UNITED STATES TRANSURANIUM REGISTRY SUMMARY REPORT TO JUNE 30, 1974 TO USAEC DIVISION OF BIOMEDICAL AND ENVIRONMENTAL RESEARCH

HANFORD ENVIRONMENTAL HEALTH FOUNDATION
Richland, Washington 99352

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by

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U. S. TRANSURANIUM REGISTRY

INTRODUCTION

This report includes general information about the Registry since its inception in late 1968, together with more detailed coverage for the past year. Previous annual reports have been made to the Atomic Energy Commission in conjunction with Additional Justification for Operating Costs (AEC Schedule 189) and numerous articles covering Registry activities have been published.[1-16]

RADIOANALYSIS OF AUTOPSY TISSUES PRIOR TO REGISTRY

A program of collection and radioanalysis of tissue samples obtained postmortem from plant workers and residents in the plant environs has been maintained at Hanford since 1949. This was for developing capability for assessing the over-all effectiveness of operating controls, safety procedures and engineering safeguards incorporated into plutonium facilities, which controlled the release of radioactive materials to the Hanford environs. Nelson et al. reported findings of some 350 autopsies.[1] Results indicated that in none of these cases permissible limits, established by NCRP and ICRP, had been exceeded. There were several earlier reports.[2,3,4] Similar studies have been carried out at Los Alamos since 1959.[5] Lagerquist et al.[6] reported on the plutonium content of several internal organs following death of an occupationally exposed Rocky Flats worker.

ESTABLISHMENT OF PLUTONIUM REGISTRY

In 1967, Dr. H. D. Bruner[7] of the Division of Biology and Medicine stressed the growing need for a center to "insure that the details of the continuing event can be correlated with the worker's subsequent health record." Extensive experimental investigation with laboratory animals had demonstrated that minute quantities of plutonium, americium and other transuranium elements could cause malignant growth in the tissues

in which they are deposited. Following discussions and meetings, the Registry idea grew and the U. S. Atomic Energy Commission asked the Hanford Environmental Health Foundation, with the cooperation of Battelle Northwest Laboratories to develop and operate such a registry. The Registry was started in August 1968. The name National Plutonium Registry was adopted but later changed to the U. S. Transuranium Registry to indicate the broader scope of the Registry. Dr. W. D. Norwood was named Director and was later succeeded by Dr. J. A. Norcross, whose ill health resulted in his resignation and Dr. Norwood was asked to resume the directorship in 1974 until a younger physician with competence in this particular field could be found. C. E. Newton, Jr. of Battelle Northwest serves as Consultant and Associate Director.

ADVISORY COMMITTEE

An Advisory Committee to assist the Registry in long-range planning was appointed in 1969. Since that time the Committee has met three times and a fourth meeting is planned for September 1974. The original membership was composed of Dr. R. D. Evans, Dr. Lloyd M. Joshel, Dr. Wright H. Langham, Dr. C. C. Lushbaugh, Dr. Thomas F. Mancuso, H. M. Parker and Dr. James H. Sterner. Two changes have since been made. Mr. J. H. Hanes, Manager of the Rocky Flats Plant, replaced Dr. L. M. Joshel, whom he succeeded as Manager at Rocky Flats and Dr. L. H. Hempelmann succeeded the late Dr. Wright Langham, whose untimely death ended a career of great contribution in the field of radiation protection.

Cooperation was solicited from the AEC contractors at the Hanford Project and only after a year of successful operation of the Registry at Hanford without serious problems, were other AEC contractors asked to cooperate.

Methods used to tell employees about the program and useful forms were then made available to the other contractors and licensees.

PURPOSE AND SCOPE OF REGISTRY

As indicated in the original Schedule 189, Request for Operating Costs, the primary purpose of the Registry is to protect the interests of workers, employees and the public by serving as a national focal

point for the acquisition and provision of the latest and most precise information about the effects of the transuranic elements on man. This is being done by (a) establishing the population at risk. To date some 5700 workers have been so identified and registered. (b) Accumulation at the local projects, on a continuing basis, of the best current estimates of the amount and location of any internal deposition of any of the transuranium elements in employees and improving these determinations by reconciliation with actual burdens found in various organs at autopsy or by alternate methods. (c) Following such employees clinically and by epidemiological methods to determine whether there may be any adverse effects of such deposits on health or longevity and (d) Recording for correlation with other known pertinent environmental work exposures. After considerable discussion it has been decided that the transuranium worker population at risk to be included in the Registry is as follows:

A Transuranic Worker is defined as one:

1) who has a deposition of a transuranic element as a result of occupational exposure as evidenced by:
   a) confirmed positive results in urine, feces, or blood
   b) confirmed positive results based on in vivo examination
   c) confirmed positive nasal smears or nose blows.

2) or whose occupational activities present a reasonable opportunity to acquire internal deposition of any of the transuranium elements in quantities greater than might be expected to be found in persons who are not occupationally exposed to transuranic elements.

   These persons can normally be identified by subjective review of the work assignment for the individual. Typical criteria include:
   a) annual or more frequent routine bioassay examination
   b) annual or more frequent routine in vivo examination
   c) frequently exposed to airborne concentrations in excess of MPC

d) frequently required to wear respiratory protection as a result of work assignment involving plutonium
e) frequently required to wear lapel air sampler.

There may be some minor modifications in this, but this will not modify the program to any appreciable extent.

There are really two principal parts of the study. (1) A study of the employee at risk, during life and at autopsy to determine if any harmful effects may be related to the deposition of these elements and to compare depositions in the body, in organs and in tissues found at autopsy with depositions estimated before death based upon urinary and/or fecal assay and/or external measurements of lung or other organs. (2) The determination whether there is any statistically significant difference in the causes of death and in years lived by workers with small depositions of transuranium elements and these parameters in others who are as similar as possible in all respects except that they do not have a deposit of transuranium elements greater than that in the general population. At the Hanford Project, much environmental and medical data is available to the Registry from the AEC Health and Mortality Study. All Hanford employees, minus the transuranium workers, will serve as one control group for comparison of longevity and causes of death with the Registry's transuranium worker group at Hanford. Data on longevity of siblings are also available from the AEC Health and Mortality Study.

Causes of death and years lived by transuranium workers, who have relatively high depositions will be compared with these parameters in workers with low or no measurable depositions, who are of the same age and sex and who live under the same general economic conditions. Similar comparisons will be made with the general populations. Mr. Ray Buschbom, a statistician with Battelle Northwest, is presently working to improve the formal study design.

The Registry, in addition to gathering data, is providing information

to the cooperating agencies who contribute to its input data. The primary responsibility with respect to reporting and publishing accidents, case histories, methods of treatment, continued surveillance and correlation with autopsy results, remains with the originating participating health groups. The Registry places considerable importance in establishing and maintaining the reliability of all input data and especially that data related to the health physics aspects due to anticipated variations among the information sources.

EARLY ACTIVITIES

During the first year of Registry operation, some forty-five contractor and licensee facilities were identified and contacted because they operated facilities in which unencapsulated transuranium elements were handled. Cooperative working relationships were solicited with medical, health physics and management staffs of these facilities. Over the years visits have been made to the principal AEC contractors, in this category, namely five major contractors at Hanford, and the major contractor at Rocky Flats, Los Alamos, Mound, Oak Ridge and Savannah River.

Typical forms for collection of medical and health physics data were developed and made available to contractors. Other forms were developed for release of medical information to the Registry when considered necessary. Information regarding the Radium Registry at M.I.T. was secured.

A regular system of policy and information guides for regular communication with the various installations was established. Pertinent medical and health physics aspects of transuranium elements are maintained in the Registry library.

At Hanford, management notified employees concerning the Registry activities and asked them to consider individual cooperation with the Registry. Following this, transuranium workers at this project were identified. At the time of periodic examination, such workers were asked to (1) allow the Registry to use medical and health physics data concerning them and (2) to consider allowing an autopsy following death to study tissues for content of transuranium elements and for any evidence of

injury which might be related to such deposition. Five hundred dollars was allowed following receipt of such autopsy tissues. This amount was later reduced to $350.00. The contract with employees is for five years and is then subject to renewal. The date for the renewal of the first contracts is this year and renewals are now being solicited. Those who do not allow autopsy usually authorize the Registry to secure medical information. It is hoped to secure cause of death on all identified transuranium workers and estimated deposition of transuranium elements before death.

DEGREE OF COOPERATION

Since cooperation with the Registry is voluntary, efforts have been made to convince management of the various AEC contractors that complete cooperation with the Registry is to their advantage and in the best interest of employers and employees.

FULLY COOPERATING COMPANY

A fully cooperating company is asked to identify the population at risk, using the definition of a transuranium worker which applies to their situation and specifically differentiates such workers from non-transuranium workers. They are identified by name, social security number, date of birth, date of employment as a transuranium worker, dates of major depositions, if any, estimated systemic depositions and organ deposition where possible, brief medical history and physical examination records or summary and major industrial exposures. Active transuranium workers are told about the Registry and asked individually if they would like to cooperate by allowing use of medical data and permitting autopsies to determine organ deposition of transuranium elements and any injury which might be related to such deposition. Of course the identity of individuals whose data is used in public health types of studies and publications is kept strictly confidential. Information for the first twenty-six autopsy cases is tabulated in Appendix A.

Terminated transuranium workers who have an estimate of positive deposition by any method are identified and by agreement with the

cooperating company the Registry is usually asked to follow these people and secure as great a degree of cooperation as possible from them. If autopsy permission is not secured, at least the cause of death may be secured if the name and address are available or social security number and birth date are available.

Cooperation of the projects who have greatest potential exposure has been quite variable. Three of the four projects having greatest potential exposure are completely cooperating. These are the Hanford Project, Rocky Flats and Los Alamos. The fourth, Mound Laboratory (Monsanto Research Corp.) in Miamisburg is cooperating in a very limited manner as follows:

MONSANTO-MOUND LABORATORY

Names, social security numbers and when possible addresses at time of termination have been supplied for terminated transuranium workers and such employees have been contacted by the Registry by letter, when possible and asked to cooperate with the Registry. For active employees, all data to the Registry is submitted through the Atomic Energy Commission in a manner to cloak the identity of the employee during employment. Only estimated depositions considered to be significant (0.01 uCi) 25% of permissible body burden are submitted to the Registry.

Employees will not be asked for permission to do an autopsy before death and at the time of death, management will decide whether to request an autopsy or not. To date no autopsy has been secured through efforts of Mound Laboratory. One autopsy of a previous Mound Laboratory transuranium worker was secured through efforts of the University of Cincinnati. This compares with 30 autopsies secured to date by Rocky Flats and 12 by Hanford. About 25% of all of the high deposition cases are at Monsanto. Efforts will be continued to try to convince Monsanto to cooperate more actively.

SAVANNAH RIVER PARTICIPATION

Du Pont (Savannah River Project) will not allow request for cooperation with the Registry of either active or separated employees during life of the employee. At the time of death of an employee the Medical Director may request an autopsy if he deems it appropriate. To date no autopsies

have been secured. Social security numbers have been supplied on some 1500 active and terminated employees identified by social security numbers only. Since errors may occur in transcribing social security numbers or for other reasons, we have asked that the first six letters of the surname be supplied and if possible the birth date. In this group, of those who can be located, the cause of death may be secured through the Social Security Administration and the states and this may be related to the estimated deposition.

OAK RIDGE NATIONAL LABORATORY

There has been little exposure to plutonium at Oak Ridge but much exposure to various isotopes of uranium. Hence, management is very loath to create any anxiety in employees by asking for their concurrence in providing the Registry with medical and deposition data. Hence they will provide only social security numbers and health physics data on those with depositions of transuranium elements exceeding 25% of maximum permissible. They are supplying data to the AEC Health and Mortality Study and have no objection to the Registry securing any of this data. We have asked if they will identify the population at risk - those considered to be transuranium workers - by social security numbers. Considerable processing of americium and californium is being done at this project and hopefully those at risk may be registered and followed. Oak Ridge will presently agree to supply deposition data only on those considered to have a deposition of 25% of the permissible body burden of any transuranium element. The Registry may follow employees considered to have a deposition greater than 25% of the permissible body burden after termination of their employment with Oak Ridge National Laboratory.

Management of the Oak Ridge National Laboratory indicate that "if an occasion arises for one of our Medical Departments to obtain tissues from one of our employees who has a body burden of one of the transuranium elements, we may perform certain studies or submit the material to the Registry. We will maintain close liaison with the Registry in any studies that we perform."

WILLED BODIES

Because only small samples of bone, fat, muscle and skin are obtainable at autopsy, errors in determining the total content of such organs by assuming uniform distribution of the transuranium element and extrapolation, may introduce a rather large error. Since the concentration in muscle, fat and skin is usually low the importance is not so great as that of bone which is considered to be one of the critical organs. While arrangements have been made to handle such whole bodies, to date no individual with a reasonably high content of plutonium (25% of mpbb or more) has been obtained. We are urging all cooperating groups to try to secure consent for willed bodies.

SEPARATED EMPLOYEES

Retired or otherwise separated employees with a relatively large exposure or estimated burden of transuranium isotope are offered medical examinations on a periodic basis. Health physics examinations are offered when needed to better evaluate status.

AEC LICENSEES

At present the following AEC licensees are cooperating with the Registry: Exxon Nuclear Company, Inc. and Donald W. Douglas Laboratories. Recent solicitation of licensees was withheld on request but a more active program has now been started.

LOCALIZATION OF TRANSURANIUM ELEMENTS IN TISSUES

As human autopsy material is analyzed it becomes increasingly evident that the cumulative dose to individual organs and tissues is most important and to determine this, the microscopic deposition is needed. In the past, autoradiographic techniques applied to human bone samples have not been successful. Recently, the technique of fission fragment track production has been used to characterize the distribution of plutonium in bone in laboratory animals.[17,18,19] The neutron irradiation of very small quantities of plutonium produces fission fragments which bombard a polycarbonate film. Using track etching techniques, the fission tracks become visible on the film. This eliminates long exposure times for bone contaminated

With small quantities of plutonium and fading of the latent image. The Jee-Miller[20] technique produces autoradiographs with both fission fragment tracts and a corresponding bone image, with no requirement for section repositioning. Specimens are exposed to neutrons in the thermal column of the Ames Laboratory Research Reactor TV-1 Facility (ALRR), or the Massachusetts Institute of Technology Research Reactor (MITRR).[21] Neutron fluence in the range of 10^{15} to 10^{16} n/cm^2 is used. During irradiation the temperature must be kept below 32° C because higher temperatures will anneal the tracks. The finished film exhibits both the fission fragment tracks and a bone image. The present state of the art is such that good autoradiographic results are only obtained when the deposition is about 40 nCi total body. No technique has as yet been worked out to secure soft tissue images, so only bone samples are being processed. The Registry is supplying appropriate samples of bone, lung, tumor and other tissue to Battelle Northwest and to Dr. Jee for autoradiographic study. Battelle samples are irradiated at the Washington State University.

PRESENT AUTOPSY PROCEDURES

Since the number of autopsies are limited, efforts are made to secure the best possible information from these, keeping in mind that determination of transuranium content of each tissue or organ is costly. Routinely we advise securing both lungs, tracheobronchial and mediastinal lymph nodes, whole liver, sternum, ribs and part of vertebrae (about 500 grams), tissue surrounding a transuranium wound deposition, regional lymph nodes into which lymphatics drain from such a wound, some teeth if available, kidneys, spleen, thyroid, testicles or ovaries, both iliopsoas muscles, fat and skin. When it is estimated that the deposition is relatively large (>10% of mpbb) additional tissues are advisable in order that unexpected high concentrations may not be missed in organs and tissues usually not sampled such as heart, prostate, gastrointestinal tract, adrenals, etc. If malignant disease exists, a sample of tumor should be secured for bioassay. Bioassay of tissues is performed at

Battelle Northwest, Los Alamos Laboratories and Rocky Flats, and efforts continue to standardize results from these laboratories. Efforts are also made to make the autopsy program for people not working with transuranium metals comparable enough with that of the Registry program that this group may be used as one of the controls for the Registry mortality study.

INFORMATION COLLECTED

Attached as Appendix A is the material collected for the first twenty-six transuranium workers at risk, upon whom autopsies have been obtained and information supplied to the Registry. Some of this material has been key punched for data processing but a greatly expanded program of data processing is needed and will be started this fiscal year. An expanded effort is being made to convince contractors that improved evaluation of accidents involving inhalation of transuranium elements should be made at the time, so that such information as particle size, shape, chemical composition, etc. may be available for assistance in working out models representing metabolism in humans. Since such occasions are not frequent, every effort should be made to secure maximum information even though the expenses may be larger than that for other types of accident investigations. Only in this way will the autopsy findings be most useful and most helpful in determining the cumulative doses to the critical organs. As improvement in data becomes available for estimating organ doses this will result in changes in the data which is collected.

RELATIVE CONCENTRATION OF Pu IN TISSUES INFREQUENTLY SAMPLED

As indicated above, there has been an increase in the number of organs routinely sampled for bioassay. The basic group is lungs, tracheobronchial lymph nodes, liver and bone. In order to avoid missing a deposition, which might be significant, three autopsies have included tissues often not sampled, such as prostate, bladder, trachea and larynx, adrenal, aorta, gastrointestinal tract, brain stem, etc. These are shown in Table II. In these, concentrations were sufficient in tissues of low concentration so that results were reasonably accurate.

TABLE I

RELATIVE CONCENTRATIONS OF Pu IN TISSUES
Tissue Concentration ÷ Concentration in Tissue Having Maximum Concentration

Registry Cases	05TM Case #0005 **C.I. ^{239}Pu ^{238}Pu Metal and Oxide B.B. 42.8 nCi (Autopsy)	01TM Case #0004 **C.I. ^{239}Pu mixed Metal, Oxide, or Nitrate B.B. 0.27 nCi	01TM Case #0006 ***A.I. ^{239}Pu mixed Metal, Oxide, or Nitrate B.B. 42.24 nCi
	15 yr. of deposition in body	16 yr. of deposition in body	17 yr. of deposition in body
TracheoBron.Lym.Nodes	1 (34.2×10^{-2} nCi/gm*)	1.8×10^{-1}	1.2×10^{-1}
Abdominal Lymph Nodes	3.6×10^{-4}		
Lungs	6.4×10^{-2}	7.9×10^{-3}	3.6×10^{-2}
Bones	2.1×10^{-3}	5.0×10^{-2}	2.2×10^{-1}
Liver	1.1×10^{-2}	1-(1.71×10^{-4} nCi/gm*)	1-(6.3×10^{-3} nCi/gm*)
Thyroid	9.6×10^{-4}		
Kidneys	6.3×10^{-5}	1×10^{-2}	2.5×10^{-2}
Spleen		8×10^{-2}	3.8×10^{-2}
Testes	2.1×10^{-4}		2.8×10^{-2}
Muscle	1.2×10^{-4}		2.1×10^{-3}
Fat	8.5×10^{-5}		7.1×10^{-4}
Pancreas	2.0×10^{-4}		
Skin			6.6×10^{-3}
Prostate	1.5×10^{-4}		
Bladder	6.8×10^{-4}		
Trachea & Larynx	1.0×10^{-4}		
Adrenal	2.9×10^{-4}	2.1×10^{-2}	1.6×10^{-1}
Aorta	1.2×10^{-3}		
Stomach	3.4×10^{-4}		
Large Intestine	7.4×10^{-5}		
Small Intestine	5.7×10^{-5}		
Heart	2.0×10^{-4}	1.3×10^{-2}	1.5×10^{-2}
Brain		5.3×10^{-4}	
Brain Stem		1.8×10^{-3}	
Lowest Concentration	Small Intestine	Brain	Fat
Highest Concentration	TBLN	Liver	Liver
Ratio $\frac{\text{Lowest Conc.}}{\text{Highest Conc.}}$	5.7×10^{-5}	5.3×10^{-4}	7.1×10^{-4}

* = Actual concentration in nCi/gm
** = C.I. = Chronic Inhalation
*** = A.I. = Acute Inhalation

MORE SPECIFIC DATA ON Pu LOCATION

As indicated in the data collected in the first 31 autopsies, the concentration in uCi per gram is obtained by dividing the sample content of Pu by the weight of the organ or sample in grams, assuming that the distribution is uniform. Various methods are used to better determine actual organ distribution in order that cumulative dose may be more accurately estimated.

PLEURA AND LUNG

In one autopsy (01AT 0100) the concentration of Pu in a large specimen of lung, including pleura and subpleural parenchyma was 58 times that of another large single section of parenchyma alone (without pleura) of the same lung. To determine whether this might be due to a relatively high concentration in pleura, separate samples of lung and of pleura from another case were analyzed. In this case the concentration in pleura was little different from that of the lung parenchyma being 1.7×10^{-3} dpm per gram of pleura and 2.22×10^{-3} dpm per gram in lung parenchyma. This suggests that the difference in concentrations in various areas of the lung was a real one and not biased by relatively high concentration in the pleura. However, such sampling is needed in several cases to validate this assumption.

CONCENTRATION OF Pu IN MUSCLE

In four cases in which muscle was assayed for Pu the extrapolated muscle content in percent of total body burden was as follows: 4.5, 2.8, 2.6 and 0.5%. The total body burden in the four cases varied from 2.9 to 40 nCi. The deposits in muscle had no consistent relationship to whether the deposit was predominantly systemic or lung and lymph nodes or to the total deposition in the ranges indicated. Exposures occurred at Hanford, Rocky Flats and Mound, to high fired and regular oxides of Pu and to mixed metal, oxides and nitrates of Pu, with no apparent difference occurring in the amount of deposition in muscle. More samples of muscle are needed to determine if this trend will continue.

Pu DEPOSITION IN FAT

In two autopsies, the extrapolated content of body fat was 0.6% and 0.1% of the total body content of Pu. More samples are needed. A large single specimen of omentum composed mostly of fat contained 7.5% of the total body content of Pu, indicating a need for further testing of omentum to determine which of its components has the higher concentration.

SKIN DEPOSITION

It is not easy to secure a representative skin sample without marring the body. The axilla appears to be the best place to secure a sample. In one case extrapolating from a small axillary sample, the estimated skin deposition was 0.2% of the total body burden of Pu.

SOFT TISSUES

Muscle, skin and fat represent about two-thirds of the total weight of the body; and in the few cases checked they contributed an average of only about 3% of the total Pu deposition. More samples of these tissues are needed in autopsies in which the total deposit is relatively great, so that the accuracy of bioassay is good.

BLOOD

Since blood samples are relatively easy to secure during life, it seems more practical to follow this practice, rather than secure blood at autopsy, as collection then may not always be simple. At Hanford twenty-three individuals with the highest estimated depositions of Pu were recently sampled for Pu content in blood and urine and no correlation was found between the two. These employees were sampled at times following deposition ranging from nine to twenty-two years. Systemic deposition estimates ranged from 6 to 400 nCi. Blood concentrations of Pu ranged from 9.5×10^{-5} to 1.5×10^{-2} dpm per gram.

BONE

Accurate estimation of the Pu content of the skeleton presents the most difficult autopsy problem because the deposition is not uniform, is relatively large and the specimens obtainable are relatively small.

Fortunately, in the case of other possibly critical organs - lung and liver - whole organs are usually obtained. The important tracheobronchial and mediastinal lymph nodes are also usually obtainable. An effort is made to secure three or four ribs, the whole sternum and the anterior portion (about half) of three vertebrae. The weight of these samples is about 500 grams. Since the weight of the skeleton is 10,000 grams in a standard seventy kilogram man, the Pu content of a 500 kilogram sample would be multiplied by twenty to obtain the Pu content for an average man's skeleton. Table II shows concentration in sternum, ribs, vertebrae and two femurs obtained from thirty-one autopsies from four different projects. In Case 05TM 0005, there is some variation in concentration from one rib to another - the range being from 0.56 to 1.20. Ratio of concentration in rib to that in sternum was from 0.64 to 4.6 except for one exceptional case which had a value of 30. The ratio of concentration in vertebrae to that of sternum ranged from 0.94 to 3 in six cases while the seventh was 17. These autopsy findings indicate a considerable error in extrapolating from such samples to the total skeleton. Since the concentration of Pu in skin, fat and muscle is so much lower than that in bone, the errors due to extrapolation are not as important. Willed bodies, with sufficient bone content of Pu to be accurately measured are badly needed so that Pu content of major bones may be assayed separately and concentrations compared with that of the total skeleton. The content of easily attainable bones, such as ribs, sternum and vertebrae, could then be related to the average skeletal content of Pu to obtain a correction factor for use in all cases. This would greatly improve the reliability of extrapolating.

While there is a need to know total skeletal deposition, it is also essential to determine microscopic location of Pu in areas of high concentration.

Pu CONCENTRATION IN ORGANS

Concentrations of Pu in principal tissues, commonly sampled, together with average and standard deviations for seven autopsies from Hanford and one from Mound Laboratory, are listed in Table III. It was

TABLE II

CONCENTRATION OF Pu in BONE SPECIMENS IN 31 AUTOPSY CASES FROM PROJECTS VI, V, I, AND II (EXPRESSED IN DIS per MIN per G)

CASE	(1) STERNUM	(2) RIBS	(3) VERTEBRA	(4) FEMUR	RATIO Rib/St	RATIO Vert/St	RATIO Fem/St	Project
06UC 0001	0.17	-	0.16	0.97	-	.94	5.7	VI
05TM 0005	0.60	3 = 0.56 4 = 0.72 5 - 0.76 6 - 1.20 7 = 0.88 Av. = 0.82	1.60	Sec of Shaft 0.24 Head 0.91 Av. 0.58	1.4	2.8	1	V
01AT 0391	0.01	0.01	0.03	-	1.0	3		I
01TM 0002	-	1+4+5+6 = 0.008	0.003	-	-	-	-	
01TM 0006	1.7	1.4	-	-	0.82	-	-	
01JA 0023	0.004	0.00	0.00	-	-	-	-	
01AT 0227	-	0.0002	0.003	-	-	-	-	
01TM 0049	0.01	0.02	0.02	-	2	2	-	
01TM 0004	-	0.02	0.02	-	-	-	-	
01AT 0100	-	0.22	0.77	-	-	-	-	
02TM 0009	0.28	0.18	0.31	-	0.64	1.1	-	II
02D0 0237	0.02	0.03	-	-	1.5	-	-	
02D0 0713	0.085	0.107	1.45	-	1.3	17	-	
02D0 0712	0.002	0.00	-	-	-	-	-	
02D0 0711	-	0.015	-	-	-	-	-	
02D0 0709	0.00	-	-	-	-	-	-	
02D0 0710	0.00	-	-	-	-	-	-	
02D0 0002	-	0.171	-	-	-	-	-	
02D0 0001	0.008	0.037	-	-	4.6	-	-	
02D0 0003	0.005	0.148	-	-	30.0	-	-	
02D0 0036	7.20	-	-	-	-	-	-	
02D0 0235	0.009	0.00	-	-	-	-	-	
02D0 0049	0.04	0.00	-	-	-	-	-	
02D0 0355	0.007	0.034	-	-	5	-	-	
02D0 0444	0.014	0.00	-	-	-	-	-	
02TM 0002	0.027	0.028	0.06	-	1	2.2	1	
02AE 0006	0.003	-	-	-	-	-	-	
02D0 0449	0.00	0.00	0.008	-	-	-	-	
02D0 0627	0.002	0.00	0.00	-	-	-	-	
02D0 0629	0.00	-	-	-	-	-	-	
02D0 0622	0.00	0.00	0.00	-	-	-	-	
# SAMPLES	23	24	13	2	11	7	2	

02D0 0713 to 02D0 0622 taken by permission from Reference 2

TABLE III

AVERAGE CONCENTRATION OF Pu IN ORGANS
IN DPM PER GRAM PER MPSB** OF Pu

Case	T.B.L.N.	Lungs	Liver	Bone	Spleen	Kidney	Remaining*
01AT 0100	585	5.48	1.52	7.8	0.078	0.091	0.062
01TM 0004	9.85	0.44	65.9	2.8	4.56	0.735	0.029
01JA 0023	4.5	13.5	0	9.0	5	0	2
01TM 0049	0.176	0.0096	0.33	0.034	0.035	0.0038	0.0038
01AT 0227	6	.022	0.028	8			
01TM 0002	4.34	1.41	11.25	2.51	0.56	0.39	0.28
01TM 0006	1.58	0.48	13.3	2.72	0.40	0.23	0.0074
05TM 0005	1460	931	22.5	2.47		0.133	0.033
Ave.	258.9	119	14.6	4.4	1.77	2.1	0.3

* Concentration in the remaining tissues is taken as being that of the lowest positive concentration in organs sampled.

** Maximum permissible systemic burden.

felt desirable to make comparisons of average concentrations of this group with those from Rocky Flats.[16] However, the deviations are so great that such comparisons of average concentrations are not meaningful.

METABOLIC PARAMETERS

Based upon animal studies, it appears that route of entry, particle size, physical and chemical composition of particles and elapsed time following deposition are important parameters in determining residence time of Pu in various organs. The deposition particles inhaled in AEC industrial and laboratory practice may be assumed to behave as polymeric ($>$0.01 uM in diameter) unless proven otherwise. In industrial practice these factors are often difficult to determine, but their significance is such as to warrant a considerable investment of funds and talent to obtain the best possible estimates at the time of occurrence of accidents involving human internal deposition of the transuranium elements.

PLUTONIUM IN TUMORS

Physicians, seeking to determine if radioactive depositions in the body caused a primary malignant disease, sometimes ask if the radioisotope that the deceased was potentially exposed to, was found in high concentration in the primary tumor. Most scientists feel that the likelihood of such a finding is small. The reasoning is that if the radioisotope was present in the original one or small number of cells, that became malignant, such cells after millions of divisions to form a tumor, would have the concentration greatly reduced, unless malignant cells preferentially concentrate the isotope later acquired by more exposure from outside the body or transfer from other body organs. This has not been found to occur in animal studies.

In a terminal cancer case, injected with radioactive Sulfur-35, highest concentration at autopsy thirteen days later was found in cancer of the breast and in the bone marrow.[21] Gottschalk et al.[22] also found a relatively high concentration of ^{35}S in tumor tissue (chondrosarcoma) and in bone marrow and a rapid turnover in most tissues. In such cases, apparently the Sulfur-35 did not cause the

malignancy, but the malignant cells were a favored site of deposition - at least for a relatively short time. It is not expected that Pu would behave in this manner since there is no reason to expect it to enter into the metabolic processes of the cell.

In one Registry case (05TM 0005), the concentration of Pu in one of the undifferentiated tumors in the lung was about the same as that in the lung tissue. There were generalized metastases of cells which were of epithelial and spindle type. The primary site of the malignancy was not evident at the autopsy. Efforts are being made to secure tissue for neutron activation autoradiographic studies to try to determine if the Pu is actually in the tumor cells or is in other compressed tissue surrounding the tumor as had been the case in animal studies at the Hanford Project.

SYSTEMIC Pu BURDENS
AUTOPSY FINDINGS vs. ESTIMATES FROM URINE

In Table IV systemic Pu burdens determined from autopsy findings are compared with systemic burdens estimated from the output of Pu in urine in thirty cases. Plutonium in lung, tracheobronchial lymph nodes and wounds is not included in the systemic burden since these may not be estimated by urine sampling with much confidence. These may be measured separately with a lung counter and a wound counter under usual conditions with a higher degree of accuracy.

Projects differ some in the levels of Pu which may be detected in the urine, depending upon the level of background measurements in the bioassay laboratories. From Table IV it may be seen that in all autopsies in which a determination of a systemic burden of Pu greater than 1.6 nCi (4% of maximum permissible), the estimates before death from urinalysis were higher by factors ranging up to 6.7. In thirty cases, highest organ concentration occurred the following number of times: TBLN - 12, lungs - 6, liver - 6, axillary lymph nodes - 1 (wound deposition case), abdominal lymph nodes - 1, muscle - 1, pancreas - 1, spleen - 1 and thyroid - 1. In cases where muscle, thyroid and pancreas were the organs having highest concentration the systemic deposition was so

TABLE IV

COMPARISON OF SYSTEMIC BURDEN ESTIMATES - URINALYSIS vs. AUTOPSY

Case Designation	Age at Death	Cause of Death	Project	Autopsy %MPSB (40 nCi)	Urine %MPSB	Ratio Est-Urine / Est-Autopsy	Organ with Maximum Concentration of Pu
01AT 0100		Coronary Infarction	I	6.4	40	6.3	T.B.L.N.
01TM 0004		General Debility - Coronary Insuf.		.68	3.4	5.0	Liver
01AT 0391		Carcinoma (Bronchogenic)		0.55	min	min / 0.55	Muscle
01TM 0002		Multiple - Emphysema-Atherosclerosis		.16	1	6.3	Liver
01TM 0006		Ischemic Heart Disease		105	90	0.86	Liver
01JA 0023		Bronchogenic Carcinoma		.02	min	min / 0.02	Pancreas
01AT 0227		Coronary Infarction		.15	min	min / 0.15	T.B.L.N.
01TM 0049		Suicide		.63	min	min / 0.63	Liver
05TM 0005		Undifferentiated CA - Primary site undetermined	V	110*	200*	1.8	T.B.L.N.
02D0 0713		Acute Myocardial Infarction	II	2.3	13.5	5.9	T.B.L.N.
02D0 0712		Acute Myocardial Infarction		0.3	0	0 / 0.3	Lungs
02D0 0711		Acute Myocardial Infarction		0.4	0	0 / 0.4	T.B.L.N.
02D0 0709		Methanol Poisoning		3.8	0	0 / 3.8	Spleen (Lung lost)
02D0 0710		Brain Tumor (Astrocytoma)		0.9	0	0 / 0.9	Lungs
02D0 0002		Carcinoma of Bladder		3.8	8.0	2.1	Lungs
02D0 0001		Suicide		1.75	< 3.0	< 3.0 / 1.75	T.B.L.N.
02D0 0003		Cancer of Stomach		1.2	0	0 / 1.2	T.B.L.N.
02D0 0036		Complications of Heart Surgery		156.0	541.0	3.5	Liver

Case Designation	Age at Death	Cause of Death	Project	Autopsy %MPSB (40 nCi)	Urine %MPSB	Ratio Est-Urine / Est-Autopsy	Organ with Maximum Concentration of Pu
02D0 0235		Chronic Lymphatic Leukemia		0.3	0	0/0.3	Lung
02D0 0040		Suicide		1.5	5.4	3.6	Axillary L.N.
02D0 0355		Cardiac Embolism Pulmonary		2.0	6.4	3.2	Lung
02D0 0444		Acute Lymphoblastic Leukemia		0.5	0	0/0.5	T.B.L.N.
02TM 0002		Ruptured Aneurysm		1.3	<3.0	<3.0/1.3	Liver
02AE 0006		Adenocarcinoma - Bronchus & Lung		0.6	0	0/0.6	T.B.L.N.
02D0 0449		Myocardial Infarction		0.3	0	0/0.3	T.B.L.N.
02D0 0627		Melanoma - Primary Site Undetermined		0	0	Bkg./Bkg.	T.B.L.N.
02D0 0629		Adenocarcinoma of Kidney with Metastases		0.6	0	0/0.6	T.B.L.N.
02D0 0622		Auto Accident		0	0	0/0	Lung
02TM 0009		Cirrhosis of Liver Liver		8.7	19	2.2**	Abdominal Lymph Nodes
02D0 0237		Myocardial Infarction with Ventricular Wall Rupture		0.23	0	0/0.23	Thyroid

** Pre-autopsy estimate of lung and T.B.L.N. deposit was zero while at autopsy 9.2 nCi were found

* Total body deposition. Lung deposition at autopsy - 27.08 nCi, T.B.L.N. - 1.33 nCi

min = minimum systemic deposition - <0.2 dpm in daily urine sample.

minute as to make the probable error of individual sample determination very great.

CAUSES OF DEATH

From Table IV it may be seen that the usual causes of death were encountered. Some of these were discussed in a previous paper.[13] There were two cases of lymphatic leukemia, 02D0 0235 and 02D0 0444. Case 02D0 0235 was one of chronic lymphatic leukemia which has not been associated with radiation exposure in animals to date or in the Nagasaki, Hiroshima cases. The deposition of Pu found at autopsy in both of these cases was extremely low, being less than one percent of the permissible (40 uCi). Case 05TM 0005 was discussed under "Plutonium in Tumors" and will receive further study. Table V indicates progress made to date in securing authorizations and completing autopsies.

CUMULATIVE ORGAN DOSE DUE TO DEPOSITED Pu

In the development of models to represent metabolism of Pu in humans, it is important to relate the content of organs at given times following its introduction into the body to the initial deposit. Such determinations are made in laboratory animals, following sacrifice at varying times following introduction of Pu of measured particle size and chemical composition. As humans, bearing Pu come to autopsy it is important to have as much of this kind of information as possible. For example at Rocky Flats, several employees received measurable depositions of high fired plutonium oxide due to a fire involving plutonium. Size of the particles in the vicinity were measured. A good place to collect representative particles breathed by a person is on the face of the person. As such employees come to autopsy, organ depositions may be related to the inhalation of Pu particles of this chemical composition and size. As enough data are collected to relate organ deposition at varying times to initial deposit it should be possible to roughly estimate organ dose, assuming uniform distribution.

TABLE V

U. S. TRANSURANIUM REGISTRY
AUTOPSY STATISTICS JUNE 1974

	Transuranium Workers Identified		Health Physics and Medical Releases		Authority for Autopsy		Autopsies Obtained		Autopsy Reports Complete	
	FY 1974	Total to Date	FY 1974	Total to Date	FY 1974	Total to Date	FY 1974	Total to Date	FY 1974	Total to Date
Hanford	68	2199	63	2132	23	525	4	12	1	8
Rocky Flats	110	1504	109	1489	10	167	4	30	0	21
Los Alamos	19	259	18	259	15	127	0	1	0	0
Savannah River	0	1559	0	0	0	0	0	0	0	0
Mound	0	322	0	0	0	0	0	1	1	1
Oak Ridge	0	0	0	0	0	0	0	1	1	1
Total	197	5843	190	3880	48	819	8	45	3	31

As detailed studies indicate concentration factors, these may be applied to determine equivalent dose in rems. Since no suitable isotopes of Pu are available for human experimentation, such methods of human study, while very slow and costly, appear to be the only way to secure good human data.

SUMMARY

This report gives some of the highlights of the U. S. Transuranium Registry since its inception in late 1968 together with more detailed information concerning the activities for the year ending April 30, 1974. Articles are referred to which describe autopsy studies to determine plutonium body content, performed since 1949 for the purpose of evaluating plant health safety programs. The purpose of the Registry is described and its administrative direction is discussed. The Registry is a data collecting agency whose success depends upon how well the data is collected by the cooperating agencies. The varying degree of cooperation of the participating companies is described. This largely depends upon the philosophy of top management and is very variable. To date some 5700 workers have been identified as transuranium workers and registered. Estimates of deposition of transuranium elements in these workers are recorded and when autopsies are obtained, these estimates are compared with autopsy measurements of organ content. Efforts are made to determine any adverse effects of the transuranium elements in workers, during life and at autopsy. Causes of death and years lived following deposition of transuranium elements are compared with these parameters in control groups, not exposed to the transuranium elements. Any available information needed which has been collected by the AEC Health and Mortality Study is available without duplication of efforts.

Information obtained by the Registry is made available to the participating agencies. Eight hundred twenty-one transuranium workers have given permission for autopsy. This number is increasing as more licensee agencies are being solicited to cooperate and as the transuranium program expands.

Willed bodies of transuranium workers with appreciable body deposition are needed to determine the transuranium content of all bones in order to minimize the error due to extrapolation from small samples to the total skeleton.

Separated employees are usually followed by the Registry, cooperation solicited and necessary health physics and medical examinations done.

A greater effort is being made to determine the exact histologic location of transuranium elements by radioautographic studies in which the tissues are exposed to thermal neutrons to produce fission tracts and speed up the otherwise very slow ionization tract formation. Autopsy material collected includes whole lungs, tracheobroncial lymph nodes, whole liver, sternum, rib and part of three vertebrae, kidneys, spleen, tumors, thyroid, gonads, muscle, fat. Other organs are occasionally secured to gradually increase knowledge of all important tissue depositions.

Measurement of organ content of transuranium elements is made at Battelle Northwest Laboratory, Los Alamos and Rocky Flats and efforts continue to standardize results.

Information collected by the Registry on each autopsy case is shown in Appendix A. Data is verified and prepared for data processing. In time it is hoped that cumulative organ doses may be calculated from the autopsy findings. Autopsy systemic deposition is compared with estimates based upon urine excretion, body counts and other methods, in an effort to improve such estimates during life.

To date organs found to have highest concentrations of plutonium are tracheobronchial lymph nodes, lungs and liver, with highest concentrations occasionally in other organs. Registry efforts are closely coordinated with the Battelle Northwest histological studies to orient the Registry operations in such a way as to secure the most needed information to aid in the determination of the metabolism of the transuranium elements in man. Plutonium concentration in malignant tumors is being studied. In the first thirty-one autopsies studied it is not felt that the cause of death was related to plutonium deposition. It is planned that thousands of transuranium workers will eventually be compared with non-transuranium workers, as to causes of death and years lived following an estimated deposition of transuranium elements. A rather large difference would have to be present to be statistically significant. The Registry program is the most sensitive method known of answering the question - is the

health of workers with small deposition being adversely affected? This becomes more important with the increasing use of plutonium in power production.

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