



2019 Scientific Advisory Committee Meeting  
Hampton Inn, Richland, WA, April 11 – 12, 2019

## 2018 SAC Recommendations & 2019 Overview

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*“Learning from Plutonium  
and Uranium Workers”*



# 2018 SAC's Comments/Recommendations

- Following the 2018 Annual Meeting, the SAC made five (5) comments and eight (8) specific recommendations





# 2018 SAC Comments

1. The proposed mission statement is improved in pointing toward using the data for biokinetic/dosimetric models
2. We are pleased with progress in demonstrating value to DOE officials. Continued progress and expansion are encouraged (see recommendations)
3. The USTUR productivity in publications this year is to be commended
4. The USTUR has shown significant effort toward identifying collaboration opportunities with outsiders this year
5. We are disappointed with the limited progress on development of DQO/MQOs





# 2018 SAC Recommendations (I)

1. To assure the confidentiality of individuals' information, add to the mission statement that all research and collaborative efforts will be in keeping with the Privacy Act requirements and IRB approval
2. Continue and enhance publication of papers and presentations with broadened scope and audience
3. Produce a list of identified potential collaborators
4. Create a Quality Assurance Plan that includes: i) *Mission Statement*, ii) data required to meet the *Mission Statement Objectives*, iii) *Measurement Quality Objectives*, and iv) quality control limits for the different measurement parameters that monitor and control the MQOs. *Quality Assurance Project Plans* may also be developed for specific collaboration needs





## 2018 SAC Recommendations (II)

5. Complete implementation of the initiative for collecting bioassay monitoring data from living Registrants
6. Need to complete 5-year, and 10-year plans by establishing benchmark completion dates for stated goals
7. Enhance relationship with WSU Tri-Cities and Pullman campuses in collaborative development of research projects and student involvement through interface at all levels of the organizations. Take advantage of doors that have been opened at the Nuclear Science Center
8. Develop a written operating procedure for control, release, and potential return of data and tissues that lists responsibilities and authorizing individuals





## Recommendation #1

To assure the confidentiality of individuals' information, add to the mission statement that all research and collaborative efforts will be in keeping with the Privacy Act requirements and IRB approval





# Mission Statement

- Follow up occupationally-exposed individuals (volunteer Registrants) by *studying the biokinetics* (deposition, translocation, retention, and excretion) and tissue dosimetry of *uranium and transuranium elements*, such as plutonium, americium, curium, and neptunium
- Obtain, analyze, preserve, and *make available for future research*, materials from individuals who had documented intakes of uranium and transuranium elements
- Apply USTUR data to *refine dose assessment methods* in support of reliable epidemiological studies, radiation risk assessment, and regulatory standards *for radiological protection of workers and general public*





# Privacy Statement

- About Us: adding *Privacy Statement* to the website

**United States Transuranium and Uranium Registries**

**Commendation from DOE**  
Department of Energy's (DOE) Associate Under Secretary for Environment, Health, Safety and Security – Matthew Moury – applauded the USTUR with a letter recognizing the USTUR's role in providing a scientific basis for radiation protection standards. The letter highlights recent research, thanks the USTUR team for its dedication to the program, and expresses a deep sense of gratitude for Registrants and their families.  
[Letter of Commendation](#)

**50 Years of Research**  
The year 2018 marked 50 years of actinide research at the USTUR. In honor of this milestone, the USTUR organized four commemorative activities:

- 2016: Special Session at the HPS Meeting
- 2016: Informational Booth at the HPS Meeting
- 2018: Special Issue of *Health Physics*
- 2018: Book of USTUR Publications (1997-2017)

**WASHINGTON STATE UNIVERSITY**

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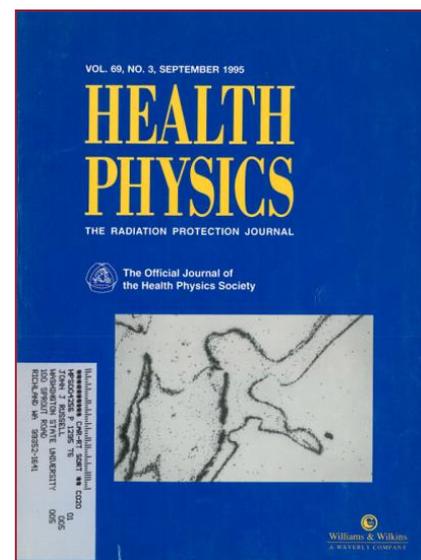
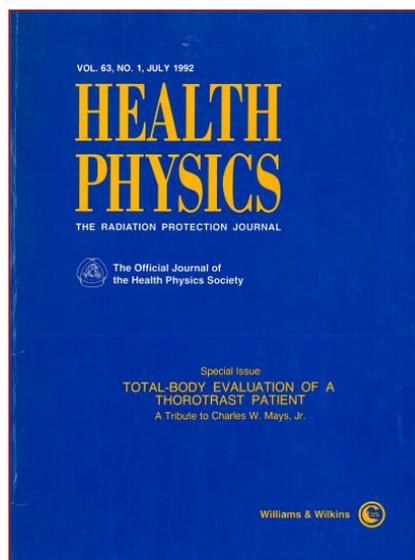
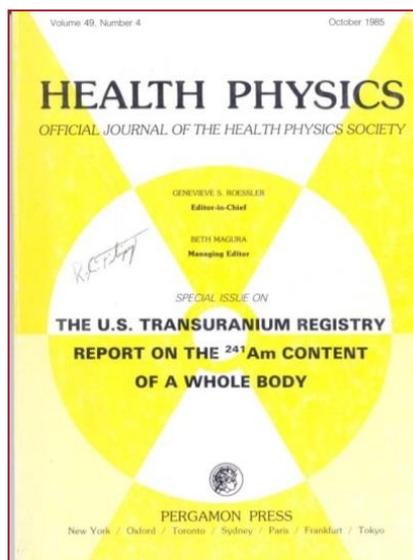
## Recommendation #2

Continue and enhance publication of papers and presentations with broadened scope and audience (external and internal)



# 4<sup>th</sup> Special Issue of Health Physics Journal (I)

- Worthington PR. (Editorial) Introduction to the USTUR special issue
- Special session's roundtable (Forum article) United States Transuranium and Uranium Registries (USTUR): A five decade follow up of plutonium and uranium workers
- Carbaugh EH. (Abstract) The Atomic Man: Case study of the largest recorded  $^{241}\text{Am}$  deposition in a human





## 4<sup>th</sup> Special Issue of Health Physics Journal (II)

1. Avtandilashvili M, Tolmachev SY. Modeling skeleton weight of an adult Caucasian man
2. Birchall A, Puncher M, Hodgson A, Tolmachev SY. The importance and quantification of plutonium binding in human lungs
3. Breustedt B, Avtandilashvili M, McComish SL, Tolmachev SY. USTUR Case 0846: Modeling americium biokinetics after intensive decorporation therapy
4. Dumit S, Avtandilashvili M, Tolmachev SY. Evaluating plutonium intake and radiation dose following extensive chelation treatment
5. Goans RE, Toohey RE, Iddins CJ, McComish SL, Tolmachev SY, Dainiak N. The pseudo-Pelger Huët cell as a retrospective dosimeter: Analysis of a radium dial painter cohort





## 4<sup>th</sup> Special Issue of Health Physics Journal (III)

6. Kathren RL, Tolmachev SY. The United States Transuranium and Uranium Registries (USTUR): A five-decade follow-up of plutonium and uranium workers
7. Tabatadze G, Miller BW, Tolmachev SY. Mapping  $^{241}\text{Am}$  spatial distribution within anatomical bone structures using digital autoradiography
8. Zhou JH, McComish SL, Tolmachev SY. A Monte Carlo t-test to evaluate mesothelioma and radiation in the U.S. Transuranium and Uranium Registries
9. Lopez MA, Nogueira P, Vrba T, Tanner RJ, Ruhm W, Tolmachev SY. Measurements and Monte Carlo simulations of  $^{241}\text{Am}$  activities in three skull phantoms: EURADOS-USTUR collaboration
10. Tolmachev SY, Avtandilashvili M, Kathren RL. Estimation of total skeletal content of plutonium and  $^{241}\text{Am}$  from analysis of a single bone





# Other Publications

11. Dumit et al. Improved modeling of plutonium-DTPA decorporation. *Radiation Research* 191: 201-210; 2019\*
12. Dumit et al. Validation of a system of models for plutonium decorporation therapy. *Radiation and Environmental Biophysics*: 2019 (e-pub)\*
13. Leggett et al. Potential improvements in brain dose estimates for internal emitters. *International Journal of Radiation Biology*: 2018 (e-pub)
14. Schneider et al. Determination of  $^{232}\text{Th}$  and progeny in human reticuloendothelial tissues using alpha particle track autoradiographic microdosimetry from Thorotrast. *Journal of Radioanalytical and Nuclear Chemistry* 318: 235-239; 2018
15. Boice et al. Response to Mortazavi et al. on detecting bone-seeking radionuclides in brain tissue. *Health Physics* 115: 389-390; 2018

\* - available in the bonus materials





# Invited Presentations

24<sup>th</sup> Meeting of the Conference on Radiation & Health, Chicago, IL, September 23 – 25, 2018

1. Tolmachev SY. *The US Transuranium and Uranium Registries: 50 years of contributions to plutonium in humans*

12<sup>th</sup> International Conference on Health Effects of Incorporated Radionuclides, Fontenay-aux-Roses, France, October 8 –11, 2018

2. Avtandilashvili et al. *The United States Transuranium and Uranium Registries: Fifty-year history of actinide biokinetic research*

Centre for Environmental Radioactivity Workshops on Human Health Effects Following Severe Nuclear Events and Particle Characteristics and Nuclear Forensics, Oslo, Norway, February 3 – 5, 2019

3. Tolmachev SY. *Radioactive actinide particles in occupationally exposed individuals*
4. Tolmachev SY. *Bioimaging of samples from the United States Transuranium and Uranium Registries – Shedding new light on the biokinetics, dosimetry, and possible biological effects of actinides in humans*





# Podium Presentations

63<sup>rd</sup> Annual Meeting of the Health Physics Society, Cleveland, OH, July 15 – 19, 2018

1. Dumit et al. *New biokinetic model simultaneously fits Ca-DTPA affected and non-affected urine bioassay data after plutonium contamination*
2. Strom DJ. *A simple visualization of the LEKSKaM 2005 model of systemic plutonium biokinetics*

12<sup>th</sup> International Conference on Health Effects of Incorporated Radionuclides, Fontenay-aux-Roses, France, October 8 –11, 2018

3. Avtandilashvili M, Tolmachev SY. *Biokinetics of soluble plutonium after wound injury treated with Ca-DTPA\**
4. Leggett et al. *Case studies in brain dosimetry for internal emitters: is more biokinetic detail needed for epidemiology?\**
5. Tolmachev et al. *USTUR: Expanding horizons for actinide biokinetics and dosimetry*

\* - available in the bonus materials





# Poster Presentations

Brazilian Graduate Student Conference (BRASCON), Columbus, OH, June 23 – 24, 2018

1. Dumit et al. *New biokinetic model simultaneously fits Ca-DTPA affected and non-affected urine bioassay data after plutonium contamination*

24<sup>th</sup> Meeting of the Conference on Radiation & Health, Chicago, IL, September 23 – 25, 2018

2. Avtandilashvili and Tolmachev. *Four-decade follow up of plutonium contaminated puncture wound treated with Ca-DTPA*

64<sup>th</sup> Annual Meeting of the Radiation Research Society, Chicago, IL, September 23 – 26, 2018

3. Dumit et al. *New compartmental model for plutonium decorporation therapy*
4. Zhou et al. *Update on causes of death among 353 former nuclear workers in the United States Transuranium and Uranium Registries*





## Recommendation #3

Produce a list of identified potential collaborators





# Potential Collaborators

- Pacific Northwest National Laboratory
- WSU-PNNL Nuclear Science and Technology Institute
- Washington State University, Department of Chemistry
- Los Alamos National Laboratory
- French Alternative Energies and Atomic Energy Commission (CEA)
- HPMC Occupational Medical Services





## Recommendation #4

Create a *Quality Assurance Plan* that includes:  
i) *Mission Statement*, ii) data required to meet the *Mission Statement Objectives*, iii) *Measurement Quality Objectives*, and iv) quality control limits for the different measurement parameters that monitor and control the MQOs. Quality Assurance Project Plans may also be developed for specific collaboration needs





# Data Quality Objectives Draft

- Available in the bonus materials

USTUR-XXXX-19

Data Quality Objectives Supporting  
U.S. Transuranium and Uranium Registries Mission



George Tabatadze  
Maia Avtandilashvili  
Stacey L. McComish  
Elizabeth M. Thomas  
Sergei Y. Tolmechev

March 26, 2019



College of  
**Pharmacy and  
Pharmaceutical Sciences**  
WASHINGTON STATE UNIVERSITY





## Recommendation #5

Complete implementation of the initiative for collecting bioassay monitoring data from living Registrants





# 2018 Activities

- Conference call with National Supplemental Screening Program: USTUR/ORAU/DOE
- Hanford Internal Dosimetry Program Manual (PNL-MA-552): urine collection protocol
- Establishing USTUR protocol (instruction to the Registrants) for 24-h urine sample collection: adoption of PNL-MA-552
- Quote from GEL laboratory for urine sample analyses (not collection): \$197 per analysis
- IRB modification





## Recommendation #6

Need to complete 5-year, and 10-year plans by establishing benchmark completion dates for stated goals [*from data generator to data user*]





# USTUR Research Goals

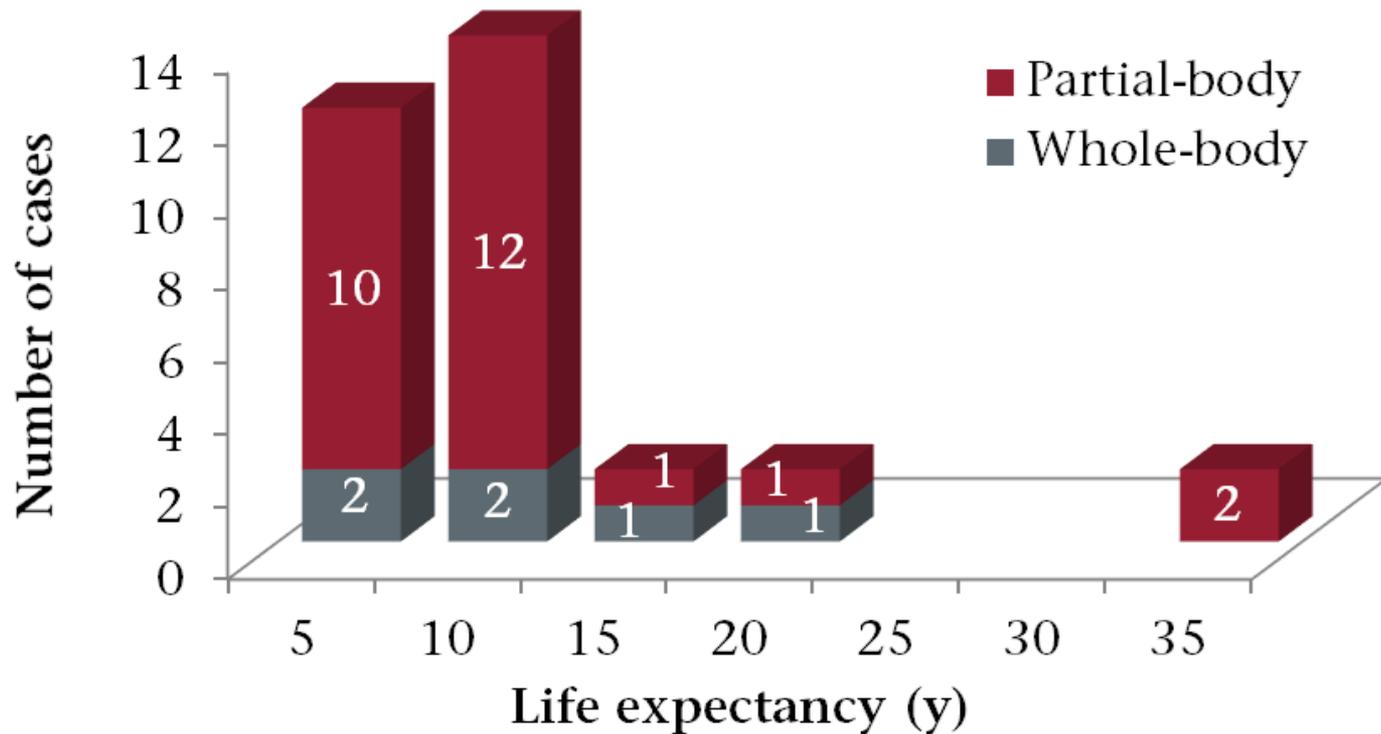
- Biokinetic modeling of individual cases
- Analysis of uncertainties in organ dose estimates
- Development of actinide decorporation models
- Study of long-term retention and distribution of actinides in the human body
- Study of exposure to beryllium and other hazardous metals associated with nuclear work





# Registrant's Life Expectancy

<https://www.ssa.gov/cgi-bin/longevity.cgi>



Expected number of living Registrants: 32 (2019)  
20 (2024)  
6 (2029)





# Operational Task Completion Dates

## Health Physics database

- All worksites except Hanford (2021)
- All cases (2029)

## Radiochemistry backlog

- Partial body cases (2020)
- All cases (2029)

## NHRTR inventory

- LANL acid solutions (2022)
- RDP frozen tissues (2024 – 2029)
- RDP other materials (2029 and beyond)





# Long-term Research Plan

## Five-year:

- $^{239}\text{Pu}$  biokinetic modeling and uncertainty analysis of 20 individual inhalation cases (post-doctoral project)
- Improvement of system of compartmental models for  $^{239}\text{Pu}$  decorporation; application to  $^{238}\text{Pu}$
- Effect of chelation on  $^{241}\text{Am}$  distribution in the body
- Beryllium analysis and biokinetics

## Ten-year:

- Analyses of single intake cases
- Pooled analysis of specific groups: *UPPU*, wound, refractory  $^{239}\text{PuO}_2$ ,  $^{238}\text{Pu}$
- Actinide distribution in the skeleton
- Minor actinides:  $^{237}\text{Np}$  and  $^{244}\text{Cm}$





## Recommendation #7

Enhance relationship with WSU Tri-Cities and Pullman campuses in collaborative development of research projects and student involvement through interface at all levels of the organizations. Take advantage of doors that have been opened at the Nuclear Science Center





# Presentations at WSU

WSU College of Pharmacy and Pharmaceutical Sciences PhD Student Orientation, Spokane, WA, August 20, 2018

- Tolmachev SY (podium). *PhD orientation talk: The United States Transuranium and Uranium Registries*

WSU Department of Chemistry Research Seminar, Pullman, WA, October 26, 2018

- Tolmachev SY (podium). *The United States Transuranium and Uranium Registries: Fifty-year history of actinide analyses and biokinetic research*

WSU Tri-Cities Japanese Dignitaries Visit, Richland, WA, January 17, 2019

- Tolmachev SY (podium). *Introduction of the United States Transuranium and Uranium Registries*

WSU College of Pharmacy and Pharmaceutical Sciences Graduate Interview Day, Spokane, WA, March 1, 2019

- Tolmachev and Tabatadze (poster). *The United States Transuranium and Uranium Registries*





## Recommendation #8

Develop a written operating procedure for control, release, and potential return of data and tissues that lists responsibilities and authorizing individuals



# USTUR Policy and Procedure Revision

- Sample Chain of Custody Modification (THEMIS)\*
- USTUR Scientific Collaboration and Data Access Policy (P106)\*

**United States Transuranium and Uranium Registries**

**CHAIN OF CUSTODY DOCUMENT**

From Location	To Location	Custody Date
C0800070 (Lab Area 100 Freezer 20)	C14000272 (Lab Area 100 Freezer 5 (176))	3/22/2019 11:27:01 AM

Samples Moved by STACELY L. MCCOY RD

Testing

Barcode	USTUR Sample #	Sample Description
08001399	USTUR-0000-580	Tissue - Frozen - Muscle: Hand (Hand Muscle: back (R))

---

Relinquished By (signature)	Date Time	Received By (signature)	Date Time
Relinquished By (signature)	Date Time	Received By (signature)	Date Time

**Return to USTUR:**

Destroyed during analysis     Returned to USTUR

Signature \_\_\_\_\_ Date Time \_\_\_\_\_

THEMIS Report Printed 3/25/2019 9:11:28:33 AM Page 1 of 1

**P106**

Created 06/92  
Revised XX/19

**Scientific Collaboration and Data Access**

Approved by *Sergei V. Tolmachev*, Director  
XXXXXX 2019

*This policy applies to research collaboration with other scientists and institutions, and to sharing Registries' data and materials with others.*

**Collaboration with other institutions is encouraged**

To maximize the scientific worth and output of the unique materials and data under its purview, the Registries encourages and actively seeks collaboration with other investigators and institutions. Collaboration is sought to complement rather than duplicate the capabilities of the Registries, and to facilitate the efforts of the Registries in achieving its primary goal. Collaboration may take the form of joint evaluations of data, tissues, or other Registries materials, preparation of articles for peer-reviewed literature, or preparation of joint research proposals to a potential sponsor.

**Confidentiality**

USTUR data shall be held in the highest confidence and every possible precaution will be taken to protect Registrants. These data include, but are not limited to: work-site medical, radiation dosimetry, and industrial hygiene histories; correspondences; and autopsy findings.

**Definition of collaborative researchers**

Data, tissues, and other unique materials collected or generated by the Registries may be made available to other scientists under the following conditions:

1. Potential research collaborators must submit to the Registries a written proposal that describes the specific materials requested, and includes the proposed usage of the requested materials.

**Dissemination of Registries' data and tissue materials**

The USTUR director must approve each individual collaborator who will have access to USTUR data and/or tissue materials by signing the administrative portion of P106 (USTUR Statement of Confidentiality).

Registries' data are classified into three levels, based on the potential for identification of the donors and dissemination of the data to other researchers. Access to the data will be restricted as follows:

**Level 1:** Data include direct personal identifiers and specific dates of events with specific sites of employment. These data are available, by written request, to medical and radiation protection groups from the work-sites of the Registrants. Access to these data is restricted by site. For example, medical

**Level 2:** Data include no direct personal identifiers; however, specific dates of events and general descriptions of the sites of employment are included. These data are available to collaborative researchers as defined above.

**Level 3:** Data include no direct personal identifiers, only general times of employment and radiologic events, and general information regarding work-sites.

Registrant data shall be sent to collaborators as PDFs that have been redacted of direct personal identifiers (name, SSN, address, phone number, fax number, email address, worker identification numbers, medical record numbers), encrypted using 256-bit technology (password protected), and copied to a removable storage device (e.g. CD/DVD, USB drive, etc.). The disk shall be shipped overnight, signature required, for receipt to the researcher, and the password will be sent to the researcher by a different means (e.g. email). Correspondence regarding Registrants shall be limited to their unique four-digit case number.

Tissues shall be shipped, for overnight delivery, in compliance with all applicable shipping regulations.

**Data Storage**

Paper and electronic files containing Registrant information must be kept in a secure location. Computers or servers that have Registrant information must be have a firewall and be password protected. Registrant data may not be stored on web-based backup systems, e.g. the cloud.

**Additional Researchers or Collaborators**

USTUR Policies and Procedure Manual

and radiation protection personnel at a work site may access data of Registrants only from that site. Signed confidentiality statements (Form 106) must be received from the responsible person(s) at the sites requesting data.

**Level 2:** Data include no direct personal identifiers; however, specific dates of events and general descriptions of the sites of employment are included. These data are available to collaborative researchers as defined above.

**Level 3:** Data include no direct personal identifiers, only general times of employment and radiologic events, and general information regarding work-sites.

Registrant data shall be sent to collaborators as PDFs that have been redacted of direct personal identifiers (name, SSN, address, phone number, fax number, email address, worker identification numbers, medical record numbers), encrypted using 256-bit technology (password protected), and copied to a removable storage device (e.g. CD/DVD, USB drive, etc.). The disk shall be shipped overnight, signature required, for receipt to the researcher, and the password will be sent to the researcher by a different means (e.g. email). Correspondence regarding Registrants shall be limited to their unique four-digit case number.

Tissues shall be shipped, for overnight delivery, in compliance with all applicable shipping regulations.

**Data Storage**

Paper and electronic files containing Registrant information must be kept in a secure location. Computers or servers that have Registrant information must be have a firewall and be password protected. Registrant data may not be stored on web-based backup systems, e.g. the cloud.

**Additional Researchers or Collaborators**

USTUR data and tissue materials are shared with approved collaborators for specific research purposes. Tissue materials may not be analyzed for purposes beyond the scope of research agreed upon prior to receipt of specimens. Data recipients may not share the materials with other researchers or perform research outside the agreed upon scope without prior approval from the Registries.

Each individual who will have access to Registries data must:

1. read USTUR procedures P106 (USTUR Scientific Collaboration and Data Access Policy) and P107 (USTUR Publications Policy); and
2. sign USTUR form P106 (USTUR Statement of Confidentiality).

**Return or Disposal of Registries' data and tissue materials**

All original printed and/or electronic files sent by the USTUR, as well as any secondary files created by the recipient that contain potentially identifiable information, must be destroyed or returned to the USTUR within 1 year of publication, or within 5 years of receipt, whichever comes first. Extensions may be requested in 1-year increments if additional time is needed.

Tissue materials that are not destroyed during analysis must be returned to the USTUR within 1 year of analysis or 3 years of receipt, whichever comes first. Extensions can be requested in 1-year increments if additional time is needed.

**Publication of data and results from collaborative research**

No publicly available or open-literature publication, or presentation, shall be made in which Registrants are identified without the prior consent of the Registrant, or the legally responsible party, unless legally required by law, regulation, or court order.

USTUR Policies and Procedure Manual

\* - available in the bonus materials





# FY2019 Activities Overview (March 31, 2018 – April 1, 2019)





# Institutional Review Board

- The Central DOE IRB is the IRB of record
- WSU completely relies on the Central DOE IRB for review and oversight of the USTUR
- August 21, 2018: continuing review submitted
- Added staff members and updated training
- September 12, 2018: IRB *approved* until *September 11, 2019*



# FY2020 Grant Renewal

- FY2020: April 1, 2019 – March 31, 2020
- **Funding increase: \$100,000**
- FY2020 budget: \$1,200,000



January 28, 2019

Renewal Proposal to Manage and Operate the  
United States Transuranium and Uranium Registries  
(FY2020)

DE-HS0000073

Submitted by:  
Dr. Sergei Y. Tolmachev, Director and P.I.  
United States Transuranium and Uranium Registries  
College of Pharmacy, Washington State University  
1845 Terminal Drive, Suite 201, Richland, WA 99354



College of  
**Pharmacy**  
WASHINGTON STATE UNIVERSITY



January 28, 2019

Renewal Proposal to Manage and Operate the  
United States Transuranium and Uranium Registries  
(FY2020): Appendices

DE-HS0000073

Submitted by:  
Dr. Sergei Y. Tolmachev, Director and P.I.  
United States Transuranium and Uranium Registries  
College of Pharmacy, Washington State University  
1845 Terminal Drive, Suite 201, Richland, WA 99354



College of  
**Pharmacy**  
WASHINGTON STATE UNIVERSITY



# Graduate Research

- Sara Dumit joint USTUR: November 1, 2015
- Dissertation title: *Development of a New Compartmental Model for Plutonium Decorporation Therapy*
- Defense: May 14, 2018



- Post doctoral fellow at Los Alamos National Laboratory: August 20, 2018





# Professional Services

Maia Avtandilashvili



National Council on Radiation Protection and Measurements



George Tabatadze



HPS Specialists in Radiation Protection



Sergei Tolmachev



National Council on Radiation Protection and Measurements





# Accepting Registrant Donations

Stacey L. McComish and Margo D. Bedell

*S. L. McComish. Registrant Statistics and IRB Changes*



# FY2019 Registrant Donations

Two donations in FY2019

- Whole-body
- Partial-body





# Health Physics Database

Maia Avtandilashvili



# FY2019 Health Physics Database Progress

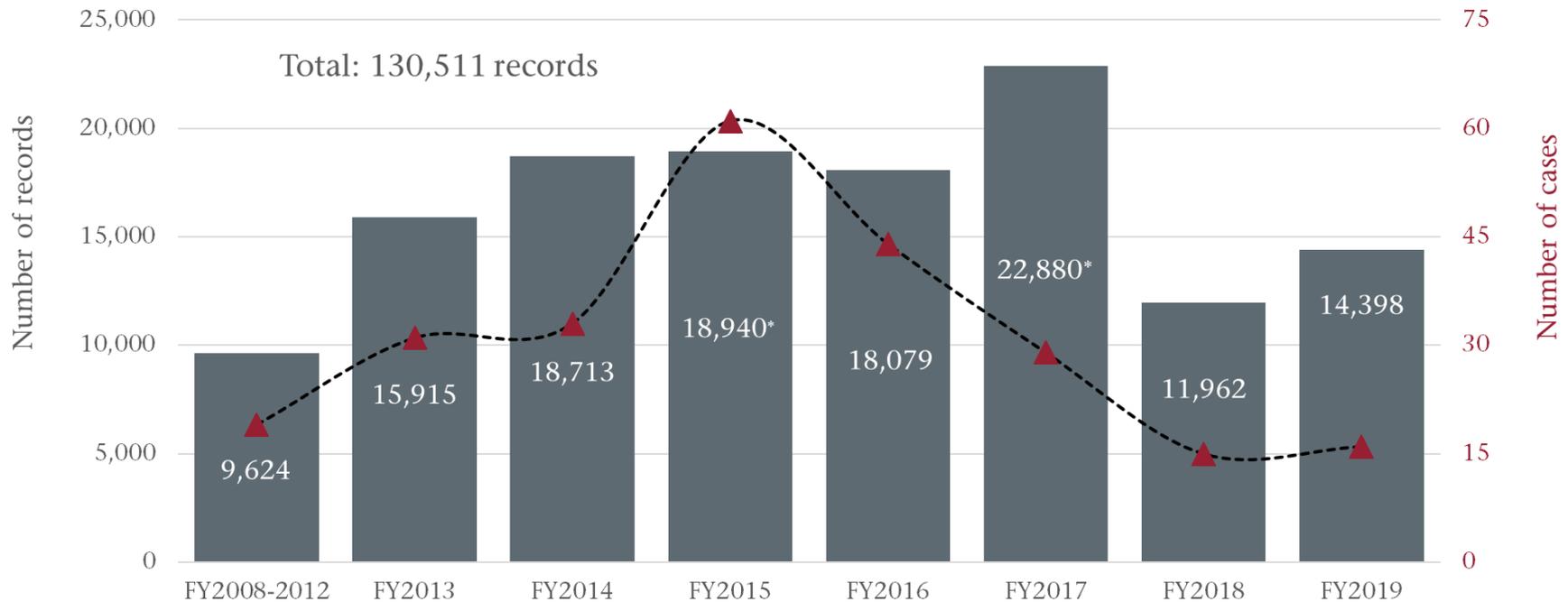
Sixteen (16) partial-body cases completed: fourteen (14) living + two (2) deceased (2004, 2018)

- ROC: 8 living + 1 deceased
- HAN: 3 living + 1 deceased
- SVR: 2 living
- MSC: 1 living





# FY2008 - FY2019 Database Progress



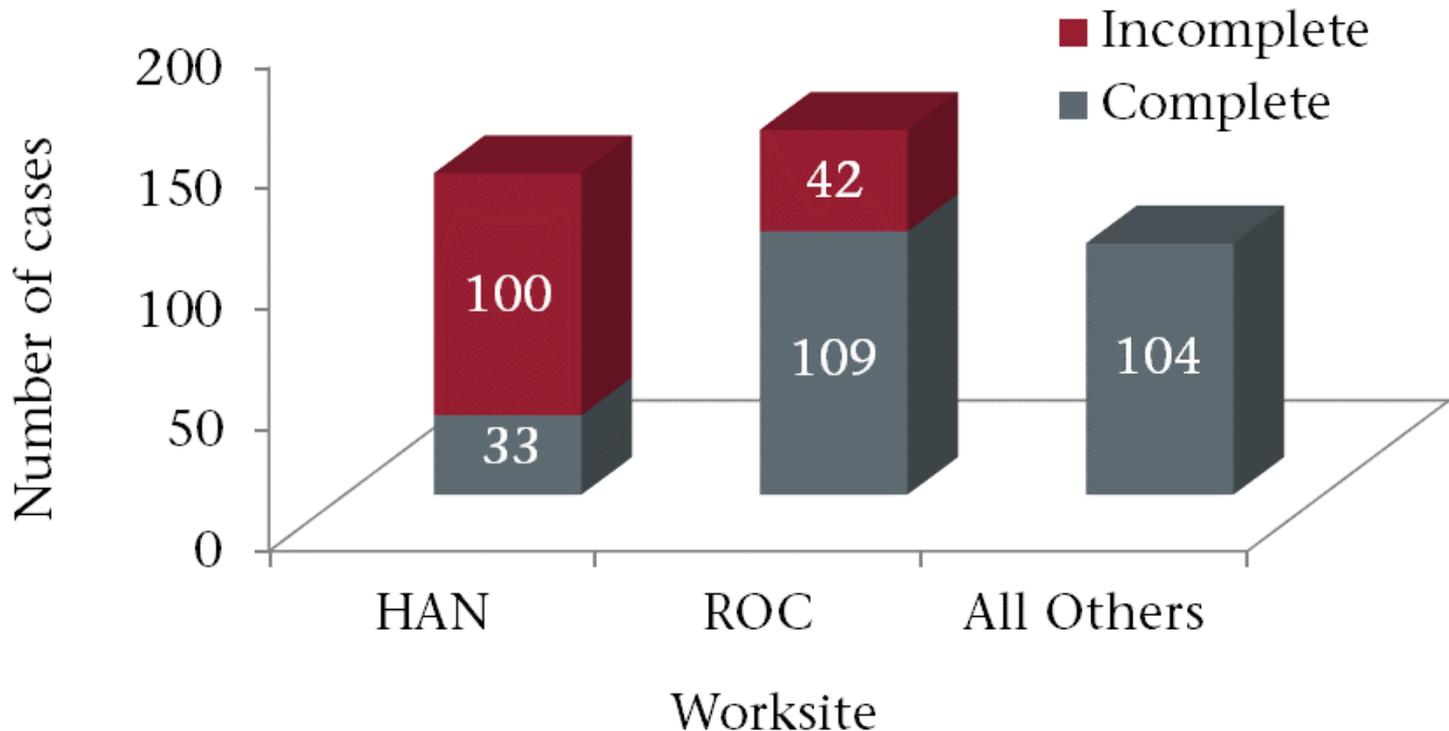
*\* Including special study cases*



# FY2019 Health Physics Database Status

As of April 1, 2019, 246 of 388 (63%) Registrant cases completed:

- 52 (100%) whole body
- 194 of 336 (58%) partial body





# National Human Radiobiological Tissue Repository (NHRTR)

Florencio Martinez, Warnick Kernan,  
Samantha Walter, and Stacey L. McComish



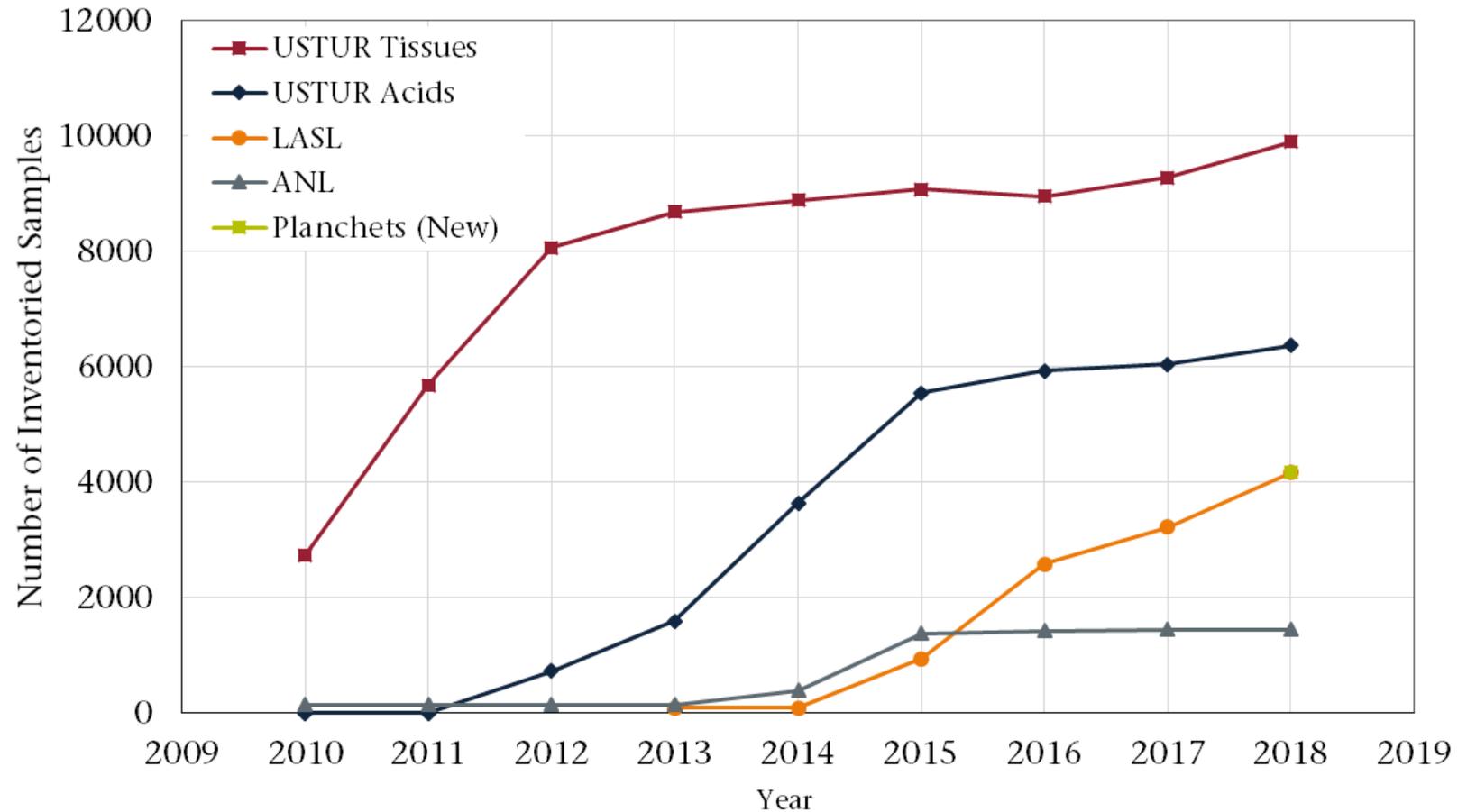
# NHRTR Material Inventory Status

- USTUR tissues and acid solutions – *Maintenance*
- Acid solutions from Los Alamos Scientific Laboratory population studies – *In progress*
- Alpha spectrometry planchets – *In progress*





# Material Inventory Data Trend





## In-house Radiochemistry

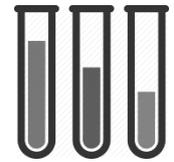
Elizabeth M. Thomas, George Tabatadze,  
Sergei Y. Tolmachev

*G. Tabatadze. FY2019 Radiochemistry Progress*



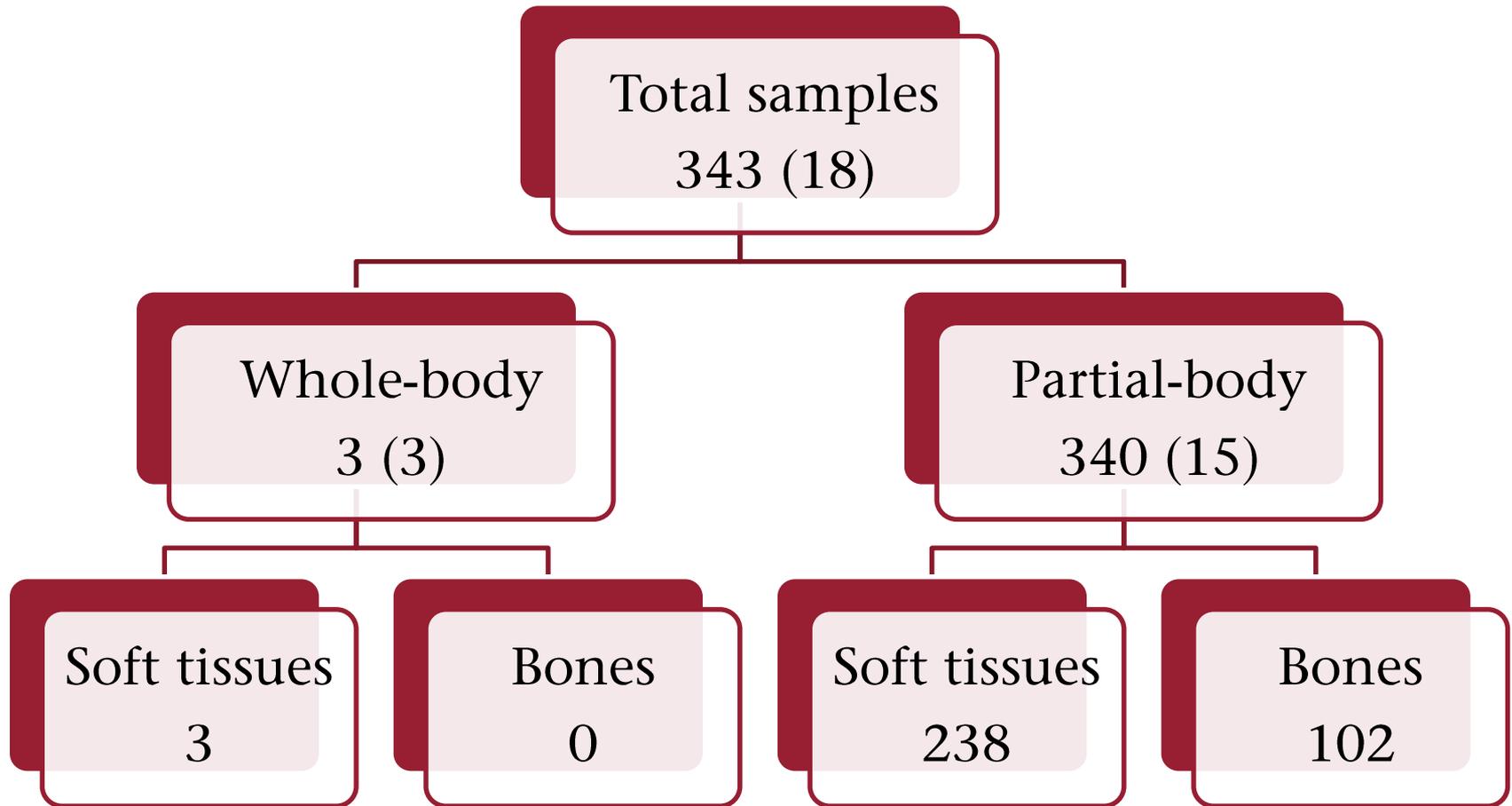
# Radiochemistry Group Activities

- Tissue sample analysis
- Radiochemistry database development
- Data and Measurement Quality Objectives





# Tissue Sample Analysis Progress





# Case Analysis Progress and Status

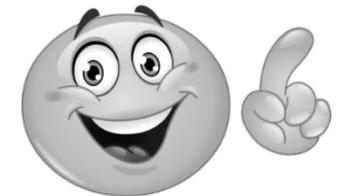
Status	Whole body		Partial body	
	FY2018	FY2019	FY2018	FY2019
Total	45	46	309	310
Complete	25	25	286	301
Incomplete	19	21	19	7
Intact <sup>†</sup>	1	--	4	2

<sup>†</sup>2017 – 2018 donations



# Radiochemistry Database: *New Functionality*

- Selection of samples for analysis
- Full integration (data exchange) with AlphaVision<sup>®</sup> database
- Summary of the results (Health Physics database)





# Research Activities

# Collaborative Research

- Plutonium decorporation therapy model; individual case modeling
- Biokinetic modeling and uncertainty analysis in radiation dose assessment
- Distribution of beryllium in human body
- Hair and nails in nuclear forensics
- Plutonium biokinetics and brain dosimetry



National Council on Radiation  
Protection and Measurements



Northwestern  
University



# WSU-PHE: Memorandum of Understanding

February 15, 2019\*

**Memorandum of Understanding (MOU)  
Between  
Washington State University, Pullman, WA, USA  
And  
The Centre for Radiation Chemical and Environmental Hazards, Oxfordshire, UNITED KINGDOM**

**ARTICLE I. PARTIES AND PURPOSE**

The Centre for Radiation Chemical and Environmental Hazards (CRCE) and Washington State University (WSU) by and through its United States Transuranium and Uranium Registries conduct programs and activities of basic and applied research, education and training, technology and information transfer, and economic development. CRCE and WSU have capabilities and expertise in conducting programs and activities of interest and potential benefit to the other.

CRCE and WSU will cooperate in efforts to establish and conduct mutually agreed upon cooperative and collaborative projects, programs, and/or activities, which will enhance the programs of each. Specific details of any cooperative/collaborative activities to be conducted, including cooperation with third parties and allocation of support and resources, shall be set forth and agreed upon in writing as a contract between parties.

This MOU also recognizes there is a separate End User Licence Agreement as signed on December 5, 2018.

**ARTICLE II. COOPERATION WITH THIRD PARTIES**

Since other universities, institutes, centers and organizations may have capabilities and conduct activities, which will benefit and support this collaboration, CRCE and WSU may identify other cooperators for joint participation in mutually agreed upon projects and activities.

**ARTICLE III. DURATION, TERMINATION**

The parties shall cooperate under this MOU for an initial period of five (5) years from the date of last signature, which may be extended by the mutual written consent of the parties. This MOU may be terminated by either party without liability at any time for any reason. Any modification shall require the written approval of the signature authority of Washington State University and the signature authority of The Centre for Radiation Chemical and Environmental Hazards, or their designees.

**ARTICLE IV. NON-BINDING NATURE**

This MOU is intended only to set forth the general understanding of the parties with respect to the subject matter herein, and does not, and is not intended to, contractually bind the parties.

**ARTICLE V. RESOLUTION OF DISPUTES**

In the event that a dispute arises under this MOU, the parties shall make every effort to resolve it themselves. Should the parties enter future contracts contemplated by this MOU, such contracts will contain a detailed resolution process.

**ARTICLE VI. CONTACT PERSONS**

<b>The Centre for Radiation Chemical and Environmental Hazards</b>	<b>Washington State University</b>
David Rhodes Centre Director Public Health England, Chilton Didcot Oxfordshire OX11 0RQ, UNITED KINGDOM Phone: 44 (0) 1235 831800 E-mail: <a href="mailto:david.rhodes@phe.gov.uk">david.rhodes@phe.gov.uk</a> Website: <a href="https://www.phe-protectionservices.org.uk/rpa/contact/locations">https://www.phe-protectionservices.org.uk/rpa/contact/locations</a>	Dr. Asif Chaudhry Vice President for International Programs PO Box 646121, Bryan Hall 301 Pullman, WA 99164-6121 Phone: 509-335-2541 Fax: 509-335-2982 E-mail: <a href="mailto:ip_admin@wsu.edu">ip_admin@wsu.edu</a> Website: <a href="https://p.wsu.edu/">https://p.wsu.edu/</a>
Anthony Riddell Internal Dosimetry Group Leader Public Health England, Chilton Didcot Oxfordshire OX11 0RQ, UNITED KINGDOM Phone: 44 (0) 1235 825036 E-mail: <a href="mailto:tony.riddell@phe.gov.uk">tony.riddell@phe.gov.uk</a>	

1

Website: <https://www.phe-protectionservices.org.uk/rpa/contact/locations>

**ARTICLE VII. SIGNATURES**

<b>The Centre for Radiation Chemical and Environmental Hazards</b>	<b>Washington State University</b>
Approved by: 	Approved by: 
_____ David Rhodes Centre Director	_____ Dr. Asif Chaudhry Vice President for International Programs
15/2/2019 Date	12/17/2018 Date
	_____ Anthony Riddell Internal Dosimetry Group Leader
18/2/2019 Date	

2

\* - available in the bonus materials





# System of Models for Plutonium Decorporation

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DOI: 10.1667/RR15183.1

## Improved Modeling of Plutonium-DTPA Decorporation

Sara Dumit<sup>1</sup>, Maia Avtandilashvili<sup>1</sup>, Daniel J. Strom<sup>1</sup>, Stacey L. McComish<sup>1</sup>, George Tabatadze<sup>1</sup> and Sergei Y. Tolmachev<sup>1</sup>

*U.S. Transuranium and Uranium Registries, Washington State University, Richland, Washington 99251-1959*

Dumit, S., Avtandilashvili, M., Strom, D. J., McComish, S. L., Tabatadze, G., and Tolmachev, S. Y. Improved Modeling of Plutonium-DTPA Decorporation. *Radiat. Res.* 191, 201–210 (2019).

Individuals with significant intakes of plutonium (Pu) are typically treated with chelating agents, such as the trisodium salt form of calcium diethylenetriaminepentaacetate (CaNa<sub>2</sub>-DTPA, referred to hereafter as Ca-DTPA). Currently, there is no recommended approach for simultaneously modeling plutonium biokinetics during and after chelation therapy. In this study, an improved modeling system for plutonium decorporation was developed. The system comprises three individual model structures describing, separately, the distinct biokinetic behaviors of systemic plutonium, intravenously injected Ca-DTPA and *in vivo*-formed Pu-EDTA chelate. The system was linked to ICRP Publication 106, “Human Alimentary Tract Model for Radiological Protection” and NCRP Report 156, Development of a Biokinetic Model for Radionuclide-Contaminated Wounds and Procedures for Their Assessment, Dosimetry and Treatment.” Urine bioassay and chelation treatment data from an occupationally-exposed individual were used for model development. Chelation was assumed to occur in the blood, soft tissues, liver and skeleton. The coordinated network for radiation dosimetry approach to decorporation modeling was applied using a chelation constant describing the second-order, time-dependent kinetics of the *in vivo* chelation reaction. When using the proposed system of models for plutonium decorporation, a significant improvement of the goodness-of-fit to the urinary excretion data was observed and more accurate predictions of post-mortem plutonium retention in the skeleton, liver and wound site were achieved. © 2019 by Radiation Research Society

### INTRODUCTION

Long-term plutonium (Pu) retention in the human body is a source of concern. If significant plutonium intake is suspected, medical countermeasures may be necessary to reduce the radiation dose to tissues and organs (1), individuals with significant plutonium intake are typically

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treated with decorporation drugs, also known as chelating agents. The U.S. Food and Drug Administration (FDA) has approved the trisodium salt form of calcium diethylenetriamine-pentaacetate (CaNa<sub>2</sub>-DTPA) for treatment of individuals with known or suspected internal contamination from plutonium, americium (Am) and curium (2). At the same time, the FDA also approved Zn-DTPA for the same indications and usage (2). Both chelating agents have proved to be an effective treatment for individuals who have been internally contaminated with these elements (3).

Ca-DTPA forms stable complexes with (i.e., “chelates”) plutonium in systemic circulation, enhancing its rate of elimination (3). Various published studies using both animal and human data have demonstrated that chelation also occurs in soft tissues and bones (4–9). Although plutonium is tenaciously retained in the skeleton (10), chelation therapy has been shown to reduce deposition and toxicity in bones (11, 12). James *et al.* (7) demonstrated that chelation treatment administered to an occupationally-exposed individual significantly reduced plutonium activity on bone surfaces and in bone marrow. Recently, Grémy *et al.* (9) observed extracellular chelation of plutonium on bone surfaces of rats. Furthermore, chelation in the liver was observed after Ca-DTPA treatment in several different studies (4, 6, 9, 13–17). Carbaugh (18) reported a human study on internal contamination with americium and showed that chelation effectively removed material from the liver, but not the skeleton, although it did prevent further skeleton deposition. Grube *et al.* (19) suggested that chelation of plutonium in the liver of a rat could be attributed to chelation that was occurring in the extracellular fluids of the liver, where the actinide is also known to be present.

After chelation treatment, plutonium biokinetics (absorption, translocation, retention and elimination) is altered by complexation of the actinide with the administered drug. Therefore, the standard biokinetic models, such as the plutonium systemic models (20, 21), which are based on the actinide’s unperturbed biokinetics, cannot be directly applied to simultaneously fit chelation-affected and non-affected bioassay data (e.g., urinary excretion data) to estimate the plutonium intake.

Radiation and Environmental Biophysics  
<https://doi.org/10.1007/s00411-018-00773-y>

### ORIGINAL ARTICLE



## Validation of a system of models for plutonium decorporation therapy

Sara Dumit<sup>1,2</sup> · Maia Avtandilashvili<sup>1</sup> · Stacey L. McComish<sup>1</sup> · Daniel J. Strom<sup>1</sup> · George Tabatadze<sup>1</sup> · Sergei Y. Tolmachev<sup>1</sup>

Received: 17 August 2018 / Accepted: 22 December 2018  
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### Abstract

A recently proposed system of models for plutonium decorporation (SPD) was developed using data from an individual occupationally exposed to plutonium via a wound [from United States Transuranium and Uranium Registries (USTUR) Case 0212]. The present study evaluated the SPD using chelation treatment data, urine measurements, and post-mortem plutonium activities in the skeleton and liver from USTUR Case 0269. This individual was occupationally exposed to moderately soluble plutonium via inhalation and extensively treated with chelating agents. The SPD was linked to the International Commission on Radiological Protection (ICRP) Publication 66 Human Respiratory Tract Model (HRTM) and the ICRP Publication 30 Gastrointestinal Tract model to evaluate the goodness-of-fit to the urinary excretion data and the predictions of post-mortem plutonium retention in the skeleton and liver. The goodness-of-fit was also evaluated when the SPD was linked to the ICRP Publication 130 HRTM and the ICRP Publication 100 Human Alimentary Tract Model. The present study showed that the proposed SPD was useful for fitting the entire, chelation-affected and non-affected, urine bioassay data, and for predicting the post-mortem plutonium retention in the skeleton and liver at time of death, 38.5 years after the accident. The results of this work are consistent with the conclusion that Ca-EDTA is less effective than Ca-DTPA for enhancing urinary excretion of plutonium.

**Keywords** Plutonium · Chelating agents · Decorporation therapy · Biokinetic modeling · Human data · United States Transuranium and Uranium Registries

### Introduction

An improved system of models for plutonium decorporation (SPD) has been developed recently at the United States Transuranium and Uranium Registries (USTUR) (Dumit *et al.* 2019). The SPD comprises three individual model structures describing, separately, the biokinetic behavior of systemic plutonium, intravenously injected chelating agent, and *in vivo*-formed chelate (actinide drug). The Coordinated Network for Radiation Dosimetry (CONRAD) approach to decorporation modeling is applied using a chelation constant to describe the second-order kinetics of the *in vivo* chelation

reaction (Breustedt *et al.* 2009). In the proposed SPD, chelation occurs in the blood, soft tissues, skeleton, and liver.

The SPD was developed using human data from USTUR Case 0212, an individual exposed to plutonium via a wound (Avtandilashvili *et al.* 2018; Dumit *et al.* 2019). To validate the SPD, data from a whole-body donor exposed via inhalation were used. USTUR Case 0269 inhaled moderately soluble plutonium and was treated extensively with both the calcium disodium salt of ethylenediaminetetraacetate (Ca-EDTA), and the calcium trisodium salt of diethylenetriaminepentaacetate (Ca-DTPA). Either of these chelation agents preferentially exchange their calcium atom with a plutonium atom, forming a rapidly excreted chelate (Pu-EDTA or Pu-DTPA). Chelation treatment data, urine measurements, and post-mortem plutonium activities in the skeleton and liver of USTUR Case 0269 were used in this study. Data from this individual have been used previously for chelation modeling studies (James *et al.* 2007; Konzen *et al.* 2016).

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# Biokinetics of Soluble Plutonium after Wound Injury Treated with Ca-DTPA

USTUR whole-body donor

- Primary intake:  $^{239}\text{Pu}$  contaminated wound
- Treatment
  - Tissue excision: 2.3 kBq
  - Ca-DTPA: 16 g in 18 injections over 2 months
- Died 40 years post intake at age 87
  - Wound site: 1.35 Bq
  - Liver: 12.2 Bq
  - Skeleton: 17.5 Bq
- Estimated total intake: 125 Bq
- Dose reduction due to Ca-DTPA: 2.6

Avtandilashvili and Tolmachev. 12<sup>th</sup> HEIR Conference, Fontenay-aux-Roses, France, October 8 - 11, 2018.

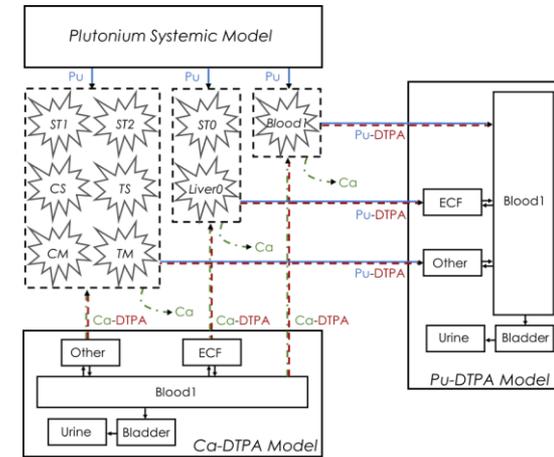
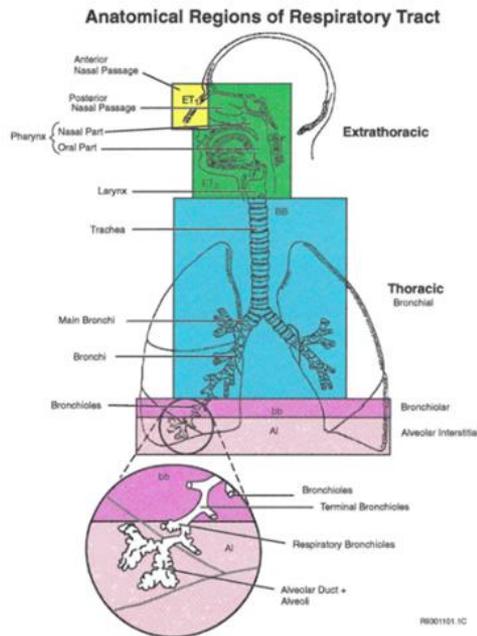




# Future Work

## Plutonium decorporation modeling

- Further improvement of the proposed system of models (Dumit et al. 2019)



## Plutonium bound fraction (LANL)

- Dissect left lung based on ICRP HRTM compartments: BB, bb, AI
- Measure  $^{239}\text{Pu}$  concentrations to evaluate bound Pu in upper airways



# Plutonium Binding in Respiratory Tract

2012 – 2014: One USTUR nitrate case (EC Epidemiological Studies of Exposed Southern Urals Populations; €16,000)

- Tolmachev (2013), Tolmachev et al. (2017) – radiochemistry results
- Puncher et al. (2017), Birchall et al (2019) – data analysis

## *Data used to derive Pu bound fraction in ICRP OIR series*

2014 – 2016: Three additional USTUR cases (DOE Joint Coordinating Committee for Radiation Effects Research; \$75,000)

- Tolmachev (2015) and Tolmachev and Avtandilashvili (2016) – radiochemistry results
- ***No data analysis***





# USTUR and LANL Collaboration

- LANL ‘volunteered’ to analyze data on plutonium binding in a USTUR wound case
- Data from the nitrate case were sent to Dr. Poudel to demonstrate computational capabilities
- Analysis report for the nitrate case was received  
*“It was estimated that the bound fraction for the case, based on the lung compartmental retention data, was ~ 0.79%. These results and the posterior means of the other parameters are in agreement with the earlier analyses of the data”*
- Data from the three additional cases will be sent to LANL to complete data analysis
- ***USTUR will dissect and radiochemically analyze remaining respiratory tract tissues from the wound case***





# Million Person Study & USTUR

## Interest

- Brain dosimetry of internally deposited radionuclides
- Worksite-specific actinide biokinetic models

## Request

- Formalin-fixed tissue sample
- Radiochemistry results and health physics data



# NCRP Letter to DOE



## NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENTS

President: John D. Boice, Jr.; Senior Vice President: Jerrold T. Bushberg; Executive Director: Kathryn D. Held  
7910 Woodmont Avenue, Suite 400, Bethesda, Maryland 20814-3095 Voice: (301) 657-2652 Fax: (301) 907-8768

May 6, 2018

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U.S. Department of Energy  
Washington, DC 20585  
email: [Pat.Worthington@hq.doe.gov](mailto:Pat.Worthington@hq.doe.gov)

Dear Dr. Worthington:

The National Council on Radiation Protection and Measurements (NCRP) would greatly appreciate help from your office *to access post-mortem radiochemical tissue analyses, bioassay data, and work histories available from the U.S. Transuranium & Uranium Registries (USTUR) for workers in our DOE studies.* **These data are needed to improve, enhance, and validate our biokinetic models to estimate organ-specific doses following the intake of radioactive elements.** This is particularly important for the workers at Los Alamos National Laboratory (LANL), Mallinckrodt Chemical Works, and Rocky Flats.

The Office of Environment, Health, Safety and Security has awarded the NCRP a grant to continue our collaboration with the study of One Million U.S. Radiation Workers. One focus is to improve the estimates of organ doses obtained from bioassay data that are used in our epidemiologic studies for risk estimation. We are working closely with Oak Ridge National Laboratory in this regard. We have found it extremely valuable to collaborate with Dr. Sergei Tolmachev to assess the post-mortem radiochemical tissue analyses that are available within the USTUR.

\* - available in the bonus materials





# USTUR Faculty at MPS Workshops

ORAU, Oak Ridge, TN

- May 2 – 4, 2018
- Oct 31 – Nov 2, 2018
- Feb 27 – Mar 1, 2019



# Beryllium and Uranium Analysis at KEEA

Donation	Self-reported, y	Results
2014	14	2018
2008	7	2018
1994	23	2018
2009	23	2018
2015	14	2019
2007	16	2019
2008	20	2019
2005	39	2019





# 50<sup>th</sup> Anniversary Events

- HPS special session on USTUR's research (2016)
- USTUR booth at the HPS (2016)
- 4<sup>th</sup> special issue of Health Physics journal (2019)
- eBook of USTUR publications 1994 – 2018 (2019)





# Thank you!

