

UNITED STATES TRANSURANIUM AND URANIUM REGISTRIES

Annual Report to the United States Department of Energy

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Background

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The United States Transuranium and Uranium Registries are unique human tissue research programs studying the distribution, dose, and possible biological effects of the actinide elements in man, with the primary goal of assuring the adequacy of radiation protection standards for these radionuclides. The Registries research is based on radiochemical analysis of tissues collected at autopsy from voluntary donors who have documented occupational exposure to the actinides. To date, tissues, or in some cases radioanalytical results only, have been obtained from approximately 300 individuals; another 464 living individuals have volunteered to participate in the Registries research programs and have signed premortem informed consent and autopsy permissions.

The Registries originated at the National Plutonium Registry which was started in 1968 as a then Atomic Energy Commission project under the aegis of a prime contractor at the Hanford site. In 1970, the name was changed to the United States Transuranium Registry to reflect a broader involvement with the higher actinides. In 1978, an administratively separate parallel registry, the United States Uranium Registry, was formed to carry out similar studies among uranium fuel cycle workers.

Orientation

In February 1992, responsibility for the operation and management of the Registries was transferred from the Hanford Environmental Health Foundation (HEHF) to Washington State University (WSU) under the provisions of a grant. Several advantages accrued from this transfer. These included immediate access to laboratory space, previously unavailable to the Registries. More significant was the combination of the management and operation of the Registries, heretofore separate albeit parallel programs, and provision for obtaining radiochemistry support via subcontract with Los Alamos National Laboratory. This organizational structural change not only carried with it the potential for reduced operating costs as well as other efficiencies associated with elimination of redundant operations, but permitted integrated planning and operations.

The transfer to the university also enhanced opportunities for collaborative research and more fully integrated the Registries research into the academic community. In this latter regard, the senior Registries research staff have faculty appointments, and the Registries provide several graduate students with the opportunity to carry out thesis research in specific areas of health physics and radiobiology. And, an important, although perhaps intangible, benefit of the relocation of the program to a major state research university is enhanced credibility for the program and greater academic freedom.

Progress and Accomplishments, 1992-93

The grant to WSU became effective in February 1992 and established the Registries operational year as February 1 through January 31. Progress and accomplishments in the initial year of the grant are briefly described in this section. A major task was to effect the transition of the Registries from HEHF to WSU, which was essentially completed within the first three months of the year. This entailed a physical move of files and a modicum of computing equipment to the university and consolidation of the management and operations of the two Registries. The files of the two Registries were consolidated, and immediate human subjects review and approval by the university

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Institutional Review Board was obtained so that operations could be continued without interruption. The Advisory Committee was reconstituted to include a public member as well as a representative of the university community.

An important startup task related to staffing. The Registries began operations at the start of the year with two full-time professional staff members who moved with the program from HEHF to the University. Staffing the Registries was achieved through the addition of two half-time graduate student research assistants, a full-time administrative assistant, a 0.3 time medical director/consultant, and a third full-time faculty member to join the two scientists who moved with the program.

An important accomplishment during the year was formalization and publication of basic Registries policies and forms. This marked the first time in their more than twenty year history that the Registries had formal, written published policies. These included a documentation of the specific criteria used for selection of registrants, communication and publications policies, and a coherent and consistent mechanism for registrant renewal. The latter calls for renewal of all registrants at five year intervals, which contrasts with past practice in which registrants at some sites and whole body donors were not renewed at all. Autopsy permission and records release forms were revised, a new informed consent form was added, and the previous medical and occupational history form combined into a single one page personal history form that not only eliminated redundancies but included provision for a more detailed history of exposure to chemicals and smoking.

DOE site visits and contacts were reinitiated, including a visit to the Savannah River Plant, and international contacts were opened with the United Kingdom Occupational Radiation Exposure Study (UNIKORNES), which will be patterned after the U.S. Registries, and the International Atomic Energy Agency. With regard to the latter, a technical committee meeting was held late in the year to discuss the need for, and development of, international registries and related activities.

Letter contact was made with all active registrants to advise them of the relocation of the Registries to the university and to obtain current addresses and work histories. Since it was not feasible to publish an annual report because of the transition, the Registries instead published a comprehensive progress report which was sent to all previous recipients of the Registries annual reports. This included not only the minutes and recommendations of the Advisory Committee but a summary of the Registries activities and operations which will be published as a separate paper in the peer reviewed literature.

A major accomplishment during the year was the publication of a series of ten papers on the evaluation of USTUR Case 1001, a whole body donor who had been injected with Thorotrast 36 years prior to death. These papers appeared as a single issue of the peer reviewed journal Health Physics. A complete list of Registries publications for the 1992-1993 Registries years is included as Appendix A.

The computerized data base was made fully functional and administrative data for all registrants -- both living and deceased -- has been entered. In addition, radioanalysis results for all deceased registrants have also been entered. Although a major effort still remains with respect to data entry, the data base is now fully functional.

The Registries took a large step forward in the establishment of the National Human Radiobiology Tissue Repository. This involved obtaining a suitable facility for the receipt and storage of approximately 20,000 individual tissue samples and solutions, including numerous frozen specimens. The inventory includes obtaining all available tissues from the radium dial painter project at Argonne National Laboratory as well as the tissue solutions and remaining tissues from registrants from Los Alamos National Laboratory, slides and other tissue materials. These will be stored in a facility rented from Sacred Heart Medical Center which was specifically designed for the Repository, and involved remodeling of an existing older building. Remodeling costs were

borne by Sacred Heart Medical Center, which shares the building, using a portion of it for their own laboratories. Approximately 3000 square feet have been leased by the Registries at favorable rates; 2000 square feet are assigned to the Repository, about half of which is dedicated to a room for cryogenic freezer storage. The remaining 1000 square feet was designed as a dissection laboratory. The first dissection on the backlog of five whole body donations was begun in January.

Deaths among the registrant population and the acquisition of new whole body donor cases, have significantly increased the backlog of tissues awaiting analysis. However, plans are being formulated to alleviate the backlog through the use of a second laboratory which could serve as a backup, as well as provide intercomparisons and other quality assurance functions.

In addition to opening new collaborative research channels, both within the university and externally, the Registries instituted a study of soft tissue concentrations of plutonium and americium. This work is still in progress, but work to date indicates that concentrations in various tissues relative to concentrations in the liver may not be linearly related. A preliminary paper was presented on the findings to date at an international meeting in Rio de Janeiro.

Planned Activities, 1993-4

Planned activities for 1993-94, the second full year of Registries operation as a part of Washington State University, can be loosely divided into major continuing activities and special projects. The bulk of the Registries efforts will be devoted to the major continuing activities, which include both technical and administrative projects and are briefly discussed below.

An important continuing activity pertains to audit, review and upgrade of the registrant files. The administrative files are now fully computerized, and a regular 5 year autopsy renewal has been implemented for all registrants. The plan is to update the files of living registrants with informed consents and current autopsy and other permissions, and, once these have been obtained, request dosimetry and medical records from their employers (or, in the case of retirees, their former employers). Since prior review of the files of deceased registrants revealed a significant number for whom dosimetry and medical data were not on file (particularly among the older cases), an effort will be made to fill in the missing data files insofar as it is practical to do so. This effort will be done in a measured and gradual fashion, at a rate of about 100 registrants per year, and will thus extend over a full five year autopsy renewal cycle.

A second major continuing activity is reduction of the backlog of tissue samples and whole body donations awaiting dissection and radiochemical analysis. With the completion of the dissection facilities, whole body takedowns are now possible, and planning for an intensive effort to complete the backlog of five cases has been completed; the takedowns will be performed as early in the year as practicable. These cases will add about 2000 additional samples to the existing backlog of several hundred awaiting radiochemical analysis at LANL. To expedite the radioanalytical process, several new practices will be implemented. For the whole bodies, sample numbers will be greatly reduced by grouping small bones (i.e. such as the phalanges) into a single sample. This can be done with no loss of relevant data. In addition, certain administrative procedures related to sample receipt, chain of custody and handling at Los Alamos will be streamlined. The key to this will be implementation of a subcontract with Los Alamos which will hopefully be consummated early in the year.

A third area involves laboratory quality assurance. Efforts will continue with respect to documentation of sample collection and preparation procedures to complement the already complete radioanalytical procedures. A subcontract will be implemented with a qualified outside laboratory to provide intercomparisons and quality control analyses for the primary laboratory at LANL. This

laboratory might also serve as a secondary facility and perform designated specific analyses to facilitate activities at the primary laboratory at Los Alamos in reducing its backlog of samples.

Continued and increased recruitment activities are planned for the year. This will include both communicating with and visiting DOE as well as other sites in order to identify and contact potential registrants.

Computer cataloging of the diverse tissue collection of the National Human Radiobiology Tissue Repository will continue as a major activity. This is a large ongoing task inasmuch as there are currently more than 20,000 individual samples in the Repository. The cataloging process will facilitate identification and use of these samples by other investigators. Collaborative studies with other institutions utilizing the unique tissue collection of the NHRTR will be actively pursued. Specific study areas to be explored relate to the initiation, promotion, and progression of the carcinogenic process. Inquiries regarding the potential use of the tissue collection have been informally received from New York University, the University of Utah, Pacific Northwest Laboratory, and the National Cancer Institute. The latter relates to a mutual interest in determining the effect of ionizing radiation on the initiation of genetic alterations in retinoblastoma and p-53 genes.

In addition to the activities more generally described above, the following specific activities will be carried out:

1. **Development of Centralized Files.** Registrant files have been consolidated, and the next step is to organize and consolidate the general administrative files for the Registries, and to attempt to retrieve and retain as much of the unclassified early material as possible. For the next year, the plan is to develop a suitable filing scheme and begin to sort through the boxed materials that were moved with the Registries from the previous contractor. This is an ongoing task that is expected to require two years for completion; completion is anticipated by January 31, 1994.
2. **Human Subjects Review.** Carefully prepared extensive documentation is a prerequisite for the annual human subjects review by the University Institutional Review Board. This task is projected for completion by April 1, 1993.
3. **25th Anniversary Report.** As 1993 marks the 25th anniversary year of the establishment of the National Plutonium Registry, the direct ancestral predecessor of the Registries, a special report is planned. This report will include an historical review of the Registries and their accomplishments, a bibliography of Registries and related staff publications, and the current status of the registries. A separate annex or volume is being considered that will include a compilation of radiochemical data. Projected completion date is July 31, 1993.

In scientific and technical areas, the primary effort will be directed towards completion of data input into the TUR data base, further upgrading and refining the data base, and continuing evaluation of the data from routine autopsies. Fundamental to this effort is development of a protocol for coding and manual entry of health physics, medical and autopsy data to permit unambiguous entry and retrieval from the TUR data base. This is no small task, as the data currently are in a variety of hard copy formats which differ from site to site and even within a specific site. The formats are not always well documented, and the data on individuals may vary from site to site. Different units are used which will require unitary conversions and some interpretation as the units are not always standard and may also be used in inconsistent ways.

It is anticipated that preparation of the coding protocol will be completed, including preliminary data entry and testing and documentation, by April 1. This will be followed by intensive data entry effort. Until the protocol is complete, it is not known how the order of the data entry will proceed

-- ie. chronological beginning with the earliest cases, entry of specific types of data (e.g. health physics or medical data) first, or entry of cases from specific site. However, it is expected that data entry will be 25-30% complete by January 31, 1994.

Efforts continue with respect to examining the concentration of actinides in various tissues collected from routine autopsy (as opposed to whole body) donors. One import aspect of this work lies in determining the value and future direction of the routine autopsy program. Preliminary results have been very encouraging and suggest that the available data are sufficient to provide some insights into relative tissue concentrations and doses at long times postexposure. In addition to the primary effort described above, several specific projects will be undertaken. These include the following:

1. Seaborg Memoirs. This involves editing and annotating for publication the World War II memoirs of Glenn T. Seaborg, Nobelist and discover of plutonium, relating to the Manhattan District Plutonium Project. It is anticipated that a manuscript will be ready for submission to the publisher by July 1, 1993, and that the published work will available in book form by December 1, 1993.
2. Actinide Dose Distribution in Bone. This is a collaborative research effort with AERE Harwell, NIST and the University of Utah involving an intercomparison of bone distribution and dose of actinides using specialized autoradiography techniques and electron spin resonance in selected Registries cases. This two year effort will be completed January 31, 1995.
3. Long Term Followup Study. This study, begun several years ago, examines the urinary and fecal excretion of plutonium and in-vivo counting results in five volunteer former plutonium workers (retirees) at the Hanford site with known measurable depositions. Additional data will be collected, and a preliminary evaluation will be made of the results to date with an eye towards publication. However, this is of necessity a continuing program that will only terminate with the deaths of the participants. An attempt will be made to expand this program to include medical followup and to a larger cohort in conjunction with PNL.
4. Uranium Kidney Toxicity. This study will be concluded and submitted for publication in a peer reviewed journal; anticipated submission date is June 1, 1993.
5. Biokinetics of Uranium Enrichments. A pilot study will be conducted in rabbits to determine if there is an enrichment effect on the biokinetics of uranium. The pilot study will be used as the basis to determine whether further studies are indicated; the pilot study will be initiated and completed by January 1994.
6. Case 246 Writeup. USTUR case 246 is an individual who died 11 years after suffering a massive accidental exposure to Am-241. The data from this case have been evaluated, and only the writeup of four papers needs to be completed. These papers will be completed and submitted for publication in a peer reviewed journal.

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