U.S. Department of Energy
Office of Inspector General
Office of Audit Services

Special Report

Meeting Medical and Research Needs for Isotopes Derived from Uranium-233

DOE/IG-0795 May 2008

Department of Energy

Washington, DC 20585

May 29, 2008

MEMORANDUM FOR THE SECRETARY

FROM: Gregory H. Friedman
Inspector General

SUBJECT: INFORMATION: Special Report on "Meeting Medical and Research Needs for Isotopes Derived from Uranium-233"

BACKGROUND

As part of its program to produce isotopes for medical, research and industrial purposes, the Department of Energy (Department) has used its unique nuclear facilities to produce thorium-229 isotopes from its inventory of uranium-233. Thorium-229 is used to create actinium-225 and its progeny isotope, bismuth-213. Both actinium and bismuth are extremely rare isotopes that are now being used in clinical trials and cancer research at organizations such as the Memorial Sloan-Kettering Cancer Center in New York. Early research results have been promising, showing improved cancer survivability rates in test populations. Consistent with these research results, a 2001 Departmental Report to Congress underscored the importance of maintaining a supply of these isotopes to support promising medical research and treatment. Specifically, the report stated that "the supply of actinium-225/bismuth-213 available as uranium-233 decay products will be inadequate if therapeutic applications for leukemia become even moderately successful and will become woefully inadequate if successfully applied to other types of cancer including prostate, breast, lymphomas, and various forms of brain cancer."

The Department's inventory of uranium-233 resides primarily at the Idaho National Laboratory (Idaho) and the Oak Ridge National Laboratory (ORNL). The Department determined that these inventories are no longer needed to meet agency mission requirements. In 2003, to aid in isotope production, Congress authorized the extraction of thorium-229 from ORNL's uranium-233 inventory prior to its disposal. Subsequently, however, Congress directed that the Department terminate the extraction process. Responsibility for disposition of uranium-233 was transferred to the Environmental Management (EM) program. Accordingly, in October 2007, at the recommendation of the Department's Nuclear Materials Disposition and Consolidation Coordination Council, the Department decided to prepare the ORNL inventory beginning in 2012 for disposal. Further, the Department decided to dispose of the Idaho uranium-233 inventory at the Nevada Test Site as low-level waste and began shipments of the material in January 2008. Because of its importance to medical and other research activities, we initiated a review to evaluate whether the Department's planned disposition of its uranium-233 inventories would permit it to meet projected domestic medical and research needs for actinium and bismuth. Shortly after initiating this review, we received information alleging that the Department was disposing of uranium-233 that had significant potential use.

RESULTS OF AUDIT

We concluded that the Department's current disposal plans provide no assurance that sufficient quantities of uranium-233 and its valuable progeny isotopes will be available to support U.S. medical and scientific research needs. We noted that:

- The Department is the only domestic producer of progeny isotopes from uranium-233 and current production is insufficient to meet medical and scientific research needs. Once the planned disposal of uranium-233 is complete, the Department will not have the means to increase isotope production to meet the dramatic projections of future needs for actinium and bismuth;

- At present, no viable alternative methods of production of actinium and bismuth have been demonstrated or proven; and,

- Uranium-233 also is used to support other Department missions such as the National Nuclear Security Administration's Test Readiness Program.

The importance of and continuing need for uranium-233 and related isotopes was confirmed by The National Academy of Sciences in its September 20, 2007, report entitled "*Advancing Nuclear Medicine Through Innovation.*" The National Academy was asked by the Department and the National Institutes of Health (NIH) to review the state of the science of nuclear medicine. The study concluded that the Department and NIH need to focus research on the development of new radionuclide production facilities and technologies as well as the development and use of targeted radionuclide therapeutics that will allow cancer treatments to be tailored for individual patients. The report also stated that several of these radionuclides, including actinium-225, are not being produced in sufficient quantities to meet existing research demand. The supply/demand balance is also affected by recent reports from researchers asserting that problems with quality and availability prevent them from using isotopes from foreign sources for human trials. The vulnerability of obtaining radionuclides from foreign sources was also underscored by the recent shutdown of a Canadian reactor, which provided many of the isotopes used in medical diagnosis and treatment.

According to senior program managers, the inventory of uranium-233 is being disposed of because there is a lack of programmatic authority to maintain the material and the infrastructure necessary to continue extracting the actinium and bismuth. Currently, the uranium-233 inventory is controlled and managed by the EM program, whose mission is to dispose of the Department's unwanted materials. The EM program tried to transfer the uranium-233 to other programs, such as the Office of Nuclear Energy (NE). However, according to NE management, which currently manages the Department's Isotope Programs, funding restrictions prohibit NE from taking possession of the inventory.

We recognize that the Department has, as a matter of policy, committed to providing isotopes only when there is no U.S. private-sector capability or when the available supply is insufficient to meet U.S. needs. In the case of uranium-233, the Department appears to offer the only viable domestic production capability. Yet, even its existing production capacity is insufficient to meet demand. Further, security and proliferation concerns

prohibit the Department from providing the source material directly to universities or industry to permit the development of a viable private sector source. Based on our consultations with program officials within the Department, we learned that given appropriate authorities and the available funding, several alternatives exist for assuring a viable inventory of these important radioisotopes. As was initially proposed for the inventory maintained at Oak Ridge, thorium-229 could be extracted from the uranium-233 prior to disposition. Alternatively, the Department could retain some portion of the uranium-233 inventory, or develop alternative methods of producing actinium-225 and its progeny isotope, bismuth-213. It should also be noted that other options are being pursued by private sector entities in an effort to create these isotopes; however, it is not yet known when or if these technologies will prove viable.

To its credit, the Department's Fiscal Year 2009 budget proposes to transfer the Nation's isotope program to the Office of Science and seeks to increase research and development in isotope production. The budget request mentions that future research and development efforts will specifically consider the results of the recent National Academy of Science report on nuclear medicine. However, without the feed material from which to produce actinium and bismuth, the research must necessarily focus only on alternative production methods -- efforts that at the least will significantly delay delivery of these potentially beneficial isotopes to the medical research community.

Should the Department elect to proceed as planned, it may dispose of a national resource that is irreplaceable. The potential for isotopes produced from uranium-233 to help save the lives of thousands of American cancer patients is widely accepted, and one top Departmental official estimated that isotopes production from ORNL stocks alone could be used to treat about 6,000 patients annually. While we are sensitive to the complex public policy implications associated with this matter, including significant budgetary issues, we believe that the Department should explore alternatives for ensuring a stable domestic supply of the important isotopes produced from uranium-233.

MANAGEMENT REACTION

Management did not concur with our recommendations but instead proposed alternative actions designed to address certain issues described in our report. Notably, the Department indicated that a merit-based peer review would be conducted to examine the needs and priorities for actinium and bismuth. Management also noted that it planned to work with NIH to address the recommendations of the National Academy of Sciences. Citing concerns with cost, security, safety and Congressional mandates, management stated that it would continue with the disposition of the uranium-233 inventories at Oak Ridge and Idaho. Management also stated that it had largely addressed our recommendation to evaluate the cost and benefits of harvesting thorium-229 from uranium-233 prior to its disposal. Should Congress direct a new strategy for the disposition of uranium-233, the Department pledged to work to establish a new framework for the disposition of the material. Management's comments are contained as Appendix 3 to our report and provide additional details regarding uranium-233 disposition decisions.

We are encouraged that the Department is taking steps to conduct a merit-based peer review to examine the needs and priorities for production of progeny isotopes discussed

in the report and working with the NIH to address medical and research isotopic needs. Management's comments, however, were not fully responsive in one important respect. While the Department has completed several evaluations regarding uranium-233 disposition alternatives for the Oak Ridge inventory, these evaluations were completed several years prior to the National Academy of Sciences report and did not consider recent medical successes, the increasing demand for these isotopes, or address alternative technologies for providing them.

Given the past and current role of the Department of Energy in supporting medical and research activities, an evaluation needs to be completed to provide Congress, the Office of Management and Budget and other stakeholders with up-to-date information on which to base important public policy decisions regarding the Department's role in producing medical and research isotopes. Management could also consider and address cost and security concerns as a part of such a study.

Attachment

cc: Acting Deputy Secretary
Under Secretary of Energy
Under Secretary for Science
Chief of Staff
Assistant Secretary for Environmental Management
Assistant Secretary for Nuclear Energy
Director, Office of Science
Manager, Idaho Operations Office
Manager, Oak Ridge Operations Office
Team Leader, Audit Liaison Team, CF-1.2

SPECIAL REPORT ON MEETING MEDICAL AND RESEARCH NEEDS FOR ISOTOPES DERIVED FROM URANIUM-233

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ENSURING A VIABLE DOMESTIC SUPPLY OF ISOTOPES

Department Plans To Dispose of Uranium-233

Should the Department of Energy (Department) carry out its disposition plans to dispose of its uranium-233, there is no assurance that a viable inventory of progeny isotopes (actinium-225 and bismuth-213) will be available to meet domestic medical and scientific research needs. Currently, the domestic production of actinium-225 is approximately 650 millicuries per year. This supply has been provided through a small inventory of thorium-229 maintained at the Oak Ridge National Laboratory (ORNL) that was extracted from uranium-233. However, according to the National Institutes of Health's (NIH) projections, demand is far greater. Specifically, NIH projects a demand for actinium-225 of 1,700 millicuries in 2008 and 6,000 millicuries in 2009. With the decision to dispose of ORNL's inventory of uranium-233, the production capability will be inadequate to meet increasing domestic demands. Further, disposal of the Idaho National Laboratory's (Idaho) uranium-233 inventory will effectively eliminate the possibility of producing isotopes from that source.[1]

The loss of the uranium-233 will have significant impact on medical research which is now requiring a greater supply of progeny isotopes than ever before. For example, ongoing research includes Phase II clinical trials for the treatment of acute myeloid leukemia at Memorial Sloan-Kettering Cancer Center in New York. The results of Phase II trials showed increased survivability of those receiving the treatment, where patients had no other treatment options. Due to the limited availability of isotopes currently being produced from uranium-233, only one Phase II trial may be done at a time. Accordingly, researchers at Memorial Sloan-Kettering have decided to focus their current research on using the actinium-225 for alpha-particle immunotherapy trials, and to postpone research work using bismuth-213.

In addition to myeloid leukemia, research is being conducted using uranium-233 progeny isotopes to treat Non-Hodgkin Lymphoma, bone marrow transplants, AIDS, as well as cancers of the lungs, pancreas, and kidneys. Each treatment application requires separate clinical trials to obtain U.S. Food and Drug Administration (FDA) approval. Unfortunately, Memorial Sloan-Kettering decided to delay Phase III clinical trial efforts for myeloid leukemia due to the extremely short supply of bismuth. Without the Department's inventory of uranium-233, there will not be adequate domestic supplies to support the Phase III clinical trial

[1] It should be noted that actinium-225 has been extracted from Idaho's inventory of uranium-233 only on a laboratory scale. Planning for pilot, and ultimately production levels, is currently ongoing.

necessary to obtain FDA approval. According to the principal researcher at Memorial Sloan-Kettering for acute myeloid leukemia, if the Department continues with its plans to dispose of its inventory of uranium-233, then all research using actinium and bismuth will be lost due to the lack of supply. The president of a medical isotope supply company has noted that the medical industry will be able to use all of the progeny isotopes that could be produced from the Department's inventory should these clinical trials prove successful.

While limited foreign supplies are available for the progeny isotopes, researchers told us that such products have quality and reliability concerns. For example, Memorial Sloan-Kettering Cancer Center has obtained actinium-225 from foreign sources; however, due to quality concerns, the Center's representatives stated that they will not use foreign sources for cancer treatment in humans, but may continue to use it in research. Further, effective treatment requires a reliable supply because, once the patient begins treatment, it must be available on an uninterrupted basis. Although we were unable to specifically verify these assertions, researchers informed us that foreign sources are not reliable enough to meet this need.

The need for uranium-233 was recently confirmed by The National Academy of Sciences in its September 20, 2007, report entitled "*Advancing Nuclear Medicine Through Innovation*." The National Academies were asked by the Department and NIH to review the state of the science of nuclear medicine and future scientific areas of research for the Department's Medical Applications and Sciences Program. The study concluded that the Department and NIH need to focus their research on the development of new radionuclide production facilities and technologies as well as the development and use of targeted radionuclide therapeutics that will allow cancer treatments to be tailored for individual patients. The report specifically mentions the promise and need for actinium-225, one of 2 alpha emitters and one of 12 therapeutic radionuclides listed as being essential to nuclear medicine research. The report also states that several of these research radionuclides are not being produced in sufficient quantities to meet the research demand.

Several alternatives exist for assuring a viable inventory of these important radioisotopes. One alternative is to extract the thorium-229 prior to dispositioning the uranium-233. The contractor at ORNL responsible for disposition estimated the cost to extract the thorium-229 at $13.7 million prior to the termination of the extraction project. Another alternative is to retain some portion of the Department's inventory of uranium-233. It is important to note, however, that due to safety and security concerns, uranium-233 will not be transferred outside of the Department. Conversely, thorium-229 and actinium-225 can be transferred and sold outside of the Department. There are also a number of other processes being considered to produce these isotopes using, for example, accelerators, cyclotrons, and reactors. Various private enterprises are in the early stages of investigating these opportunities in order to meet the market demand. Each of the processes under investigation have their respective costs and benefits but it is not known when or if any of these will prove to be useful and affordable to the medical and research community. At present, none of the alternative technologies being considered have resulted in the actual production of actinium and bismuth.

Finally, we noted that uranium-233 also has value to support other Department missions such as the National Nuclear Security Administration's Test Readiness Program. According to the pre-decisional draft Implementation Plan for the Disposition of Surplus uranium-233, the decision to dispose of the ORNL inventory of uranium-233 was made, in part, based on the sufficiency of the uranium-233 in Idaho to meet potential future needs. However, in October 2007, the Department approved the Nuclear Materials Disposition and Consolidation Coordination Committee's recommendation to dispose of the Idaho inventory as well; therefore, there will no longer be any inventory to meet on-going programmatic needs.

Programmatic Authority

Based on our discussion with several Department program officials, we learned that there is currently a lack of programmatic authority to maintain the material and infrastructure necessary to continue providing progeny isotopes from uranium-233. Both the Idaho and ORNL uranium-233 inventories are now controlled and managed by the Office of Environmental Management (EM) whose mission is to dispose of these unwanted materials. Given this responsibility, EM is proceeding with short-term

actions to dispose of these materials as waste. EM's decision-making process considers various issues crucial for deciding whether to dispose of materials. One of the decision points is whether the material should be retained as a national resource. EM determined that uranium-233 should not be retained as a national resource because there is no program with an identified current use and funding to take custody of the inventory. Further, EM is under pressure to dispose of the Idaho inventory quickly since the license for a disposal cask to transport the uranium-233 expired on November 30, 2007. To avoid the cost of constructing and licensing a new cask, the Department is taking steps to extend this license for one year and is trying to dispose of the uranium-233 by September 30, 2008.

Prior to reaching its disposal decision, EM tried to transfer the uranium-233 to other programs, such as the Office of Nuclear Energy (NE). However, no programs stepped forward to take control of the material since EM required the adopting program to assume responsibility for managing the uranium-233 and paying for the disposition costs. To retain this material, programs must have current projects with current funding sources – a circumstance that does not currently exist.

NE currently manages the Department's Isotope Programs and would appear to be a likely Programmatic Secretarial Office to take custody of the uranium-233 inventory at Idaho. However, according to NE management, it lacks a Congressionally-approved programmatic mission and appropriated funds to take possession of the inventory. Additionally, NE has no program that can assume the disposition costs. For example, NE's Isotope Program has placed the need for isotopes derived from uranium-233 as one of its top priorities. However, the Isotope Program does not have the budget or programmatic authority to take control of uranium-233 feedstock materials that are necessary to produce these isotopes.

The Department's Fiscal Year (FY) 2009 budget request, however, seeks to transfer management of the Isotope Program to the Office of Science and devote more funding and attention to meeting the demand for research and medical isotopes. Under the proposal, all isotope-related facilities and funding would be transferred to the Office of Science and a number of research-related initiatives not funded in FY 2008 by NE would be funded at nominal

amounts. The FY 2009 budget request mentions that future research and development efforts will specifically consider the results of the recent National Academy of Science's report on nuclear medicine. Without the feedstock material from which to produce actinium and bismuth, however, research must necessarily focus only on alternative production methods – efforts that will at the least significantly delay delivery of these valuable isotopes to the medical research community.

Disposal Impacts

By pursuing disposition of its uranium-233, the Department is poised to dispose of a national resource. Although other means of producing these isotopes are currently under investigation by the research community, it is not yet known whether any of these will come to fruition. The facilities that originally produced this material have all been closed and decommissioned. To produce uranium-233 using existing facilities, such as the Idaho National Laboratory's Advance Test Reactor, program officials indicated that it would take approximately 1,000 years to replace the 320 kg of uranium-233 stored at Idaho. Another alternative is to produce the actinium-225 using accelerators or reactors; however, this requires chemical processing and/or separation steps that are yet to be determined. The current cost estimate to dispose of Idaho's inventory of uranium-233 is approximately $5 million. Alternatively, the current cost to store Idaho's inventory of uranium-233 is approximately $60,000 per year. However, the maintenance and storage costs of uranium-233 will grow over time because, due to the radioactive decay process, the material becomes increasingly more difficult to manage.

More important than the cost to replace or retain this material, is the potential for it to contribute to vital national interests. There is real promise for it to help save the lives of thousands of American cancer patients – in fact one top Departmental official estimated that these isotopes could be used to treat 6,000 patients annually. Also, should the nuclear renaissance expand to include research into proliferation resistant thorium cycle reactors, this material could be vital. Further, this material could help the nation explore space, offering an alternative to the plutonium powered radioisotope thermoelectric generator technology

that is currently deployed on NASA's deep space missions, as well as other important uses. However, if the Department continues with its plans to dispose of the uranium-233 none of these will come about.

RECOMMENDATIONS

We recommend that the Under Secretary of Energy, working with the Under Secretary for Science:

1. Prior to final disposal of the Department's inventory of uranium-233, evaluate the costs and benefits of:

    a. retaining the uranium-233 for the production of progeny isotopes;
    b. extracting the thorium-229 and continuing with disposition of the uranium-233; or,
    c. producing progeny isotopes using other technologies, such as an accelerator or reactor.

2. Work with the Office of Management and Budget and Congress, as necessary, to identify funding sources and approaches to meet demands for the isotopes discussed in this report.

3. Identify an appropriate Programmatic Secretarial Office to take responsibility for the material or identify means whereby industry can assume custody of the material if the decision is made to retain or extract isotopes from the uranium-233

MANAGEMENT REACTION

Management expressed concerns that many of the recommended corrective actions directed in this report have been previously implemented. Further, it noted that the current disposition strategy for the Oak Ridge uranium-233 had been directed by Congress. Alterations to the current strategy would have a significant impact on the safety and security postures in Building 3019 at ORNL and would require a change in Congressional mandate.

As to Recommendation 1, management stated that the analysis called for has been largely addressed through previous evaluations. Management stated, however, that the Office of Science will employ a merit-based peer review process to examine the needs and priorities for production of progeny isotopes discussed in this report, in the context of the broader needs for other research isotopes, and alternative production technologies. Regarding Recommendation 2, the Department stated it is working with the National Institutes of Health (NIH) to address the

recommendations of the National Academy of Sciences pertaining to the production of research isotopes in the broader context of needs across both industry and research. Should Congress direct an alternative strategy for the disposition of uranium-233, the Department will work to establish a new framework for the production of progeny isotopes. Management felt that this approach was consistent with Recommendation 3, which directs the Department to identify an appropriate Programmatic Secretarial Office to take responsibility for the material if a decision is made to use uranium-233 for isotope production.

AUDITOR COMMENTS

We are encouraged by management's proposals but remain concerned that the planned actions are not fully responsive to our recommendations. While we recognize that management previously evaluated disposition options for the Oak Ridge uranium-233 inventory, these evaluations were completed prior to the recent National Academy of Sciences report and did not consider the latest medical successes or the significant increase in projected demand for the isotopes discussed in the report. For example, one cost study referenced by management, "*Evaluation of the Options for Disposition of the U-233 Inventory at Oak Ridge National Laboratory*," was completed in April 2005. Another study, "*Environmental Assessment for the U-233 Disposition, Medical Isotope Production, and Building 3019 Complex Shutdown at the Oak Ridge National Laboratory*," was issued in December 2004.

Both of the studies (provided to us by management after we received its comments on our draft report) supported thorium extraction over continued storage of the Oak Ridge inventory. None of the studies, however, compared the cost of producing progeny isotopes through alternative technologies such as accelerators. This evaluation needs to be completed to provide Congress, the Office of Management and Budget and other stakeholders with up-to-date information on which to base an important public policy decision regarding the Department’s role in the production of medical and research isotopes. The evaluations also could be useful in examining the security and cost concerns that management identifies as one of the primary drivers for declining to interrupt the Oak Ridge disposal efforts.

Finally, we are pleased that the Department now intends to work closely with NIH. Such interaction could be critical in identifying funding and authorization sources for producing these valuable isotopes. Management's comments on the third recommendation are responsive. However, the efficacy of this recommendation is

dependent upon the Department successfully interacting with Congress and the Office of Management and Budget as advocated in Recommendation 2.

Appendix 1

OBJECTIVE

The objective of this audit was to evaluate whether the Department of Energy's (Department) planned disposition of its uranium-233 inventories would permit it to meet projected domestic medical and research needs for actinium and bismuth isotopes.

SCOPE

The audit was performed from March 2007 to May 2008 at the Idaho Operations Office, Battelle Energy Alliance, LLC, and CH2M-WG Idaho, LLC in Idaho Falls, Idaho. We also obtained information from the Oak Ridge Operations Office in Oak Ridge, Tennessee; and the Isotope Program in Washington, D.C. The audit scope was limited to the disposition plans of uranium-233.

METHODOLOGY

To accomplish the audit objective, we:

- Reviewed Federal regulations and Departmental directives and guidance related to isotopes and uranium-233;
- Reviewed prior reports issued by the Office of Inspector General;
- Reviewed reports by the National Academy of Sciences and American Nuclear Society on isotopes;
- Reviewed the Idaho National Laboratory's Cooperative Research and Development Agreement to use Idaho's uranium-233;
- Held discussions with a researcher at Memorial Sloan-Kettering Cancer Center;
- Held discussions with companies in the isotope supply industry;
- Held discussions with program officials from Department Headquarters and sites reviewed, including representatives from the Office of Nuclear Energy, the Office of Science, and Environmental Management; and,
- Analyzed information provided by the organizations reviewed to determine disposition plans and other uses for uranium-233.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objective. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objective. Specifically, we assessed internal controls regarding the Department's disposition plans for uranium-233. Because our review was limited, it would not necessarily have disclosed all internal control deficiencies that may have existed at the time of our audit. Also, we examined the establishment of performance measures in accordance with the Government Performance and Results Act of 1993 as it related to the audit objective. Performance measures were identified at the Idaho National Laboratory and the Isotope Program. Finally, we did not rely on computer-processed data during the audit; therefore, we did not conduct reliability assessments on the data.

An exit conference was held on May 23, 2008, with the Associate Under Secretary for Energy, as well as representatives from the Offices of Environmental Management, Nuclear Energy, and Science.

PRIOR AUDIT REPORTS

Office of Inspector General Reports

Management of the Department's Isotope Program (DOE/IG-0709, November 2005). The Department of Energy (Department) had not always provided researchers with the isotopes needed to conduct planned research. Since 1998, independent reviews, many of which were sponsored by the Department, have noted that the Isotope Program did not fully support production of research isotopes and that it had not adequately served the needs of the research community. Even though the Department recognized in the 2005 Isotope Program Plan that the current structure of the Program has had a "severe chilling effect on several promising areas of medical research in the United States," it did not take what we considered to be adequate action to address production issues. The Isotope Program Director stated that the Program is receiving frequent requests for other research isotopes that it will be unable to fulfill, including actinium, lutetium, and barium. For example, the Department is at its production limit for actinium, and the Director stated that the Program would sell more of this isotope if more could be produced. The price of actinium-225, from Fiscal Year (FY) 2002 to FY 2003, increased from about $580 to $1,203 per unit. According to the FY 2005 Isotope Program Plan, if the Department could produce a reliable supply of certain isotopes, there would be immediate use for them in medical research with some moving to clinical trials and widespread application. Further exacerbating this problem, the National Cancer Institute and the Society of Nuclear Medicine expect there to be a dramatic increase in the use of medical isotopes by the research community for a broad range of efforts.

Other Reports

Advancing Nuclear Medicine Through Innovation (National Academy of Sciences, September 2007). Advances on the horizon in nuclear medicine could substantially accelerate, simplify, and reduce the cost of delivering and improving health care. However, the Department's Nuclear Energy Isotope Program is not meeting the needs of the research community because the effort is not adequately coordinated with National Institutes of Health activities or with the Department's Office of Biological and Environmental Research. Public Law 101-101, which requires full-cost recovery for Department-supplied isotopes, whether for clinical use or research, has restricted research isotope production and radiopharmaceutical research. For targeted radiopharmaceuticals to have a larger role in cancer treatment, the following key issues must be resolved: more stable labeling methods for alpha emitters, particularly actinium-225 and astatine-211, to maximize the therapeutic potential of therapeutics labeled with these radionuclides. The radionuclides most frequently described as being essential to nuclear medicine research includes actinium-225. Several of the research radionuclides are not being produced in sufficient quantities to meet the research demand.

The U.S. National Isotope Program: Current Status and Strategy for Future Success (American Nuclear Society, March 2005). Overall, this report found that the U.S. isotope program is in a state of crisis, and immediate action is needed to address the major program issues. The issues specifically directed at the Department include:

- Research & Development (R&D) isotopes are not available at reasonable prices due to declining resources and policy change in the Department's Isotope Program.

- Elimination of Department R&D funding is impacting development of future isotope applications; and,

- Failure to provide the necessary leadership to reverse the decline of the Department's Isotope Program.

Department of Energy
Washington, DC 20585

MAR 2 7 2008

MEMORANDUM FOR GREGORY FRIEDMAN
INSPECTOR GENERAL

FROM: C.H. ALBRIGHT, JR.
UNDER SECRETARY OF ENERGY

RAYMOND L. ORBACH
UNDER SECRETARY FOR SCIENCE

SUBJECT: Draft Report on "Meeting Medical and Research Needs for Isotopes Derived from Uranium-233"

This memorandum is in response to the subject draft report issued on February 12, 2008. We appreciate the opportunity to comment on the findings identified in, and the recommendations resulting from, the Inspector General's (IG) review. We have reviewed the IG's recommendations and have concerns that many of the corrective actions directed in the report have been previously implemented. Further, the current disposition strategy of the Uranium-233 material has been directed by Congress. Alterations to the current strategy would have a significant impact on the safety and security postures in Building 3019 at ORNL and would require a change in Congressional mandate.

Recommendation 1, which calls for analyses to assess the costs and benefits associated with using Uranium-233 to produce progeny isotopes, has been largely addressed through previous evaluations. The Office of Science (SC) will employ a merit-based, peer review process to examine the needs and priorities for production of progeny isotopes discussed in this report, in the context of the broader needs for other research isotopes, and alternative production technologies.

SC's proposed peer review process for determining needs and priorities for research isotopes is consistent with Recommendation 2, which directs the Department to identify funding sources to meet the demand for isotopes discussed in the report. In addition, the Department is working with the National Institutes of Health to address the recommendations of the National Academy of Sciences pertaining to the production of research isotopes in the broader context of needs across both industry and research.

Should Congress direct a new strategy for the disposition of Uranium-233, DOE will work to establish a new framework for the disposition of the material. This approach is consistent with Recommendation 3, which directs the Department to identify an appropriate Programmatic Secretarial Office (PSO) to take responsibility for the material if a decision is made to use Uranium-233 for isotope production,

The attached comments on the draft report include the perspectives of the Office of Nuclear Energy, the Office of Science, and the Office of Environmental Management.

Attachments

cc: T. Harms, S-3
M. Lewis, CF-1.2
H. Smith, EM-3.1
S. Johnson, NE-2
D. Miotla, NE-3
T. O'Connor, NE-33
O. Lowe, NE-34
J. Pantaleo, NE-34
J. Rispoli, EM-1
I. Triay, EM-2
J. Owendoff, EM-3
F. Marcinowski, EM-10
C. Gelles, EM-12
R. Orbach, S-4
P. Dehmer, SC-2
G. Malosh, SC-3
G. Boyd, ORO
S. McCracken, ORO

bcc: J. Boone, EM-6
J. Venneri, SC-41
J. Miller, ORO

Comments on
Inspector General Draft Report
"Meeting Medical and Research Needs for Isotopes Derived from Uranium-233"

We recommend that the Under Secretary of Energy, working with the Under Secretary for Science:

Recommendation 1

Prior to disposal of the Department's inventory of Uranium-233, evaluate the costs and benefits of: a.) retaining the Uranium-233 for the production of progeny isotopes; b.) extracting the Thorium-229 and continuing with disposition of the Uranium-233; or c.) producing progeny isotopes using other technologies, such as an accelerator or reactor.

Management Comment

The current course of action for disposition of Uranium-233 has been recently reviewed and endorsed by the Department; in addition, there are significant safety and national security drivers for the disposition project. Subsections a) and b) of this recommendation are not supportable since the report does not fully explore or properly recognize these actions.

The Department has evaluated and documented costs associated with retaining the Uranium-233 for the production of progeny isotopes, as well as extracting the Thorium-229 and continuing with the disposition of the Uranium-233. In 2005, at the direction of Congress, the Department re-scoped the Uranium-233 project to terminate isotope extraction and expedite down blending and disposal of this material. It must be noted that Congress has registered its opposition to continued extraction of Thorium-229 from Uranium-233 prior to disposal. The facility design is being finalized and facility construction is scheduled to begin in 2009; Uranium-233 processing activities are scheduled to begin in 2012. The Nuclear Materials Disposition and Consolidation Coordination Committee (NMDCCC) undertook a rigorous process in consultation with all elements of the Department which reviewed the disposition plans for Uranium-233 and recommended continuation of the disposition activities; this recommendation was accepted by the Department. There are no additional facts in this report that provide a basis for further studies or estimates prior to proceeding with disposal of the Uranium-233 material. Moreover, there is no mandate, nor is funding available, to alter the current disposition strategy for Uranium-233.

Changing the current strategy would invite significant cost, schedule, safety and national security issues. For example, if it is decided that the Thorium-229 extraction process should be revisited, the Department would incur costs for the revised design, as well as costs associated with the resulting delays to the current project schedule. In addition to those project costs attributable to schedule delays, any delay in the project will increase safety and security costs dramatically.

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In the area of safety, timely completion of this project is required in partial response to the Defense Nuclear Facilities Safety Board (DNFSB) recommendation 1997-1 which identified concerns with the integrity of packaging of the Uranium-233 materials, and required an extensive program of inspection and repackaging to ensure the continued long-term safety of the material in storage. Subsequent inspection activities have satisfied the DNFSB's concerns regarding the long-term safety of the material. However, delays in the project will re-open the question of long-term safety and force the Department to revisit the DNFSB recommendation.

In the area of security, approximately $5M per year is expended to deal specifically with the security issues associated with Building 3019. Delay in the execution of this project will not only result in incurring these costs over a longer, indefinite period but require significant additional one-time security costs (~$25M) as well as an escalation of the $5M annual costs to about $15-20M per year. This is because the execution of this project in a timely fashion is a key to satisfying the requirements for meeting the design basis threat (DBT) in Building 3019. Delays in the project will result in the need to re-open this issue and will require additional security expenditures.

The Department's FY 2009 Congressional budget request transfers responsibility for the Medical Isotopes program from the Office of Nuclear Energy to the Office of Science, and includes additional funds for research isotope development and production in response to the needs of the scientific community for commercially-unavailable research isotopes. The Department's current policy for production of isotopes, including research isotopes, is that the production costs must be fully recovered from the customers; as such, the Department does not produce isotopes speculatively. The Office of Science, beginning in FY 2009, will examine the production of progeny isotopes discussed in this report using other technologies, such as an accelerator or reactor. The ultimate decision on whether to produce research isotopes will depend upon a merit-based peer review process. However, a decision to use Uranium-233 to produce isotopes will also require a new Congressional mandate.

Recommendation 2

Work with the Office of Management and Budget and Congress, as necessary, to identify funding sources and approaches to meet demands for the isotopes discussed in the report.

Management Comment

The Department's FY 2009 Congressional budget request transfers responsibility for the Medical Isotopes program from the Office of Nuclear Energy to the Office of Science. If approved by Congress, SC will determine the development and production of research isotopes by peer review, consistent with other basic research efforts within SC. The peer review will be based on established criteria including, but not limited to, non-proliferation and national security concerns, prioritized interest by the nuclear medicine and broader research community, costs, safety concerns, whether specific isotopes can be

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obtained through more desirable alternative methods, programmatic interests, and budget needs and constraints.

SC, working with NE, has established a Working Group with the National Institutes of Health to address the recommendations of the National Academy of Science's report, and has initiated preparations for a workshop to bring together industrial, federal, and research stakeholders to discuss the needs, priorities, and potential paths-forward for meeting the U.S. commercial and research isotope needs.

Peer review and NIH working group activities designed to identify funding sources and approaches to meet demands for research isotopes will take place during FY 2008 and FY 2009. The earliest the outcome of these efforts may be reflected with regards to the Office of Management and Budget and Science will be the FY 2011 budget formulation process.

Recommendation 3

Identify an appropriate Programmatic Secretarial Office to take responsibility for the material or identify means whereby industry can assume custody of the material if the decision is made to retain or extract isotopes from the Uranium-233.

Management Comment

The Office of Environmental Management (EM) currently has responsibility for the disposition of the material, and will continue to move toward disposal, as directed by Congress, until such time that Congress directs an alternative disposition pathway. Should Congress provide new direction and funds to the Department to pursue the production of progeny isotopes using Uranium-233 (either through extraction of Thorium-229 or other means) then DOE will establish a new framework for the disposition of the material.

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