OFFICE OF THE SECRETARY
CORRESPONDENCE CONTROL TICKET

Date Printed: Feb 11, 2004 18:38

PAPER NUMBER:	LTR-04-0064	**LOGGING DATE:**	02/10/2004
ACTION OFFICE:	CHRM		
AUTHOR:	Mr. Carl Holder		
AFFILIATION:	WA		
ADDRESSEE:	CHRM Nils Diaz		
SUBJECT:	Concerns the Fast Flux Test Facility		
ACTION:	Information		
DISTRIBUTION:	RF		
LETTER DATE:	02/03/2004		
ACKNOWLEDGED	No		
SPECIAL HANDLING:			
NOTES:			
FILE LOCATION:	ADAMS		
DATE DUE:		**DATE SIGNED:**	

H-4486.2

HOUSE JOINT MEMORIAL 4043

State of Washington 58th Legislature 2004 Regular Session

By Representatives Delvin, Hankins, Grant, Schoesler, Clements, Mastin, Pettigrew, Cox, Skinner, Newhouse, Jarrett, Chandler, Clibborn and Kessler

Read first time 01/30/2004. Referred to Committee on Technology, Telecommunications & Energy.

TO THE HONORABLE GEORGE W. BUSH, PRESIDENT OF THE UNITED STATES, AND TO THE PRESIDENT OF THE SENATE AND THE SPEAKER OF THE HOUSE OF REPRESENTATIVES, AND TO THE SENATE AND HOUSE OF REPRESENTATIVES OF THE UNITED STATES, IN CONGRESS ASSEMBLED, AND TO SPENCER ABRAHAM, THE SECRETARY OF THE DEPARTMENT OF ENERGY:

We, your Memorialists, the Senate and House of Representatives of the State of Washington, in legislative session assembled, respectfully represent and petition as follows:

WHEREAS, Governor Locke recently launched "Bio 21" with the express intention to strengthen, enhance, and expand the biotechnology businesses for the people of Washington State through merging science, health, education, and research projects, encouraging partnerships from public and private participations; and

WHEREAS, The "Bio 21" document was prepared under the leadership of the Technology Alliance of Washington in January 2004 at the direction of Governor Locke, recognizing that Washington State ranks 46th out of 50 states in obtaining research funding grants; and

WHEREAS, The "Bio 21" document answered the question that Washington State does have unique assets at the intersection of biotechnology and information technology that should be exploited for the benefit of Washington's economy encompassing some of the most important companies in the world in the technology sectors, including software, biotechnology, wireless communications, aerospace technology, energy, environmental technology, and nanotechnology; and

WHEREAS, Governor Locke has accepted the recommendations of the Washington Competitiveness Council's January 2002 report to examine Washington's ability to compete and create jobs in a global economy; and

WHEREAS, Governor Locke recognizes that Washington State is the home of a unique United States Department of Energy (U.S. DOE) property, the five billion dollar Fast Flux Test Facility (FFTF) complex, located in the Tri-Cities, that

could allow Washington State to provide a national center for radiopharmaceutical production that would bring in five hundred million dollars in private capital immediately to make these facilities market ready, benefiting the people of Washington State, the Nation, and the World, through improved health care; and

WHEREAS, "Bio 21" recognizes fields of advanced science such as radiopharmaceuticals for diagnostic and therapeutic medical procedures with five billion dollars of market sales by 2008 projected by the U.S. DOE and the National Cancer Institute with tens of millions of these procedures being performed annually; and

WHEREAS, United States Secretary of Health and Human Services Tommy Thompson, on October 8, 2002, requested that U.S. DOE give "...the (community re-use commercialization) proposal every consideration..." for utilization of these facilities which could meet expanded national health care needs and provide a consistent national domestic supply of medical isotopes, which are now over ninety percent imported; and

WHEREAS, The 30,000 member organization, the United States Radiological Society of North America, as of December 2003, is seeking the establishment of a United States radionuclide production facility to handle the projected growth in food security, homeland security, and health care that drives expanded United States isotope production requirements;

NOW, THEREFORE, Your Memorialists respectfully pray that the U.S. DOE act on United States District Court Judge Edward F. Shea's ruling to prepare the Environmental Impact Statement (EIS) to determine the final disposition of the unused FFTF property and that the U.S. DOE avoid every irretrievable action that could jeopardize future uses, and we request that the U.S. DOE FFTF complex be privatized to a qualified party for the production of medical isotopes and other energy related issues. Further, Your Memorialists call on Secretary of Energy Spencer Abraham to immediately call a multicabinet meeting represented by the United States Departments of Energy, Health and Human Services, Homeland Security, and Agriculture and Washington State representatives to discuss multiagency uses.

BE IT RESOLVED, That copies of this Memorial be immediately transmitted to the Honorable George W. Bush, President of the United States, Spencer Abraham, Secretary of the Department of Energy, the President of the United States Senate, the Speaker of the House of Representatives, and each member of Congress from the State of Washington.

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Opinion

Medical Radionuclide Supplies and National Policy: Time for a Change?

Thomas S. Tenforde[1]

The use of radionuclides in diagnostic and therapeutic procedures is currently one of the fastest growing areas of medicine. The strong growth of the United States radiopharmaceutical market during the past decade has been fueled by the United States Food and Drug Administration (FDA) approval of several effective diagnostic and therapeutic radiopharmaceutical products. A challenge to sustaining the growth of this market, however, is posed by the limited domestic availability of radionuclides for laboratory and clinical research during the early stages of developing and testing new radiopharmaceutical products. The supply of radionuclides provided by the Isotope Programs Office (IPO) of the United States Department of Energy (DOE) for radiopharmaceutical products that are at an early developmental stage in many instances has been unreliable over the past several years. This problem and a possible resolution based on a major shift in the commitment and policy of the United States government on supplying medical radionuclides are the major topics addressed in this article.

Recent Growth of the Radiopharmaceutical Market

On the basis of a review of the sales of radiopharmaceutical products from 1998 to 2002, the consulting firm Frost & Sullivan [1] has predicted that the compound annual revenue growth rate of the total United States radiopharmaceutical market will be 10.2% during the period 2001–2008. This growth projection is close to the prediction made in a report issued in 1998 by a DOE expert panel that the annual growth in revenues from sales of diagnostic and therapeutic radiopharmaceutical products in the United States would average 10%, with a confidence range of 7–16%, over the period 1996–2020 [2]. The projection of the DOE expert panel was based on a review of four independent market surveys performed from 1994 to 1998.

Diagnostic Radionuclides

Of the nearly 15 million nuclear medicine procedures performed in the United States each year, more than 90% involve the use of radiopharmaceutical products for disease diagnosis, primarily in the diagnosis of cancer and cardiovascular disorders. The rapid growth of the diagnostic radiopharmaceutical market was launched in the early 1970s with the development and routine availability of molybdenum-99 generators for the production of technetium-99m used in diagnostic imaging. After the introduction of the ^{99}Mo–^{99m}Tc generator, the compound annual growth rate of the ^{99m}Tc radiopharmaceutical market was a remarkable 74% per year over the period 1972–1977. After the market was well established, it continued to grow at a slower, but progressive, average annual rate of approximately 5%.

Several other diagnostic radiopharmaceutical products have been used successfully over the past three decades, including thallium-201 for imaging myocardial perfusion and the positron emitters fluorine-18 (as FDG) and rubidium-82 for positron emission tomography (PET) analysis of cardiac perfusion and myocardial viability. FDG has also proven to be effective for the diagnosis and staging of treatment of several major classes of cancer and neurologic diseases. As a result of FDA approval for the broad-scale use of FDG for PET applications, the compound annual growth rate of the FDG market has averaged 38% over the period 1997–2002. The market growth rate for this radiopharmaceutical product is anticipated to continue at an average rate of 31% per year from 2001 to 2008 [1].

Therapeutic Radionuclides

Until the late 1990s, the relatively small therapeutic radiopharmaceutical market was dominated by the use of iodine-131 for treat-

Received September 30, 2003; revised after accepted October 2, 2003.

The views expressed in this article are those of the author and do not necessarily represent those of the National Council on Radiation Protection and Measurements.

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AJR 2004;182:575–577 0361–803X/04/1823–575

ing hyperthyroidism and thyroid cancer, phosphorus-32 for the treatment of polycythemia vera, and strontium-89 and samarium-153 for palliating the pain associated with advanced bone cancer. This situation is beginning to change with the approval by the FDA of prostate cancer brachytherapy using implanted palladium-103 and iodine-125 seeds. In addition, in 2002 and 2003 the FDA approved for the first time the use of two radiolabeled antibody products for the treatment of cancer. These radiopharmaceutical products, both of which have been shown to be effective in the treatment of non-Hodgkin's lymphoma, are Zevalin ([ibritumomab tiuxetan] Y2B8-anti-CD20 monoclonal antibody labeled with yttrium-90, IDEC Pharmaceuticals, San Diego, CA) and Bexxar ([tositumomab] B1-anti-CD20 monoclonal antibody labeled with iodine-131, Corixa, Seattle, WA).

Problems with Radionuclide Supplies

The advances in brachytherapy and radioimmunotherapy over the past decade have set the stage for a rapid expansion in the use of radiopharmaceutical products for the effective treatment of cancer. However, as pointed out in the latest market survey by Frost & Sullivan [1], the growth of the therapeutic radiopharmaceutical market may be severely limited by the lack of a reliable supply of radionuclides for clinical trials of new products. This problem is especially serious for new and novel classes of radionuclide products. For example, early phase I and II clinical trials at the University of California Davis Medical Center showed that 2IT-BAT-Lym-1 labeled with copper-67 was more effective than ^{131}I-labeled Lym-1 antibody in treating B-cell non-Hodgkin's lymphoma patients [3]. The ^{67}Cu radioimmunotherapy trial was delayed, however, because of the inability to obtain a steady supply of this radionuclide from the DOE.

Similarly, the α-emitter bismuth-213, when conjugated to the HuM195 monoclonal antibody, has shown promising results in the treatment of acute myelogenous leukemia. In addition, preclinical research with models of prostate carcinoma and other types of cancer indicate that short-range alpha particle radiation from ^{213}Bi or its parent radionuclide, actinium-225, may be extremely effective in treating a wide variety of cancers [4]. In many cases, these cancers are difficult to treat effectively using radioimmunotherapy procedures that involve β-emitting radionuclides. However, the supply from the DOE of ^{225}Ac to generate ^{213}Bi has been extremely limited, and clinical trials with ^{213}Bi have not moved forward as rapidly as initially planned.

Finally, in addition to ^{67}Cu, there is an increasing demand for other radionuclides such as holmium-166, lutetium-177, and rhenium-186 that offer a desirable combination of short half-lives, favorable beta energies, and gamma emissions at energies suitable for imaging the whole-body distribution of radioactivity. The chemistry for binding these radionuclides to targeting molecules such as monoclonal antibodies is also well understood and relatively easy. Unfortunately, the lack of abundant and reliable supplies of these radionuclides represents a serious limitation to their eventual use in large-scale clinical trials.

Role of the DOE

The initial stages of preclinical and clinical testing of novel radionuclides such as those discussed earlier offer little or no financial incentive for commercial suppliers of medical radionuclides to produce these radionuclides on a routine basis. The medical community must therefore turn to the DOE or foreign suppliers as a source of promising radionuclides that are not available on the commercial market. The DOE, under the authority of the Atomic Energy Act of 1954, holds the responsibility for producing radionuclides needed for research, medical, and industrial applications. Much to its credit, the DOE and its predecessor organizations, the Atomic Energy Commission and the Energy Research and Development Administration, sponsored the development of the gamma camera, PET technology, and many radiochemical procedures for the production of short-lived medical radionuclides—^{99m}Tc, ^{90}Y, and ^{213}Bi, among others. However, despite early successes in developing important nuclear medicine technology, the radionuclide production program at the DOE is in rapid decline, and many of the radionuclides that are urgently needed for medical research and clinical applications cannot be supplied in adequate quantities or in a timely manner.

Financial Problems of DOE

Multiple factors have contributed to the inability of the DOE to meet the radionuclide requirements of the medical community in an adequate manner, the most serious of which is financial. In the mid 1990s, the congressional appropriation for the IPO (then known as the Isotope Production and Distribution Office) averaged $18 million per year, including capital funds. By fiscal year 2002, the IPO appropriation had decreased to $17 million, including capital funds. In the same time period, the sales of radionuclides produced at DOE national laboratories with funding by the IPO had declined from an average of $15 million per year in the mid 1990s to $8 million in fiscal year 2002. Over the past 8 years, the total funding for IPO from federal appropriations and radionuclide sales has therefore declined by approximately a factor of 2 when adjusted for inflation.

In an effort to increase the supply of radionuclides for medical applications, the IPO has undertaken several efforts to privatize radionuclide production programs conducted at DOE national laboratories. These efforts have had mixed results. An outstanding example of successful privatization was the transfer of the ^{90}Y production program at the Pacific Northwest National Laboratory to NEN Life Science Products (now a subsidiary of Perkin Elmer Life Sciences). During the period 1996–1998, the worldwide sales of ^{90}Y by the Pacific Northwest National Laboratory increased 14-fold, and the rapid market growth continued after transfer of the program to NEN in 1999. During the period 1996–2001, the average annual growth rate of ^{90}Y sales was 119% per year. The success of the ^{90}Y program and its privatization by DOE have been important factors in making ^{90}Y one of the most promising new therapeutic radionuclides, with a growing United States and worldwide market.

In contrast, other privatization efforts by the DOE have been unsuccessful. In the latter half of the 1990s, the IPO undertook an effort to convert the annular core research reactor at Sandia National Laboratory in New Mexico, a reactor used for defense-related programs for more than two decades, into an operational state suitable for the production of ^{99}Mo and other radionuclides. The primary goal of this project was to develop a United States supply of ^{99}Mo for ^{99m}Tc generators in the event of a disruption of the ^{99}Mo supply received from Canada and other nations. After several years and a large expenditure of capital funds, the IPO attempted unsuccessfully to privatize the project at a stage when considerably more work remained to be done to bring the reactor into an operational state for radionuclide production. An effort to privatize the operation of calutrons at the Oak

Ridge National Laboratory for the enrichment of stable radionuclides used as targets for reactor-generated medical radionuclides was similarly unsuccessful.

Because of a lack of federal funding, the IPO recently undertook an effort to privatize the radiochemical harvesting of thorium-229 from aged stockpiles of uranium-233 at the Oak Ridge National Laboratory. The ^{229}Th is highly valued as a source of the α-emitting medical radionuclides ^{225}Ac and ^{213}Bi, which are obtained as radioactive decay products. On October 9, 2003, the DOE announced that a contract had been awarded to Isotek Systems to down-blend enriched ^{233}U as part of the cleanup of legacy wastes at the Oak Ridge National Laboratory and during this process to extract ^{229}Th as a useful byproduct. Isotek Systems will also work with its partner Theragenics and with the Pacific Northwest National Laboratory through a cooperative research and development agreement to develop an optimized process for extracting ^{225}Ac from the ^{229}Th. The extraction and supply to medical centers of the purified ^{225}Ac will be carried out at no cost to the DOE. The concept of linking the retrieval of useful medical radionuclides to the cleanup of nuclear waste materials at DOE sites is innovative, and it will be interesting to follow progress in this new program.

Other Problems Faced by the DOE

Because of the severely declining IPO budget for radionuclide production, IPO now requires customers to preorder radionuclides during the preceding fiscal year under a program known as the Nuclear Energy Protocol for Research Isotopes (NEPRI). The orders are peer-reviewed for merit by an advisory panel appointed by DOE, and the customers must prove that they have adequate resources to pay for the quantities of radionuclides that they preorder. On the basis of this information, the IPO decides on the types and quantities of radionuclides that it will produce during the next fiscal year. In view of the difficulty of predicting the quantities of radionuclides needed in early stages of preclinical and clinical research, the NEPRI program is clearly an incentive for IPO customers to seek alternative sources of medical radionuclides.

Another serious problem faced by the IPO is the deteriorating condition of many aging facilities used for radionuclide production in the national laboratories. In addition, the reactor and accelerator facilities on which the IPO relies are used primarily for physics experiments, and only limited time is available for radionuclide production. In an attempt to improve its radionuclide production capability, the IPO has supported a multiyear effort to develop a 100-MeV proton beam line at the Los Alamos Neutron Science Center accelerator at the Los Alamos National Laboratory in New Mexico. This facility, the completion of which is behind the original schedule, should be an asset in the effort to improve the domestic supply of accelerator-produced research and medical radionuclides.

Finally, as of fiscal year 2003, the IPO has lost all congressionally appropriated funding for support of research on innovative medical radionuclide products. This research was funded through an advanced nuclear medicine initiative that had received $2.5 million per year in fiscal years 2001 and 2002. The loss of these funds marks an end to all radionuclide process development research supported by the IPO.

Overcoming the Problem

A renewed commitment by the federal government is needed to revitalize and adequately fund a strong national radionuclides program. Because of frequent delays in supplying radionuclides for early stages of clinical research and the inability to complete facility upgrades in a timely and cost-effective manner, the DOE has lost credibility as the primary government supplier of medical radionuclides. One possible remedy for this situation would be to directly involve the National Institutes of Health (NIH) as a lead agency with the capability of convincing Congress of the importance of a reliable domestic supply of radionuclides for research and medical applications. In this model, the NIH would exert its strong management and marketing skills to secure adequate funding for producing urgently needed medical radionuclides, and would provide "pass-through" funding to the DOE for radionuclide production activities at its national laboratories.

During the past decade, the NIH and the DOE have jointly sponsored several workshops on medical radionuclide needs and availability issues, the latest of which was held September 15–16, 2003. The proceedings of these workshops have been documented in reports, but they have not led to a firm agreement for collaboration between the NIH and the DOE in strengthening the national supply of radionuclides for research and medical applications. What may ultimately be needed is a decision by Congress to transfer responsibility for medical radionuclides to the NIH, with the IPO serving as a supporting agency under a memorandum of agreement that imposes rigorous program management controls.

This path forward must be coupled with a firm federal commitment and adequate funding to rebuild the supporting infrastructure for reliable radionuclide production, including the upgrade of existing facilities and the development of new dedicated radionuclide production facilities, the creation of new training opportunities for the next generation of radiochemists, the provision of greater incentives for collaboration between the government and private sector radiopharmaceutical manufacturers, and the development of more effective mechanisms for transferring to the private sector the production of mature radionuclide products.

These shifts in federal policy and the organizational structure of the national medical radionuclides program would represent a major step toward enhancing and sustaining the rapid development of new radiopharmaceutical products for the diagnosis and treatment of cancer and other major diseases.

References

1. Frost & Sullivan. *Radiopharmaceutical markets.* Mountain View, CA: Frost & Sullivan, 2002. report A161-50
2. DOE expert panel. *Forecast future demand for medical isotopes.* Washington, DC: United States Department of Energy, 1998. DOE/SCUREF cooperative program project 130
3. O'Donnell RT, DeNardo GL, Kukis DL, et al. A clinical trial of radioimmunotherapy with ^{67}Cu-2IT-BAT-Lym-1 for non-Hodgkin's lymphoma. *J Nucl Med* 1999;40:2014–2020
4. McDevitt MR, Ma D, Lai LT, et al. Tumor therapy with targeted atomic nanogenerators. *Science* 2001;294:1537–1540