



Beryllium in the Tissues of Weapons-site Workers

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*“Learning from Plutonium and Uranium
Workers”*

National Plutonium Registry – The USAEC Vision



The US Transuranium Registry (USTR)

UNITED STATES TRANSURANIUM REGISTRY
SUMMARY REPORT JULY 1, 1974 TO OCTOBER 1, 1975
TO ERDA DIVISION OF BIOMEDICAL AND
ENVIRONMENTAL RESEARCH

by

W. D. Norwood, M.D. and C. E. Newton, Jr.

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.



The U.S. Transuranium & Uranium Registries – FY2008

Washington State University College of Pharmacy United States Transuranium & Uranium Registries

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Mission of the USTUR

The mission of the USTUR is to study the uptake, translocation and retention (biokinetics) and tissue dosimetry of uranium, plutonium, americium, and other actinides in occupationally exposed humans (workers), over their whole lifetime (from exposure through full lifespan), and to serve as a national and international resource for testing and improving the application of excreta monitoring and other contemporary bioassay data to predict tissue dose rates measured at autopsy. These studies are fundamental to evaluating and improving the reliability of, and confidence in, both prospective and retrospective assessments of tissue doses and risks from intakes of actinide materials through inhalation, ingestion, or contaminated wounds.



This page was last updated on November 26, 2007. ustunwebmaster@tricity.wsu.edu

USTUR Website – Stacey McCord MS (Webmaster)

Washington State University College of Pharmacy
United States Transuranium & Uranium Registries

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The National Human Radiobiological Tissue Repository

Resources for Radiation Dosimetry and Biological Effects

The National Human Radiobiological Tissue Repository

The NHRTR is one component of the United States Transuranium and Uranium Registries (USTUR). It contains frozen tissues, tissue solutions, microscope slides, and paraffin blocks that were collected by the USTUR at the autopsy of workers with documented intakes of plutonium, americium, uranium, and thorium.

The NHRTR is a Great Resource

The samples in the NHRTR are available to qualified scientists who are interested in conducting studies of localized tissue doses, studies of micro-distribution of the actinide elements, or studies of radiation induced molecular changes.

The NHRTR archives thousands of solutions containing acid dissolved tissues from each USTUR case. These solutions are available to qualified scientists for further research.

The NHRTR Collection is Unique and Well Documented

USTUR, Washington State University
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This Presentation

- Introduce USTUR Registrant Program (DOE Grant to WSU)
 - Sample scope and tissue donor status
- Co-exposure to Actinides and Beryllium
 - Self-reporting IH exposures
- National Human Tissue Repository (NHRTR)
 - Specimen storage/Inventory database
- Internal Database and Web Publication of Case Data
 - Health Physics/Radiochemistry/**Pathology**.
- Beryllium Biokinetics (ICRP Systemic Metabolic Model)
 - Qualitative/quantitative analysis of Be in tissues
- Conclusions – Application of NHRTR tissues/USTUR IH data?



USTUR Registrant Status (October 31st, 2008)

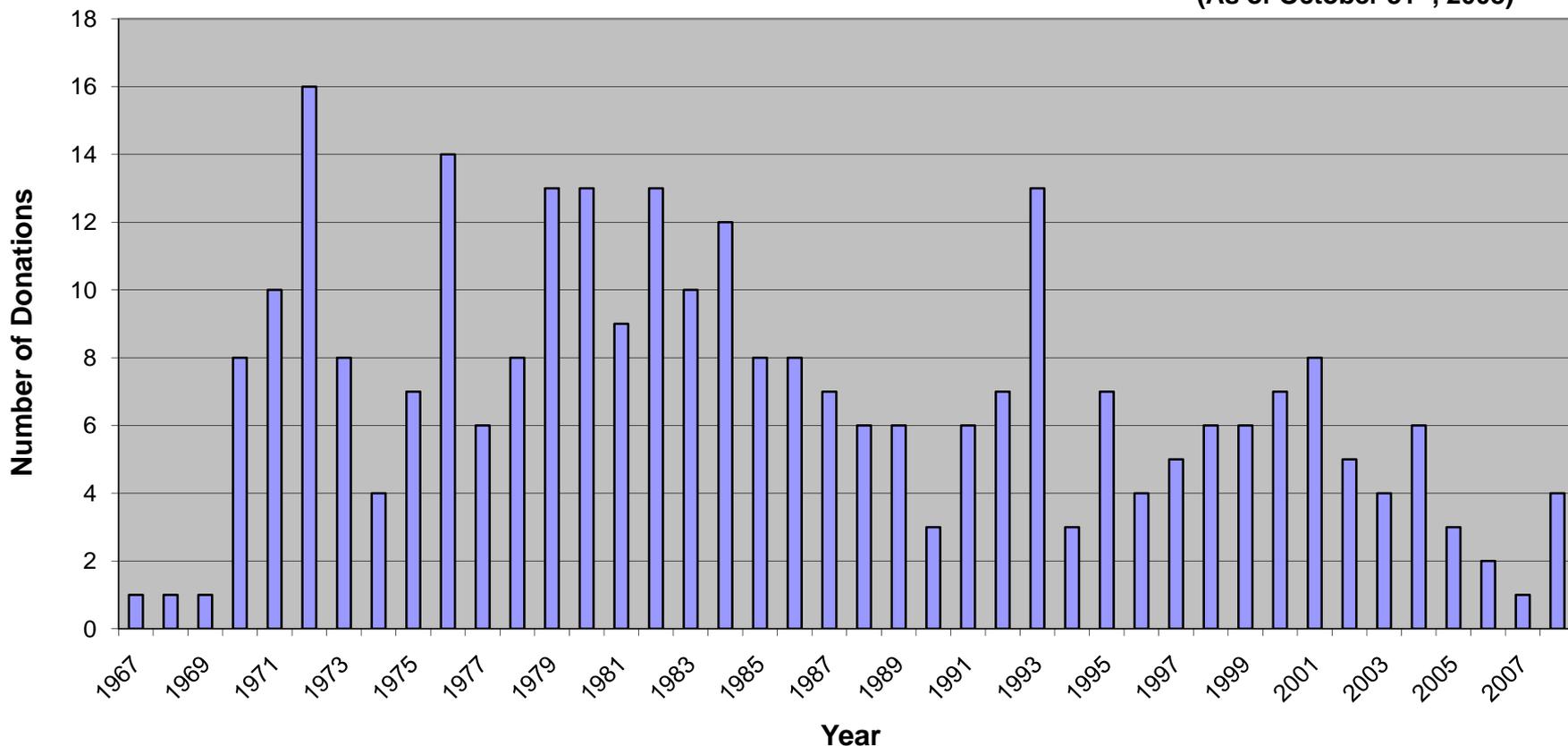
<u>Total Active (Living) and Deceased Registrants:</u>	<u>423</u>
Living Registrants:	94
Potential Partial-body Donors:	73
Potential Whole-body Donors:	14
Special Studies:	7
Deceased Registrants:	329
Partial-body Donations:	289
Whole-body Donations:	35
Special Studies:	5



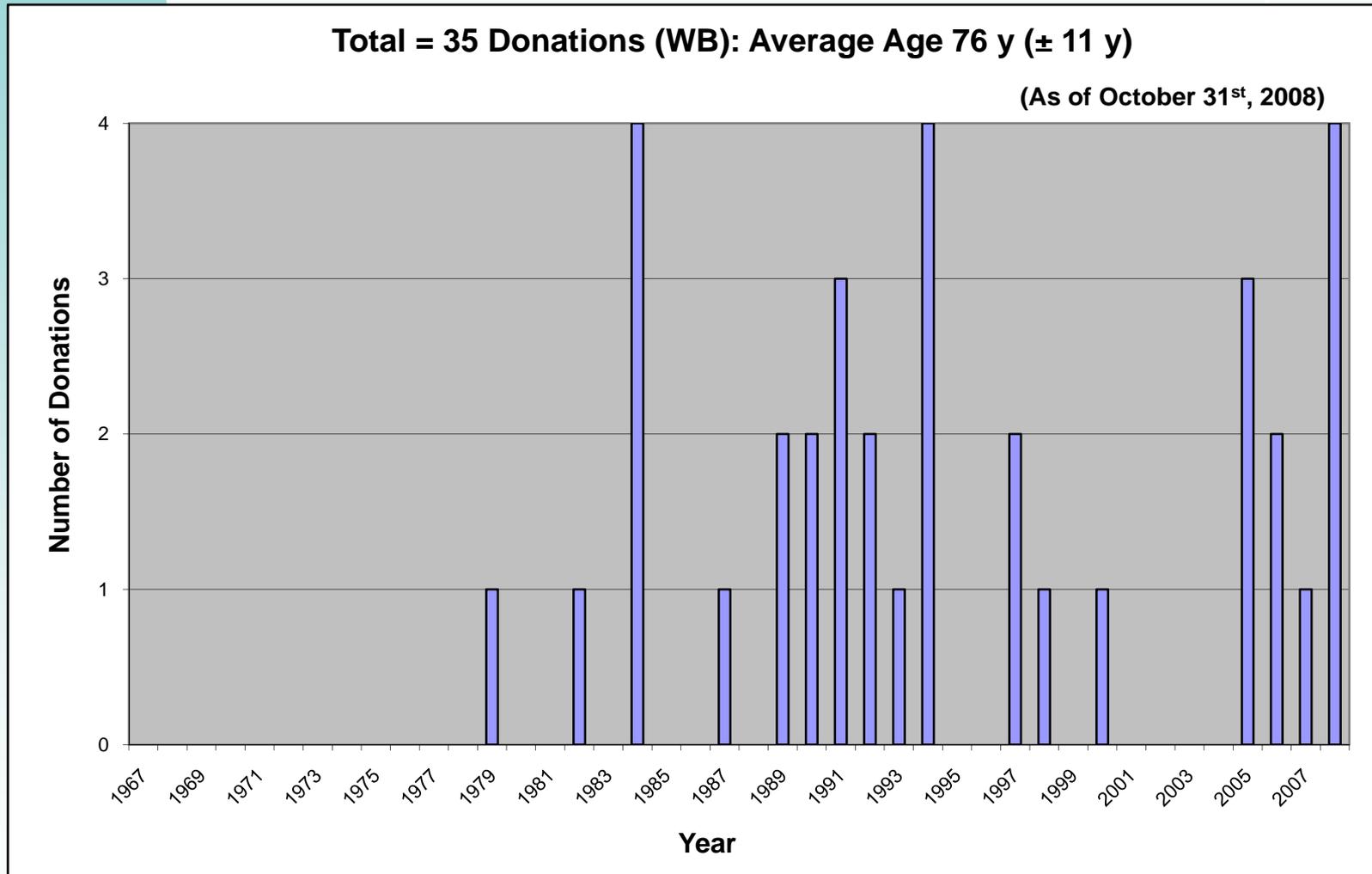
The Registries: Historical Profile of Partial Body Donations (Routine Autopsy Cases)

Total = 289 Donations (RO): Average age = 67 y (± 12 y)

(As of October 31st, 2008)



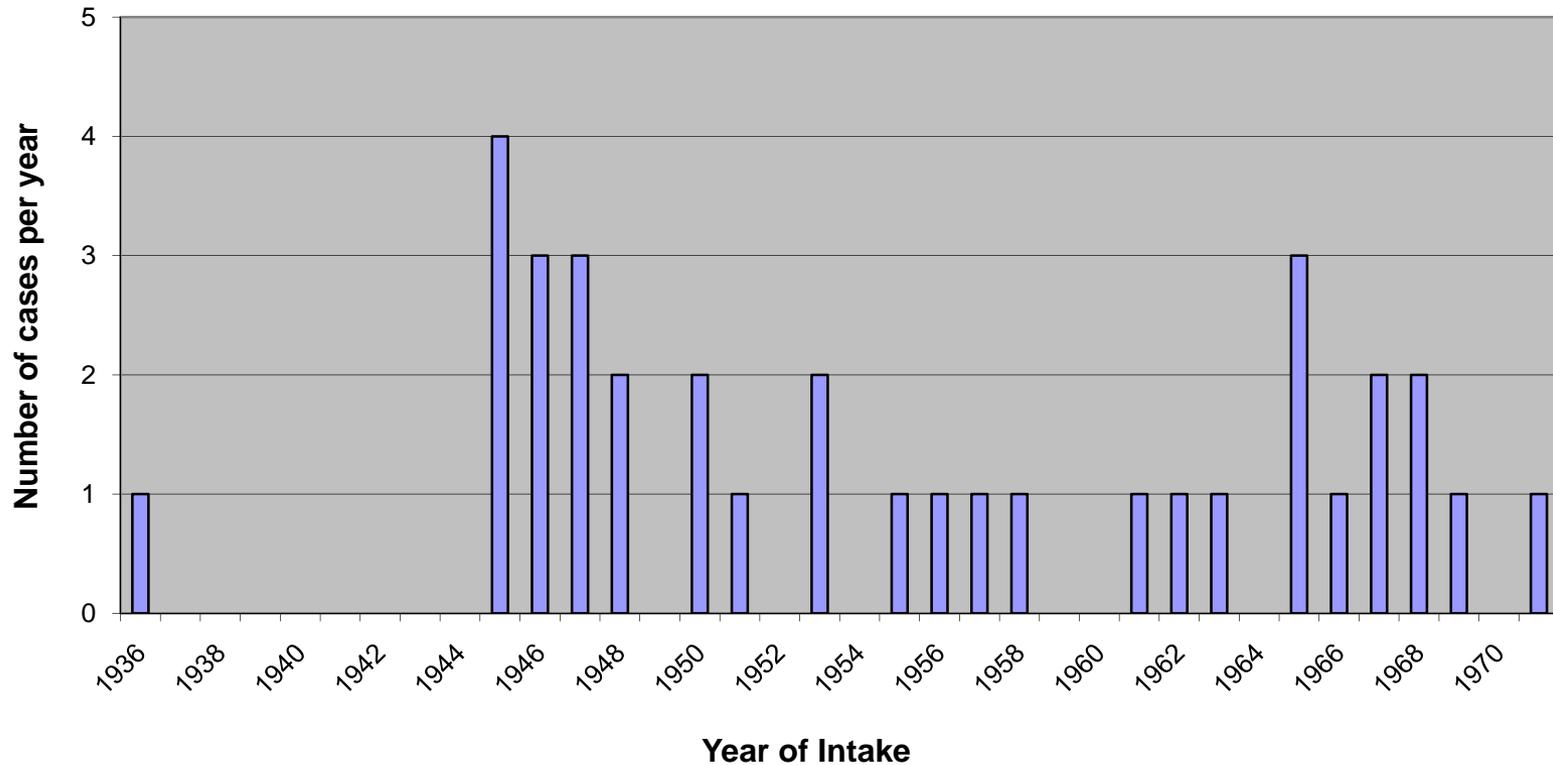
USTUR: Historical Profile of **Whole Body Donations**



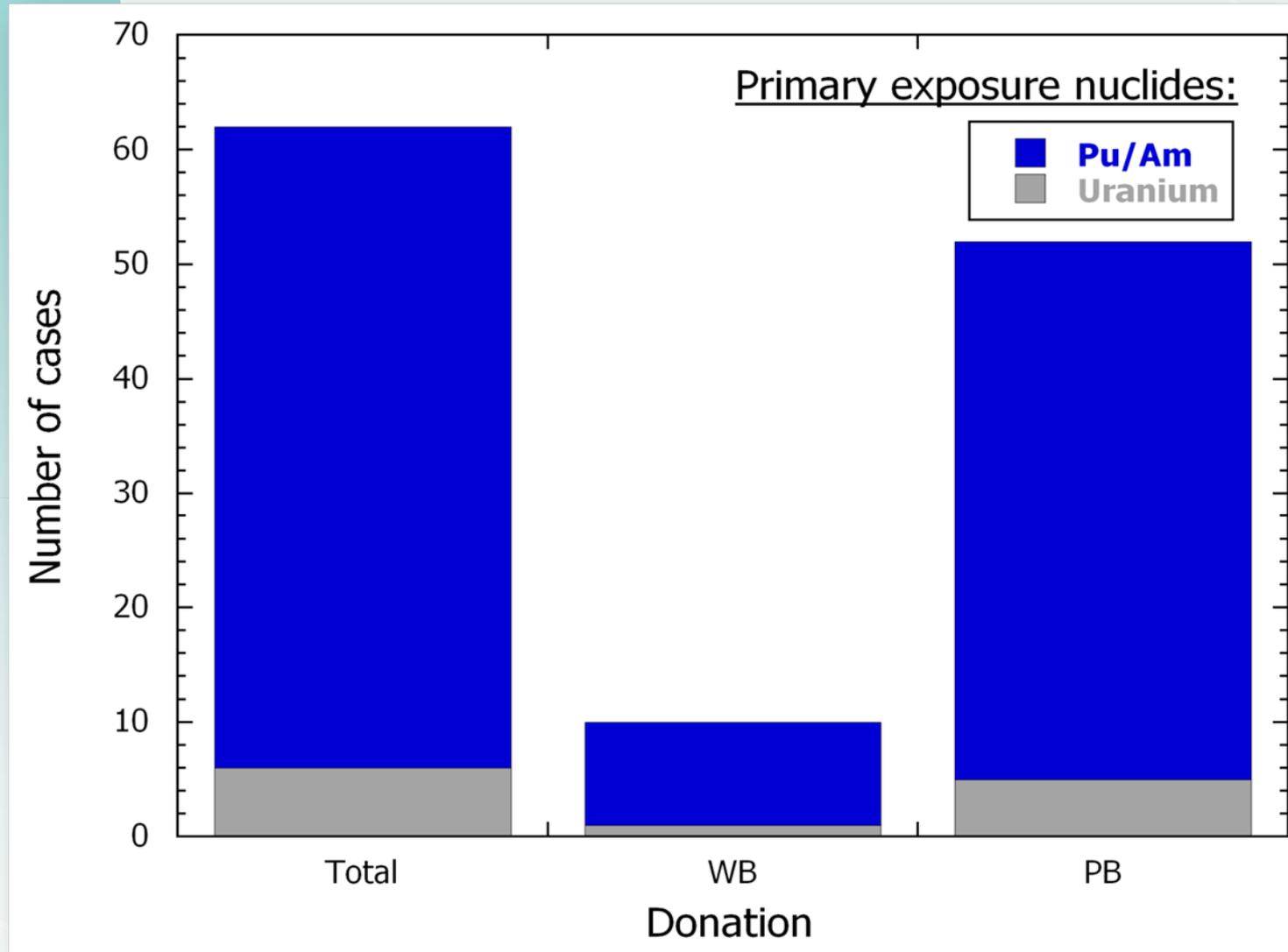
Year of Actinide Intake for Whole Body Donors

Average follow-up 40 y (± 12 y) - Cumulative follow-up 1392 person-y

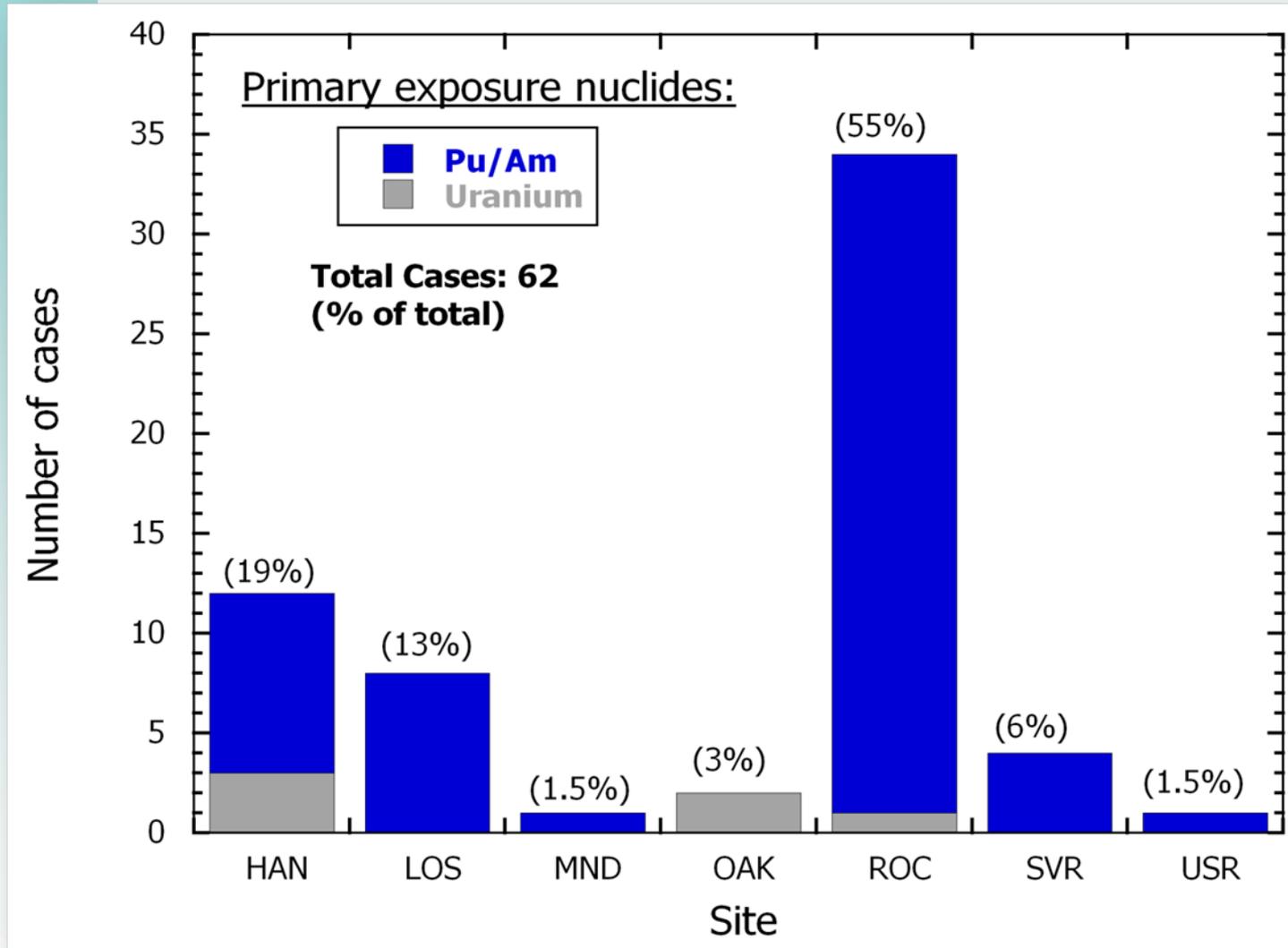
(As of October 31st, 2008)



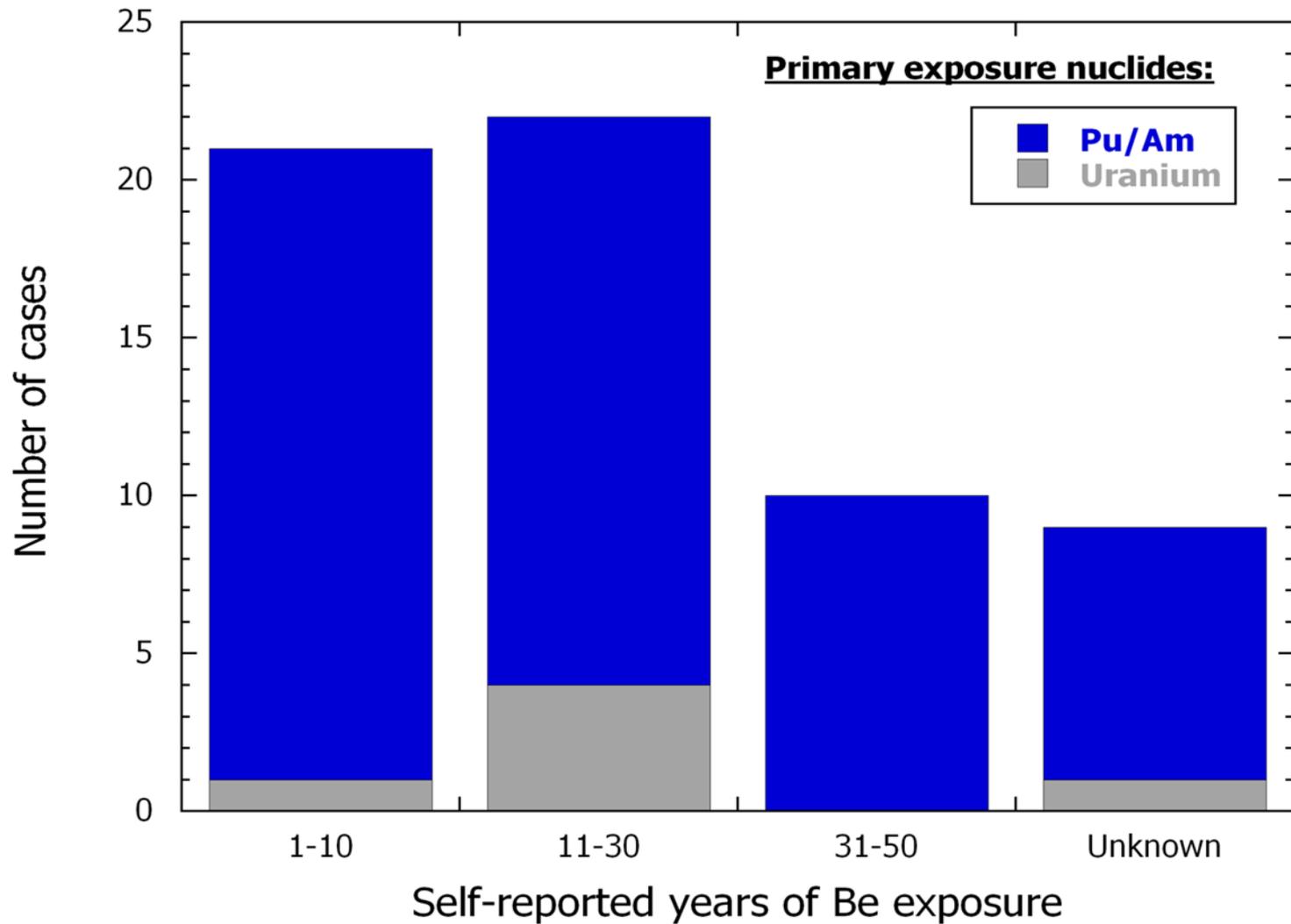
USTUR Donors With Self-Reported Be Exposure



USTUR Donors With Self-Reported Be Exposure (By Site)

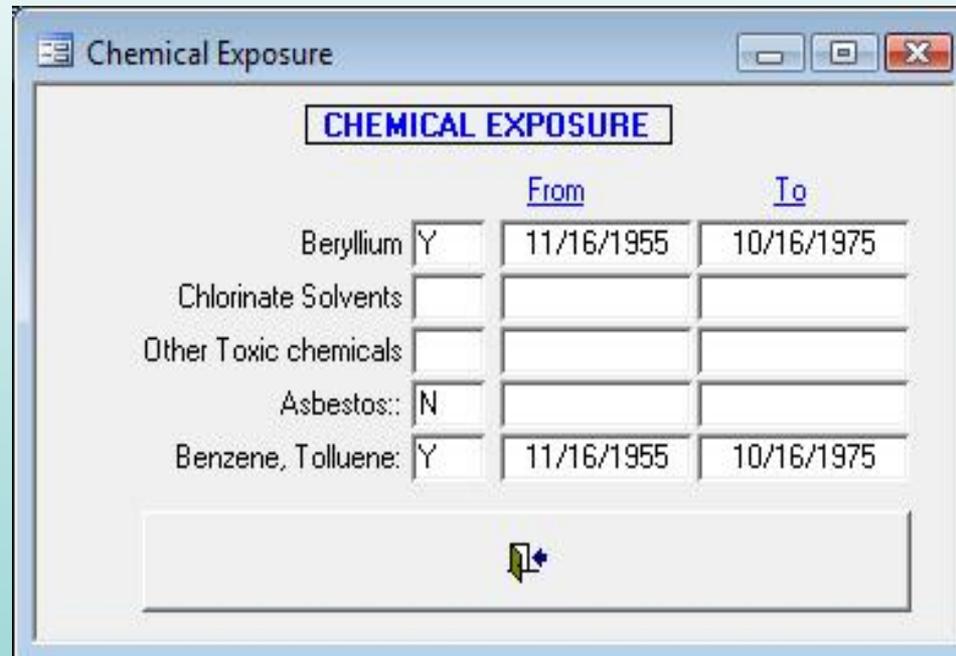


USTUR Donors' Self-reported Years of Be Exposure



USTUR Internal Database – “Chemical Exposure” Form

- This indicates each Registrant’s **potential** exposure to chemical hazards, e.g., beryllium, asbestos
 - **Caveat: data are taken directly from self-reported exposure questionnaire – NOT (yet) verified by industrial hygiene records**



The screenshot shows a window titled "Chemical Exposure" with a table of exposure data. The table has columns for chemical names, a response (Y/N), a start date (From), and an end date (To). Below the table is a scroll bar.

		From	To
Beryllium	Y	11/16/1955	10/16/1975
Chlorinate Solvents			
Other Toxic chemicals			
Asbestos::	N		
Benzene, Toluene:	Y	11/16/1955	10/16/1975

Critical Need for Confirmatory IH Records

- Historically 'non-specific' questionnaire (e.g., for Case 0846)

Original Registration (1995 Form)

Have you ever worked or been exposed to any of the following:

Beryllium Yes No Asbestos Yes No Benzene, Toluene Yes No

Chlorinated Solvents Yes No Other Toxic Chemicals Yes No

Dates (From - To) _____

USTUR/DOE has formally requested IH records for all Registrants - 55 received to date!

Re-registration (2005 Form)

Medical Exposure History

Have you ever worked or been exposed to any of the following:

	no	yes	no	dates(from-to)
Beryllium	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Asbestos	<input type="checkbox"/>	<input type="checkbox"/>		
Chlorinated Solvents	<input type="checkbox"/>	<input type="checkbox"/>		
Benzene, Toluene	<input type="checkbox"/>	<input checked="" type="checkbox"/>		11/55 / 1-67
Other Toxic Chemicals	<input type="checkbox"/>	<input type="checkbox"/>		



E.g., Case 0846 – High Level Chronic $^{241}\text{AmO}_2$ Inhalation (Chelated) + Be



NHRTR – FY2008: THEMIS™ Bar-coded Sample Inventory Chain of Custody/Database System



The Management Information System (THEMIS™)

- Assigns a unique barcode to each individual sample.
- Records a sample's mass or volume.
- Tracks the sample's current location as it is moved within the NHRTR facility (e.g., from one freezer to another).
- Tracks the sample's location as it is 'shipped' to an external laboratory for radiochemical analysis.

The image displays two overlapping windows from the THEMIS software. The top window, titled 'Sample Info', shows details for USTUR Case # 0846, USTUR Sample # 023, and Sample Barcode 08000044. It includes fields for Collection Class (NHRTR), Collection (USTUR), External Case # (n/a), Current Location (HALL FREEZER 1), Date Received (4/8/2008 2:31:52 PM), By (Stacey L. McCord), From (DMS), Description (desc), Seal Pack (Clear Plastic Bag), Mass Type (Autopsy), Sample Type (Tissue - Autopsy), Tissue Type (Gland), Tissue (Pancreas), Acid Type, Amount (126.6 g), and Comments (dissected into pieces for fixation). The bottom window, titled 'Sample History', shows a list of movements for the same sample. It includes fields for USTUR Case # (0846), USTUR Sample # (023), Sample Barcode (08000044), Collection (USTUR), and Description (desc). The history table shows the following entries:

Released To:	Received From:	Custody Date:
HALL FREEZER 1	HALL FREEZER 2 - STACEY L. MCCORD	4/11/2008 10:20:40 AM
HALL FREEZER 2	C08000005 (HALL FREEZER 1) - STACEY L. MCCORD	4/11/2008 10:19:30 AM
C08000005 (HALL FREEZER 1)	HALL FREEZER 1 - Stacey L. McCord	4/8/2008 3:01:56 PM
Stacey L. McCord - HAND DELIVERED	Accessioned Container C08000005	
DMS	Stacey L. McCord - HAND DELIVERED	4/8/2008 2:31:52 PM
	Container Entered	

The bottom window also shows a record count of 5 of 7 (Filtered) and a 'Form View' button.

USTUR Internal Database – Pathology

Search Pathology

Case Number Search

Search Pathology

Case Number Search

ICD Search Results

Case No	Relation to Death	ICD-9-CM	Description	Source	ICD-10	Description	Source
▶ 0013	0	199.0	Malignant neoplasm without specification of site: Disseminated	D	C45.9	Mesothelioma: Mesothelioma, unspecified	D
0084	0	163.9	Malignant neoplasm of pleura: Pleura, unspecified	D	C45.0	Mesothelioma: Mesothelioma of pleura	D
0161	1	199.1	Malignant neoplasm without specification of site: Other	A	C45.9	Mesothelioma: Mesothelioma, unspecified	A
0256	0	163.9	Malignant neoplasm of pleura: Pleura, unspecified	D	C45.0	Mesothelioma: Mesothelioma of pleura	D
0648	0	163.9	Malignant neoplasm of pleura: Pleura, unspecified	a	C45.0	Mesothelioma: Mesothelioma of pleura	A
0677	0	162.9	Malignant neoplasm of trachea, bronchus, and lung: Bronchus and lung, unspecified	A	C45.7	Mesothelioma: Mesothelioma of other sites	A
1040	0	163.9	Malignant neoplasm of pleura: Pleura, unspecified	D	C45.0	Mesothelioma: Mesothelioma of pleura	D

Pathology Database – Case Report

Example Pathology Report for Case 0002



Pathology Report

*United States Transuranium and Uranium Registries
Washington State University - Tri-Cities*

Case No: 0002

ICD-9-CM and ICD-10 codes

<i>Relation*</i>	<i>ICD-9-CM</i>	<i>Source</i>	<i>Description</i>	<i>ICD-10</i>	<i>Source</i>	<i>Description</i>
0	434.91	D	Occlusion of cerebral arteries: Cerebral artery occlusion, unspecified: with cerebral infarction	I63.9	D	Cerebral infarction: Cerebral infarction, unspecified
1	436	D	Acute, but ill-defined, cerebrovascular disease	I64	D	Stroke, not specified as haemorrhage or infarction
2	414.00	D	Other forms of chronic ischemic heart disease: Of unspecified type of vessel, native or graft	I25.1	D	Chronic ischaemic heart disease: Atherosclerotic heart disease
3	599.0	D	Other disorders of urethra and urinary tract: Urinary tract infection, site not specified	N39.0	D	Other disorders of urinary system: Urinary tract infection, site not specified
4	564.7	A	Functional digestive disorders, not elsewhere classified: Megaecolon, other than Hirschsprung's	K57.9	A	Diverticular disease of intestine: Diverticular disease of intestine, part unspecified, without perforation or abscess
5	424.1	A	Other diseases of endocardium: Aortic valve disorders	I35.8	A	Nonrheumatic aortic valve disorders: Other aortic valve disorders
6	515	A	Postinflammatory pulmonary fibrosis	J84.1	A	Other interstitial pulmonary diseases: Other interstitial pulmonary diseases with fibrosis
7	492.8	A	Emphysema: Other emphysema	J43.9	A	Emphysema: Emphysema, unspecified

**0 = underlying cause of death; 1-7 = contributing causes of death in order of severity (1 = most severe)*



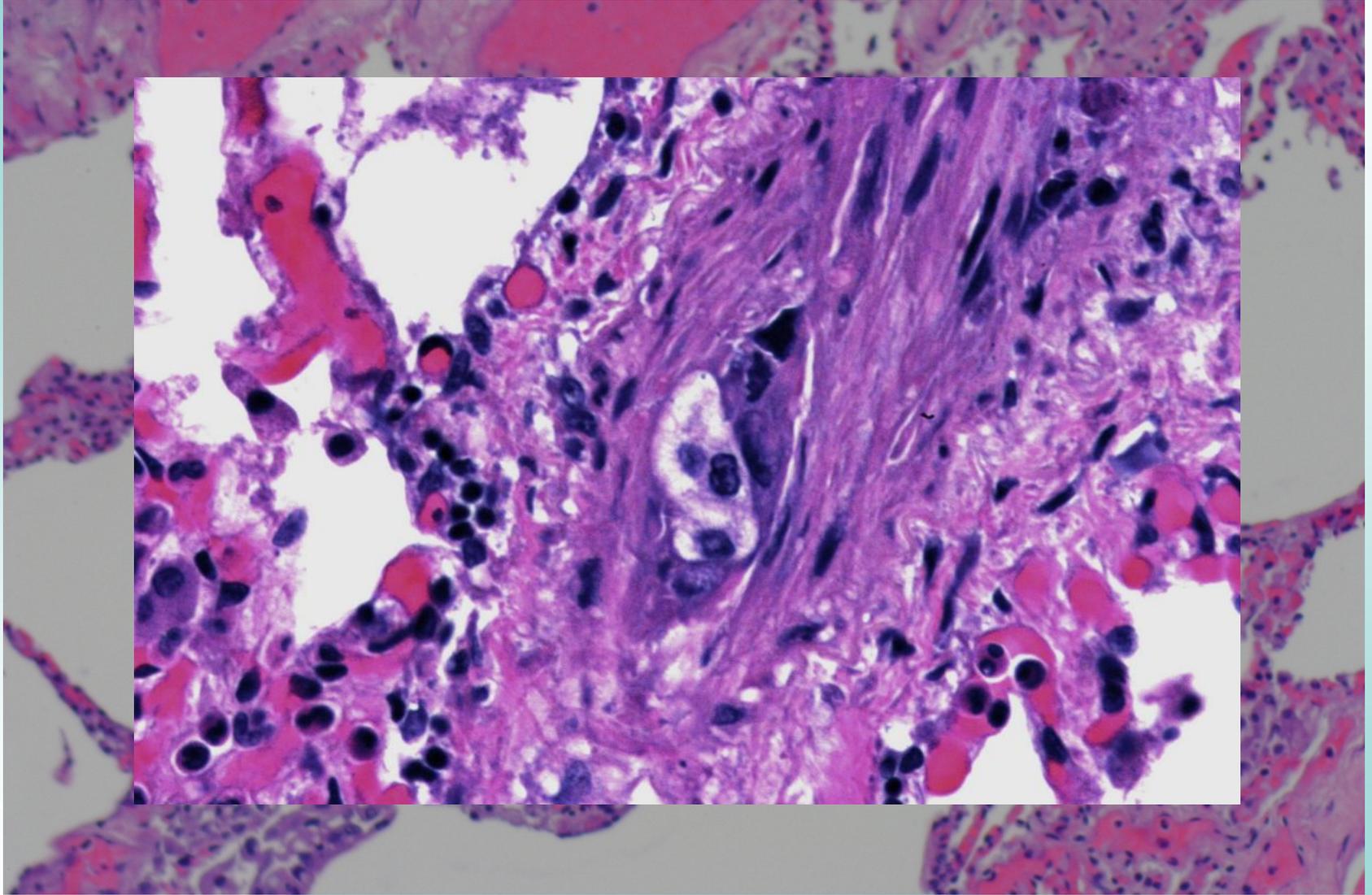
Case 0695 – Partial Body Donation (August, 2008) – First Diagnosis of “Berylliosis” in USTUR Registrant

UNITED STATES TRANSURANIUM REGISTRY AUTOPSY REPORT

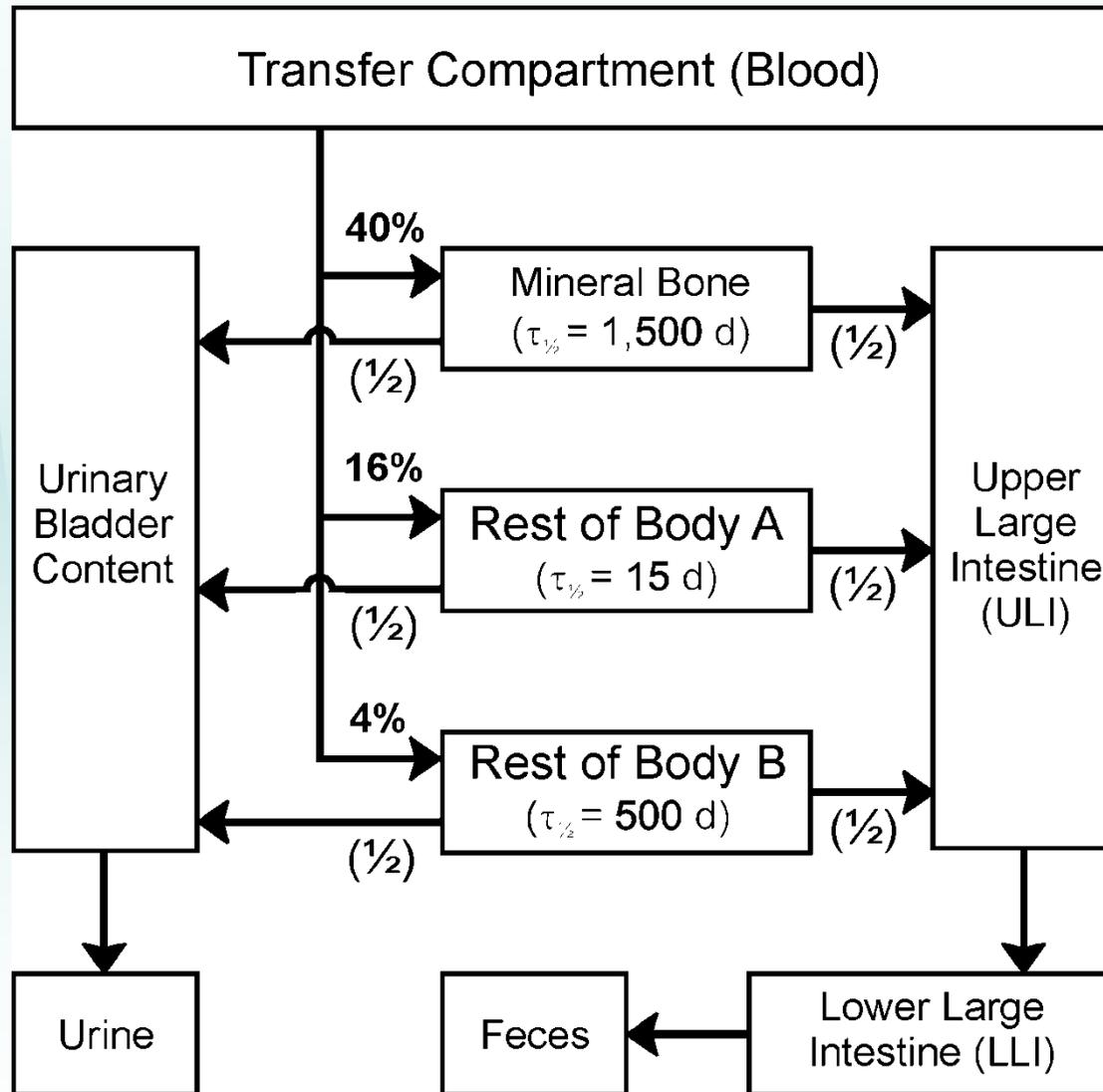
PATHOLOGICAL DIAGNOSES

1. Metastatic, moderately to poorly differentiated adenocarcinoma of the colon (Stage IV) with:
 - a. Primary lesion, cecum
 - b. Metastatic involvement of the lymph nodes (mediastinal, mesenteric and perihepatic), bilateral hemidiaphragms, bilateral lungs, liver, spleen and bone marrow
 - c. Associated complications including jaundice and peripheral edema.
2. Berylliosis with history of occupational exposure to beryllium.
3. Focal acute bronchopneumonia.
4. Arteriosclerotic cardiovascular disease with:
 - a. Mild to moderate coronary artery atherosclerosis
 - b. Mild atherosclerosis of the aorta.
5. Benign prostatic hyperplasia.

Lung Pathology in USTUR Case 0695



Beryllium Biokinetics – ICRP Systemic Metabolic Model



Limits of Detection in Be Analysis (Mass Spectrometry)

- Digested samples (with Be separation)

ICP-OES: 0.5 ng/mL – Maxwell et al., 2008

ICP-MS: 0.00005 ng/mL – Agilent 7500ce Tech. Note

- Non-digested samples

LA-ICP-MS: 100 ng/g (geological samples – Tiepolo et al., 2004)

SIMS: 100 ng/g (biological tissue – Duckett et al., 2000)



Be Separation – USTUR Tissue Samples



- **Chemical separation: DIPEX®-TEVA® resins**
(Maxwell et al., Talanta 2008)
 - **Sample in 30 ml of 0.1M HF – 0.1M HCl**
- **USTUR samples in 6M HCl**
Need to convert to 0.1M HF – 0.1M HCl

Test Tissues – USTUR Case 0817

- Primary exposure to Pu (Rocky Flats)
- 37-y (self-reported) exposure to Be
- ^{239}Pu concentration in tissues (Bq/kg wet)
 - Lung: 38.0 ± 0.1
 - Femur (shaft): 2.2 ± 0.2
- Digested sample aliquots
 - Lung: ~ 25 g in 40 mL acid solution
 - Femur ~13 g in 75 mL acid solution

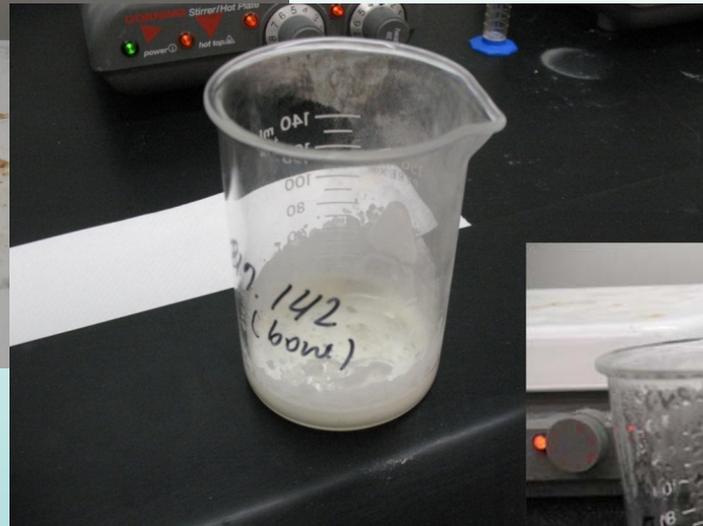


USTUR Laboratory Test Procedure

- Original femur sample (in 75 mL 6M HCl)



- Aliquot dried



- Re-dissolved in 35 mL 0.1M HF – 0.1M HCl
 - no CaF_2 precipitate (bone or lung)
 - ready for Be separation!



Conclusions – Application of NHRTR Tissues to Beryllium Toxicology?

- **USTUR Registrants (actinide exposure cases followed for several decades) include a substantial number of cases with chronic exposure to beryllium (also often asbestos).**
- **Self-reported beryllium exposure can be verified from site industrial hygiene records.**
- **The NHRTR holds thousands of acid-digested tissue samples, frozen tissues (and pathology specimens).**
- **Acid-digested tissues can be processed readily for beryllium separation.**
- **Tissue/specimen resource is available for collaborative research.**



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