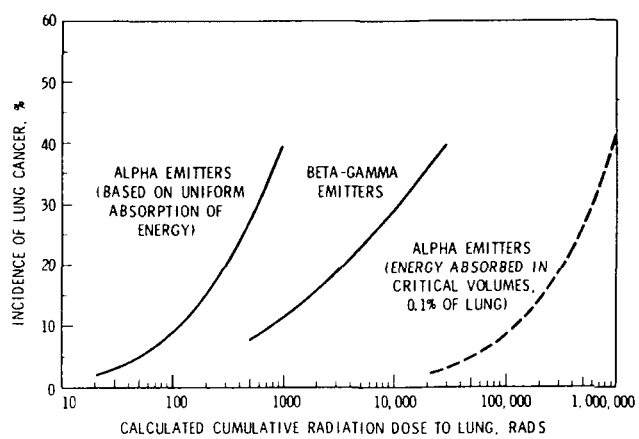

Figure V–3.—Comparative relationships between the incidences of lung cancer and radiation doses from inhaled beta-gamma and alpha emitters in experimental animals. The dose to the lung from alpha emitters was calculated in two ways: assumed absorption of energy in the total lung mass and assumed absorption of total energy in only 0.1% of the lung mass. The radiation energy from beta-gamma emitters was assumed to be absorbed throughout the total lung mass.

are "parallel." Regardless of the nonuniform distribution of the alpha dose the mean rad dose ratios between beta-gamma and alpha emitters for comparable tumor incidences range between only about 5 and 20, and no assumptions regarding the carcinogenicity of individual particles are needed or implied. Thus, a comparison of relatively uniform beta-gamma irradiation with nonuniform alpha irradiation can be derived solely from toxicity data. The appropriate models needed to describe the complete sequence of events leading to cancer are of secondary importance to a valid determination of the relative toxicity of the two radiations—the most fundamental criteria in any hazard assessment.

According to Geesaman (1968), tissue damage rather than radiation is the proximate cause of cancer. Tamplin and Cochran (1974) suggest that irradiation of a critical architectural unit of a tissue (e.g., a hair follicle) at a sufficiently high dose rate is a requirement for cancer induction. The results of experimental animal studies which bear upon these two views are from studies of low LET radiation in which the entire lung and, therefore, all the "critical architectural units," regardless of the number, are irradiated, and from studies in which a specific target tissue is irradiated.

Figure V–4 shows that lung tumor incidence increases with dose for rats given bronchial implants containing ^{32}P or ^{106}Ru. Tumor incidence is virtually zero at 10^3 rad and about 60% at 10^6 rad. The radiation dose was calculated for a specific target tissue, that is, the basal layer of the bronchial epithelium. Because of the size of the implanted pellet it is likely that many of these target cells were irradiated.

Data in Figure V–4 for five species of animals given ^{60}Co wire implanted in their lungs show lung tumor incidences ranging from about 8 to 40%, in all but one instance, for total doses of 10^5–10^6 rad to either the entire lung or to the esophagus. It is of interest that the entire lung is irradiated, including any and all possible "critical architectural units," at high dose rates, yet the tumor incidence is not unity. Also of interest is the similar response shown for the several species used with the possible exception of the rat lung, the highest cancer incidence point. The observation of tumor incidences well below unity is true also for the whole-body exposures to X-irradiation in which the entire lungs and body of rats received doses near 10^3 rad. Although these were acute exposures, the entire lung was irradiated.

The high doses from the implanted sources and the process of implanting the sources as well caused severe localized reactions. However, such lesions do not appear to be a requirement for cancer induction, because the whole-body exposures from external sources do not involve severe necrosis although pneumonitis and fibrosis can result at high exposure levels.

These data from experimental animal studies involving low LET radiations lead one to conclude that there probably is not a critical structure in the lung analagous to the hair follicle in the skin of a specific strain of rat which, if irradiated at a dose of 10^3 rad, will produce lung tumors in high yields.

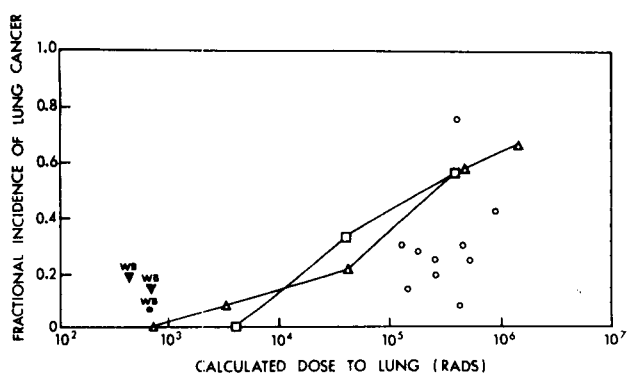

Figure V–4.—Fractional Incidence of Lung Cancer in Animals Exposed to Low LET (β,X,γ) Radiation

- ○ ^{60}Co implant. Rats, mice, hamsters, rabbits, guinea pigs (Warren and Gates, 1968).
- △ ^{106}Ru implant. Rats (Laskin *et al.*, 1963).
- □ ^{32}P implant. Rats (Laskin *et al.*, 1964).
- ● X-ray. Rats (Koletsky and Gustafson, 1955).
- ▼ X-ray. Rats (Castanera *et al.*, 1968).

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A Review of the Natural Resources Defense Council Petition Concerning Limits for Insoluble Alpha Emitters

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A REVIEW OF THE NATURAL RESOURCES DEFENSE COUNCIL PETITION CONCERNING LIMITS FOR INSOLUBLE ALPHA EMITTERS

by

J. W. Healy, C. R. Richmond, and E. C. Anderson

The interpretations of the potential effects of insoluble alpha-emitting particles in the lung, as described in the document supporting the Natural Resources Defense Council petition of February 14, 1974, are reviewed in light of present evidence. It is concluded that the theories upon which the proposal is based are not in accord with the evidence and that the theories do not correctly predict the outcome of experiments actually using such particles.

I. INTRODUCTION

On February 14, 1974, the Natural Resources Defense Council (NRDC) submitted a petition to the U. S. Atomic Energy Commission (AEC) and the Environmental Protection Agency (EPA) requesting that they amend their standards as said standards apply to insoluble particles of plutonium and other alpha-emitting "hot particles."[1] (The terminology of "hot particles" is that of the NRDC and refers to particles which contain more than 0.07 pCi of insoluble alpha emitters.) In support of their petition, the NRDC included a report by Drs. Arthur R. Tamplin and Thomas B. Cochran which provides the basis for the proposal.[2]

The question of the possible biological effects from radioactive particles which can irradiate small quantities of tissue to large physical doses has been of interest to the scientific community and radiation protection groups for many years. In several studies involving large extrapolations of available data, an enhanced tumor production from numbers of such particles has been predicted.[3,4] However, the tenuous nature of the evidence and the indirect methods of arriving at the answer have, in general, prevented these predictions from gaining acceptance in the biomedical community, and the standards have continued to be based upon other evidence.

In view of the current interest in this question and the somewhat unusual procedure of submitting the proposal through legal channels rather than through scientific review, it was felt that an examination of the allegations and conclusions would be useful in informing those concerned as to the validity of the bases. This report, therefore, reviews in some detail the basis for the NRDC proposal and briefly indicates the experimental information available on the question.

II. THE CONTENTION

While it is difficult to condense the arguments of an author without running the risk of changing his meaning or emphasis, we will briefly summarize in this section, for the orientation of the reader, our understanding of this contention. However, it is urged that reference be made to the original document[2] to obtain their full viewpoint. It is our impression that the following are the key technical items upon which the petition is based.

1. The responsible standards-setting organizations, the International Commission on Radiological Protection (ICRP) and the National Council on Radiation Protection (NCRP), have given no guidance on the question of localized radiation dose resulting from an alpha-emitting particle.

2. In Tamplin and Cochran's words, the Geesaman hypothesis indicates that "when a critical architectural unit of a tissue (e.g., a hair follicle) is irradiated at a sufficiently high dosage, the chance of it becoming cancerous is approximately 10^{-3} to 10^{-4}." The Geesaman hypothesis was published in 1968 in a Lawrence Radiation Laboratory report[5] (now Lawrence Livermore Laboratory) but was never published in the open literature. In this theory, Geesaman relied upon a theoretical

investigation of the dose distribution around a particle in the lung and estimated sizes above which cell death would result in no cancer. In an addendum,[6] he used data on the induction of tumors in rat skin and the relation of these to atrophied hair follices as a result of radiation. Perhaps his conclusions can best be stated by quoting from the conclusions section of the addendum.[6]

"Summing up, intense radiation exposure of mammalian skin and lung tissue commonly results in cancers. Tissue injury and disturbance are a primary consequence of intense radiation insult, and are observed in association with carcinogenesis. Albert has exhibited a simple proportionality between skin carcinoma and atrophied hair follicles. No general description of precarcinogenic injury exists, but in a crude sense the available observations are compatible with the idea of an injury-mediated carcinogenesis. Cancer is a frequent instability of tissue. Since tissue is more than an aggregate of cells, and has a structural and functional unity of its own, it would not be surprising if some disrupted local integrity, a disturbed ordering, comprises a primary pathway of carcinogenesis. The induction of sarcomas with inert discs of Mylar, cellophane, Teflon, and Millipore is indicative that such a mechanism exists. Presumably mitotic sterilization is an important factor in any carcinogenesis mediated by radiation-induced tissue injury. The functional relation of this factor to the carcinogenic response may be quite different from a linearity in the surviving mitotic fraction.

"While regrettably unquantitative, the hypothesis of an injury-mediated carcinogenesis is suggestively descriptive. If the respiratory zone of the lung contains a structure analogous to the rat hair follicle, and if a radioactive particulate deposited in the respiratory zone has the capacity to disrupt one or more of these structures and create a precancerous lesion, then cancer risks of the order of 10^{-3} and 10^{-4} per particle can be expected for burdens much less than 10^{8} particles."

Again, however, the reader is urged to review the original document to obtain the full argument.

3. In deriving present limits for alpha emitters in the lung, Tamplin and Cochran indicate that no factor was included to account for the non-uniform distribution of radiation in the lung as is done in the ICRP and NCRP formulation of bone dosimetry. It was pointed out that such a distribution factor could be defined by:

$$DF = \frac{\text{number of cancers (non-uniform distribution)}}{\text{number of cancers (uniform distribution)}}$$

"Since direct experimental evidence are not available....,"[2] they chose to attempt a definition of this factor from the Geesaman hypothesis including the quantitative derivation of probability of cancer induction derived from rat skin hair follicles.

4. As regards human data, they discuss the case of a skin lesion from plutonium embedded in the epidermis; a purported case of synovial sarcoma due to contamination during handling of a carboy; the Los Alamos cases which date back to the Manhattan Project and are dismissed as not having received particles of sufficient activity; and a group of exposed Rocky Flats workers which are, again, dismissed on the grounds that the time since exposure has not been long enough for cancer to develop. In the first case, the statement of the pathologist that "their similarity to known precancerous epidermal cytological changes, of course, raised the question of the ultimate fate of such a lesion....."[7] seems to be interpreted as proof that cancer would have developed. In the second case, a series of circumstantial inferences is quoted to "prove" that the cancer was due to plutonium.

5. Since the Geesaman hypothesis,[6] as given in his earlier reports, seems to have no dependence of effect on radiation dose or amount of activity per particle but states that the effect is due to the number of particles, Tamplin and Cochran modify this hypothesis by establishing a critical particle size below which the effect will not be noted (i.e., a threshold?). Their basis is given by the following quotations:[2]

"Not all particles would be expected to result in these high cancer probabilities. As the particle size or specific activity per particle is reduced so is the dosage to the surrounding tissue. Indeed, at sufficiently small particle size or specific activity, one would expect the radiation insult to behave similar to uniform irradiation. The study of Albert on induction of cancer in rat skin indicates a precipitous change in the dose response curve as the dosage exceeds 1,000 rem.[55] ..... This suggests

that a particular level of tissue damage must occur before this unique carcinogenic response occurs. The experiments of Laskin *et al.* indicate a significant carcinogenic response in the lung at 1400 rem, suggesting a comparable sensitivity of lung tissue.[56] Geesaman indicates that the tissue repair time in the lung is of the order of one year.[57] It therefore seems appropriate, but not necessarily conservative, to accept as guidance that this enhanced cancer risk occurs when particles irradiate the surrounding lung tissue at a dose rate of 1000 rem/yr or more. .....using Geesaman's lung model, a particle with an alpha activity between 0.02 pCi and 0.14 pCi is required to give a dose of 1000 rem/yr to irradiated lung tissue. For purposes of establishing a maximum permissible lung particle burden we will use 0.07 pCi from long half-lived (greater than one year) isotopes as the limiting alpha activity to qualify as a hot particle."

Reference 55 in the above quotation is to Albert *et al.*;[8] reference 56 to Laskin *et al.*;[9] and reference 57 to Geesaman.[5]

6. From their definition of a "hot particle," Tamplin and Cochran derived values for occupational exposure by comparing the risk of lung cancer from dose rates of 15 rems/yr to the lung to assumed risks from particles of 1/1000, 1/2000, and 1/10 000 per particle. They then recommended as ".....a somewhat arbitrary compromise and ..... not the most conservative value....."[2] the use of a risk of 1/2000 per hot particle in determining the maximum permissible lung burden for insoluble alpha-emitting radionuclides in hot particles. From this they arrived at a value of 2 particles or 0.14 pCi for a reduction in the maximum permissible lung burden by a factor of 115 000.

For individual members of the public, a value of 0.2 hot particle, while recognizing the disparity in risk occasioned by a fractional number of particles per person, is recommended along with a value of 0.07 hot particle as the average lung burden for members of the public. Limiting values for soil contamination and accidents are also derived by similar considerations.

III. PARTICLES AND RADIATION DOSE

The origin of the NRDC proposal lies in the very non-uniform radiation dose to the tissue surrounding a radioactive particle. For this reason, we will initially provide some description of the nature of this non-uniformity and the application of the concept of radiation dose to biological problems.

A. The Radiation Dose around a Particle

The unique feature of a particulate source of radioactive material (particularly for an alpha emitter because of the short range of the alpha particle) is the rapid change in dose or dose rate as one moves away from the particle and the relatively small amount of tissue exposed to the dose. If one ignores the details of the Bragg curve, the dose in a uniform density tissue at reasonable distances from the particle follows the inverse square law for alpha particles. For the lung, the presence of the alveoli and air passages results in varying degrees of absorption, depending on the actual mass of tissue encountered, so that the inverse square relation is distorted by the varying absorption and the dose pattern may be non-symmetrical. Geesaman[5] has approximated this dose pattern by assuming a cubical lattice representing the air spaces in the human, while Anderson and Dean[10] have used micrographs and computer programs to calculate the pattern for the hamster.

The effect on the calculated dose of varying the volume over which energy deposition is averaged is shown in Fig. 1. (This is not the radial dose distribution, which extends only from the particle surface to the maximum alpha range and for which the

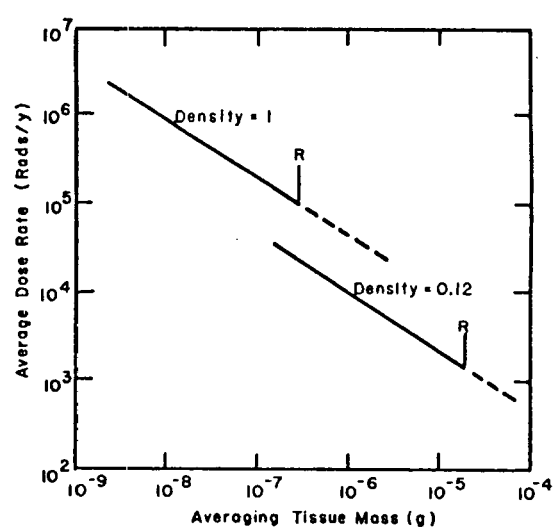

Fig. 1. Calculated dose rate averaged over different distances from a 0.28-pCi particle vs the tissue mass involved in averaging. R represents the range of the particle.

abscissa would be distance.) The calculations are for a particle of 0.28 pCi of ^{239}Pu in tissues of two different densities. It is assumed that the energy loss per unit path length is constant so that the alpha particle deposits energy uniformly along its path. The range in unit density tissue is taken as 40 μm,[11] with the range for other tissues scaled to the tissue density. The doses given are annual doses averaged over the volume of tissue given. The curve indicated as density = 1 is calculated for unit density tissue, and the curve for density = 0.12 is for a uniform tissue having a density of 0.12, corresponding to the average bulk density of Geesaman's lung model at half inflation.[5] No correction was made for the self-absorption in the particle, although this should be negligible for these small PuO_2 particles in comparison to the errors caused by other assumptions. The annual doses are given both in rads which can be converted to rems by the conventionally used quality factor of 10.[12] It must be emphasized that this conversion to rems is particularly uncertain for this case, since there are no data which can be used to assess the relative effects of alpha radiation and the reference radiation in this particular geometry of irradiation.

Figure 1 is intended to indicate the wide variation in dose which can be calculated by different assumptions of averaging volume. Even here we have minimized the dose to individual cells by plotting the average over the volume to the fraction of the range considered. The dose to an individual cell at differing distances varies even more than this average.

We have not considered in this calculation the photon dose from x rays or infrequent gamma rays from either ^{238}Pu or ^{239}Pu, since the focus of the discussion is on alpha-particle effects. It should be noted, however, that these photons are more penetrating and will result in lower doses at distances beyond the range of the alpha particles.

B. Limitations on the Usefulness of Radiation Dose

Calculations such as those given in the preceding section are interesting and have been made by various individuals for many years. The question remains as to their usefulness and meaning in assessing a biological problem.

The primary use of radiation dose, in practice, is as a physical parameter to be used in correlating and extrapolating experimental data on biological effects on an empirical basis. Thus, the present limits for radiation exposure are based upon observations of effects in humans for whom the dose has been estimated. There is no *a priori* basis for assigning an effect to a given dose, since our understanding of the basic mechanisms of radiation carcinogenesis and the influence of cellular interactions is completely inadequate. Thus, radiation doses are meaningful only when related to empirical data on the outcome. As a corollary, the further one extrapolates from the experimental conditions under which the dose-effect relationship is measured, the greater the uncertainty. Thus, predicting the behavior of the effects on individual cells or aggregates of cells in a functioning organ from *in vitro* studies in cell culture is a very wide extrapolation which ignores the very different environment of the cells in the organ and the potential interactions which occur among cells. (Such *in vitro* studies, however, are of great interest for other reasons, such as studies of the mechanisms of damage at the cellular level.) Similarly, extrapolating from the effects of a partial organ irradiation to a full organ (or vice versa) can lead to a misestimate. 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.

A further factor of importance in the use of physical dose as a correlating concept is the exact method of expression of dose. That is, if a correlation with effect is established using one method of calculating the dose, it is not valid to apply this correlation if another basis for dose calculation is chosen. As an illustration which, incidentally, seems pertinent to the problem at hand, Vaughan[13] indicates that 90% of the ionization along an alpha particle track formed in unit density tissue is contained in a cylinder of 0.01-μm radius with the axis of the cylinder along the track. For an alpha particle with 5.15-MeV initial energy, the range is about 40 μm. The average dose to this limited volume, therefore, is about 6×10^6 rads, with even higher average doses for smaller radii and at the peak of the Bragg curve. For a 1000-g

organ of unit density tissue, the current occupational limit of 1.5 rads (15 rems) per year, even assuming homogeneous distribution of the alpha tracks, means that about 0.25 mm^3 of tissue is irradiated to doses above 4×10^6 rads, or if a dose of 1000 rads were chosen, a volume of some 1500 mm^3. Since unit density tissue was chosen for this illustration, the results do not compare with those for a particle using the Geesaman model. However, it is clear that even a "homogeneous" distribution of alpha radiation through a body of tissue results in considerable non-uniformity in dose distribution. Further, for the example chosen, one could express the limits as 15 rems to the 1000 g of tissue or as a limitation on the volume of tissue exceeding a given dose. For example, no more than 0.3 mm^3 of tissue shall exceed 4×10^7 rems or no more than 1500 mm^3 shall exceed 10 000 rems. Although the latter methods of expression involve numbers that are frighteningly high in more normal context, all three methods define the same total energy deposition. However, note that it would be highly improper to apply the 15-rems value to the dose along the track just as it would be improper to apply the dose along the track to the dose arising from an assumption of uniform tissue distribution.

A specific point in the Tamplin-Cochran dissertation[2] is the use of the "distribution factor" (DF) in calculating the dose in rems for internal emitters and is supported by the fact that a DF of 5 is used in calculating the dose for bone. They then indicate that a DF should be applied to lung. However, it must be realized that a dose calculation was not used to arrive at the present maximum permissible body burden for plutonium.[14] Instead, a comparison of biological effects (primarily on bone) was made between plutonium and radium. On the basis of these data, it was deduced that plutonium in the body is 2.5 times as harmful as radium on a microcurie basis. Since the maximum permissible body burden for radium had been established from studies of humans as 0.1 μCi, the maximum permissible body burden for plutonium was set at 0.04 μCi.

The dose considerations quoted by Tamplin and Cochran arose in an attempt to use these experiments, and others with strontium, to provide a physical formulation of the results which could be used for extrapolation to other bone-seekers. For the purpose of such calculations, it was *assumed* that radium was uniformly distributed in bone. Further, it was assumed that 90%, or essentially all, of the plutonium in the body was in bone. Since the individual plutonium disintegration liberated about half of the alpha energy of one disintegration of radium with its accompanying daughter products, the foregoing damage ratio of 2.5 on a microcurie basis becomes 5 on an average energy-delivered (dose) basis.

The key to this comparison lies in the assumptions. We know, for example, that radium is *not* uniformly distributed in bone. In fact, if anything, it is more non-uniformly distributed than plutonium. However, the deposition sites are different from those of radium so that the plutonium affects a different, and more sensitive, portion of the bone. One could presumably eliminate the confusion caused by the distribution factor by redefining the critical organ to include only the sensitive portion of the bone and comparing the dose to this region from plutonium and radium. We also note in passing that the more recent examination of the distribution of plutonium in animals indicates that only about 40 to 50% of the plutonium is in the bone. If this were true in the comparison animals (as seems likely), then the actual distribution factor for bone calculations should be 10 rather than 5.

We have introduced this rather lengthy discussion on bone dose calculations to indicate, once again, the difficulty in applying dose calculations and concepts derived for one use to a different problem without full understanding of what was done. In the above case, the salient feature is that radium is non-uniformly deposited so that some sections of the bone receive doses orders of magnitude greater than others.[15] The distribution factor is not intended to indicate greater localized dose from plutonium but, rather, that the distribution in bone is different from that of radium on a gross basis.

C. Previous Guidance

An interesting point in the Tamplin-Cochran document is: "It is important to recognize that the ICRP has given no guidance with respect to non-uniform irradiation of the lung by insoluble alpha-emitters such as insoluble plutonium particles." They then quote one of many statements made by the ICRP[16] and other groups which indicate that there is no clear evidence as to whether the effect of the

non-homogeneous dose is greater or less than that of the homogeneous dose. They interpret this statement as: "In effect, the ICRP is saying that there is no guidance....." A quote from the NCRP follows concerning the significant volume of tissue which concludes: ".....For example, if a single particle of radioactive material fixed in either lung or lymph node might be carcinogenic, the averaging of dose either over the lung or even over one cubic centimeter may have little to do with this case."[12]

While we do not feel that it is useful to quote such bodies at length, there is evidence that the problem has been considered since the early days of the derivation of limits. One of the earlier statements arose from a Tri-Partite Conference in 1949[17] at which scientists from the United Kingdom, Canada, and the United States were arriving at the conclusions which were later applied by many of these same people in the ICRP and NCRP recommendations: "In relation to the possible pathological effects of radioactive particles in the lungs, Dr. Hamilton pointed out that the cells in the immediate neighborhood of a dust particle containing 1 or 2% of plutonium would be subjected to a dose of about 400 r/day. The general opinion which emerged from the discussion was that the carcinogenic effect per unit volume is probably considerably less for the irradiation of small masses of tissue than for large." This conclusion undoubtedly affected the practice of calculating dose as the average dose to an organ at that time and comprises definite guidance on the handling of such problems. However, the matter did not rest there, since several national and international groups continued investigation from that time to the present, with frequent statements as to the lack of definitive information.[16,18-21] However, in spite of the indications of periodic questioning and reviews, there has been no revision in the practices which they recommended of using the average organ dose as a basis for establishing standards.

From the above, it seems clear that the ICRP and the NCRP *did* furnish guidance on the pertinent dose to be used for standards-setting: the use of an average calculated dose to an organ, with full recognition of the non-uniform distribution of dose around the particle. In spite of numerous reviews of the question over the intervening years, they have reiterated this guidance by not changing it. It is difficult to support any claim of no guidance in view of this record on the part of bodies which have traditionally been in the forefront of recognizing potential problems (i.e., genetic effects) and providing generally conservative recommendations.

One recommendation of the NCRP[12] (while perhaps not completely applicable to the particle case as is shown by their example situation quoted earlier) is of interest when combined with Geesaman's estimate of a particle size above which cancer would not be expected due to cell death.[5] The NCRP statement is, "Simplifications in practice hinge largely on reporting a single representative protection dose for a limiting organ system even when the actual irradiation is grossly non-uniform. The representative dose is taken as the highest that can be obtained by averaging over a prescribed significant volume. The implication of this concept ..... is that any redistribution of a given dose within such a volume does not materially alter the radiation response. It is usually assumed that the 'significant volume' should be of the order of one cubic centimeter. This will be grossly conservative under most circumstances, and in special situations use of a larger volume is justified." It is not clear why the NCRP recommended a significant volume rather than a significant mass, since this results in averaging over a smaller mass in the lung than in other tissues due to the density difference.

However, if we calculate the dose over 1 cm^3 of lung tissue with an average density of 0.12 g/cm^3 for the "hot particle" of 0.07 pCi derived by Tamplin and Cochran,[2] we obtain a dose of only 0.055 rad or 0.55 rem per year. Thus, one would require an activity of 1.9 pCi to reach the limit of 15 rems per year for this single cubic centimeter of tissue (or an activity of 15 pCi for a single cubic centimeter of unit density tissue). Geesaman[5] quotes an activity for a 1-μm-diameter particle of ^{238}Pu as 60 pCi and arrives at a conclusion that ".....unless the source size, s, is smaller than or of the order of 0.25 μ the yearly flux will be lethal for all epithelial populations in the exposed volume. The source size condition will only be slightly less stringent for endothelial populations $s < 0.35$ μ." The implication of the above is that no cancer will

develop for particles larger than those described since the cells are killed. According to the constants used by Geesaman, a 0.25-μm particle would have an activity of about 2.5 pCi, which compares with the 2 pCi to give 15 rems to one cubic centimeter of tissue. Thus, if Tamplin and Cochran had chosen to use this available NCRP guidance along with the Geesaman study, their conclusions would have been considerably different.

IV. THE GEESAMAN HYPOTHESIS

The Geesaman hypothesis was published as a Lawrence Radiation Laboratory (now Lawrence Livermore Laboratory) report in February 1968,[5] with an addendum in October 1968[6] containing the quantitative estimates of cancer production. This work has never been published in the open scientific literature but remains an unreviewed and unrefereed study.

Since his conclusions seem to be based primarily upon the studies of follicular cancer produced in rat skin, we quote below those sections of the report in which he uses these data with his references and footnotes deleted.

"Albert's study of radiation-induced carcinoma in rat skin gives some quantitative description of a high-dose carcinogenic situation. Since such descriptions are rare, and since Albert's results have implications to risk analysis in general, his experiment is outlined here.

"A skin area of 24 cm^2 was exposed to electron radiation with various depths of maximum penetration. ..... In all cases the response scale at sufficiently high doses was large, ~ 1 to 5 tumors per rat at 80 weeks after exposure. It was noted by Albert that when the dose was normalized to a skin depth of 0.27 mm, the three response curves became continuous. Since this depth is near the base of the hair follicle which comprises the deepest reservoir of epithelial cells of the germinal layer, it was suggestive that this might be a critical region in the observed carcinogenesis. The suggestion gained significance from the observation that most of the tumors are similar to hair follicles, and that in the nonulcerogenic dose range the number of tumors per rat was in nearly constant ratio (1/2000 to 1/4000) with the number of atrophied hair follicles..... Thus the carcinogenesis in this experiment was remarkably correlated with the dose to and the specific damage of a particular skin structure. When exposures were made with stripe and sieve patterns of roughly 1-mm scale, geometrical effects were observed; most notably the cancer induction in the sieve geometry was suppressed at doses of 1700 R, but not at doses of 2300 R. The reduction, however, was again consistent with the reduction in damage as characterized by atrophied hair follicles.

"For perspective it is valuable to relate these observations to cellular descriptions. Carcinogenesis in Albert's experiment is maximum in the neighborhood of 2000 R. It is well documented *in vitro* and to a lesser extent *in vivo* that the fraction of mitotically competent cells as measured by clonal formation decreases in a nearly exponential fashion with the dose. From these results a surviving mitotic fraction of approximately 10^{-5} would be expected in a population of germinal epithelial cells exposed to 2000 R. Even in this pre-ulcerative dose regime the cell population suffers severe mitotic injury. It is significant that Albert's dose response curves show no simple relationship with the surviving fraction of mitotically competent epithelial cells. There is certainly no exponential decrease of the response in the neighborhood of D_{37}, and, in fact, the tumorigenesis is maximum in a dose region where the population of mitotically competent cells should be initially depleted by about 5 orders of magnitude.

"To summarize this important experiment, a high incidence of cancer was observed after intense local doses of radiation, and the carcinogenesis was proportional to the damage or disordering of a particular skin structure."

The reasoning leading from this information, plus a discussion of other experiments with high doses and particle sources leading to the conclusion (quoted earlier) of a cancer risk of 10^{-3} to 10^{-4} per particle, is not given but is presumed to result from the correlation with atrophied hair follicles from Albert's experiments.

There is a similarity between this work and the theory propounded by Virchow in 1863 that the cause of cancer is chronic tissue damage.* This

*We are indebted to Dr. Roy E. Albert, New York University, for this line of reasoning.

theory was disproved by experiments which showed that cancer can be produced by very potent substances that vary widely in their capacity to cause cancer, whereas many agents which cause damage do not cause cancer. Thus, while there is a frequent association between tissue damage and cancer, there are types of cancer and types of damage for which no association exists.

There are several aspects of the data from the skin experiments used by Geesaman, as well as information published later from the same series of experiments, which should force some modification of the proposal but are not included in the Tamplin-Cochran document. These and their implications for the Geesaman hypothesis are reviewed below.

A. Type of Tumor

In a 1961 paper, Albert *et al.* first explored the tumors resulting from irradiation of rat skin with ^{91}Y beta rays.[22] Two strains of rats were used with the tumor types and frequencies as given in Table I. They indicate the Holtzman strain to be similar to the Sprague-Dawley strain, but the animals were considerably older (~ 40 weeks compared to ~ 20 weeks for the Sprague-Dawley).

A variety of tumor types were obtained. In Fig. 2, we have plotted the dose-incidence curve

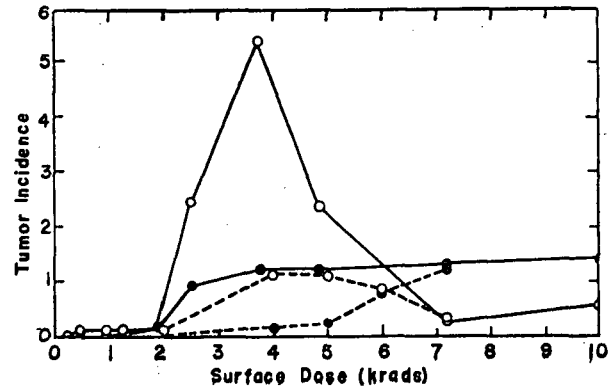

Fig. 2. Tumor incidence per animal vs surface dose of electrons: (——) Sprague-Dawley strain; (---) Holtzman strain; (-O-) adnexal tumors; and (-●-) other tumors.

for both strains for the predominant tumor type (follicle and sebaceous or "adnexal") and the sum of all other types. The incidences were corrected for the unidentified tumors by assuming these to arise in the same proportion as the identified ones. It is of interest to note the wide disparity between the response curves of the adnexal tumors and those of other types, as well as the disparity between the curves for the two strains (whether due to strain or age is not determined). Since the remainder of the experiments focused upon the adnexal tumors, with

TABLE I

TUMOR TYPES AND FREQUENCIES FROM IRRADIATION OF RAT SKIN

	Dose (rads)									
Sprague-Dawley Strain	10 000	7200	4870	3750	2500	1900	1225	950	470	230
Initial number of rats	12	12	13	14	15	10	15	23	25	24
Epidermoid carcinoma	9	11	6	5	5	1	0	0	0	0
Adnexal tumor	5	2	26	62	23	3	1	3	3	1
Connective tissue tumor	2	1	0	1	1	1	1	0	1	0
Squamous papilloma	0	0	6	6	3	0	0	0	0	0
Cysts	0	0	1	2	0	0	0	2	1	1
No pathologic examination	8	5	8	17	19	0	2	0	0	0
Total	24	19	47	93	51	5	4	5	5	2

Holtzman Strain	7200	6000	5000	4000	2000	1000	500
Initial number of rats	9	10	8	11	16	20	50
Epidermoid carcinoma	7	6	1	2	0	0	0
Adnexal tumor	2	7	6	11	2	0	1
Connective tissue tumor	0	0	0	0	0	0	1
Squamous papilloma	2	0	0	0	0	0	0
Cysts	0	0	0	0	0	0	0
No pathologic examination	3	4	3	3	0	0	1
Total	14	17	10	16	2	0	3

data on other types discarded, the information is aimed at a very specific tumor type even for the organ considered: rat skin.

B. Volume of Irradiated Tissue

As was discussed earlier, the extrapolation from one condition of irradiation or method of expressing dose to another must be done with great caution and a full understanding of the parameters involved. How, then, do the conditions of the rat skin experiments compare with those of the particle irradiation?

The particle doses typically involve tissue quantities of tens of micrograms (see Fig. 1). In the rat skin experiments, areas ranging from about 5 to 30 cm^2 were used with depths from about 0.4 to about 1.5 mm. Thus, the tissue volumes ranged from about 0.2 to about 5 cm^3 or, for unit density tissue, 0.2 to 5 g.[8,23-25] This is an extrapolation in tissue volume on the order of 10^3 to 10^5.

There are several observations in the rat skin experiments which are pertinent to the validity of extrapolation. In one series of irradiations, exposures were made through two grids which provided 1-mm-wide bars of irradiation area with one grid masking all except a third of the area and the other all except a sixth of the area.[23] In addition, a mask (sieve) with circular holes which permitted an exposed area of a third of the uniform area was used. From these data, it was noted that the response with the smaller areas was lower even though the total dose to the area (expressed in gram-rads) was in the vicinity of the uniform dose required to produce the maximum incidence of adnexal tumors. In other words, the delivery of a specific amount of energy to a given overall area of skin resulted in fewer tumors when the energy was delivered at higher doses but to smaller subareas. Geesaman correctly points out that this suppression occurred at 1700 rads but not at 2300 rads.[6] However, the 2300-rads value for the uniform irradiation is well past the dose of maximum tumor induction, and there has been a significant drop in the incidence for this condition. Therefore, it is difficult to attribute this effect to other than the oversaturation of the response. Albert *et al.* conclude from this work: "The experiments reported here indicate that, in a limited dose range, the non-uniform radiation pattern has the effect of reducing both chronic hair follicle damage and tumor formation."[23]

In the studies of the association between hair follicle damage and tumor formation, Albert *et al.* noted that the damage to the hair follicles across the irradiated area was not uniform, with the major damage occurring at the center of the area and considerably lower damage at the edges.[24] From other data, it appears that the dose across the area was reasonably uniform and that the effect was due to something other than non-uniform dose. From this and the preceding work, Albert *et al.*[24] conclude: "Two observations indicate the importance of the size of the irradiated area on the magnitude of hair damage: (1) the follicles along the margin of the irradiated area are relatively uninjured compared to the follicles in the center of the irradiated area..... (2) there is a suppression of follicle damage when the irradiation is delivered in a sieve pattern..... These observations strongly suggest that the pathogenic mechanisms for the development of both irreparable hair follicle damage and skin tumors depend upon both the dose and the *amount of skin irradiated*" (emphasis added).

Thus, the data and conclusions in the papers used by Geesaman to justify his work (and quoted by Tamplin and Cochran[2] as "biological evidence" supporting their contentions) strongly suggest that extrapolations to smaller tissue volumes may not be legitimate.

C. Species Dependence

We have alluded earlier to the difference in response curves for skin tumor formation occasioned by either the strain difference or the age of the rats used. In a paper subsequent to the Geesaman proposal, Albert *et al.*[25] repeated some of their studies using mice as the experimental animal, since it had been noted that the response of mouse skin is different, with relatively few tumors and most tumors being epidermoid carcinomas rather than adnexal tumors.

The results of this experiment confirmed the previous findings that adnexal tumors, noted as the most probable outcome in rats, were rare in mice and that the total number of tumors produced in mice was only 15 to 20% of those in rats for comparable conditions. The lack of adnexal tumors was attributed to the fact that the hair follicles in the mouse are more radiosensitive than those in the rat. As a result, little follicle atrophy is noted in the

mouse -- either the follicles remain intact or they are destroyed.

The results of this experiment indicate clearly the difficulties of applying results from one organ to another. Even though skin was the target in both cases, the differences in structure between rat skin and mouse skin caused a completely different outcome upon irradiation. The outcome upon comparison to a different organ such as the lung, where follicle structures or functions do not even exist, would seem to make the final conclusion by Geesaman one of sheer speculation.

D. Volume of Follicle Irradiated

In the original studies of rat skin response, Albert *et al.* used electron beams which had an approximate linear decrease in dose with depth.[8,22-24] The relation between dose at the tip of the hair follicle, lying at a depth of about 3 mm, was established by noting that the tumor incidence curves for electrons of various penetrations coincided when the dose was expressed as the dose at a depth of 0.3 mm.[8] However, it can be noted that the entire follicle was irradiated to this dose or greater.

To test the dependence of the effect of doses to various portions of the follicle, Heimbach *et al.* used the Bragg peak of alpha radiation produced by a cyclotron.[26] The energy of a 37-MeV alpha beam was adjusted by the use of aluminum absorbers in the experiments so that the Bragg peak fell at depths of 0.12, 0.35, and 0.55 mm. Since the Bragg peak can produce dose rates up to 5 times that along the early portion of the track, this enabled investigation of doses delivered to various parts of the follicle. The results indicated that the response curves coincided when the dose was expressed as minimum dose to any point along the hair follicle. The tumor types were identical with those found with electrons, and there was once again a correlation between tumors and atrophied hair follicles, with the ratio between tumors and atrophied hair follicles of about 1/9000.

From this experiment, the authors concluded that the entire hair follicle must be irradiated to produce tumors. The minimum penetration alpha radiation used did not irradiate the lowest part of the follicle and did not induce tumors. The authors then suggested: "The findings reported here can be explained on the basis that the hair follicle is reparable from cells originating at any point along its length, and that the capacity for such repair is inversely related to the degree of damage sustained by the part of the follicle minimally damaged. The existence of a 'critical depth' in skin of about 0.3 mm which was demonstrated with electron radiation ..... can be explained on the basis that the follicle tips, which received the minimum dose to the follicles, were the most protected part of the skin epithelium and, therefore, contained the critical reservoir of cells for replacing the more superficial and more heavily irradiated cells."[26]

Since the hair follicle is a few tenths millimeters long (several hundred μm) and the range of an alpha particle is about 50 μm, these results strongly suggest that a single alpha-emitting particle, even if it could be placed in rat skin, would not produce tumors. Thus, in the statement of the Geesaman hypothesis, "If the respiratory zone of the lung contains a structure analogous to the rat hair follicle, and if a radioactive particle deposited in the respiratory zone has the capacity to disrupt one or more of these structures....., then cancer risks of the order of 10^{-3} to 10^{-4} per particle can be expected."[6] The second conditional clause does not follow unless the first is modified to further redefine the hypothetical structure to a size where it will be fully irradiated by the particle (i.e., less than ~ 100 μm). A further necessary condition is that such structures be located throughout the lung with such a frequency that the particle will irradiate one with a probability approaching unity. This appears to be stretching an already tenuous theory beyond the realm of credibility.

V. THE TAMPLIN-COCHRAN APPLICATION

In the Tamplin-Cochran interpretation of the Geesaman work,[2] they introduce the concept of a "critical architectural unit" in the following passage: "Now what are these experiments trying to tell us? Certainly a reasonable interpretation of these experimental results is: when a critical architectural unit of a tissue (e.g., a hair follicle) is irradiated at a sufficiently high dosage, the chance of it becoming cancerous is approximately 10^{-3} to 10^{-4}. This has become known as the 'Geesaman hypothesis'."

There are significant differences, however, in the statement by Geesaman and that quoted above. Geesaman states his theory as conditional: i.e., "If the respiratory zone ..... contains a structure analogous to the rat hair follicle....."[6] Thus, in the Tamplin-Cochran version there is a progression from "if" to "when," with no evidence or attempt to indicate what this critical architectural unit may be. Further, they imply that *any* hair follicle will be a "critical architectural unit," while Geesaman carefully refers to structures ".....analogous to the rat hair follicle."[6] We have seen earlier that mouse skin hair follicles do not fit the Geesaman description, since they are not analogous in their response.

The second part of Geesaman's conditional statement indicates that ".....if a radioactive particulate deposited in the respiratory zone has the capacity to disrupt one or more of these structures and create a precancerous lesion....."[6] has been changed to indicate that when the structure is ".....irradiated at a sufficiently high dosage, the chance of it becoming cancerous is approximately 10^{-3} to 10^{-4}."[2] Thus, the hypothetical statement of the possibility of disruption and cancer formation has become, in translation, a statement of fact.

It is of interest that Tamplin and Cochran use the same probability of cancer formation for particles deposited in the lung that Geesaman states for the condition that the particle actually irradiates the hypothetical structure. We can deduce from this something of the character of this supposed structure. From Table III of the Tamplin-Cochran report, the mass of tissue irradiated to 1000 rems per year around a 0.07-pCi particle is 65 μg with the lung at half-inflation. Geesaman, for this condition and his cubical lattice lung model, estimates the range of an alpha particle to be between 335 and 1000 μm, depending upon the path through the lattice.[5] The experiments with alpha particles and rat hair follicles indicate that the full "analogous structure" must be irradiated,[26] which can only occur if the 65 μg of tissue surrounds the particle. Thus, we can conclude that the structure has a mass of 65 μg or less, since the probability of the particle lodging at the center would seem to be low. From the Tamplin-Cochran assumption that the probability of cancer for a particle lodged in the deep respiratory zone is the same as Geesaman's probability assuming the structure to be irradiated and damaged, it is apparent that the number and spacings of the structures must be assumed to be such that *each* particle will irradiate one. (Otherwise, the probability of the particle lodging close enough to irradiate the structure must be included in their estimates.) In a 1000-g lung, there must be greater than 10^7 such structures, each of which weighs less than 65 μg. It appears from this type of estimate that the "critical architectural unit" is any group of cells rather than an identified structure, as is implied by the comparison with the hair follicle.

The second change in interpretation introduced by Tamplin and Cochran is the minimum activity of a particle to produce cancer. This could logically follow from Geesaman's second conditional statement concerning the ability of the radiation to disrupt one or more of the structures.[6] However, the consequences of introducing such a threshold on the radiation response when the entire lung is irradiated are of interest. If one irradiates the full lung, obviously *all* of the hypothetical structures will be irradiated. If one assumes the disruption of these structures to be the sole cause of radiation-induced cancer and there were more than 1000 to 10 000 such sites in the lung, then the incidence would remain at zero until the threshold dose (1000 rems) was reached. The incidence would then increase rapidly above this to 100% or greater. If there are fewer than this number of sites (with a probability of 10^{-3} to 10^{-4} of producing cancer per site when irradiated), then obviously the probability of a particle irradiating the site must be included. There may be causes of radiation-induced cancer other than the mechanism of tissue disruption. These could result in a gradual increase in incidence below the threshold, but the response from the architectural unit mechanism postulated would still increase to 100% when the threshold is exceeded. This pattern does not conform to any known data on cancer incidence dose-effect relations for full lung irradiation.

It is of interest that the Tamplin-Cochran interpretations of the theory receive only minimal, if any, justifications. For example, there is no

attempt to identify the structure in the lung responsible for the effect, nor is it explained how one can extrapolate from the effects on a hair follicle to the effects in a lung which contains no unit even similar in function or structure to the hair follicle and sebaceous gland of the rat skin. Data on these tumors and their incidence, which have appeared since the original Geesaman postulation and which throw considerable light on the hypothesis, have been ignored. It can only be concluded that a more thorough and comprehensive study could have changed the conclusions of the document.

VI. THE HUMAN DATA

People have been exposed to plutonium during various uses of the material over the past 30 years. Tamplin and Cochran have chosen a few of these experiences, some to discount on the basis of their threshold theory and others to support their contention. Although we profess no special knowledge in the field of medicine, we will analyze their contentions on the basis of biological and health physics experience.

A. The Lushbaugh Report

In 1962, Lushbaugh and Langham reported on a lesion associated with plutonium in a wound.[7] The patient, while machining plutonium metal, received a wound which was later excised. Some 4 years after the accident, he noticed a nodule which, upon measurement, still contained some 0.08 μg of plutonium (~5000 pCi). Lushbaugh reported on the histological examination of the lesion, and the quotation appearing in the Tamplin-Cochran report arose from this paper: "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 pre-cancerous 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" (emphasis added). Following this quotation, Tamplin and Cochran indicated that ".....less than 0.1 μg of Pu-239 produced pre-cancerous changes in human tissue." They refer several sentences later to "this pre-cancerous lesion....." and state that this proves that a single ^{239}Pu particle ".....irradiates a significant (critical) volume of tissue and is capable of producing cancer." In other words, they manage, in the space of a few sentences, to move from ".....similarity to known pre-cancerous epidermal cytologic changes....." and expressed uncertainty on the part of the pathologist on the eventual outcome to a conclusion that cancer will result. We believe that the uncertainty expressed by the expert should be given proper weight in the conclusion.

In point of fact, examination of the autoradiograph in the Lushbaugh paper indicates very clearly that the lesion contained a number of small particles, since several points of origin of alpha particle "stars" can be discerned. Further, the author indicates the lesion containing the plutonium had a volume of 27×10^{-5} cm^3 or, for unit density tissue, a mass of some 27 μg. Reference to Fig. 1 would indicate that a single particle would deliver an alpha dose to only about 0.3 μg in unit density tissue.

In a subsequent paper, Lushbaugh *et al.* describe the result of the study of 8 such lesions resulting from plutonium in wounds in which the plutonium had resided for periods of time ranging from 0.5 to 8 years.[27] They indicate, "The lesions were found to vary morphologically in an orderly manner related roughly to the length of time the plutonium had been present. All were confined to the dermis. The size of the nodule depended on the dispersion of the particles present rather than the duration of the lesion. The largest nodule was about 2 mm in greatest dimension." They conclude in the discussion, "Although this study is based on too few small lesions to evoke much confidence in these retrospective interpretations, the conclusions may be warranted that metallic plutonium implanted in the skin in minute amounts elicits a foreign-body reaction of granulomatous type, which after subsiding in cellular activity becomes fibromatous." No reference is made in this paper to cancerous or similarity to pre-cancerous lesions.

These lesions are the most severe changes which have been reported in humans as a result of plutonium and, as such, require the question of wound

contamination to be taken seriously in radiation protection programs. However, to extrapolate these to cancers, in view of the uncertainty on outcome expressed by the pathologist, and especially to extrapolate to lung cancer seems to be an unjustifiable step.

B. The Gleason Case

The information available to the authors on the Gleason case is primarily that presented by Dr. Arthur R. Tamplin in the appendix of the Tamplin-Cochran document.[2] This involves the case of an individual who handled a crate containing a leaking carboy of ^{239}Pu solution and later developed a synovial sarcoma of the left hand.

In the initial analysis of this case, Tamplin indicates that the occurrence of this type of cancer is less than the total skin cancer death rate, since the prognosis for this type of cancer is poor. He concludes, "Thus it is highly unlikely that anyone who handled this crate would spontaneously develop this sarcoma on the contaminated hand....." This, of course, is not the question of interest, since the *a priori* condition that cancer did develop is given and the question is now whether there is evidence that indicates whether the plutonium was involved. Tamplin introduces evidence from animals that injection of 1 μg of ^{239}Pu into the skin of rats produced fibrosarcomas in 5% of the animals.[28] The relevance of this information appears remote, since these tumors were of a different type and arose from different tissues than the synovial sarcoma. (This is similar to the extrapolation from follicular tumors in the rat skin to lung tumors in the humans.) We know of no evidence, nor do Tamplin and Cochran produce any, that this type of tumor has been produced by radiation. However, in view of the ubiquitous nature of radiation as a carcinogenic agent, it would appear as a definite possibility providing that the proper critical tissue is irradiated (presumably the synovial membrane or the synoid capsule). It would appear that this would require something other than an injection into the dermis. Thus, the question to be examined is whether there is a reasonable probability that plutonium could have penetrated to the critical tissue under the conditions of the purported exposure.

Early in the discussion, Tamplin states: "There is little reason to doubt that this small amount of liquid (0.01 milliliter) or even more *found its way* below the surface of Mr. Gleason's palm" (emphasis added). It is our experience that plutonium does not "find" its way through skin, even though there is water exchange across the skin. The skin has been shown to be an excellent barrier to prevent the passage of many materials,[29] including plutonium.[30] Thus, some mechanism such as a break in the skin (wound) must be postulated and of such a depth and location that the critical tissue is involved.

The incident occurred on January 8, 1963. According to the Tamplin account, a survey was conducted on Mr. Gleason's home, clothing, and automobile on January 19, 1963. The results apparently were negative, or they would have been mentioned. It is indicated earlier when referring to Mr. Gleason's handling of the crate: "This could not have occurred without contaminating the palmar surface of his left hand, which was bare." It is difficult to see why the contamination should preferentially go to the *left* hand. Other portions of the body and the shoes presumably would also be susceptible. However, if a sufficient quantity to deposit 0.1 μCi (0.01 ml of a 160-μg/ml solution) were on the left hand, experience has indicated that such contamination transfers rapidly to other objects, including clothing and items handled such as tools or even the automobile steering wheel. The fact that these surveys, even 11 days later, did not detect significant contamination would indicate that not much was initially present.

Tamplin further indicates that urine samples collected subsequent to January 20 gave negative results and, "The only thing that this demonstrates is that no detectable level of Pu-239 was found." Later he indicates that negative findings in the feces and urine were obtained in April 1970 and, again, dismisses the results on the grounds that little is absorbed into the body. The latter conclusion is, of course, dependent upon the type of material used. As an illustration of a worst case, Johnson *et al.* injected plutonium oxide particles with a count mean diameter of 7 μm subcutaneously into dogs.[31] They found that the translocation to

the body occurred rapidly, with on the order of 0.25% of the plutonium recovered from other tissues. Assuming this very low translocation of PuO_2 to apply to the nitrate and using Langham's equations[32] for the excretion, we find that, for the 0.1 μCi postulated by Tamplin, urine samples should have indicated on the order of 0.2 disintegration per minute in the period around January 20. This level is easily detectable by adequate analysis. Of greater applicability to the soluble nitrate case is a wound described by Schofield *et al.*[33] Here the material was plutonium oxalate, and they estimated that, without treatment, about 0.1% of the material in the wound would have been excreted in the 10- to 20-day period and 0.08% in the 20- to 30-day period. For a postulated wound burden of 0.1 μCi of this soluble material, one would expect, therefore, on the order of 20 disintegrations per minute per day excretion in the urine or some 200 to 1000 times the detectable level for most analyses. The later analyses are also significant in that they indicate the lack of a source of relatively insoluble material continually leaching into the blood.

The physical examination by Dr. Roy Albert seems to be significant in several respects. While the details are not given, there is no mention of a wound or other break in the skin through which plutonium could enter. Further, the solution was undoubtedly very acidic to retain the plutonium in solution. Such shipments are usually made in nitric acid. There is no indication given that the medical examination showed any signs of acid reaction with the skin. (Nitric acid can produce a yellow discoloration even when no overt burn occurs.) In a later conclusion, Tamplin indicates that the deposition ".....may have occurred through a small cut or via a sliver." One can only speculate on the size of cut required to introduce the plutonium in a position to irradiate the critical tissue, but it is important to note that the medical examination, which presumably included questioning of Mr. Gleason, did not reveal any indication of such a wound or sliver. (Tamplin presumably is referring to a contaminated sliver of material other than that of the carboy, since there is no indication that it was broken.)

From the above evidence, we can only conclude that the association between cancer and plutonium is speculation. The subject did handle the carboy, but subsequent examinations showed no contamination, and urine and medical history provided no indication of plutonium deposition.

C. The Los Alamos Cases

In referring to the exposures of 25 individuals exposed to plutonium some 30 years ago during the Manhattan Project,[34] Tamplin and Cochran indicated that the exposures were to insoluble plutonium and, hence, of interest. However, they discount this experience on the grounds that 14 of the 25 subjects worked in plutonium recovery operations and were exposed to droplets of plutonyl nitrate: "A droplet 1 u in diameter ($0.5\ u^3$) would therefore contain only 6×10^{-4} pCi compared with a 0.07 pCi particle of PuO_2." However, no justification is given for the assumed drop size, which appears to be very small based on attempts to produce particles by evaporating droplets from a nebulizer. For comparison, fog has a particle size of 5 to 50 μm and mists of 50 to 100 μm. If we assume the particles to be the size of fog particles, then the plutonium content would range from 0.16 to 160 pCi* -- well within the range of the definition of the "hot particle."

A summary of particle size measurements for various operations using plutonium is given in Table II.[35,36]

The aerosol from the Rocky Flats fire was generated by high-temperature condensation of PuO_2 in a manner perhaps not unlike fume formation in the wartime reduction processes. In addition, it is similar to those aerosols measured at the Los Alamos Scientific Laboratory in connection with the operations of fluorination and reduction. The lathe operation is not typical of the wartime operations, and the resuspension aerosol from cleanup is quite different from the others, although this distribution undoubtedly occurred during the wartime exposure. As a best estimate of the aerosol involved in the Los Alamos exposures, we have considered the 0.32-μm mass median diameter (MMD) with a σ_g of 1.83 μm, along with the estimates of deposition in these individuals.

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*For a 1-μm-diameter droplet containing 40 g/liter of ^{239}Pu with a specific activity of 0.0614 Ci/g but still assuming unit density for the solution, we obtain 1.3×10^{-3} pCi.

TABLE II

PARTICLE SIZE MEASUREMENTS FOR PLUTONIUM OPERATIONS

Source	Mass Median Diameter (μm)	Geometrical Standard Deviation, σ_g (μm)	Mass Fraction as "Hot Particles"[a]
Rocky Flats Fire	0.32	1.83	0.15
Fluorination of Nitrate	0.45	1.55	0.23
Reduction to Metal	0.32	1.62	0.10
Lathe Operation	0.26	1.44	0.01
Cleanup	1.90	1.80	0.97

[a]Diameter greater than 0.6 μm.

TABLE III

ESTIMATED "HOT PARTICLE" BURDENS OF LOS ALAMOS WORKERS

Diameter (μm)	Incremental Mass Fraction	Activity (pCi/particle)	Activity (nCi/man)	Particles (per man)
0.6 - 0.7	0.05	0.09	20.0	2.22×10^5
0.7 - 0.8	0.033	0.14	13.2	9.4×10^4
0.8 - 0.9	0.022	0.20	8.8	4.3×10^4
0.9 - 1.0	0.015	0.28	5.9	2.2×10^4
1.0 - 1.2	0.015	0.44	5.9	1.4×10^4
1.2 - 1.4	0.007	0.72	2.8	3.9×10^3
1.4 - 1.8	0.0057	1.34	2.3	1.7×10^3
			Total	4.0×10^5

The number of "hot particles" from an aerosol of this distribution was calculated by numerical integration in given particle size ranges above 0.6 μm. It was further considered that the total of 2.5 μCi of plutonium in these 25 men was 10 μCi at the time of exposure to allow for subsequent elimination. On this basis, the total number of particles in various size ranges is given in Table III.

The process of pulmonary deposition would not significantly distort the deposition in this range since, for more than 90% of the mass range represented, the pulmonary deposition fraction varies only in the ranges of 0.2 to 0.32. Thus, if the lung cancer per particle estimate of 10^{-3} to 10^{-4} given by Geesaman[6] were valid, we would expect some 1000 to 10 000 lung cancers in this group. Exposure has been for 30 years, so that a significant portion of the lifetime has passed with no cancers developing.

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.

D. The Rocky Flats Workers

Tamplin and Cochran discuss the 25 individuals exposed to plutonium during a fire in 1965.[35] They compare the lung burdens in these individuals with the lung burdens in the beagles which developed lung cancer by noting, ".....it is significant to note that in the experiments reported by Park *et al.*, the beagle dog with the smallest lung burden, i.e., 0.2 μCi, developed lung cancer. The highest burden in Table V is comparable to the lowest beagle exposure; the lowest exposure ....., the 19 cases with lung burdens in the 0.24 uCi range, are only an

order of magnitude less than the lowest beagle exposure." The fact that they are, in this case, using microcuries rather than numbers of particles leads to the conclusion that they are referring to radiation dose to the lung, yet they neglect to point out the difference in size between the beagle lung and the human lung -- a factor which would make the human dose about an order of magnitude lower than that of the dog with a comparable burden.

It is of passing interest that the lack of cancer in these Rocky Flats workers is dismissed on the grounds that only 9 years have passed, which is not adequate to produce cancer. We concur in this statement but note that Tamplin argues strongly for the production of a synovial sarcoma, in spite of the lack of evidence of exposure, in a matter of a few years after the incident. (Times are not given in his report, but the accident occurred in 1963 and the report of Dr. Wald, referred to by Tamplin and Cochran, was submitted in 1973, indicating that the cancer was well developed by this time.)

VII. EVIDENCE ON PARTICLE DOSE EFFECTS

As was indicated in an earlier section, those groups charged with providing safe limits for radiation exposure have consistently utilized the average dose to an organ as a basis for the limiting quantity of radioactive material. That is, the dose is calculated as though the energy were uniformly distributed through the organ. In the earliest of these recommendations, the opinion was undoubtedly based upon meager direct evidence plus the knowledge of radiation biology of those involved, and cautions as to the uncertainty of the procedure were appropriate (and still are, since full and complete data will require some years to accumulate). However, as evidence has accumulated, such cautions refer to a much narrower range of uncertainty. It is the purpose of this section of the report to summarize briefly some of the more pertinent information which can be used in assessing the question of particle dose but is not included in the Tamplin-Cochran document.

Two reviews on the question of particle dose have appeared in the past year.[38,39] The first[38] focused on the general question of whether the non-uniform dose distribution in an organ is more or less hazardous than the uniform distribution (i.e., in Tamplin-Cochran's appraisal, is the distribution factor appropriate to the particulate situation greater or less than one?). The conclusion, from the evidence available at that time was ".....that the preponderance of the evidence indicates that the use of an average lung dose is appropriate in limiting exposures and may well be conservative." The second review was a more complete examination of all of the information available on plutonium and other isotopes in the lung, with emphasis on the particle question. The conclusion of this review was similar to that of the first. We will not, here, pursue again all of the evidence but will provide a brief description of some of the pertinent results. While these experiments are selected because of the way in which they illustrate the results, we would also note that neither of the reviews found evidence which indicated the particle dose to be more harmful than the uniform dose.

Little *et al.*[40,41] administered ^{210}Po (an alpha emitter) intratracheally to hamsters both with and without iron oxide. The administration with iron produced agglomerations (effectively particles) of the ^{210}Po on the iron oxide particles, while the administration without iron produced a more uniform distribution as was shown by autoradiographs. Sanders[42] performed experiments with inhalations of both $^{238}PuO_2$ and $^{239}PuO_2$ prepared in the same manner in rats. The $^{238}PuO_2$ behaved in such a manner that it appeared to be more soluble and provided a more homogeneous dose to the lung. Both of these experiments led to the conclusion that the homogeneous distribution is more effective in producing cancer than the particulate distribution (i.e., the DF for the particulate is less than 1). Dolphin[43] quotes Lafuma as reporting ".....greater toxic effects including cancer in rats following deposition of curium-242 in lungs compared with equal amounts of plutonium-239 activity. This he attributes to the diffuse nature of the curium deposit and the particulate nature of the plutonium, as shown by autoradiographs."

In studies with beta emitters in the lung, Cember[44] concluded, ".....the carcinogenicity of a given amount of absorbed radiation energy increases up to a point, as the absorption of the energy is spread out, both time- and space-wise. From a practical point of view, this means that, for a given

total amount of absorbed energy, low-level, continuous exposure of the total lung may be more carcinogenic than the same amount of energy delivered acutely to a restricted volume." Thus, there is evidence that the same effect may be true for beta radiations.

Current experiments at the Los Alamos Scientific Laboratory provide a direct test of the Geesaman theory in that the particles are carried to the lung by the bloodstream and are lodged in immobile positions in the capillaries. Here they are in position to irradiate the surrounding tissue in patterns little, if at all, different from those administered by inhalation or intratracheally. However, they do not agglomerate or move about so that the results can be ascribed to a fixed particle and the dosimetry examined. In the first experiment,[45] particles of $^{238}PuO_2$ of 180-μm diameter were used in rats. Although a lesion similar to the one described by Lushbaugh[7] developed, it did not affect the well-being of the animal, and no cancers developed in 32 animals sacrificed from 120 to 400 days after implantation or in a group of 6 animals allowed to live out their lifetime. It is estimated that the radiation energy from this particle, if averaged over the lung of the latter 6 animals, would have delivered a dose of 2 500 000 rads (or 25 000 000 rems). Such a dose to the full lung would have caused very early death and is many orders of magnitude above that at which increased incidence of cancer is noted.

In an experiment currently in progress,[46,47] uniform-sized microspheres (10-μm-diameter) of ZrO_2 are used with intermixed PuO_2 to provide particles of differing activities, and these are introduced into the lungs of hamsters by the above technique. In the first study in this experiment, 8 groups of 60 animals each were injected with 2000 such particles, with the plutonium content of each particle ranging from 0.07 to 59.4 pCi. Essentially all of animals have now died, with only two lung cancers observed. (Three other cancers in the exposed animals occurred in organs other than the lung.) The dose rates to the lungs of those animals, when calculated as the average dose to the lung, ranged from 13 rads per year (130 rems per year) to 12 000 rads per year (120 000 rems per year). This is a range over which one would expect high tumor incidence and, in fact, premature death from pulmonary inefficiency if the material had been distributed homogeneously. Since the survival curves of the individual groups did not differ from those of the controls and the total tumor incidence was low, one can only conclude that the DF for plutonium in particulate form must be less than one. In the continuation of this study, some 1900 hamsters have received 1.6×10^8 microspheres.[48] As of October 1974, the minimum time of exposure has been 50 weeks,* which is comparable to or longer than the tumor induction times observed by Little *et al.* in their experiments with more uniformly distributed ^{210}Po. In fact, only three lung tumors (including the two observed in the first study) have, as yet, developed from the microsphere exposures. While this study is as yet incomplete, the very low tumor incidence again indicates a low effectiveness of the particles in inducing lung cancers as compared to more homogeneously distributed alpha emitters, as well as the failure of the Geesaman hypothesis to correctly forecast the results of this experiment.

VIII. DISCUSSION

There appear to be few further conclusions which can be drawn. The preceding review has indicated that the Tamplin-Cochran conclusions are based upon a hypothesis which requires considerable extrapolation of the data upon which it is based. Later evidence, of the same nature as was used in the derivation (i.e., rat skin data), does not support the assumptions of the original model. The Tamplin-Cochran interpretation of the model not only fails to take into account the later evidence but appears to present the hypothesis as fact. The supporting evidence on human data which they present are based upon unsupported assumptions and distortions of the words of the authors they quote. Most importantly, they fail to use or acknowledge direct evidence on the effect of radioactive particles. Such evidence indicates that the basic damage model which they use overestimates badly the carcinogenic effects of radioactive particles. We conclude,

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*Reference 48 indicates that ".....by the spring of 1974....." these exposures had been attained. The intent was to indicate progress to the time of preparation of the paper. The administrations were actually completed in September 1973.

therefore, that the application of the average organ dose to the establishment of limits is still appropriate, although experimentation to narrow existing uncertainties on the effects of non-uniform dose distribution should continue.

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C O P Y

September 9, 1974

The Enewetak Council

On September 7, 1974 the Director of Territorial Affairs, Mr. Stanley S. Carpenter, announced that in answer to a longstanding request from the people of Enewetak, fifty (50) people would be permitted to return to live on Japtan at the earliest possible time, subject to certain restrictions. The restrictions are designed for your safety and will apply until you are notified that they have been altered.

We ask that the following restrictions be duly noted and accepted by the Council in that your assurances in this regard will comply with one of the criteria which can help insure an early return:

(1) No visits are permitted on the northern islands from Runit to Biken.

(2) Scrap collection and stockpiling can be undertaken only with approval of the District Administrator's Representative.

(3) Visits to Enewetak Island must be coordinated between the District Administrator's Representative and the site manager of Enewetak Base.

(4) Visits to other southern islands may not be made without the specific prior approval of the District Administrator's Representative and, then, only in accordance with his instructions.

We appreciate your early consideration of the above and are hopeful that we can have some written expression from your Council that these restrictions are understood and will be fully observed.

(Signed) Peter T. Coleman
Deputy High Commissioner
Trust Territory of the Pacific Islands

(Signed) Harry U. Brown
Office of Territorial Affairs
Department of the Interior

(Signed) M. R. Biles
U.S. AEC
Atomic Energy Commission

COPY

ORDINANCE

of the

COUNCIL OF ENEWETAK

WHEREAS Mr. Stanley Carpenter, Director, Office of Territorial Affairs, Department of Interior, informed the Council of Enewetak that their long-standing request to establish a settlement of fifty (50) persons on Japtan Island, Enewetak Atoll, will be permitted, and

WHEREAS the conditions existing on Enewetak Atoll require that certain safety precautions be taken with respect to the movements and activities of the members of the settlement and the Trust Territory of the Pacific Islands, the Department of Interior and the Atomic Energy Commission have suggested certain precautions and limitations in a memorandum to the Council on September 9, 1974, and

WHEREAS the Council is in full agreement with those precautions and limitations,

NOW THEREFORE THE FOLLOWING ORDINANCE IS ADOPTED:

Section 1. This ordinance shall apply to all persons residing or visiting on Japtan Island, Enewetak Atoll, in connection with the temporary settlement there.

Section 2. No person shall visit or enter into that area in the northern and western part of Enewetak Atoll bounded by Runit Island in the east and Biken Island in the west and including all the intervening beach, island and reef areas.

Section 3. No person shall collect or stockpile scrap from any island in the Atoll, except with the prior approval of the District Administrator's Representative for Enewetak.

Section 4. No person shall visit Enewetak Island without coordinating that visit with the District Administrator's Representative (who shall coordinate all visits with the site manager of Enewetak Base).

COPY

Section 5. No person shall visit the island of Kidrenen, Robewon, Boken, Mut or Ikwren without first obtaining specific approval from the District Administrator's Representative and any such approved visit shall only be made in accordance with his instructions.

Section 6 This ordinance shall be enforceable by the District Administration and violation thereof shall be punishable by a fine of One Hundred Dollars ($100.00) and the Council pledges its full assistance in enforcement.

Section 7. This ordinance shall remain in full force and effect until notification is received from the District Administrator that these precautions and limitations are no longer needed.

CERTIFICATION

I, John Abraham, hereby certify that the foregoing ordinance was considered by the Council of Enewetak Atoll, assembled at Enewetak Atoll, on the 9th day of September, 1974, at which a quorum was present and duly enacted by unanimous vote.

(Signed) John Abraham

JOHN ABRAHAM
Magistrate

(Signed) Sam Livai

SAM LIVAI,
Scribe

Approved this 11th day of September, 1974.

(Signed) Oscar DeBrum

OSCAR DeBRUM
District Administrator
Marshall Islands District
Trust Territory of the
Pacific Islands

COPY

AGREEMENT BETWEEN THE DEFENSE NUCLEAR AGENCY AND THE DEPARTMENT OF THE INTERIOR TO PROVIDE FOR DRI-ENEWETAK SETTLEMENT AT JAPTAN ISLAND, ENEWETAK ATOLL, M.I.

This Agreement made this third day of January, 1975, by and between the Defense Nuclear Agency, hereinafter referred to as "DNA", as project manager for the Department of Defense, and the Department of the Interior, acting through the Office of Territorial Affairs, hereinafter referred to as "DOI".

WHEREAS, the dri-Enewetak desire that an advance party not to exceed fifty (50) people be permitted to return to Japtan Island, Enewetak Atoll, M.I.; and

WHEREAS, DOI announced to the dri-Enewetak on 7 September, 1974 that such an advance party could return to Japtan Island; provided however, no return could take place prior to execution of an agreement between the United States of America and the Government of the Trust Territory of the Pacific Island (TTPI) transferring Enewetak Atoll back to TTPI;

NOW THEREFORE, the parties agree as follows:

1. A group of dri-Enewetak, not to exceed fifty (50) in number, may return to Japtan Island as soon as reasonably practicable after execution of an agreement between the United States of America and TTPI transferring Enewetak Atoll to TTPI.

2. It is expressly understood that the islands of Enewetak Atoll, because of the presence of radioactive contamination, deteriorated physical structures and debris, pose a potential hazard to the health and safety of the dri-Enewetak; further, the support capabilities of DNA on the

Atoll are limited. Accordingly, the dri-Enewetak will reside only on Japtan Island and will not visit the radioactively contaminated northern islands; further, the dri-Enewetak will not go to other islands for the purpose of gathering materials or scrap and generally they will in no way hinder DNA operations on the Atoll. Movement other than as herein specified will be in accordance with agreements between TTPI and Field Command, Defense Nuclear Agency (FC DNA).

3. DOI is responsible for providing or assuring the provision of all necessary subsistence and support for the dri-Enewetak at Japtan Island.

4. DOI is responsible for assuring compliance on the part of the dri-Enewetak with all restrictions and regulations now or hereafter adopted by DNA, and generally for the administration of civil and criminal law among the dri-Enewetak. In furtherance of this requirement, DOI will assure that a resident representative of TTPI is assigned to live on Enewetak Atoll.

5. DNA will provide, on a reimbursable basis, emergency support and assistance to the dri-Enewetak, as and if available. The determination of what constitutes an emergency support requirement and of the availability of such support will be made by DNA.

6. This Agreement will be implemented by TTPI as representative of DOI and FC DNA as representative of DNA.

COPY

IN WITNESS WHEREOF, the parties hereto have executed the Agreement as of the day and year first above written.

DEFENSE NUCLEAR AGENCY

By: (Signed) Warren D. Johnson

WARREN D. JOHNSON
Lieutenant General, USAF
Director

DEPARTMENT OF THE INTERIOR

By: (Signed) Stanley S. Carpenter

STANLEY S. CARPENTER
Director, Office of
Territorial Affairs

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UNITED STATES
ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION
WASHINGTON, D.C. 20545

February 6, 1975

Lt. Gen. Warren D. Johnson, USAF
Director, Defense Nuclear Agency
Washington, D.C. 20305

Dear General Johnson:

Your letter of January 8, 1975, to Major General Ernest Graves has been forwarded to us for reply. It is the view of ERDA staff that the U.S. Environmental Protection Agency (EPA) comments on the Enewetak Draft Environmental Impact Statement reflect a considerable degree of insight into the important issues of this complex task and are in fact a very favorable response.

Speaking to those items related to radiological aspects in the EPA analysis of proposed actions, we believe there are adequate answers to all of the questions posed and concerns expressed. Several of the EPA concerns are covered by actions taken or planned since the DEIS was drafted.

ERDA staff response to EPA questions and concerns is contained in a report entitled "Staff Review of EPA Comments on the DEIS for Cleanup, Rehabilitation, Resettlement of Enewetak Atoll." This deals with the radiological aspects of the EPA analysis. A copy of the report is enclosed for your use.

Our response to the EPA comments is, of course, predicated on the assumption that ERDA will provide support for those activities planned and initiated by AEC. If additional discussions are needed to assist you with comments on the DEIS, we would be glad to help.

Sincerely,

Martin B. Biles, Director
Division of Operational Safety

Enclosure:
As stated

February 4, 1975

STAFF REVIEW OF EPA COMMENTS ON THE DEIS FOR CLEANUP, REHABILITATION, RESETTLEMENT OF ENEWETAK ATOLL

In their comments, EPA expressed reservations regarding the environmental impact of actions proposed in the DEIS and stated that more information was needed in certain areas to fully assess this impact. EPA comments noted that radiation protection criteria and cleanup criteria recommended by AEC had been previously accepted as upper limits with the additional qualification that population doses be maintained as low as practicable.

The following comments are provided for those specific items of EPA concern under the general heading, Radiological Aspects:

1. Current Sampling Needs

Regarding brackish water lenses on islands to be inhabitated, the Enewetak Atoll Master Plan indicates that rainwater is to be used for drinking water. Vol. II, Section D, page 4-26 of the DEIS indicates that rainwater from the roofs of houses will drain into a 3,780 gallon cistern. A supplemental 3,200 gallon cistern will be provided with each house to guarantee an adequate water supply. A common well will serve each cluster of houses. Plans are to use well water for washing clothes and dishes and for bathing.

AEC Task Group recommendations number 2h and 10, Vol. II, Section B, pages 25 and 29, of the DEIS state that wells for human use should be drilled only on the southern islands and that an underground lens water sampling and analysis program should be conducted with samples taken over a period of at least 12 calendar months.

ERDA staff have recognized need for additional information on lens water quality at Enewetak Atoll, but believe that this is not grounds for delaying cleanup and resettlement. Soon after publication of NVO-140, a ground water sampling program was initiated by ERDA through the Division of Biomedical and Environmental Research and the Nevada Operations Office, on 7 of the larger islands of Enewetak Atoll. This program, designed and conducted

jointly by Lawrence Livermore Laboratory and the University of Hawaii, utilizes a total of 15 drilled wells, 11 of which are 40 feet deep and 4 of which are 200 feet deep. Objectives include determination of radionuclide and stable element concentrations, cycling mechanisms, bacteriological content, recharging rates, etc.

In addition, ERDA is initiating on Enjebi (JANET) an experimental agricultural program to evaluate, among other things, the significance of ground water contaminanats (radionuclides) to the potential internal dose to man in the Enjebi environment. It is anticipated that these programs, which are being continued for an indefinite period, will provide a good understanding of the ground water systems on all islands which are planned as residential islands before actual resettlement occurs.

The primary question to be answered by the lens water study is the use that can be made of underground lens water by people when they return.

For the 50 people who are to return to Japtan Island prior to cleanup of the atoll, additional water catchment tanks are to be provided on Japtan for storage of rainwater for drinking and cooking. It is understood that additional details on the early return to Japtan Island are to be presented in a report entitled "Early Return Program Operational Plan," that is to be made a part of the EIS.

Regarding sampling for airborne radioactivity, ERDA staff hold the position that sampling actual conditions is the ideal approach for determining the radioactivity content of ground level air on the various islands in the atoll. However, this can be done only after the islands are inhabitated. An important consideration is that some of the activities of the residents themselves will produce dust. The next best approach would be to sample levels of radioactivity in air during cleanup operations. This prompted recommendation number 11 by the AEC Task Group in Vol. II, Section B, page 30, of the DEIS. This recommendation states that a comprehensive air sampling program should be conducted over a period of 12 consecutive months coincident with and in support of cleanup operations. Such sampling should be performed by those providing health physics support for cleanup operations under direction of the agency having responsibility for cleanup as contained in Task Group recommendation 7a, page 27, and 15, page 31. The results of this air sampling

effort should be documented in a comprehensive final report from the cleanup agency. See Task Group recommendation number 14, page 31. These samples would be analyzed for all radionuclides that could be found, including uranium.

2. Future Sampling

The need for base-line surveys of radionuclide body burdens in the Enewetak people prior to return and subsequent to return, as a check on their status and to assure that exposure criteria are not being approached or exceeded, is established in Task Group recommendation 12, page 30. The responsibility for long-term radiological monitoring of the people and environments rests with ERDA. See part 1.4, page 1-4, Vol. I of the DEIS. Two divisions within ERDA carry out this responsibility, namely, Division of Biomedical and Environmental Research for followup of the people, and Division of Operational Safety for followup of the environment. The current followup being provided for Bikini Atoll people by the Brookhaven National Laboratory and the University of Washington with assistance from the Lawrence Livermore Laboratory, acting as contractors for ERDA, will be expanded to cover the Enewetak people and their environment when they return to their homes. The responsibility for funding these efforts currently rests with ERDA.

Considering that cleanup and rehabilitation of Enewetak Atoll is a U. S. Government action, we suggest the following specific wording to describe the responsibilities of the major agencies:

"The agreed division of DOD, DOI, and ERDA (AEC) responsibilities for the proposed cleanup, rehabilitation, and resettlement of Enewetak Atoll has evolved over the past several years as a result of various memoranda, interagency meetings, and other discussions and documentation. The governmental agency responsibilities essentially have been and are:

Energy Research and Development Administration (Atomic Energy Commission)	--- conduct a radiological survey prior to cleanup and rehabilitation; prepare judgements and recommendations on radiological cleanup and provide them to DOD and DOI; conduct future periodic followup radiological surveys as necessary; and maintain periodic monitoring

	of the health status of the resettled people and of the radioactivity in the environment subsequent to rehabilitation.
Department of Defense ----------	conduct an engineering survey prior to cleanup; maintain facilities from which to base surveys, cleanup, and rehabilitation; develop an environmental impact statement; and perform cleanup operations including debris disposal and radiological control during such operations.
Department of the Interior ----------	rehabilitate the atoll (e.g., planting of crops, housing, construction, etc.) to permit the people to be as self-sufficient as possible."

3. Recommended Cleanup and Disposal Plan

The AEC Task Group objectives in making recommendations for cleanup of plutonium in soil was first to assure that a group of qualified experts would be assembled to carry out the recommendations, and second, to provide cleanup criteria specific enough to assist these experts in making good day-to-day decisions on cleanup of islands and at the same time not so specific that there can be no room for flexibility in application to account for conditions yet to be discovered or encountered during actual operations.

General guidance on cleanup of plutonium is presented in Task Group recommendations 6, 7, and 8, pages 27 through 29, in Vol. II, section B, of the DEIS. Objectives and justification are given for removal of contaminated soil. More detailed guidance is given in Appendix III of Section B, on how the 40 pCi/gm and 400 pCi/gm are to be applied.

The Task Group objective was to recommend an approach to application of numerical cleanup criteria that would achieve the greatest dose reduction for the effort and dollars expended. The 400 pCi/gm guide was viewed as an upper limit of contamination with removal of such soil required at or above this value on any island where it may be found and at any depth below the surface of islands. The

40 pCi/gm guide was viewed as a lower limit below which corrective actions would not be required because of the presence of plutonium alone. Guidance for cleanup of contaminated soil in the range between 400 and 40pCi/gm is presented on page III-9 of section B. This guidance states that removal of contaminated soil is better justified for the larger islands that may someday contain permanent housing than for small islands. The guidance specifies that once the decision is made to take action, the objective is a substantial reduction in plutonium soil concentrations with reduction to the lowest practicable level, not just reduction to some prescribed numerical value.

ERDA staff believe that the Task Group recommendations and associated material are specific enough to guide the actions and decisions of a qualified group who are assembled to carry out cleanup actions at Enewetak Atoll.

The next subject for EPA concern, paragraph 2 on page 2, regarding disposal of contaminated soil, should be better considered by DNA staff and will not be addressed in this review.

4. Recommended Rehabilitation and Resettlement Plan

The radiological implications of use of the northeastern islands for subsistence and commercial production of coconuts were not overlooked in development of input material for the DEIS. The practical means for avoiding exposures at Enewetak Atoll range all the way from recommending against any return of people to the atoll to other severe actions such as restricting use of any local foods and importing all food. Justification for recommended actions is contained in the AEC Task Group report presented as section B of Vol. II of the DEIS. The purpose in recommending use of the northeast islands for raising coconut was to provide the people as much land as possible for production of copra, their primary cash crop, not to provide an adequate supply of coconut for food. Coconut grown in the southern islands will be more than adequate for food. However, it was recognized that anywhere coconuts are grown in the atoll, whether for food or copra production, there will be some use as food. Use of the northeastern islands for growing coconuts increases the land area for this crop from about 830 acres to about 1,200 acres. An increase of 50% in agricultural land is a significant factor especially where useable land is limited. See table 3-1, Vol. II, section D, of the DEIS for the areas of various islands.

As for the additional radiation exposure that would be received by allowing people living on the southern islands to eat coconut from the northeast islands (KATE through WILMA), a review of predicted

doses does not support the EPA comment that virtually all of the predicted dose received by the Enewetakese under the proposed plan is due to this decision. To examine this one must compare the predicted doses for whole body, bone, and bone marrow given in the Task Group Report and make a judgement on conditions that are most likely to occur. Thirty-year doses may be compared using Living Patterns A and B, Tables 1, 2, 3, and 4, Vol. 2, Section B of the DEIS.

In Table 1, page 32, Living Pattern B, importing pandanus and breadfruit reduced the 30-year whole body dose from 4.4 to 2.2 Rem, a reduction of 2.2 Rem. Importing coconut and tacca further reduces the dose from 2.2 to 1.9 Rem, a reduction of 0.3 Rem. Importing meat makes a reduction from 1.9 to 1.3 Rem, a reduction of 0.6 Rem. Placing restrictions on use of islands KATE through WILMA for production of pandanus, breadfruit, and meat gives the greatest benefit in reducing dose. Adding coconut from KATE through WILMA (tacca makes a small contribution by comparison) to the diet of people living on and taking their food from southern islands will increase their 30-year whole body dose from 1.0 to 1.3 Rem. (See Living Pattern A, Table 1, page 32.) The comparable 30-year mineral bone dose will increase from 3.8 to 6.2 Rem. (See Table 2, page 33.)

Dose comparisons for maximum annual dose for whole body and bone marrow can be made using Appendix IV of the Task Group Report in Section B, Tables 3, 4, 5, 8, 9, and 10*. Taking the KATE through WILMA coconut and tacca out of the diet reduces the annual bone marrow dose from 0.200 to 0.092 Rem. (See Tables 3, 4, and 5, pages IV-15 and 16.) Most of this reduction is due to coconut. Putting this coconut into the diet of those living on southern islands would increase the annual bone marrow dose from 0.047 to 0.155 Rem. The comparable increase in annual whole body dose is from 0.039 to 0.107. (See Tables 8, 9, and 10, pages IV-18 and 19.)

In making these comparisons, there is a very important factor to consider, namely, these are the increases in dose that are predicted assuming that all of the coconut eaten by those living on southern islands comes from KATE through WILMA. In fact, coconut used as food on southern islands will be a mixture with much coming from the village islands. Doses somewhere between Living Patterns A and B and between Patterns 1 and 2 are expected.

*Values for January 1974 or January 1984 used depending on which time gave the highest dose.

Use of the northeast islands for coconut production increases the amount of available land, compared to the area of southern islands, by 50 percent. This means that the quantity of copra produced could roughly increase a similar amount as would the cash income from this crop. This is an important benefit. The additional exposure that will come from use of these coconuts as a part of the coconut in the diet is expected to be very low and well within the recommended radiation criteria.

Application of the "as low as practicable" concept in an effort to determine marketability of copra from Enewetak would not guarantee that the product would be acceptable to those outside the atoll. The AEC Task Group addressed this question and decided it could not determine what level of radioactivity in copra would unquestionably be found acceptable. Detectable quantities of radionuclides from atmospheric tests of nuclear explosives will be found in copra from Enewetak Atoll and in copra from other atolls as well. The recommendations for rehabilitation of Enewetak make about 1,200 acres available for copra production. When handled through normal channels, this copra will be added to that produced from approximately 76,000 acres represented by the total production in the U. S. Trust Territories.

In terms of annual production, it is quite uncertain what the total production of copra under the recommended restrictions might be. The total land area of the atoll is about 1,800 acres of which roughly 1,200 or about 65 percent is being returned and could be available for growing coconuts. The actual amount will be less than this, considering the areas that are to be devoted to housing, the runway, and other uses. Part D, Vol. II of the DEIS, page 4-51, presents estimates of the annual copra production for Enewetak considering the uncertainty of yield of nuts per tree. Using the yield point of an average of 50 nuts per tree, the entire atoll production may be as much as 500 tons/yr. If only 65 percent of the atoll is returned, this would be reduced to 325 tons/yr. The annual income could be 0.65 X $40,000 or $26,000/yr at the current price of copra. About 1/3 of this would come from copra produced in the northeast islands.

As to the amount of ^{90}Sr and ^{137}Cs that would be in copra from Enewetak, page 583, NVO-140, indicates that the average concentrations of ^{90}Sr and ^{137}Cs in dried coconut meat samples (considered for this comparison to be the same as copra) are as follows:

	Concentration pCi/g	
	^{90}Sr	^{137}Cs
KATE-WILMA	0.347	6.19
ALVIN-KEITH	0.034	0.687

If the ALVIN-KEITH production is twice the KATE-WILMA value, the average concentration of ^{90}Sr and ^{137}Cs in Enewetak Atoll copra would be:

Average Concentration - pCi/kg	
^{90}Sr	^{137}Cs
138	2,781

The important factors in copra production and processing may be stated briefly. In the Marshall Islands, coconuts which take about a year to mature are harvested and the meat extracted from the shell and husk. Pieces of coconut are sun dried (or dried in ovens) and stored under cover until picked up by a copra boat that visits each island or atoll several times a year. Fresh coconut meat is about 50 percent water, 30-40 percent oil, and 10-20 percent copra meal by weight. The copra consists of the fraction that is oil and meal.

For processing, copra is washed and run through a press which extracts the oil leaving a residue which is copra meal. The oil which is used in foods and cosmetics, has a very low mineral content and very low levels of radioactivity. The radioactivity ends up in the copra meal which contains about 20 percent protein and 5 percent oil. The meal is a good quality animal feed and may be used for dairy cows.

As for considering the acceptability of Enewetak copra as an item of export from the atoll, the Bureau of Radiological Health, Food and Drug Administration (FDA) has recently published radionuclide concentrations for use as guides applicable to foods. (See Radiation Data and Reports, Vol. 15, No. 10, October 1974.) Using an assumed average food consumption rate of 1.71 kg/day and the Federal Radiation Council Radiation Protection Guides (RPG's), the following guidance was derived:

	Range I (pCi/kg)	Range II (pCi/kg)	Range III (pCi/kg)
^{137}Cs	0-360	360-3,600	3,600-360,000
^{90}Sr	0-20	20-200	200-2,000
Types of Action recommended:	Periodic confirmatory surveillance	Quantitative surveillance - routine control	Evaluation and additional controls as necessary

FDA uses these guides to evaluate radioactivity in certain indicator foods imported into the U.S. Analysis of samples of imported foods collected in the U.S. in 1973 gave the following results:

RADIONUCLIDE CONTENT OF IMPORTED FOODS

	^{137}Cs	^{90}Sr
Fish	26-232	0.8-5.4
Cheese	ND*	5.2-101.7
Coffee	ND*-189	9.18-37.8
Tea	135-436	14.2-593
Cocoa	ND*-163	36.7-94
Cashew nuts	28-189	1.59-25.2

All of the imported items except fish had some samples with radioactivity levels into Range II of the FDA guides for ^{90}Sr. Tea showed samples into Range II for both ^{90}Sr and ^{137}Cs. The estimates of average concentrations for Enewetak copra fall into Range II for ^{90}Sr and ^{137}Cs which, according to the FDA criteria as used with U.S. imports, would require that levels of radioactivity be measured in a quantitative way with routine control. Levels falling into Range III would require an evaluation as recommended by EPA.

*ND-Not detectable.

Regarding the question of permitting fishing in all of the lagoon, seafood at Enewetak Atoll is among the lowest of all contributors to radiation dose to people living in the atoll. The doses to people, both annual and for longer times out to 70 years, are presented in the DEIS. The dose estimates include contribution from both plutonium and strontium coming through the seafood pathway and thus are directly related to the radioactivity in the lagoon bottom sediments. The AEC Task Group did not feel that it would be productive to try to do a detailed evaluation of all possible combinations of remedial actions and restrictions. The Group directed its efforts toward what was considered a reasonable number of options for exposure reduction and control that presented actions against the primary pathways for radionuclides giving the most dose to man. These actions ranged all the way from recommending no return to the atoll, which would have a severe impact on the people, to complex and costly actions requiring removal and replacement of contaminated soil. ERDA staff believe that if there are actions or restrictions that will minimize exposures other than those recommended, the amount of dose saved would be very small.

Regarding the ban on coconut crabs and actually sampling crabs in the northern islands, an effort was made to sample coconut crabs throughout the atoll. Samples were found only on the islands of BRUCE, GLENN, JAMES, KEITH, and LEROY. See page 543, NVO-140. Coconut crabs could be found only on these southern islands.

Regarding health physics support for cleanup, this is covered in Task Group recommendation 7a, page 27, Part B, Vol. II, of the DEIS.

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UNITED STATES
ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION
WASHINGTON, D.C. 20545

April 4, 1975

Major General W. E. Shedd, USA
Deputy Director for Operations
and Administration
Defense Nuclear Agency
Washington, D. C. 20305

Dear General Shedd:

In response to your request of February 28, 1975, enclosed herewith is ERDA's detailed response to the comments of the People of Enewetak concerning the Draft Environmental Impact Statement for the Cleanup, Rehabilitation and Resettlement of Enewetak - Marshall Islands. I understand that Dr. Bruce Wachholz, of my staff, and Mr. Earl Eagles, of your staff, have been in regular communication regarding this effort.

We do not feel that impact statements are the proper forum in which to conduct the resolution of scientific issues. We believe that the National Environmental Policy Act (NEPA) requires that judgments be made on the basis of the best scientific information available. The basis of that information is generally the scientific literature. The issues raised by Mr. Mitchell via his appendices have never been published in scientific journals or presented at scientific meetings. While NEPA requires consideration of responsible opposing points of view, we do not believe that it requires that every proposed theory be addressed via impact statements, nor that they should become vehicles for the dissemination of opinion outside of the scientific peer review processes.

Nevertheless, we have provided comments addressing the issues raised by Mr. Mitchell and by Drs. Martell, Geesaman and Tamplin. Responses to the latter two have previously been published and you might prefer to reference them rather than include them in your Final Statement. The response to Dr. Martell previously has not been published since his theory as described in Appendix II has been available for only a short period of time. You will note that this response is an extremely detailed analysis of Dr. Martell's theory. Even though we do not feel

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that an impact statement is the proper forum for discussion of these issues, we have provided this detail since Mr. Mitchell has on several occasions requested, both verbally and in writing, a full and detailed reply to Dr. Martell. If this response to Dr. Martell is used, we strongly urge you to include it in its entirety; if this response to Dr. Martell is not used we would appreciate its return. However, we feel that it would be detrimental and perhaps lead to erroneous conclusions if it were edited or fragmented.

Our response to Mr. Mitchell's letter is provided for your use as you think appropriate.

We appreciate the opportunity to be of assistance to you and hope that our responses will be helpful in resolving the issues and in allowing the cleanup of the Atoll to proceed.

Sincerely,

James L. Liverman

James L. Liverman
Assistant Administrator
for Environment and Safety

Comments on the Submission of the
People of Enewetak Concerning the Draft Environmental
Impact Statement for the Cleanup, Rehabilitation
and Resettlement of Enewetak - Marshall Islands

Page 1, lines 12-23 - "It is difficult enough for the layman to comprehend what the experts in the various radiological science fields are saying about the effects of radioactivity, but that difficulty is compounded many times over the differences of opinion found among the experts, by the realization that even the experts agree that the long term effects of some of the more dangerous radionuclides are not known by anyone at this time and may not become known for many years to come, and it is unsettling to learn that the standards used for the kinds and amounts of radionuclides to be tolerated in the environment and in man are criticized by reputable experts as unreliable and inadequately conservative."

Comments: While Drs. Martell, Geesaman, Tamplin and Cochran have expressed strong opinions regarding plutonium, they are not recognized as experts in plutonium by the national and international scientific community. Assessment of the hazards of radioactivity and the recommendation of standards are methodically and continually reviewed by persons most knowledgeable and experienced in evaluating the available relevant data. This is true both for national bodies such as the National Council on Radiation Protection and Measurements (NCRP) and the National Academy of Sciences (NAS), and for international bodies such as the International Commission on Radiological Protection (ICRP) and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). None of the "experts" referred to have been or are members of any of these bodies, nor have their theories, as described in the author's* submission, been presented through the normal channels of scientific communication. In contrast, those individuals in this country and abroad who are recognized as experts

*"Author" herein refers to Mr. Mitchell.

because of their published research on plutonium and their analyses of the hazards of plutonium have regularly been members of or advisors to such bodies. These bodies have consistently adopted a conservative philosophy regarding recommendations. Reputable scientists consistently have taken a conservative, scientific and unemotional approach to matters of radiation protection. Since these recommendations and resulting standards are inherently conservative, the term "inadequately conservative" becomes a relative one which essentially questions "How conservative is conservative?". One can be conservative to the point where standards are meaningless.

Page 2, lines 12-15 - "And it is in the assessment and, if possible, elimination of the radiobiological health risk that they are the most dependent upon the United States government."

Comments: Based upon the hypothesis of a linear relation ship between exposure and effect, the total elimination of any radiobiological health risk at Enewetak is an unrealistic objective which cannot be attained. Some exposure and therefore the possibility of some risk must be accepted if the people are to return. This risk, however, is expected to be very small.

Page 2, lines 15-19 - "The Defense Nuclear Agency and the Atomic Energy Commission have already devoted great amounts of time and money to assessment and remedy of radiological problems presented by this program, but more will have to be done and it will have to be done over a long period of time."

Comments: The author is aware that the Energy Research and Development Administration (ERDA) anticipates continued selected radiological monitoring of both the Enewetak environment and the people; it

is planned to fund these and other related programs in excess of $2 million during fiscal year 1976.

Page 3, lines 11-14 - "It is an absolute kind of responsibility to both return the people to their home and eliminate the likelihood of so much as a single radiation induced illness or anomaly."

Comments: This objective, while commendable, can never be assured. While no absolute assurance can be given, the predicted exposure levels are considerably below those in which populations have lived for centuries. No radiation induced illness or anomaly is expected at the predicted levels. As the author indicated, the effects of extremely low level radiation exposures over a long period of time are not known; it is doubtful that they will ever be known with any degree of accuracy. If the return of the people is deferred until all is known with the assurance requested, it may be some time before relocation can be affected.

Page 6, line 14 to Page 7, line 11 - "The survey of radiological conditions at Enewetak Atoll in 1972 under the auspices of the Atomic Energy Commission is, we believe exceptionally good as far as it goes, but we have been advised by capable experts in the field that more work remains to be done and that the qualifications of the four-member Task Group which supervised the conduct of the survey, the assessment of its data and developed final recommendations are open to question. It is also apparent that as detailed and elaborate as that survey was, follow-up

gathering of data and careful assessment of that data is absolutely essential, particularly with respect to the risk to health from all low-level, long-life radionuclides and especially the danger posed by those alpha-emitting radionuclides known as hot particles, such as Plutonium-239 and Americium-241.

"We do not wish to detract from the qualification of the members of the Task Group, but in a field involving so many specialties and where equally expert opinions differ markedly, it is imperative that the Task Group for follow-up studies be enlarged to include scientists known to take the most conservative approach to radiation protection, such as Drs. E. A. Martell at the National Center for Atmospheric Research, Arthur R. Tamplin at Lawrence Livermore Laboratory, and Donald P. Geesaman, at the University of Minnesota. Their presence in the Task Group, or their participation in some other direct way in designing methods to be used for the gathering of information and its evaluation is strongly recommended."

Comments: The "AEC Task Group on Recommendations for Clean-up and Rehabilitation of Enewetak Atoll" was established by the AEC General Manager and requested to prepare recommended criteria and guidance for clean-up and rehabilitation of Enewetak Atoll for consideration by the Commission. The thirteen-man Task Group consisted of four units: Drafting Group (4), Headquarters Liaison (2), Interagency Liaison (3), and Advisors (4). Comments and recommendations on draft reports were obtained from the Environmental Protection Agency (EPA), Health, Education and Welfare (HEW), and several of the National Laboratories and University contractors. Thus, the ERDA recommendations rest not only on the qualifications of the four-man Drafting Group, but on the broader base of expertise available to ERDA from numerous sources. In addition, the "four-member Task Group" did not supervise the conduct of the environmental survey at Enewetak Atoll. The survey was conducted by research scientists from Lawrence Livermore Laboratory, University of Washington and the University of Hawaii.

While the Task Group made recommendations regarding clean-up and rehabilitation of the Atoll and for later follow-up studies and surveys that were approved by the Commission, the Task Group's responsibilities ended with the approval of their recommendations. Therefore, it is irrelevant to consider enlarging the Task Group. In addition, any new task group would have no additional results to evaluate at this time, or for perhaps years to come. It should also be noted that the recommendations of the Task Group are lower, and therefore more conservative, than the maximum exposure limits recommended by national and international bodies.

Plutonium-239 and Americium-241 are not known as "hot particles", but are two of many radioisotopes which can be aggregated under certain conditions to form such particles. "Hot particle" is a term defined by some (Natural Resources Defense Council) as a particle with a minimum of 0.07 pCi of long half-lived alpha-emitting radioisotopes, and which is insoluble in lung tissue.

Whether or not the author's advisors are "capable experts in the field," "equally expert," etc. is the author's opinion. Thus far they have not received support from the scientific community at large. Furthermore, the participation of those with extremely conservative philosophies may lead to decisions based on no effective standards. Resolution of scientific issues and differing philosophies should be conducted through normal scientific channels rather than on a day-to-day basis at Enewetak.

Page 7, lines 12-16 - "The 1972 radiological survey (NVO-140) must be regarded as an impressive beginning of long-range radiological assessment and monitoring of the Enewetak environment with appropriate emphasis placed upon not only the marine and terrestrial environments but upon the radionuclide pathways to man."

Comments: NVO-140 is the most comprehensive radiological assessment and monitoring ever carried out on a marine and terrestrial environment. The results of the Enewetak Radiological Survey, except for minor areas identified in the ERDA Task Group Report (sampling of water lenses and air over longer periods of time), were found to be an exceptionally complete data base for the purpose of evaluating conditions and for making decisions on clean-up and rehabilitation. Twelve month studies of lens water and air sampling are already in progress. No additional radiological studies other than those identified in this document are warrented or planned prior to the start of clean-up operations.

It should also be noted that the Survey not only considered but focused on radionuclide pathways to man. Various diets and quantities of ingested foods were considered in deriving potential radiation exposure via these routes; exposure via inhalation was also estimated.

Page 6, lines 16-18 - "As we shall discuss more fully below, more information is needed about the presence of hot particles."

Comments: The evidence to date does not support the position taken by those who advocate the hypotheses regarding hot particles. (See comments on NRDC, Dr. Geesaman and Dr. Martell.)

Page 7, lines 18-20 - "The long range effects of Strontium-90 and Cesium-137 and other nuclides in the food web cannot be known without experimental planting."

Comments: Conservative estimates can and have been made on the basis of a considerable body of information available. We agree, however, that the full significance of strontium-90, cesium-137 and other nuclides in the specific food web at Enewetak cannot be precisely evaluated without experimental planting. For this reason ERDA has already funded and initiated a research effort to study the uptake of various radionuclides in seedlings and plantings on the island of Enjebi where conservative assumptions indicate that recommended levels of exposure might be exceeded, thereby preventing the immediate return of the people to the island. Although applicable to general considerations, this effort is principally directed at the specific question of if and when the Enjebi people might be permitted to return to that island.

Page 7, lines 21-26 - "And as time goes on, scientific knowledge of the nature and effect of radioactivity is bound to improve and new techniques for remedial measures will be found. These scientific advancements will be lost to the Enewetak people unless the United States government assumes a long-range commitment of the kind we suggest here."

Comments: Anticipation of the development for startlingly new remedial measures to counteract the effects of radiation does not appear realistic in this situation since those techniques which are available have limited usefulness for specific situations, and at the extremely low levels of exposure considered here there is no way of determining the effectiveness of any such technique, nor is any need for same anticipated for this population. Historically, the U. S. Government has had a long-term commitment to the welfare of the Marshallese people. This concern is expected to continue.

Pages 8-11 - The Hot Particle Problem - The comments of NRDC, Geesaman and Martell are addressed separately following their respective comments.

Page 8, lines 12-17 - "For a discussion of the seriousness the hot particles problem we attach as Appendix II, E. A. Martell, "Basic Considerations in the Assessment of the Cancer Risks and Standards for Internal Alpha Emitters," (Statement presented at the public hearings on plutonium standards sponsored by the United States Environmental Protection Agency, Denver, Colorado, January 10, 1975)."

Comments: Dr. Martell's conclusions are reached independent of those who advocate the "hot particle" hypothesis. Although he reaches the conclusion that standards should be reduced, the logic by which he justifies his position cannot be considered as evidence for the "hot particle" argument as advanced by Drs. Geesaman, Tamplin and Cochran (see Martell's comments, page 8). The hot particle as previously defined is not synonymous with the hot particle as used by Martell.

Page 8, lines 25-27 - "It is highly likely that inhalation of very small amounts of plutonium gives rise to a high risk of lung cancer."

Comments: There is no question that inhalation of relatively large quantities of plutonium will lead to lung cancer. It is not clear what is meant by "very small amounts."

Page 8, line 27 to Page 9, line 2 - "And the DEIS completely fails to address the recent findings of Martell and others that hot particles may very well be a causative factor in a number of other disorders."

Comments: The "...recent findings of Martell..." were presented at public hearings in Denver, Colorado, on January 10, 1975, as stated on page 8, lines 15-17, and were appended as Appendix II. These "...findings of Martell..." are reviewed separately (see "Comments on Appendix II: 'Basic Considerations in the Assessment of the Cancer Risks

and Standards for Internal Alpha Emitters'").

Page 9, lines 12-16 - "In addition, the ^{241}Am concentrations range up to 8.2 pCi/g averaged over the top 15 cm depth of soils, with $^{241}Am/^{239}Pu$ ratios varying widely and ranging up to 3.5 (NVO-140, Vol. 1, p. 507)."

Comments: The Survey does report (page 507) that ratios of activities of Am-241-to-Pu-239, 240 in Enewetak soil range up to 3.5. However, it goes on to indicate that the highest ratios are for those islands which have the lowest absolute amounts of Am-241 and Pu-239. In a communication with D. W. Wilson, author of this section, he explained that the high ratios result from comparing two numbers which are themselves small and near the limit-of-detection; consequently, the 3.5 value is not significant. (All ratios greater than 1.0, moreover, were calculated for samples taken from the southern islands of the Atoll.) The more meaningful ratios are listed in Table 14, page 98, of the Survey. Those ratios are for the northern islands and they average about 0.40 with the largest being 0.51.

Page 9, lines 16-18 - "Due to further radioactive decay of ^{241}Pu, the ^{241}Am activity concentrations can be expected to double over the next 50 years."

Comments: We agree that the amount of ^{241}Am will increase from the decay of the parent nuclide ^{241}Pu. The maximum ^{241}Am activity which can result from the decay of ^{241}Pu is 2.6% of the initial ^{241}Pu activity. This maximum ^{241}Am level is reached in 69.6 years; after 17 years 65% of the maximum ^{241}Am activity is present and at 20 years 71% is present. The time since most of the tests at Enewetak is about 20 years. On this basis alone the ^{241}Am levels at Enewetak will increase by less than 50% above present levels.

Page 9, lines 21-22 - "The DEIS limits consideration of $^{239+240}Pu$ to inhalation risks."

Comments: The statement is in error. The DEIS includes also doses to various organs resulting from the ingestion of $^{239,240}Pu$ via food chains. See, for example, Table 235, p. II-48, Vol. II for integral doses from the marine food chain; Table 239, pp. II-53 to II-55, Vol. II for dosage from ingestion of terrestrial foods assuming diet at the time of return for each of the island groups; Table 240, pp. II-56 to II-58, Vol. II for dosage from ingestion of terrestrial foods assuming a 10-year post return diet for each of the island groups. The critical organ (bone) dose resulting from the ingestion of $^{239,240}Pu$ is insignificant when compared to the dose from all other radionuclides.

Estimates of doses for residents of Enewetak Atoll for various living and dietary patterns presented in the Enewetak Radiological Survey Report, NVO-140 and in the Task Group Report considered the critical organ for the most sensitive segment of the population and all pathways and all significant contributors (radionuclides) to this exposure.*

Page 9, lines 22-25 - "However significant uptake of Pu from the gastrointestinal tract has been observed in young mammals and similar uptake may occur in young children."

Comments: This statement is partially correct. Absorption of plutonium from the gastrointestinal tract is as much as 100 times greater

*Dose assessments were made for the fetus, the newborn, children and adults, using exposure levels in the highest year predicted. Because of the extremely small (<0.001%) contribution to the bone dose due to plutonium, the transuranic elements were not included in this age-related assessment.

in the newborn rat than in the adult. A similar effect of enhanced absorption of normally non-absorbed substances is observed in the newborn of other animal species. If such an effect occurs in the human infant, it will probably persist for only a few days following birth. However, the predominantly milk diet consumed during this period is a very poor source of transuranic elements.

There is no indication that a similar increased uptake would occur in young children.

Special calculations of dose resulting from ingested plutonium have not been made for the infant or child. The available data on metabolic behavior of the transuranic elements in the infant and child indicate that no significant underestimate of hazard will result from considering the total population as adults.

Because of the very long retention of transuranic elements in man, most of the radiation dose deposited in infants or children following ingestion will be delivered when the child has grown to a much larger size. The radionuclide is not only diluted by this growth process, but, in the important instance of bone, is buried under new bone growth and its alpha particles largely shielded from the radiosensitive cells on the bone surface. Thus, the smaller intake of radionuclides by the infant or child results, over the life span, in a very much smaller radiobiologically significant dose than the metabolic models predict using adult intake parameters.

Page 9, line 25 to Page 10, line 14 - "In addition the uptake of americium in soils by vegetation is substantially higher than plutonium uptake. Similarly americium is readily taken up from the gastrointestinal tract and accumulated in the liver, spleen and bone of mammals, and thus undoubtedly in man.

"Based on these considerations it is possible that uptake of americium in the food chain and its accumulation in the liver and skeletal tissue of man may be the critical path for exposure to internal alpha emitters in the Enewetak Atoll area. The radiological survey is seriously inadequate with respect to americium distribution in both vegetation and in edible marine life to assess the consequent body burdens and health consequences to future atoll inhabitants."

Comments: We agree that ^{241}Am might contribute more to the alpha dose from ingestion than plutonium. The use of ^{241}Am data in the ingestion dose evaluations for Enewetak Atoll in "Enewetak Radiological Survey," NVO-140, 1973, are as follows:

Marine Food Chain - ^{241}Am data were included in the dose assessment. ^{241}Am was non-detected in most of the fish samples analyzed. In such cases the value used for assessment was the detection limit (<0.03 pCi/g wet).

Terrestrial Food Chain - $^{239,240}Pu$ was detected in terrestrial products and the relative significance of Pu was evaluated for this pathway. $^{239,240}Pu$ contributes less than 0.001% of the bone (the critical organ) dose via this pathway. After maximum ingrowth of ^{241}Am, the ^{241}Am concentration will increase by ~50%. Assuming that the Am uptake of americium in soils by food plants is an order of magnitude greater than for plutonium and that the absorption of Am across the gastrointestinal tract is two orders of magnitude greater than for Pu, the Am contribution at the time of maximum ingrowth is about 1% of the total initial bone dose. With later generations the proportion of dose resulting from the transuranic elements will increase due to a decrease in the total dose resulting from the radioactive decay of many of the fission products.

A more precise estimate of the relative increase in ^{241}Am

levels and the potential concentrations of ^{241}Am relative to $^{239,240}Pu$ can be made from data available in "Enewetak Radiological Survey," NVO-140, 1973 (Ref. 1), from a report by V. E. Noshkin et al., "Transuranics at Pacific Atolls, 1. Concentrations in the Waters at Enewetak and Bikini," UCRL-51612, 1974, (Ref. 2), and from more recent data of Noshkin at Enewetak Atoll (unpublished) (Ref. 3). These data are considered for several different compartments at Enewetak Atoll.

Water Concentrations

a. One crater and one lagoon sample have been analyzed for both ^{241}Pu and $^{239,240}Pu$. The $^{241}Pu/^{239,240}Pu$ ratios were 1.14 and 2.56 with a mean of 1.85 and a standard deviation of 1.0. This average ratio has been used to estimate the ^{241}Pu activity in other compartments. The calculations have also been made using a ratio of $^{241}Pu/^{239,240}Pu$ of 3.0 which is slightly more than $X + 1\sigma$ (i.e., 1.85 + 1.0 = 2.85).

b. Lagoon surface water has an average $^{239,240}Pu$ concentration of 39 fCi/l (Ref. 2, Ref. 1). Using a ratio of 1.85 $^{241}Pu/^{239,240}Pu$ the ^{241}Pu activity is 72 fCi/l. The ratio of ^{241}Am to $^{239,240}Pu$ is 0.11 (Ref. 3); therefore, the ^{241}Am activity is 4.3 fCi/l. The maximum ^{241}Am activity which will result from decay of present levels of ^{241}Pu is 72 (0.026) = 1.87 fCi/l. This is a 43% increase over present ^{241}Am activity. The total ^{241}Am which will result is 6.2 fCi/l which is 16% of the $^{239,240}Pu$ activity.

Plankton

Concentrations in pCi per gram wet weight of ^{241}Am and $^{239,240}Pu$ in plankton samples are 0.23 and 0.39 respectively (Ref. 1). Using the factor 1.85 for $^{241}Pu/^{239,240}Pu$, the ^{241}Pu concentration would be 0.72 pCi/g. Maximum growth from this level of ^{241}Pu will be 0.72 (0.026) = 0.019 pCi/g. Relative to the present ^{241}Am level of 0.23 pCi/g this represents an 8% increase. The total ^{241}Am is 0.23 + 0.019 = 0.249 pCi/g. Relative to the $^{239,240}Pu$ levels this is 0.249/0.39 = 0.64 or 64%.

However, a more realistic situation is that the plankton will always reflect the same ratio of ^{241}Am to $^{239,240}Pu$ as they do to the present water concentrations. Therefore, the increased ^{241}Am water concentrations resulting from the "grow in" from ^{241}Pu will lead to ^{241}Am concentrations in plankton which are 85% of the $^{239,240}Pu$ concentrations.

Fish

The average concentration of ^{241}Am and $^{239,240}Pu$ is 0.11 and 0.25 pCi/g respectively (Ref. 1). ^{241}Am was non-detected in most fish samples and the value 0.11 pCi/g represents the value obtained when the detection limit is assumed to be a real concentration. Again using 1.85 as the ^{241}Pu to $^{239,240}Pu$ ratio the ^{241}Pu concentration is 1.85 (0.25) = 0.46 pCi/g ^{241}Pu.

The maximum ^{241}Am which can grow in from this level of ^{241}Pu is 0.46 (0.026) = 0.012 pCi/g. Relative to the present ^{241}Am concentrations of 0.11 pCi/g this represents an 11% increase.

The total ^{241}Am will be 0.11 + 0.012 = 0.122 pCi/g; compared with the $^{239,240}Pu$ of 0.25 pCi/g this is 0.122/0.25 = 0.49 or 49% of the $^{239,240}Pu$ levels.

However, a more realistic situation is that the fish will always reflect the same ratio of ^{241}Am to $^{239,240}Pu$ as they do to the present water concentrations. Therefore, the increased ^{241}Am water concentrations resulting from "grow in" from ^{241}Pu will lead to ^{241}Am concentrations in fish which are 64% of the $^{239,240}Pu$ concentrations.

Sediment Concentrations and Ratios

The ratio of ^{241}Am to $^{239,240}Pu$ in lagoon sediments is 0.37 and for the craters if 0.29 (Ref. 1). These data will be shown to correspond very well with ratios observed in the soil. The ^{241}Am and $^{239,240}Pu$ concentrations are 172 and 463 mCi/Km^2 respectively. The ^{241}Pu concentration is therefore 1.85 (463) = 857 mCi/Km^2. The maximum ^{241}Am activity from ^{241}Pu is therefore 0.026 (857) = 22 mCi/Km^2. This will be a 13% increase above present levels of 172 mCi/Km^2. The total ^{241}Am activity will be 172 + 22 = 194 mCi/Km^2 which is 194/463 = 0.42 or 42% of the $^{239,240}Pu$ activity.

Soil Concentrations

The average soil concentration of $^{239,240}Pu$ for the northern half of Enewetak Atoll is 12 pCi/g (Ref. 1). The $^{241}Am/^{239,240}Pu$ ratio in the soil at Enewetak is 0.36 (Ref. 1). Therefore, the present ^{241}Am concentration is ($^{239,240}Pu$ 12 pCi/g) (0.36 $^{241}Am/^{239,240}Pu$) = 4.3 pCi/g ^{241}Am.

Assuming the same ratio for $^{241}Pu/^{239,240}Pu$ of 1.85, the ^{241}Pu activity is 1.85 (12) = 22 pCi/g ^{241}Pu. The maximum grow in of ^{241}Am from this level of ^{241}Pu is 22 (0.026) = 0.57 pCi/g ^{241}Am.

When the calculated increase from ^{241}Pu of 0.57 pCi/g ^{241}Am is compared to 4.3 pCi/g of ^{241}Am now present it represents a 13% increase. The total ^{241}Am will be 4.3 + 0.57 = 4.87 pCi/g. When compared with the 12 pCi/g of $^{239,240}Pu$ present, the ^{241}Am level will be 41% of the $^{239,240}Pu$.

Ground Water

The average $^{239,240}Pu$ concentration in the ground water on Enjebi is 5.4 fCi/1 (Ref. 3). Using the 1.85 factor the ^{241}Pu concentration is 10 fCi/1. Americium-241 concentrations have not yet been measured but assuming a similar ratio for ^{241}Am to $^{239,240}Pu$ in both the lagoon water and ground water an estimate of the ^{241}Am in ground water can be made. 5.4 fCi/1 $^{239,240}Pu$ in ground water (4.3 fCi/1 ^{241}Am in lagoon water)/39 fCi/1 $^{239,240}Pu$ in lagoon water = 0.6 fCi/1 ^{241}Am in the ground water. Decay of ^{241}Pu leads to a 43% increase in ^{241}Am concentration and the total ^{241}Am activity is 16% of the $^{239,240}Pu$ activity.

Vegetation

Over 400 vegetation samples were analyzed during the Enewetak survey. There were only 3 samples where both ^{241}Am and $^{239,240}Pu$ were detected. The average values for these 3 samples were 0.44 pCi/g

$^{239,240}Pu$ and 0.053 pCi/g ^{241}Am. The ^{241}Pu concentration is 1.85 (0.44) = 0.82 pCi/g. The maximum ^{241}Am activity resulting from this level of ^{241}Pu is 0.026 (0.82) = 0.021 pCi/g ^{241}Am which is a 40% increase above present ^{241}Am concentrations. The total ^{241}Am activity is 0.053 + 0.021 = 0.074 pCi/g which is 0.074 pCi/g/0.44 pCi/g = 0.168 or 17% of the $^{239,240}Pu$ concentration.

Page 10, line 19 to Page 11, line 10 - "The resuspension measurements and calculations which relate the air contamination to the soil contamination are not immediately compelling, and deserve a much more careful analysis than I have given them. I would be surprised if the analysis is meaningful to factor of 100, when used to determine public health guidelines. Resuspension is poorly understood, it is sensitive to windspeed, soil characteristics, vegetation, humidity, rainfall, mechanical disturbance, physical and chemical history of plutonium particles in soil. How then does one consider the exposure of children throwing dry sand on a windy day at the beach? I would anticipate large fluctuations about the implicit exposure levels, which, even for the limiting soil contamination guidelines and predicted air concentrations associated with these guidelines will be approximately a maximum permissible lung burden."

Comments: The issues raised by Dr. Geesaman are not new. We are well aware that all of the variables which are identified have not been analyzed with respect to their individual or combined influence upon resuspension factors. For that reason additional air sampling studies will be carried out for a period of twelve months, as described in the DEIS.

Even though measurements made primarily reflect airborne plutonium from worldwide fallout levels and cosmic ray activity, because of the uncertainties identified the assumptions made in deriving the various

organ doses due to the inhalation of plutonium are quite conservative. A constant air concentration of plutonium is assumed, consisting of low solubility, optimal size particles for deep lung deposition; furthermore, cases for both surface soil concentrations of plutonium and average soil plutonium concentrations are calculated. The conservatism of these factors is apparent in that the average person is not likely to be constantly exposed to an air dust loading of 100 $\mu gm/m^3$; in addition, all resuspended particles of plutonium will never be of an identical and optimal respirable size.

In view of the author's stated uncertainties it is not clear what the basis is for the conclusions stated, or their derivation or justification. In the absence of any of these it must be regarded as opinion.

Page 11, lines 15-20 - "Concerning the standard employed by the DEIS for maximum permissible plutonium contamination of soils at Enewetak, Dr. Martell points out that 'There are no ICRP standards for soil levels of Pu and the actinides or for lifetime exposures to internal alpha emitters.' (Personal Communication.) And he provides the following critique of the standards adopted by the AEC Task Group for Enewetak."

Comments: Numerical values of radiation exposure and concentrations of plutonium in soil were recommended by the Task Group as guides for use in evaluating radiological conditions at Enewetak Atoll only. Such guides were not intended as and are not to be considered as primary standards. These guides were used as limits in evaluating remedial action options in order to recommend actions and restrictions that will ensure that exposures of people when they return will not exceed the basic FRC, ICRP and NCRP standards. These considerations are the basis for actions and

restrictions recommended in the DEIS. While there is no national or international standard for plutonium expressed as a concentration in soil, the guides recommended, 40 and 400 pCi/g, were derived using the best current information relating such soil concentrations to possible exposure to man. The guidance for cleanup of contaminated soil was selected such that exposures of people are expected to be well within the basic standard. This guidance has been approved by EPA for use at Enewetak.

The statement that, "There are no ICRP standards...for lifetime exposures to internal alpha emitters;" is in error. All ICRP standards for internal emitters are based upon the assumption of lifetime exposure.

Page 11, line 21 to Page 12, line 4 - "The recommendation that plutonium contaminated soils, with levels not exceeding 40 pCi $^{239+240}Pu/g$ of soil averaged over 15 cm depth, is suitable for human habitation, can be very seriously questioned.

"The State of Colorado Board of Health has adopted interim standards for Pu contamination limits in soils in land areas for residential use, specifying that ^{238}Pu levels shall not exceed 2 dpm (0.91 pCi) per gram of surface soil (i.e., averaged over the top 1 cm depth of soil)."

Comments: The information quoted from Dr. Martell's "personal communication" relative to an interim standard for plutonium in soil adopted by the State of Colorado Board of Health is grossly misleading. The guidance referred to does not apply to cleanup or removal of soil containing plutonium or to restrictions on use of plutonium contaminated land as Dr. Martell's communication implies. After conduct of an appropriate hearing, the Colorado Board accepted 2 dpm/g or 1 pCi/g

of plutonium in soil as requiring special techniques of construction upon such property. These special techniques are intended to minimize plutonium resuspension by construction activities. This guidance is irrelevant to development of plutonium cleanup guidance for Enewetak Atoll.

FRC, ICRP, and NCRP have not taken a position, except to indicate that value judgments and risk/benefit/cost judgments should be derived for each specific situation. Therefore, it is unrealistic for standards agencies to develop standards applicable to a broad range of circumstances. This is also why specific guidance is often developed for particular circumstances. The Task Group 40-400 pCi/g and the 1 pCi/g cited by Dr. Martell are both examples of guides for plutonium in soil developed for a completely different purpose and for very different conditions. Inherent in both guides are considerations of what is necessary and feasible. Inherent in both is the assumption that neither is absolutely safe. Neither of the guides should be considered as generally applicable standards.

Assuming that basic standards can be met, it is reasonable to assume that the guide selected for each set of circumstances involving protection of people from radiation exposure would be the lowest level that is feasible within the standard, a level that is attainable without a level of effect which is not justified by the commensurate degree of reduction of risk. This is the idea behind the "lowest practicable" concept.

If the wording is examined carefully, the comparison is made between the recommended cleanup criteria and the Colorado "interim standards" in land areas for residential use. It should be noted that Case 3, the recommended cleanup plan, would limit the residence locations of the Enewetakese to the southern islands of the Atoll, at least initially. According to Table 3-8, p. 3-70, Vol. I of the DEIS, the mean plutonium concentration in soil on most of these southern islands varies from 0.04 to 0.07 pCi/gm (ranging from 0.004 to 1.1 pCi/gm), with one island showing a mean concentration of 0.63 pCi/gm (range 0.2-2.0), all of which are below the interim guideline established by the State of Colorado and referred to by Dr. Martell. While these are mean values over 15 cm of soil depth, the islands consisting of the initial islands of habitation show a mean value of 0.04 with a range of 0.004 to 0.31. Even if the total quantity of plutonium in this maximum sample were located in the top 1 cm of soil (a most unlikely situation), the concentration would be 4.5 pCi/gm, reasonably comparable to the Colorado guidelines.

The recommendations for Enewetak are based upon minimal contraints to the living patterns and the diet of the people after their return. Colorado criteria did not consider such factors. Furthermore, the Colorado values are not based upon any demonstrated health hazard to man, but rather are based upon an arbitrary factor times the plutonium concentration in Colorado soils resulting from worldwide fallout.

Page 12, lines 4-6 - "It is noteworthy that the AEC has not established that this standard is unduly conservative..."

Comments: It is obvious that, where environmental quality is the only relevant consideration, there can be no such thing as an "unduly conservative" standard and we do not question the prerogative of the State of Colorado to apply such a standard in those areas where Federal control and regulation is not exclusive. Where other factors must be considered along with environmental factors, ERDA (AEC) has not endorsed Colorado's interim guidelines for plutonium concentration in soil.

Page 12, lines 6-10 - "...it is not apparent that the AEC has requested the ICRP or NCRP to make specific recommendations with respect to standards for Pu in soils applicable to chronic exposure to the general public, including children."

Comments: As stated above the various standards setting bodies have not provided explicit guidance because of the flexibility needed to permit implementation of the requirement that exposures be reduced to levels as low as practicable in each individual situation. However, both the NCRP and the EPA are currently reevaluating the desirability and the potential need for additional guidance in this area.

Page 12, lines 15-20 - "...for most Enewetak soils the top cm contains substantially higher levels of Pu per gram than the 15 cm depth average. Thus, for example, at location 101 on Pearl, the top 1 cm depth shows 400 pCi ^{239}Pu/g, whereas the average over 15 cm depth is about 60."

Comments: While Dr. Martell is correct that "for most Enewetak soils the top cover contains substantially higher levels of Pu per gram than the 15 cm depth average," there are also locations where higher plutonium

concentrations are found below the top cover of soil (Janet, locations 135, 142, 143, 144, 901; Irene, 24, 27, 51, 100; Alice 24; Belle 35, etc.). None of the islands containing these levels of Pu are expected to be village islands; furthermore, the Task Group recommendations included "Recovery of plutonium in soil at concentrations greater than 400 pCi/g $^{239,240}Pu$ at any depth these levels are found. Also, recovery of contaminated soil sufficient to reduce surface levels to a value well below 40 pCi/g $^{239,240}Pu$" (p. 5-80, Vol. I; emphasis added). Comparison of these values with the Colorado guidelines, therefore, is grossly misleading. (Refer to comments on author's page 11, line 21 to page 12, line 4.)

Page 12, lines 23-26 - "There are recent research developments which are expected to lead to reductions in acceptable organ burdens of Pu in man by a factor of 100 to 1000 or more."

Comments: There are no recent research developments of which we are aware that are expected by knowledgeable experts "to lead to reductions in acceptable organ burdens of Pu in man by a factor of 100 to 1000 or more." If Dr. Martell is aware of research data which would justify such changes, it would be expected to be distributed to the scientific community so that the ICRP and NCRP might consider the implications.

Page 12, line 26 to Page 13, line 3 - "In my opinion it is likely that a 10 pCi lung burden of insoluble alpha emitting particles will give rise to significant adverse health effects for lifetime exposures."

Comments: Similarly, if Dr. Martell has evidence that "a 10 pCi lung burden of insoluble alpha emitting particles will give rise to significant adverse health effects for lifetime exposures," we would

expect to have such data presented for review and evaluation by the scientific community. Until such time as evidence is available, these conclusions remain as stated by Dr. Martell as "my opinion."

Page 13, line 16 to Page 14, line 6 - "Further explanation of the plutonium cleanup criteria developed by the AEC Task Group is necessary. (DEIS, Vol. II, Tab B, pp. III-8 to III-11.) We have already mentioned the questionable wisdom of the 40 pCi/g standard. For any concentrations exceeding 400 pCi/g the Task Group recommendations require removal of the soil. But in the range between 40 and 400 pCi/g, the DEIS standards call for 'corrective action ..... on a case-by-case basis.' (Vol. II, Tab B, p. III-9.) Certain criteria are offered for guidance in the exercise of this judgment, but they appear to be entirely too unspecific and subjective. Once a decision is made to take corrective action, 'the objective is to achieve a substantial reduction in plutonium soil concentrations, and further, to reduce concentrations to the lowest practicable level, not to reduce them to some prescribed numerical value.' (Ibid. Emphasis added.)"

Comments: As stated in the DEIS, decisions regarding correction action for plutonium concentrations in soil between 40 and 400 pCi/gm $^{239,240}Pu$ will be on a case-by-case basis. Many specific factors enter into such a decision for which definite statements and numbers are inappropriate: location, environmental factors (e.g., wind and wave action); soil matrix; soil use; frequency and duration of human, animal or crop contact; risk/benefit balance; significance of removal, etc. To establish predetermined criteria for those and other variables is unrealistic. Judgment must be used to determine what can be done without doing more harm than good.

Page 14, lines 7-10 - "Nor is it entirely clear who will be making these 'case-by-case' decisions. Presumably it is the 'team of experts' referred to in the recommendations of the Task Croup (Vol. II, Tab B, p. 27), but we are not told who they are or how they will be selected."

Comments: Defense Nuclear Agency is responsible for cleanup of Enewetak Atoll. Staff for radiological support of cleanup operations will

be selected by that Agency. The AEC Task Group recommended inclusion of experts from a Public Health Service group, which is now part of the EPA, in the team that will interpret radiation and radioactivity measurements and provide advice and guidance in the field on cleanup actions, as was done for Bikini Atoll cleanup.

Page 14, lines 11-15 - "This whole approach must be explained and justified, especially at a time when the EPA is conducting hearings around the country on plutonium soil standards for precisely the purpose of developing 'numerical values' for the maximum concentrations permissible."

Comments: EPA has conducted public hearings in Washington, D.C., and in Denver, Colorado, to "evaluate the environmental impact of plutonium and the other transuranium elements and to consider whether new guidelines or standards are needed to assure adequate protection of the general ambient environment and of the public health from potential contamination of the environment by radionuclides of these elements." It can be seen from the above that the purpose of the hearings was to determine whether or not additional or new guidelines or standards are required; it was not the purpose of the hearings to set new standards or to specifically develop plutonium soil standards, much less "for precisely the purpose of developing 'numerical values'...". These activites may or may not subsequently take place, but the hearings were held to obtain information relevant to the above stated objectives which appeared in the Federal Register. It is expected that in time EPA may provide additional guidance pertaining to plutonium soil standards, but it is not at all clear at this time that this guidance will consist of numerical values, even as FRC guidance in

the past has not referred to numerical values.

Page 14, lines 18-28 - "Before any final standards are set for the radiological cleanup of Enewetak, the International Commission on Radiological Protection should be called upon for plutonium and actinide standards applicable to air, water, soils and food concentrations for both soluble and insoluble activities, applicable to long-range exposure to the general public. Application should also be made to the U. S. Environmental Protection Agency for special hearings for the same purpose. Consideration should also be given to the desirability of requesting the United Nations Scientific Committee on the Effects of Atomic Radiation to conduct hearings and set these standards."

Comments: It is doubtful if UN hearings or additional EPA hearings would bring to light any information not already known and considered, or that ICRP would address the specific question of what would be acceptable for Enewetak cleanup. ICRP policy leaves to each nation a degree of flexibility in applying the basic standards. The only organizations having experience in cleanup and rehabilitation of an atoll lies within ERDA, EPA, HEW, DOD and DOI.

The request for EPA public hearings on plutonium soil contamination standards appears inconsistent with the preceding paragraph on page 14 which states that such hearings are now being held around the country.

Furthermore, the EPA has already reviewed and evaluated the recommendations of the Task Group. The recommendations were approved by the EPA. Since the EPA has approved the guidelines recommended, it would appear redundant to request the EPA to hold hearings on this specific issue after they have made their decision.

It should also be noted that there are in existence applicable ICRP standards for air and water (and by extension, food) for both soluble and insoluble forms of these isotopes for long-range exposure to the general public. Thus the only issue is the one of soil standards, which has been discussed at length previously.

Page 15, line 5 to Page 16, line 7 - "Removal and Disposal of Radiocontaminated Materials. These comments relate to the proposed removal and disposal of contaminated scrap metal and soil treated in the DEIS at Vol. 1, §§5.3.3.3 and 5.5.

All radiocontaminated scrap metal on the Atoll has been identified and will be removed, as of course it must be, but the precise method of disposal has not been determined. Four alternative methods are discussed: ocean dumping of the loose scrap, concrete encapsulation in the Cactus and Lacrosse craters at the north end of Runit islet, or removal to the United States mainland for storage. We appreciate the practical and political difficulties presented by the various disposal methods which would remove the scrap from the Atoll entirely, but the People of Enewetak are adamantly opposed to any disposal upon or within the environs of the Atoll. Ocean dumping, according the DEIS (Vol. I, § 5.5.2.1), was rejected 'in view of complications.' Disposal of the United States mainland was disfavored for similar reasons. (Vol. I. § 5.5.2.4). Disposal on the Atoll must be rejected and the other methods should be explored, the necessary permits and authority obtained and disposal off the Atoll selected as the preferred method.

"Removal and disposal of contaminated soil presents more serious cost and practical difficulties, but here again the complete removal and off-Atoll disposal of all contaminated soil must be the stated objective of the program.

"Even using the high plutonium contamination standard set by the Task Group (40 pCi/g, etc.), the total amount of Atoll soil which would have to be removed and disposed is 779,000 cubic yards. (Vol. I § 5.5.2). If the soil standards are lowered as they should be, that volume will increase."

Comments: The comments pertaining to disposal of contaminated material are most appropriately dealt with by agencies other than ERDA because of the legal, political and fiscal implications.

Page 16, lines 15-18 - "...but a clear decision must be taken to study and fully assess the relation of soil removal to dose reduction (including the risk from airborne hot particles) and the likely ecological effects of soil removal and replacement."

Comments: An assessment of the relation of soil removal to dose reduction is discussed in the DEIS, Vol. II, Section 13, pp. 8-14.

Page 16, line 26 to Page 17, line 11 - "The AEC Task Group has wisely recommended the establishment of 'team of experts' to monitor the execution of the radiological cleanup phase of the program. (DEIS, Vol. I, pp. 5-79, 6-5). Even if the Task Group is enlarged as we have suggested and specific soil standards are developed and implemented, this monitoring group will perform a crucial function. Thus, it is important that its membership be carefully selected. It is imperative that radioscientists of the most conservative cast be included in the monitoring group. Here again, we suggest that the names of Drs. Martell, Geesaman, Tamplin and Cochran.

"And the on-site authority of the monitoring group should be clearly defined, with all important or unexpected problems to be referred to the enlarged Task Group."

Comments: As we stated earlier, the function and responsibilities of the Task Group were terminated when the Commission approved its recommendations.

The scientific approach used in development of radiation protection standards and practices is inherently conservative. The basic standards of the FRC, which according to law must be implemented by Federal agencies, are in themselves conservative. Recommendations by the AEC Task Group contain additional safety factors and provisions for checking the effectiveness of remedial actions and restrictions. In our opinion, the Enewetak cleanup field operation is not the proper forum to pursue debates and discuss issues between individual scientists where there can be no early

resolution. The hypotheses of Drs. Martell, Geesaman, Tamplin and Cochran are subjects for proper scientific debate. This is best conducted through the medium of technical journals and scientific meetings, not in day-to-day deliberations at Enewetak Atoll.

Page 17, lines 13-19 - "We are in full agreement with the AEC Task Group recommendations for test plantings, lens water and air sampling. (Vol. I., pp. 5-80 to 5-81). But it is not clear whether these recommendations have been implemented. They must be and the studies should be commissioned to the best scientists and technicians available, under the over-all guidance of the enlarged Task Group. All of these studies must deal explicitly with the hot particle problem."

Comments: All of the recommendations referred to here have been implemented and either are or soon will be underway. Additional information on these specific projects is available from DNA.

Any potential hazard due to hot particles would result from their inhalation; consequently the lens water and test plantings projects are not relevant to the "hot particle" issue. Characterization of resuspended particles will be conducted as a part of the air sampling project, however.

Page 17, line 21 to Page 18, line 8 - "AEC Task Group recommendation 12 (Vol. 1, p. 5-81) calls for 'Baseline surveys of body burdens and urine content of Cs-137 and Sr-90...for the Enewetak people prior to return to Enewetak Atoll, and periodically thereafter.' But here, too, it is not clear whether a firm commitment to long-range radiological health monitoring of the Enewetak population has been made, and, if so, precisely how it will be implemented.

"A fully adequate radiological health program must be designed, funded and implemented. It can and should include the people of Bikini, who will one day soon be resettled, the exposure victims at Rongelap and Utirik Atolls and the Enewetak people.

"The final impact statement should address this question and state clearly whether such a program is planned and what it will include."

Comments: Provision for long-term periodic radiological health monitoring of the Enewetak population, including analyses for strontium, cesium and plutonium, has already been arranged.

Page 18, lines 8-10 - "It too must deal with the health effects of hot particles and all forms of low level radiation, with emphasis on internal emitters."

Comments: It is not clear whether "It" refers to the Final Statement or to the radiological health monitoring program to be established. If the former, the issue is discussed in our response to the comments of Drs. Martell, Tamplin and Geesaman. If the latter, it is not a realistic request. Criteria justifying the initiation of any controlled epidemiologically and radiologically valid study are not present. Studies of "the health effects of hot particles and all forms of low level radiation" are seldom practical even under controlled laboratory conditions; even at exposure levels considerably above the potential levels discussed here, health consequences are either not seen or are of questionable significance. To identify a health effect in a very small population resulting from extremely low levels of respirable particles, which may or may not be present, of questionable significance is very difficult even in controlled laboratory environments, and we expect that it would be impossible to do so with the population on the Atoll. Health effects from these causes in the population under discussion are not expected to be seen. To study any relationship between morbidity or mortality and the anticipated levels of exposure to radiation is a considerably different situation from monitoring the people to ascertain the levels of internal emitters to which they might be exposed. The latter will be done, as stated above, but it is not planned to do the former.

Page 22, lines 19-23 - "But at the same time all of the radiological investigations recommended here should be undertaken and high confidence results obtained as soon as possible so that they can be used to revise and improve the radiological cleanup phase before moving forward with it."

Comments: The additional radiological investigations recommended by the Task Group have already been funded and initiated. If all of the recommendations suggested by the author had to be undertaken and high confidence results obtained in order to revise and improve the radiological cleanup phase before proceeding, the return of the Enewetakese might have to be abandoned or delayed a good many years.

Comments on Appendix II: "Basic Considerations in the Assessment of the Cancer Risks and Standards for Internal Emitters" by Edward A. Martell*

Page 2, lines 13-17 - "...and the tobacco smoke radioactivity results[14]. The latter results imply that as little as a few picocuries of insoluble alpha emitting particles in the lung may give rise to a significant risk of lung cancer and other serious health effects in the chronic exposure case."

Comments: The Public Health statistics correlating tobacco smoking and incidence of lung cancer and other diseases do not distinguish selectively between the alpha emitters and the rest of the tobacco smoke as causative agents. Extensive epidemiological observations suggest that the etiology of lung cancer in smokers is different from that in irradiated populations. The excess risk of lung cancer produced by radiation persists for at least three decades after single or briefly fractionated exposures; it does not show any appreciable return toward normal levels for twenty years following an initial 8-12 year latency. On the other hand, when smoking is continued for a prolonged period and then terminated, excess risk remains constant for only 1-3 years after which a steady decline to normal occurs in 10-14 years. The striking difference in the temporal pattern of excess mortality in former smokers and in irradiated humans indicates, contrary to Dr. Martell's suggestion, that the etiology is different in the groups. Uranium miners who have stopped smoking do not show this pattern of

*The author referred to herein is Dr. Martell.

declining risk typical of unirradiated populations; about 30% of the cancer deaths in uranium miners have occurred in former smokers even though more than half of them had not smoked for five years or more. This suggests that the effects of the smoke as a whole, or apart from the contained alpha emitters, are probably much more important than the permanent effects of the small amounts of alpha emitters in the smoke, in regard to the mechanism of induction of the associated lung cancer.

While Dr. Martell provides evidence regarding the presence of very small quantities of alpha emitting radionuclides in definitive structures of the tobacco leaf, his conclusions go considerably beyond the data provided.

Page 2, lines 28-29 - "And for long term exposures, unacceptably high tumor risks appear to be associated with picocurie burdens of internal alpha emitters."

Comments: If this conclusion is based upon the tobacco smoking statistics, the previous response is applicable here also.

Page 3, lines 1-5 - "It also is possible that the critical health effects for alpha emitting particles are the incidence of atherosclerosis and other degenerative diseases of the cardiovascular system. The published evidence supporting these conclusions is briefly reviewed below."

Comments: The evidence which the author presents in support of his conclusions is reviewed below.

Page 4, lines 13-16 - "The alpha radiation-induced bone tumor incidence in dogs is observed to be proportional to the square of the alpha dose[19] implying that a sequence of two or more low probability events must be involved."

Comments: This is true and should be noted for future reference. It should also be noted that this dose-incidence relationship indicates not only an increase in tumor incidence with increasing dose size and dose rate (associated with dose size), but also an increase in tumorigenic

effectiveness per unit dose with increasing dose size and dose rate. In this kind of dose-incidence relationship, and referring to the rising portion of the dose-incidence curve, the effectiveness of the dose decreases with decreasing dose and dose rate.

Page 4, lines 16-18 - "This is consistent with the two-mutation and multiple-mutation theories of cancer[20,21] based on the age distribution of cancer in man."

Comments: There is a great weight of evidence in favor of multi-event mechanisms of carcinogenesis that require not only the cell initiating events (malignant cell transformation) but also promotional events such as local tissue damage or damage of structure and function of more remote but relevant organs or systems by one or a combination of agents or conditions. This type of complex mechanism is consistent with the type of dose-incidence relationship described for the production of bone cancer in dogs by internal alpha-emitting radionuclides.

Page 4, lines 18-27 - "On the basis of these considerations the production of a malignant cell involves a sequence of events, as follows: (1) production of a viable mutated cell; (2) clone growth from the mutated cell; (3) production of a second viable mutation in one or more of the clone; (4) growth of a clone of doubly-mutated cells; etc. Thus, for a two-mutation sequence, the tumor risk would be proportional to the $R^2t^2(t/T_c)$, where R is the alpha dose rate, t is the time of exposure, and T_c is the mean life of the normal cell and singly mutated cell. The term (t/T_c) represents the influence of the growth of the clone of the singly-mutated cell on the long-term risk."

Comments: Assuming that this formula is appropriate for the continuous alpha particle irradiation from internal alpha emitters, with very high LET, short track in tissue, and high cell sterilizing and killing efficiency and effect within short distances of the sources, and applying to it various dose rates (R), a given constant time of exposure (t) and a given constant mean life of normal cell and singly mutated cell (T_c), the formula seems to indicate that for varying internally administered amounts of alpha emitter

(continuous alpha irradiation), i.e., different doses and associated dose rates, the tumor incidence would be proportional to the square of the dose or the square of the dose rate, and the incidence per unit dose would increase in proportion to increasing dose or increasing dose rate. This is compatible with the dose-incidence relationship for alpha radiation-induced bone tumor incidence in dogs cited by the author in lines 13-16, page 4 (see comments on that sentence above). This kind of dose-incidence relationship for alpha emitters (involving continuous irradiation) indicates decreasing effectiveness of doses in the rising portion of the dose-incidence curve with the decreasing dose rate that is associated with decreasing dose.

It is difficult to reconcile these findings with the author's next statement, as follows:

Page 4, line 28 to Page 5, line 3 - "This tumor risk relationship makes it abundantly clear that a linear extrapolation to low dose rates is not only not conservative for alpha radiation induced tumors, but rather that there is a marked inverse dose-rate vs. risk relationship."

Comments: Reference is made to the immediately preceding set of comments. For varying amounts of internally administered alpha emitter of a given type, the continuous irradiation occurs over a constant time of exposure, but the dose rate (and the total accumulated dose in a given time) depend directly on the amount of alpha emitter administered. Both dose and dose rate are relevant and important in internal alpha radiation induction of cancer. In the author's formula, if the only parameter that is varied is the dose rate (R), this would also vary the dose proportionally for a constant time of exposure. On this basis there is a direct relationship between incidence (or risk) and dose rate or dose size.

Perhaps what the author intended, but did not make clear and explicit, was that the total dose should be kept constant by varying both the dose rate (R) and the time of exposure (t) such that the product of the two (the total dose) would always be the same. Under these circumstances, as one increases the dose rate (R) one decreases the exposure time (t) proportionally, and the consequent reduction of the function t/T_c reduces the value of $R^2t^2(t/T_c)$ which is related to incidence or risk. However appropriate the use of the formula may be for estimating a two-mutation sequence from some kinds of radiation from external sources, it is artificial and neither appropriate nor realistic for tumor incidence or risk for continuous irradiation from internal alpha emitters which cannot be limited to varying times of exposure in relation to dose rate, and it requires presumptions on the interrelationships among dose rate, time of exposure, total dose, relevant induction dose, and latent period in internal alpha radiation induction of tumors, as well as the assumption that a two-mutation sequence is, or is equivalent to, the mechanism of cancer induction.

Page 4, lines 3-24 - "There is an increasing body of published experimental evidence that reflects this trend.

"Speiss and Mays[22] observed that for ^{224}Ra alpha radiation induced bone sarcoma in man, the tumor incidence per rad approximately doubled for a four-fold increase in the spacing of ^{224}Ra injections and that the observed incidence of bone tumors per rad in children was nearly twice that for adults. Upton et al.[23] show a significantly higher incidence of tumors in mice for a given neutron dose at more protracted periods of exposure. Moskalev and Buldakov[24] showed that fractionation of the administered ^{239}Pu dose over larger periods of time increased bone tumor induction. The higher tumor incidence per rad for the smaller lung burdens of crushed $^{239}PuO_2$ microspheres observed by Sanders[11] seems best explained by the limited alpha irradiation of large numbers of cells by numerous very small, mobile particles of low activity per particle (see below). Hamsters subjected to low alpha doses from ^{210}Po distributed quite homogeneously in the bronchiolar-alveolar region show a marked increase in the lung tumor incidence per rad at very low doses and dose rates[25]. And the incidence of bronchial cancer

in uranium miners reflects a higher tumor risk per rad at the lower doses[26] for this low dose rate exposure group. The tobacco radioactivity results[14] indicate a significant tumor risk for the cumulative alpha radiation dose from ^{210}Po in insoluble particles in the bronchi of smokers, involving much lower dose rates."

Comments: Here the author indicates that "there is an increasing body of published experimental evidence that reflects this trend", i.e., referring to "marked increase dose-rate vs. risk relationship." Then the author cites various reports to support this.

It is well known that fractionation or protraction (reduction of dose rate) of doses that as intensive doses are in the range of high doses that are relatively inefficient (per rad) for carcinogenesis (i.e., in the declining part of the dose-incidence curve following the peak at the most efficient dose level), owing to excessive cell sterilization or destruction, will increase the efficiency of such doses. It is also well known that fractionation or protraction of a dose that as an intensive dose is in the rapidly rising portion of a dose-squared dose-incidence relationship (an efficient dose) will reduce the effectiveness and efficiency of the dose. It is the dose rate influence on these efficient doses that is important in considering the possible influence of dose and dose rate reduction to levels of interest in radiation protection. The author neglects this distinction in his selection of reports for presentation in this paragraph.

Sanders[11], in describing the material administered to the rats, states that it was derived from crushed $^{238}PuO_2$ microspheres; the animals did not receive the crushed $^{238}PuO_2$ microspheres, as is implied by Dr. Martell. Prior to administration the material had been stored in a saline solution for a long period of time and had been altered to a physico-chemical form which was 70% ultrafilterable and apparently was in a non-crystalline form of plutonium since it had no detectable x-ray diffraction pattern.

Page 5, line 25 to Page 6, line 20 - "Based on the above considerations it is evident that the tumor risk is optimized when a very large number of cells and their descendants are subjected to only a few widely spaced alpha interactions with the small target afforded by the cell chromosomes. This follows necessarily from the fact that most alpha interactions with cell chromosomes lead to the subsequent mitotic death of the cell, as Barendsen has shown[17,18]. The production of a malignant cell calls for a sequence of two or more low probability events and thus cannot be speeded up by the application of massive alpha doses, but rather only by subjecting a much larger number of cells to a limited number of interactions. Additionally, assuming that the tumor risk to the tissue subjected to alpha irradiation is proportional to $R^2t^2(t/T_c)$, explained above, it is apparent that the alpha activity concentration or the activity per particle which is equated to a given tumor risk decreases with increasing time of exposure and also that a given risk can be attributed to smaller cumulative doses when the time of exposure t is appreciably longer than the mean life of the cell, T_c. Brues[27] and Burch[28] both pointed out that the two-mutation theories of carcinogenesis[20,21] would imply an exceptionally high effectiveness of widely spaced radiation for tumor production. It is proposed that just such a dose rate relationship serves to reconcile the observed significant tumor risk in cigarette smokers with the presence of a persistent lung burden of insoluble smoke particles involving a total of only a few picocuries of ^{210}Po[14].

Comments: Here the author does recognize the high cell sterilizing or killing efficiency of alpha radiation in attempting to further his argument that tumor risk is optimized at very low dose. This argument and his additional argument, on the basis of the assumption that the tumor risk to the tissue subjected to alpha irradiation is proportional to $R^2t^2(t/T_c)$, that "the alpha activity concentration or the activity per particle which is equated to a given tumor risk decreases with increasing time of exposure and also that a given risk can be attributed to smaller cumulative doses when the time of exposure t is appreciably longer than the mean life of the cell, T_c", are rather enigmatic with respect to dose and dose-rate relationships with effect, but are subject to the previous (above) comments on the author's pages 4 and 5.

The dose-squared relationship between alpha radiation induced cancer incidence and dose (as in the dog experiments referred to) indicates increasing

effectiveness and efficiency of dose in the rising portion of the relationship curve until the curve changes to a plateau before declining at still higher doses. According to this, the rising portion of the downwardly convex curve shows decreasing efficiency with decreasing dose. Under actual conditions, different amounts of a particular alpha emitter in a particular form and distribution within an organ irradiates cells and tissues for the same period (t) and with the same decay kinetics, and therefore the dose rate (R) and the dose are determined by the amount of the alpha emitter taken in or present. The use of the formula $R^2t^2(t/T_c)$ with proportional variation of R and t to achieve constant dose for examination of the influence of variation in dose rate and time of exposure may be useful for external sources of radiation which can be controlled with respect to R and t, but this manipulation is artificial and unrealistic for internal alpha emitters which are not subject to such control of the variation in time of exposure.

Page 6/ lines 21-23 - "If the above tentative conclusions are correct, then the same considerations must apply in the assessment of tumor risks for hot particles."

Comments: The correctness of "the above tentative conclusions" are subject in part, at least, to previous (above) comments on the author's pages 4, 5 and 6.

Page 6, lines 26-28 - "Raabe et al.[29] report an apparent rate of dissolution of $^{238}PuO_2$ in lung fluid which is two orders of magnitude higher than that observed for $^{239}PuO_2$ particles."

Comments: The $^{238}PuO_2$ dissolution experiments referred to were not carried out using "lung fluid", but rather a synthetic serum simulant. In addition, these experiments were conducted in vitro, not in vivo as is implied.

Page 7, lines 5-8 - "In addition the $^{238}PuO_2$ particles exhibited a very significantly lower density than the $^{239}PuO_2$ particles[30], indicating a highly faulted structure and weakened intermolecular bonding for the $^{238}PuO_2$ particles."

Comments: Early measurements of density of PuO_2 with the Lovelace Aerosol Particle Separator system were highly variable due to experimental errors, with values averaging about 10 g/m^3; this value was reported for $^{239}PuO_2$. Improved techniques were developed by the time the $^{238}PuO_2$ experiments were conducted and the particle densities measurements were more constant and probably more accurate with average values around 8 g/cm^3. That this difference in reported density indicated "...a highly faulted structure and weakened intermolecular binding for $^{238}PuO_2$..." is speculation by the author and appears somewhat oversimplified.

Page 7, lines 8-12 - "Fleischer[31] proposes that the apparently higher dissolution rate for $^{238}PuO_2$ may be explained by the alpha recoil nucleus ablation of the surface layers of the particles, with a fragmentation rate proportional to the specific alpha disintegration rate and with variable sizes of fragments ranging up to $\sim 10^4$ atoms."

Comments: Fleischer suggested that aggregate recoil explains the increased dissolution rate of $^{238}PuO_2$ over $^{239}PuO_2$. This is more likely to be a radiolytic effect occurring at the surface of the particle, but the exact mechanism has not been unequivocably demonstrated.

Page 7, lines 12-14 - "The poorer structural integrity of the $^{238}PuO_2$ particles may give rise to an increase in the size range of the ejected fragments."

Comments: The reference to "...poorer structural integrity of the $^{238}PuO_2$..." gives the impression of being a factual statement; in point of fact it is the author's speculation, and possibly an erroneous one. When $^{238}PuO_2$ is prepared in a manner identical to the preparation of $^{239}PuO_2$, investigators do not feel that the $^{238}PuO_2$ has "poorer structural integrity" or lower density than $^{239}PuO_2$, although it does have a lower median particle size. This alone could account for a higher solubility rate, insofar as the $^{238}PuO_2$

particles would have a larger surface area per unit mass (or activity) than $^{239}PuO_2$ particles.

Page 7, lines 14-17 - "Such small fragments, ranging up to tens of angstroms in diameter or more, would pass readily through the 0.1 μm diameter pores of the membrane filters used in the dissolution experiments(29)."

Comments: Whether small ablation fragments, if they are formed, can pass readily through a membrane filter rated at 0.1 μm pore has not been demonstrated. This assumption, while perhaps reasonable, is an assumption of the author.

Page 7, lines 23-27 - "Another explanation for the apparently higher solubility of $^{239}PuO_2$ than $^{238}PuO_2$ is the possibility that the intense alpha radiolysis of the lung fluid at the surface of the particles leads to the production of chemically active free radicals which in turn react with PuO_2 molecules on the particle surface."

Comments: Presumably a typographical error occurred in identifying the isotopes; we expect that "...higher solubility of $^{239}PuO_2$ than $^{238}PuO_2$ is..." should read "...higher solubility of $^{238}PuO_2$ than $^{239}PuO_2$ is...".

In the experiments referred to (29), "intense alpha radiolysis of the lung fluid", with the formation of free radicals, is one explanation for the increased dissolution rate observed in $^{238}PuO_2$ particles; a more realistic explanation is that the increased dissolution rate is due to the intraparticle radiolytic effects. A 0.44 μm diameter $^{238}PuO_2$ particle emits only 12 alpha particles per minute and a $^{239}PuO_2$ particle of the same size emits only 3 alpha particles per hour. In well buffered solvents such as were used in the dissolution experiments, radiolysis products are probably quickly inactivated at the slow rate and in the small quantities that they are formed.

Page 8, lines 2-6 - "However this dissolved plutonium undoubtedly would be slowly redistributed in the lung in the same fashion as that reported by Moskalev[34] for inhaled soluble compounds of plutonium, resulting in a highly non-uniform distribution, with hot spots located predominantly in the sub-pleural region of the lungs."

Comments: That "...this dissolved plutonium undoutedly would be slowly redistributed in the lung..." (emphasis added) is a source of confusion. The material that is redistributed in the lung is the material that does not become solubilized, e.g., PuO_2 particles, or polymerized $Pu(NO_3)_4$. The solubilized plutonium enters the bloodstream and is translocated to the liver or the skeleton; this has been shown quite clearly in both the rat and the dog.

Page 8, lines 6-8 - "This gradual conversion of the soluble plutonium compounds to small colloidal size particles at focal points of activity may be the result of the self-chelating properties of tetravalent plutonium in solution."

Comments: It is not clear what is either meant here or what assumptions have been made to reach this conclusion.

Page 8, lines 9-11 and line 17 - "In recent studies of rat inhalation of $^{238}PuO_2$, Sanders[11] has demonstrated a substantially increased risk per rad for small lung burdens of aged, 'crushed' $^{238}PuO_2$ microspheres."
"...the greater mobility and wider redistribution of the $^{238}PuO_2$ microspheres..."

Comments: The material to which Sanders[11] exposed rats was not "'crushed' $^{238}PuO_2$ microspheres." It was matèrial derived from crushed $^{238}PuO_2$ microspheres, as was explained previously (see comments on the author's page 4, lines 3-24).

In addition, it should be pointed out that the smallest initial alveolar deposition in this study was 5 nCi, or about 300 times the current maximum

permissible occupational lung burden for humans of 0.016 nCi/gm (1000 gm lung). The low rad dose, in contrast to this deposition, was due to the rapid alveolar clearance of the inhaled ^{238}Pu.

Page 9, lines 20-22 - "It is proposed that these two tumors may be attributed to secondary protons ejected by alpha interactions with hydrogen atoms. The expected yield is one proton per 10^4 alpha interactions."

Comments: It is not exactly clear that it is the author who is making the proposed mechanism of induction of the two tumors referred to, nor is the basis for the proposed conclusion clear, nor is any evidence presented to support it.

Page 10, lines 18-21 - "These effects plus the accompanying chromosome structural changes can give rise to the earlier incidence not only of cancers, but the whole pattern of diseases of the cardiovascular and renal systems[37,38]."

Comments: The author, referring to the fact that radiation can damage or destroy cells that produce blood platelets and leukocytes, states that, "These effects plus the accompanying chromosome structural changes can give rise to the earlier incidence not only of cancers, but the whole pattern of diseases of the cardiovascular and renal systems[37,38]." This statement, the manner in which it is made, and the sweeping implications of it, are misleading, unaccompanied by adequate meaningful explanation or foundation, and attempt to factionalize mechanistic connections which are so remote and speculative, and neglectful of known aspects of the mechanisms, as to be practically meaningless. The references (37, 38) do not provide substantive support for the sweeping mechanistic aspects of the statement.

Page 10, lines 22-26 - "Let us review the mounting evidence which suggests that inhaled insoluble alpha emitting particles may be the agent of atherosclerosis and thus give rise to an increased risk of death by early coronaries and strokes. Atherosclerosis is reported to be present in every instance of partial or complete arterial occlusion and every case of coronary thrombosis[39]."

Comments: Reference 39 is identified as a 1940 paper in The American Heart Journal on arteriosclerosis of the coronary arteries and the mechanism of their occlusion. In a study of 100 cases of recent coronary occlusion, the authors of this paper reported that "arteriosclerosis was observed in every instance in which either a partial or complete arterial occlusion was found." These authors also reported on the later sequelae of arteriosclerosis, including calcium deposition in the plaques and even bone formation in some cases following calcium deposition. They stated the following: "Judging from the recorded, and our own, anatomic observations, it appears that the process of arteriosclerosis consists primarily of an intimal lipoidosis and collagenous thickening, and further, that the end result is intimal fibrosis brought about with the aid of capillary channels which proliferate in response to the fatty change and intimal thickening. The ingrowth of vessels into the plaque must be considered, then, as basically repairative and granulation tissue-like in nature. If the vascularization of a plaque does not keep pace with the lipoid change, or if the delicate intramural channels become obstructed in any of the ways previously mentioned, the ensuing circulatory deficiency leads to necrosis of the lipoid zone, and produces an atheromatous 'abscess.' This establishes the second phase of the vicious cycle, for the necrotic foci may now precipitate localized hemorrhages, with progression of the arteriosclerotic process, and incidentally, occlusion of the luman. The extent of the local hemorrhage is dependent upon

the ratio of the size of the capillary affected to the degree of associated intimal degeneration. Finally, then, the lesion must be the expression of the interrelationship between fatty change, vascularity of the wall, and intimal necrosis. Calcification and bone formation characterize ultimate healing of the lesion."

Page 11, lines 1-3 - "Recently Benditt has shown[40] that the human atherosclerotic plaque is a monoclonal proliferation of a mutated cell of the artery wall, and thus an arterial tumor."

Comments: Clarification of this matter requires explanation of what the paper of reference (40) by Benditt and Benditt (1973) actually reports and shows.

First, it should be pointed out that early in embryonic development of mammalian females there is random inactivation of one or the other of the two x-chromosomes in various cells. Thus, the female becomes a mosaic of two cell types, each type having one or the other of the pair of x-chromosomes active with respect to x-linked glucose-6-phosphate dehydrogenase isoenzymes. The two cell populations reproduce true to type in this respect throughout somatic growth, it is thought. Benditt and Benditt (1973) referred to Linder and Fartler as having examined the nature of the cell population in benign uterine smooth muscle tumors* by investigating the pair of x-linked isoenzymes.

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*The following definitions might be useful:

Mutation: a change in the character of a gene that is perpetuated in subsequent divisions of the cell in which it occurs.

Tumor: a swelling.

Neoplasm: an abnormal mass of tissue that grows more rapidly than normal and continues to grow after the stimuli which initiated the new growth cease; may be either benign or malignant.

Cancer: any of various types of malignant neoplasms.

It should be noted that these terms are not synonymous. A neoplasm may or may not be a cancer, and "tumor" is not equivalent in meaning with "cancer." Similarly, the proliferation of a mutated cell does not necessarily result in a tumor.

Benditt and Benditt (1973) (author's reference 40) investigated by this means individual atherosclerotic plaques from various regions of the aorta and common iliac arteries of 4 human females. The data were reported to show that the fibrous caps of the atheromatous plaques were composed of cells that produce solely or predominantly one of the two isoenzymes, whereas samples of artery wall media and intima were regularly composed of a mixture of the two isoenzyme cell types.

These investigators considered an alternative to the injury-repair hypothesis of spontaneous atherosclerosis on the basis of the following considerations: cells of spontaneous atherosclerotic lesions differ from cells of normal artery wall and cells populating a repair site in size, composition of associated extracellular material (e.g. preponderance of collagen rather than elastin), and in the absence of intercellular junctions. These investigators stated that these differences and the results of their enzyme analysis of plaques and normal vessel components imply that atherosclerotic plaques in human beings arise by another mechanism. They stated that these features suggest two possibilities: either the cells of atherosclerotic plaques derive from a population of cells different from those of the normal arterial media or they are transformed cells, and if the latter is so, cells of atherosclerotic plaques, like those of the benign smooth muscle tumors of the uterine, could be expected to be monoclonal. It is at this point that Benditt and Benditt seem to have used the term, monoclonal, to suggest origin not only from one of the two isoenzyme cell types of the female but from a single transformed cell. In this latter context they stated that the mechanism compatible with the monoclonal nature of atherosclerotic plaques is mutation, and that the likely causes are chemical mutagens or viruses.

All that the actual data (isoenzyme data) in this paper (Benditt and Benditt) really show is that the plaques arise solely or predominantly from one or the other of the two embryonically determined isoenzyme cell types, with differentiation or metaplasia of the cells of either type in certain characteristic ways under the atherosclerotic circumstances, and not that plaques necessarily had origin from single (versus multiple) cells of the isoenzyme cell type predominating. The actual data did not show that cell mutation was involved, as is stated by the author of the document under review.

Benditt and Benditt acknowledge the possibility that the reason for the sole or predominant presence of one or the other of the two isoenzyme cell types in the plaques is not a monoclonal origin but rather some process selecting from one or the other of the two cell types.

Benditt and Benditt did not actually define the atherosclerotic plaque as an arterial tumor as the author of the document under review seems to imply in relation to his reference to the paper by Benditt and Benditt.

Page 11, lines 3-4 - "Elkeles[41-43] has observed anomalously high concentrations of alpha activity at the calcified plaque sites."

Comments: Elkeles (1966) (author's reference 42) pointed out the well known fact that calcium deposition in various soft tissues is a manifestation of aging. Elkeles referred to a paper by Blumenthal et al. who microincinerated human aortas and showed that calcium was deposited in the media after 20 years of age, and emphasized that such deposits increase with age and precede the formation of intimal plaques. Blumenthal et al. also observed that the ratio of calcium phosphate to calcium carbonate in the aortas is similar to that in bone.

It should be pointed out here that whether or not the calcium deposits in blood vessels may be regarded as an irritant leading to damage and repair in the formation of plaques, there are subtle to obvious changes in parts of some blood vessels (e.g., aorta, coronary arteries, renal arterioles) that somehow provide a receptive environment for deposition of calcium (dystrophic calcification). Calcium deposition may be especially marked in conditions involving excessive demineralization of bone, as in advanced osteoporosis of aging, osteitis fibrosa, and parathyroid disorders, and with elevation of blood levels of calcium, from whatever cause. The deposition of calcium in blood vessels as a consequence of damage of bone of experimental animals after internal administration of substantial doses of bone-seeking alpha emitters has been observed.

Elkeles (to whom the author referred) pointed out that certain radioactive substances are deposited with the calcium in the skeletal system. He reported that in elderly patients, the alpha particle activity per unit net weight of aorta, although variable, tended to follow the degree of calcification. He studied the abdominal aorta, coronary arteries, pulmonary artery, and ribs and costal cartilage. Ash % and alpha activity rose with age only in the aorta and coronary arteries. In pulmonary arteries, ash % did not rise and alpha activity declined with age. Pulmonary arteries were chosen as the control arteries because they are histologically similar to aorta but not subject to atherosclerosis except in cases with long-standing pulmonary hypertension. In costal cartilage there was no increase in ash with age and the alpha activity declined with age. Turner et al. and Mayneord were cited as having reported that the radioactivity of bone ash does not increase with age.

In short, Elkeles reported that in those elastic arteries which are the most common sites of atherosclerosis, there is increase of both ash and alpha activity with age, and advanced the concept that progressive deposition of calcium together with small amounts of alpha emitters lead to subtle injury and reactive changes of connective tissue in arterial walls leading to atherosclerosis.

However, as mentioned above, there are changes in some parts of some vessels which precede and provide a receptive environment for deposition of calcium and the alpha emitters that behave like calcium metabolically and go with calcium, e.g., from bone to vessel walls. Much larger doses of alpha radiation than the amounts measured by Elkeles are required to damage arteries to the point of causing substantial increase in calcium deposition. Increasing blood pressure with age should be highly suspect as one condition which may contribute to subtle but progressive changes in aorta, coronary arteries, and perhaps even renal and other arterioles to some extent, which may provide the conditions favoring calcium deposition. Just as atherosclerosis occurs in pulmonary arteries under the conditions of pulmonary hypertension, atherosclerosis in aorta or coronary arteries and damage of renal arterioles are associated with general hypertension or increases in blood pressure with age.

Page 11, lines 4-7 - "In addition atherosclerosis plaques normally occur in the main and abdominal aortas and the coronary arteries, but rarely in the pulmonary arteries[42,44]. This distribution suggests a respiratory origin for the mutagenic agent."

Comments: Here the author assumes that atherosclerotic plaques are the result of alpha radiation induced cell mutations and suggests that the alpha emitters responsible originate from the lung (presumably inhaled) because

the pulmonary arteries rarely develop atherosclerotic plaques. This would imply that inhaled alpha emitters that get into the blood are trapped efficiently in their first passage in the blood stream through the pulmonary veins, heart, coronary arteries, and perhaps the rest of the vascular tree except that virtually none is left in the blood by the time the blood reaches and services the pulmonary artery. The author does not discuss this matter, or the fate of alpha emitters absorbed from the gastrointestinal tract, or the mechanisms by which alpha emitters may be taken up so specially in aorta, coronary arteries, etc. on the first passage of the blood containing them.

The sentences which are the subject of these comments represent a very poor argument for the respiratory origin of the causative agent, for the nature of the causative agent, or for the reason for the rarity of atherosclerosis in the pulmonary artery. It is highly unlikely that there would be no alpha emitters passing through the blood of the pulmonary artery or of its vasa vasorum after inhalation and ingestion of alpha emitters that were in a state allowing them to pass into the blood.

Page 11, lines 8-10 - "Attempts to reproduce arterial lesions in animals by chemical, mechanical and nutritional means have not produced plaques similar to those of atherosclerosis in man(40)."

Comments: The author's reference (40) is to the paper by Benditt and Benditt (1973), whose statement in this matter is as follows: "Chemical, mechanical, and nutritional manipulations have been used in animals in an effort to reproduce lesions like those of atherosclerosis in man: none of these experimental lesions yields wholly satisfactory copies of lesions of the human disease."

The next sentence in the Benditt and Benditt paper is as follows: "Spontaneous atherosclerosis occurs in chickens and, as we have found, produces lesions that strikingly resemble those of man."

The fact that certain types of experimental manipulation may have failed so far to reproduce wholly satisfactory copies of lesions of the human disease does not mean that some of those lesions which have been produced are wholly irrelevant or that radiation is the only agent that would be perfectly successful. Experimental manipulation with radiation has not succeeded in meeting this requirement either. Since other animals are not wholly like humans it has been difficult, but it is not necessarily impossible for the future, to produce good copies of the human disease by experimental manipulation of factors other than radiation. Perhaps investigation of the spontaneous lesions in chickens would provide valuable clues.

Page 11, lines 10-12 - "However atherosclerotic plaques have been directly induced in human arteries by intensive irradiation with x-rays and radium(45)."

Comments: The reference (45) is to a paper by Sheehan (1944) on what Sheehan calls an uncommon or at least rarely described lesion, i.e., foam cell plaque, observed in the intima of irradiated small arteries (100 to 500 microns external diameter) in several irradiated organs. The lesion was described as a plaque-like thickening of intima due to collection of foam cells alone or foam cells mixed with various other cells, fluid, fibrin or hyaline material, between endothelium and internal elastic membrane. Although pathological changes were found sometimes also in adjacent internal elastic membrane, media and adventitia, these structures were often normal. The plaque may cause marked narrowing or even occlusion of the lumen. Thrombosis, fibroblastic proliferation or deposition of elastic tissue in the thickened

intima seldom result. The foam cell plaques were found in small arteries in organs subjected to radiation therapy (large doses) by roentgen rays and/or gamma rays from radium sources. The paper states that the plaques probably result from migration of lymphocytes and monocytes into the intima from the blood stream and subsequent transformation (meaning differentiation or metamorphosis) of these cells into foam cells by their ingestion of lipids which have been freed by the dissolution of red cells in the intima or which have accumulated in the intima after passage across portions of the endothelium that was rendered more permeable than normal by irradiation. The paper contained a casual or incidental statement to the effect that the foam cell plaques in irradiated small arteries closely resemble the early lesion of atherosclerosis. If this were true, it would be indicative of some of the kinds of changes which may occur in vessels before, and presumably responsible for, subsequent deposition of calcium. It is interesting to point out, however, that earlier in this paper, Sheehan indicated that foam cell plaque was an uncommon or at least rarely described lesion.

Page 11, lines 15-17 - "For all of these reasons it is proposed that inhaled insoluble alpha emitting smoke particles are very likely to be the mutagenic agent which gives rise to atherosclerosis in cigarette smokers."

Comments: This statement is a string of poorly founded presumptions covered by previous comments.

Page 11, lines 18-21 - "If this is the case, similar increased risk of early coronaries are to be expected for other groups of individuals who are occupationally or environmentally exposed to the inhalation of insoluble alpha emitting particles of respirable size."

Comments: "If this is the case" is a poorly founded presumption, for reasons covered in previous comments.

Page 11, line 26 to Page 12, line 2 - "Very significant increases in the incidence of early coronaries as well as lung cancers and cancers at other sites is observed among cigarette smokers[46] with insoluble alpha emitting particle burdens of only a few picocuries of ^{210}Po in the lung[14] and similar total alpha activity per 100 grams of arterial wall tissue[41-43]."

Comments: This sentence is misleading in tying the alpha activity of arterial wall tissue to the statement about incidence of diseases among cigarette smokers. The references (41-43) refer to Elkeles' papers reporting alpha particle activity in calcified atherosclerosis and in coronary artery disease, based on measurements in plaques and vessels, where it is most likely that calcium, and alpha radioactivity with it, increase after alterations of the arterial tissue that lead to the rest of the atherosclerotic mechanisms have occurred (see comments on page 11, lines 3-7 and 10-12).

Page 12, line 3 to Page 13, line 2 - "By comparison, plutonium workers exhibit plutonium organ burdens ranging from a few picocuries to a few nanocuries or more[47,48]. And although there has been no epidemiological study of the age-incidence of heart disease and cancer among plutonium workers, the limited published information bearing on this question is more disturbing than reassuring. Most often cited is the medical experience of 26 plutonium workers at Los Alamos[49,50], usually accompanied by a statement to the effect that none of the medical findings for this group can be attributed definitely to internally deposited plutonium. With equal justification one may state that most of the serious medical findings in this group can be attributed to plutonium. One member of the original group died in the early 1950's. Cause of death is not reported. Another died of a coronary at age 38. A third suffered a coronary occlusion but recovered and was well compensated. A fourth developed a hamartoma of the lung and his right lower lobe was surgically removed in May 1971. A fifth had a melanoma of the chest wall. A sixth had a partial gastrectomy for a bleeding ulcer. One subject suffered loss of teeth, apparently due to damage to the lamina dura of the jaws which show the earliest effects in beagles given toxic doses of plutonium. Another subject has gout. The full medical history of this group, now mostly in their fifties, has not yet completely unfolded. Only 12 of these 26 plutonium workers were exposed to plutonium inhalation. Which of the observed effects were experienced by the inhalation exposure group? Regardless of the distribution, the medical experience of this small group thus far provides no basis for complacency about the health consequences of plutonium exposure.

"Hanford employees and others whose autopsy tissue samples exhibited plutonium levels in excess of 5 fCi/g died mainly of coronary heart disease and other cardiovascular effects and to a lesser extent of cancer and pulmonary emphysema[47]."

Comments: The author's discussion here, of what he calls "the limited published information" on plutonium workers with plutonium organ burdens, cannot be categorized as a scientific analysis or discussion of the problem, but rather as his subjective reaction and opinion. In our opinion the Los Alamos workers with plutonium burdens and the autopsy cases in the Transuranium Registry do not constitute an adequate sample for the assessment of the incidence of any type of disease. We have not and do not feel that it would be purposeful to compare the incidence of various diseases with the national figures for such small samples. Adequate comparison data for the incidence of disease is not available for morbidity in the living members of the Los Alamos group. The autopsy data may show significant bias due to the selection process in obtaining permission for autopsies.

Page 13, lines 2-6 - "Based on evidence reviewed above it appears that atherosclerosis is a cancer of the artery wall and thus that coronary heart disease and other diseases of the cardiovascular and renal system are expected effects of inhaled plutonium and of other insoluble alpha emitting particles."

Comments: Whereas previously the author had referred to the human atherosclerotic plaque of the artery wall as an arterial tumor (author's page 11), he here states that atherosclerosis is a cancer of the artery wall. No evidence is presented which identifies atherosclerosis as a cancer. The "evidence" referred to is a discussion of the author's opinions regarding past and present plutonium workers.

This sweeping generalization and string of presumptions are poorly founded, for reasons given already in previous comments above.

Page 13, lines 6-8 - "An adequate assessment of the magnitude of these risks can only be obtained by a comprehensive medical follow-up of all past and present plutonium workers."

Comments: We fully agree with the author that there is need for a proper epidemiologic study of workers with plutonium burdens, and ERDA is now developing definite plans for such a study. The continuation of such studies, as well as the pertinent experimental research, are certainly worthy of support and encouragement.

Page 13, lines 8-12 - "Until the age distribution of these effects among plutonium workers is fully assessed, any claim by the proponents of nuclear energy that there is little risk associated with the MPLB (maximum permissible lung burden), 16 nCi of plutonium, or fraction thereof, is totally unjustified."

Comments: The use of the phrase "these effects among plutonium workers", without specification, suggests that the author has already concluded or presumed, on the basis of "the limited published information" (his term on his page 12), that all of the deaths, causes of death, and diseases among plutonium workers that he mentions on his pages 12 and 13 are "effects" of plutonium rather than natural or other specific causes, despite statements he attributes to the investigators of "the medical experience of 26 plutonium workers at Los Alamos[49,50]" to the effect that "none of the medical findings for that group can be attributed definitely to internally deposited plutonium". On his page 12, the author states: "With equal justification one may state that most of the serious medical findings in this group can be attributed to plutonium", and this he states apparently on the basis of his examination of the limited published information and his speculations.

Where objective scientific assessments of risk are concerned, we do not think that the justification of the assessments or related claims should depend on whether or not one is a proponent or opponent of, or indifferent to, nuclear energy or its alternatives.

That any risk associated with the MPLB, or fractions thereof, is totally unjustified is an opinion of the author. The evidence presented by the author cannot be considered supportive of his conclusions in light of the preceding comments. The opinion that there is no fraction of the MPLB at which the risk becomes insigificant appears unrealistic.

Page 13, lines 12-14 - "The growing evidence suggests that as little as a few picocuries of alpha activity in the lung, in arterial tissue, and in other organs gives rise to a significant cancer risk."

Comments: If the statistics relating cigarette smoking and lung cancer are the basis for the statement concerning lung, there is still a question concerning the relative importance of the few picocuries of alpha activity as compared with the influence of the rest of the smoke (see previous comments on the author's page 2, lines 13-17). The case for cancer risk in arterial tissue, if it refers to the author's postulate that atherosclerotic plaques are arterial tumors, or cancers, is poorly founded (see previous comments on the author's pages 10 and 11). We are not clear what data has been provided to support the statement about "other organs", whichever the author meant by this term, and "a few picocuries of alpha activity."

Page 13, lines 15-17 - "The published evidence, reviewed above, clearly indicates that a linear extrapolation to lower doses and dose rates is not conservative for internal alpha emitters."

Comments: Little in this statement is clear with respect to meaning: not the "published evidence" or what is "reviewed above" that is pertinent to the statement, not the level of dose or dose rate (and associated efficiency for the effect) from which extrapolation linearly is supposed to be "not conservative", not the shape of the dose-effect curve that is regarded as nonconservative as compared with the linear one, not the meaning of "conservative", not the effect being considered in the statement, and not the

kinds of alpha emitters referred to or their properties. Again, this is a sweeping and poorly founded generalization. See also previous comments on the author's pages 4 and 5.

Page 13, lines 17-19 - "The initial effects of alpha interactions with cell chromosomes are irreversible and thus will vary linearly with alpha dose rate."

Comments: On his page 3, the author states: "When alphas interact with the chromosome or its gene in the nucleus of the cell, the dense ionization in the track of the alpha particles give rise to closely spaced breaks which bring about a wide variety of irreversible chromosome structural changes, or mutations. X-ray and γ-ray interactions give rise to a diffuse distribution of ions, resulting in widely spaced individual breaks, most of which can undergo repair by recombining without structural change. Thus permanent structural changes for x-rays and γ-rays are proportional to the square of the dose, with greatly reduced incidence at low dose rates. By contrast, structural changes resulting from alpha interactions are directly proportional to the number of interactions and are independent of alpha interaction rates."

The proper interpretation or expression of the content of the quoted statement under comment and the quoted statements in the comments, is that for alpha radiation the incidence of induced chromosomal structural changes increases linearly (proportionally) with increasing dose, and also with dose rate under realistic conditions for internal alpha emitters where dose rate and dose are dependent upon amounts of alpha emitter present. On this linear relationship basis the effectiveness of the alpha radiation per unit dose (efficiency) is independent of dose rate, as contrasted with the dose-squared dose-effect relationship for x- or γ-rays and the dependence of effectiveness and efficiency on dose size and dose rate. However, it should

be pointed out that either the linear or the dose-squared dose-effect relationship pertains only to the point of saturation of effect, with no further increase in the specified effect with further increase in dose. Furthermore, at very low doses of alpha radiation, if there were any reduction in efficiency of production of any particular type of chromosomal effect or other effect, which could be possible, this would indicate the possibility of an effect-reducing influence of reduced dose-rate.

Page 13, lines 19-22 - "However, the cumulative effects of internal alpha emitters gives rise to an increase in the populations of mutated cells (cells with viable structural changes in their chromosomes) and in the health consequences of such changes."

Comments: This is true insofar as it means that the increasing dose with continuous irradiation increases the incidence of mutated cells capable of reproduction, but only up to the point at which the continuing irradiation and increasing dose begins to sterilize or kill more of such reproductively capable mutated cells than it is producing. Compared with x- or γ-rays, alpha particles are highly efficient for killing or reproductively sterilizing cells, so that for equivalent dose parameters, the fraction of cells surviving and capable of reproducing themselves as well as carrying chromosomal aberrations and mutations, is very small for alpha radiation. But the amount of tissue damage and disorganization, which requires larger doses for production than does chromosomal aberration or mutation, and which may also be an important factor in mechanisms of carcinogenesis, is relatively greater for the high LET alpha radiation.

Page 13, lines 22-23 - "Therefore the tumor incidence per alpha disintegration must increase with decreasing dose rate."

Comments: This sentence seems enigmatic, non-sequitus and perhaps incompatible with the author's previous sentence. Perhaps it depends upon what the author means by his newly injected dose parameter, "per alpha disintegration," as compared with his meaning of "dose" (rad?) and of "decreasing dose rate." If he intends to mean by "decreasing dose rate" the decreasing dose rate in an organ with increasing time after a given alpha emitter burden to that organ, and then intends to relate this lowered dose rate with the delayed appearance of cancer after a long latent period, it should be pointed out that the earlier high dose rate may be the rate more associated with the cancer induction. On the other hand, if he intends to mean a comparison of different dose rates, initially or later on, based on different amounts of alpha emitter burden given to an organ initially, then the interpretation of his remark depends upon whether he is comparing high dose - high dose rate levels which are relatively inefficient for cancer production (by virtue of overkill of cells) (see comments on the author's pages 4, 5 and 13) with lower dose and dose rate levels, or comparing different dose and dose rate levels in the region of ascending dose-incidence relationship.

It should be pointed out again that the author apparently regards chromosomal structural changes or mutations as constituting the mechanism of carcinogenesis and has indicated that the chromosomal effects of alpha radiation are directly proportional to the number of alpha interactions, independent of alpha interaction rates, and vary linearly with alpha dose rate. The linear relationship between effect and dose or dose rate indicates lack of dependence of effect per unit dose on dose size or dose

rate. Therefore, it does not follow that tumor incidence per unit dose, on the basis of a mechanism that has a linear dose-effect relationship, will change with change in dose size or dose rate.

Page 13, lines 23-26 - "For this reason a given cancer risk is equated with smaller cumulative alpha doses and with much smaller internal alpha emitter burdens as the period of exposure decreases.

Comments: This is an enigmatic statement, but taken literally appears to be unfounded for the same reasons given and referred to in comments on the previous sentences on this page and on the author's pages 4 and 5.

Page 14, lines 1-9 - "By contrast, the cellular effects of X-rays and γ-rays are largely repairable at low dose rates. This stems from the fact that the diffuse distribution of ion pairs produced by such radiation results in widely spaced single chromosome breaks which repair themselves readily. For these reasons the relative biological effectiveness of alpha particles, compared to X-rays and γ-rays increases continuously with decreasing dose rate. Thus alpha radiation acquires a greatly increased biological significance relative to soft radiation in the production of tumors and other health consequences of chromosomal structural changes."

Comments: The first two sentences of this paragraph are essentially correct. The third sentence is essentially correct, but it should be pointed out and emphasized that the relative biological effectiveness of alpha particle irradiation, compared to x-radiation and γ-radiation as standards, increases with decreasing dose rate not because the effectiveness of alpha radiation changes with change in dose rate but because the effectiveness of the standard radiation (x- or γ-radiation) decreases with decreasing dose rate. The effectiveness of the alpha radiation is independent of dose rate and proportional to dose.

The 4th sentence of this paragraph is also subject to this qualification and to others of preceding comments relating to it.

Page 14, lines 10 to Page 15, line 2 - "There are several other lines of evidence which reinforce the possibility that alpha interactions with cells play a unique role in human cancer production. The distribution of cancer sites in the bronchi, in the lymphatic system, in arterial tissue, in the liver and bone, all involve sites at which insoluble alpha emitters are known to accumulate. Anomalously high concentrations of alpha activity have been observed at the bronchial cancer sites[51], at cancer sites adjoining lymph glands in other organs[52,53] in atherosclerosis plaques[41-43], at liver cancer sites in thorotrast patients[54], at bone tumor sites in the radium dial workers[55], etc. The difficulties of producing lung cancer by external radiation has been pointed out by Warren and Gates[35,36]. The absence of cancers in muscular tissue, except at sites of thorotrast injection or plutonium injection, also is relevant to this issue. All of these observations reinforce the possibility that one or more of the chromosomal structural changes which characterize a malignant cell must be brought about by alpha interactions and not by low intensity X-rays or γ-rays. In this connection, the determination of the nature of the structural differences between the healthy and the malignant cells of each organ could shed some light on this important question."

Comments: The first sentence of this paragraph indicates that the paragraph will present "...several other lines of evidence which reinforce the possibility that alpha interactions with cells play a unique role in human cancer production."

If the author intends that the word "unique" be used in the strict sense of the word, e.g. single or sole, it should be pointed out that no type of radiation effect has been observed which cannot be caused by other agents or conditions, and that no type of effect of alpha radiation has been observed that cannot be caused by other kinds of ionizing radiations. The differences between effects of various types of ionizing radiations are quantitative rather than qualitative, and are owing to differences in relative biological effectiveness, LET, distribution, etc.

The next two sentences in the paragraph refer to observations of high concentration of alpha activity at sites of cancer. In regard to bronchial cancer sites, the author refers to a paper on distribution of polonium in

pulmonary tissues of cigarette smokers. In regard to cancer sites in the lymphatic system, the author refers to a paper entitled, "Only vertebrates with a lymphatic system are subject to malignant disease," and to a note to the Health Physics Journal, entitled, "The lymphatic system--a storehouse of long-stay deposits of inhaled radioactive particles. Although high concentrations of plutonium are seen in the tracheo-bronchial lymph nodes of dogs following the inhalation of plutonium, it is an unusual site for primary malignant neoplasms. The most common neoplasm seen under these conditions is metastatic from the lung. The author's references to anomalously high concentration of alpha activity in atherosclerotic plaques, which he has designated as arterial tumors, are subject to previous detailed comments on earlier pages of his paper. The liver cancer sites in thorotrast patients agree well with the deposition of administered sizeable amounts of thorium oxide and the consequent tissue damage, as do the bone tumor sites in radium dial workers agree well with the deposition of sizeable amounts of ingested bone-seeking alpha emitters and the consequent bone damage.

The 4th sentence of the paragraph states: "The difficulties of producing lung cancer by external radiation has been pointed out by Warren and Gates[35,36]." Such experimental difficulties have more to do with species and strains of animals, getting high enough radiation doses from external sources into the lungs or into what may be appropriate lung structures for the species and strain of animal, without severely damaging too much lung tissue in other ways or other tissues between the radiation source and the lung and thereby causing competing earlier causes of death than the tumors of interest. Some laboratories have been producing lung tumors in experimental animals by means of radiation from external sources. There have also been reports of epidemiological studies showing increased incidence of lung tumors in human beings

following irradiation from external sources. The author's statement should not be taken to mean that radiation from external sources cannot cause lung cancer.

The 5th sentence of this paragraph states: "The absence of cancers in muscular tissue, except at sites of thorotrast injection or plutonium injection, also is relevant to this issue." The author does not develop further the relevance or the issue referred to, or indicate the types of cancers to which he is referring. This statement should not be taken to mean that other radioactive isotopes injected into similar regions, or irradiation from external sources in one or another mode, cannot cause similar cancers.

In the 6th sentence of this paragraph, perhaps the author is giving the purpose for his previous two sentences. He states: "All of these observations reinforce the possibility that one or more of the chromosomal changes which characterize a malignant cell must be brought about by alpha interactions and not by low intensity x-rays or γ-rays." Although this sentence has enigmatic characteristics, a mixture of confusing qualifications, we will take it literally and state that it is not well founded and is neglectful of the evidence for x-ray and γ-ray induction of mutations, chromosomal aberrations, and cancer.

Page 15, lines 3-13 - "It is also observed that the relative significance of chemical agents, viruses and radiation in the incidence of human cancer is not known. Details of the mechanisms of cancer induction by chemical agents and viruses also are poorly understood. And the proposed chemical carcinogens in cigarette smoke and in polluted urban environments have not been demonstrated to be carcinogenic at the low concentrations involved. For all of these reasons it is deemed likely that radiation, and alpha radiation in particular, may be the principal agent of human cancer. In view of such a possibility, it is very disturbing to note that the U.S. National Cancer Institute, now spending about one-half billion dollars per year on cancer research, has completely neglected the field of radiation induced cancer research."

Comments: It is obviously true that "the relative significance of chemical agents, viruses and radiation in the incidence of human cancer is not known."

It is true that the "details of the mechanisms of cancer induction by chemical agents and viruses also are poorly understood." However, we would point out that many experts in carcinogenesis would regard these mechanisms as better understood than the mechanisms of cancer induction by radiation.

The 3rd sentence of this paragraph states flatly and without elaboration that "the proposed chemical carcinogens in cigarette smoke and in polluted urban environments have not been demonstrated to be carcinogenic at the low concentrations involved." Even if this were true, it may be only a question of more time and investigation, as it has been with understanding the effects of radiation. Furthermore, the same might be said for the low alpha radiation activity by itself in regard to cigarette smoke, as compared with the effects of the rest of the smoke (see previous comments on the author's page 2).

The fourth sentence of this paragraph states: "For all of these reasons it is deemed likely that radiation, and alpha radiation in particular, may be the principal agent of human cancer." The "reasons" referred to in this paragraph, even if they were true, would hardly be reasons for anything but further research, and they certainly do not provide an acceptable scientific basis for this enormously sweeping generalization and summary dismissal of all other known and suspected agents and conditions which may cause or help to cause human cancer.

The fifth sentence implies that NCI has greater interest in etiological factors other than radiation but ascribes this interest to a misdirection of the NCI program.

Page 15, lines 14-16 - "Published evidence[39-45] indicates that atherosclerosis is a tumor of the artery wall and that the alpha activity at the calcified plaque site is likely to be the mutagenic agent."

Comments: This "evidence" has already been reviewed. Nowhere is evidence presented that atherosclerosis is a tumor of the artery wall or that alpha activity is likely to be the mutagenic agent. This statement is presented as fact, whereas it is the author's opinion.

Page 15, lines 16-19 - "If so the major causes of death in the general population - coronary disease, other cancers, and strokes - may in large part be attributable to internal alpha emitters from natural and pollutant sources."

Comments: The phrase "If so" conditions the remainder of the sentence to be true only if the preceding sentence is factual, which has yet to be proven. The sweeping generalization is poorly founded, as has been previously discussed.

Page 15, lines 19-21 - "If so, fallout plutonium and alpha emitting contaminants must already be contributing to increased health risks and life shortening to the general public."

Comments: Again the sentence is a conditional one based upon the preceding conditional sentence. By this time the author's conclusions have progressed considerably beyond the data presented in his references. The author has not presented any evidence to support this supposition.

Page 15, lines 21-26 - "Cigarette smoking causes increased risks of early coronaries, lung cancer, cancers at other sites, and other health effects[46], with about 15 years reduction in life expectancy for those who regularly smoke 2 packs of cigarettes per day or more (attributable to lung burdens of only about five picocuries of ^{210}Po in excess of that of nonsmokers).

Comments: The author flatly states the parenthetical expression as if it were fact. There is complete disregard for any and all mechanisms of cancer induction other than that postulated by the author.

Page 15, line 28 to Page 16, line 3 - "Although these levels are only about 10 percent of the ^{210}Po organ burdens of heavy smokers, the effects may be correspondingly greater because the total population is exposed, and the inhalation exposures begin at birth."

Comments: The author here states that the "effects (due to fallout) may be correspondingly greater (than those due to cigarette smoke)." The sentence implies as fact that health effects resulting from smoking are due to ^{210}Po organ burdens; this unverified assumption is the author's.

Page 16, lines 4-12 - "If the health risks attributable to fallout plutonium exceed 10 percent of the risks of heavy smoking, then inhalation exposure at ~20 times fallout (the surface soil concentration of plutonium which corresponds to the interim soil standard adopted by the Colorado Board of Health in 1973) would give rise to organ burdens more than twice that of heavy smokers. Exposing children to such levels would be tantamount to their smoking four packs of cigarettes per day, beginning at birth. This estimate assumes, as I believe to be the case, that the inhaled, insoluble radioactive smoke particles give rise to the serious health effects of smoking."

Comments: Such numbers relationships have little meaning when the basic assumptions are so poorly founded (see earlier comments). The author is building assumption upon assumption, which he acknowledged in lines 10-12.

Page 16, lines 13-21 - "For the estimate of organ burdens which may result from the inhalation of soil contaminants, it is common practice to attempt to determine the average surface soil concentrations, the applicable resuspension factors, inhalation exposure patterns, particle size distributions, lung retention, clearance and translocation patterns and rates, etc. The large cumulative errors and uncertainties in the prediction of the ultimate organ burdens from long-term exposure to contaminated surface soils and urban dusts by such a long sequence of complex processes serve to make this procedure an almost useless exercise."

Comments: While we agree that there are uncertainties in the procedures which the author describes, we do not agree with the author's opinion that such calculations are useless exercises. Where uncertainties exist, efforts are made to be conservative, thereby overestimating any potential hazard. Because of this procedure, any errors are likely to be in the direction of conservatism.

Page 17, lines 5-8 - "For this reason, surface soils with one picocurie of plutonium per gram (the Colorado interim soil standard) should contain an estimated 10 to 100 pCi of plutonium per gram of insoluble soil particles of respirable size."

Comments: The conclusion again is a supposition of the author for which no evidence is presented, as is suggested by the word "should."

Page 17, lines 8-11 - "Such a soil level should lead to plutonium lung burdens of 5 to 50 picocuries by age 20, or 15 to 150 picocuries by age 60, with correspondingly higher concentrations in the lymph nodes, liver and bone."

Comments: This observation follows if the premise upon which it is based is true (see comments above).

Page 17, lines 11-13 - "Thus the Colorado interim soil standard is hardly a safe of acceptable standard unless it can be shown that such levels of plutonium have no serious long term health effects."

Comments: Assuming the preceding assumptions to be fact, the author now states that, "Thus..." This conclusion is no more valid than the assumptions upon which it rests, for which no evidence is presented.

Page 17, line 20-25 - "Thus the high tumor risk for the hot $^{238}PuO_2$ particles(11) can be variously attributed to (a) the mobility of the smaller particles (b) the recoil ablation and/or dissolution rates which increase with specific activity and with surface area of hot particles and (c) the irradiation of larger numbers of cells with scattered protons (an effect that may be significant for very hot particles)."

Comments: The reference to "the hot $^{238}PuO_2$ particles(11)," is misleading. As was stated previously (see author's page 8, lines 9-11), the material used was neither $^{238}PuO_2$ nor in particulate form (see comments on the author's page 4, lines 3-24). Furthermore, the author's definition of "hot... particles" here is not clear. It is the "monomeric" ^{238}Pu, with its consequent exposure of more "'target' epithelial cells" which reference 11 attributes as the cause of the higher tumor incidence. Recoil ablation, scattered protons, etc. are not discussed in reference 11.

Page 18, lines 1-4 - "For these reasons, the insoluble alpha emitting smoke particle, uranium oxide, thorium oxide and other alpha emitting particles of moderate to low specific activity may be expected to give rise to a higher tumor risk per alpha disintegration or for a given cumulative dose."

Comments: It is not at all obvious what "these reasons" are, nor what they do or are supposed to support. If the "reasons" are what immediately precedes the statement, there is little upon which to base a judgment other than the assumptions upon which the author bases his speculations. If the "reasons" are the preceding 17 pages, these have been discussed in detail previously.

Page 18, lines 5-7 - "Similarly plutonium-239 in mixed fallout particles may be expected to produce more tumors per disintegration than is the case for pure $^{238}PuO_2$ and $^{239}PuO_2$."

Comments: That this "may be expected to produce more tumors per disintegration" depends upon the validity of the assumptions of the author.

Page 18, lines 7-11 - "However although larger burdens of hot particles will be required for a given tumor risk, such risks can be expected to increase with both alpha specific activity and with particle surface area, and the effects should occur earlier for a given burden of smaller particles of higher specific activity."

Comments: This sentence is enigmatic, starting with "a given tumor risk" which is subsequently variable, ending with "a given burden" which earlier was larger (larger than what is not stated), and meanwhile varying specific activity, surface area and time. Nor is it clear that it is consistent with the two preceding sentences and earlier statements regarding the relative risk of high specific activity versus low specific activity particles.

Page 18, lines 12-15 - "The above considerations make it obvious that the present practice of averaging the alpha dose over the whole lung or some arbitrary fraction thereof[10-13] is a highly questionable and grossly misleading procedure at best."

Comments: There is nothing "obvious" about the "above considerations," whether "above" refers to the same page or to the preceding 17 pages (see also comments on the author's page 13, lines 15-17). These "considerations" consist of a string of hypothetical assumptions which the author portrays as fact and upon which he bases his conclusions.