Nuclear Science Advisory Committee
Isotopes Subcommittee

Co-chairs
Ani Aprahamian
Donald Geesaman

A Strategic Plan for the Isotope Development and Production for Research and Applications Program

Presentation to NSAC
27 July 2009

Report Status and Versions

July 20, 2009 — 18 July version sent to NSAC
Still needed final formatting
Some budget numbers (e.g. ARRA) need finalizing

Significant mistake in isotope separator recommendation
Discussion was correct

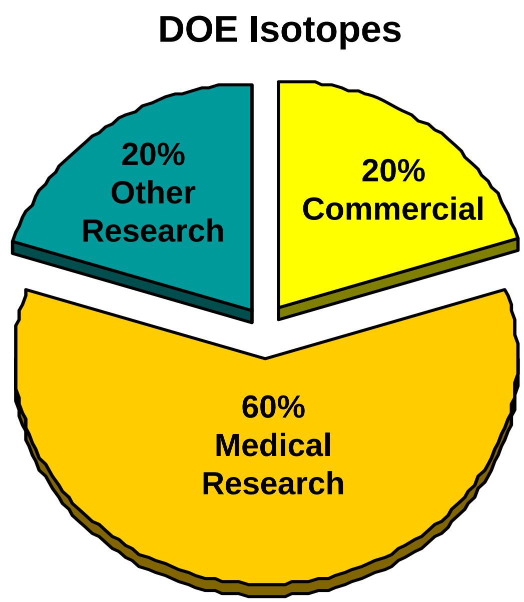
I assume this will be the basis of our discussions

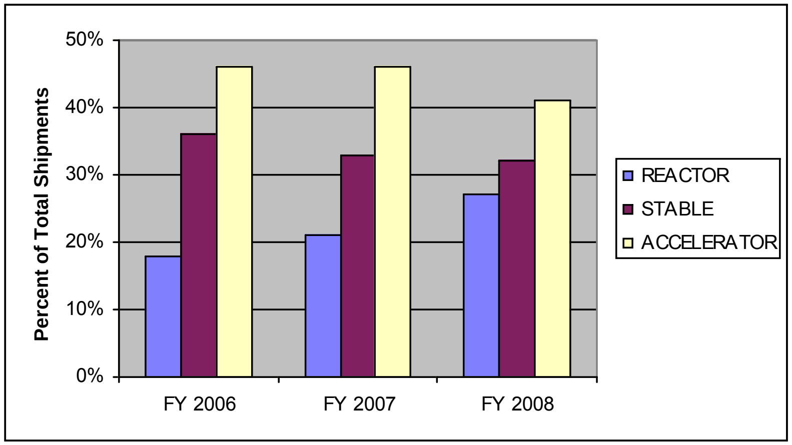
July 24, 2009 — Printed version available to NSAC
Reformatted so page numbers have changed slightly
Cover included
Mistake in recommendation corrected
A number of small grammar corrections but no other corrections

Executive summary including recommendations available to the public. The public should understand that the report has not yet been accepted and these are not yet NSAC's recommendations.

DOE's Isotope Development and Production for Research and Applications Program

- Produce and sell radioactive and stable isotopes, associated byproducts, surplus materials, and related isotope services.
- Maintain the infrastructure required to supply isotope products and related services.
- Support R&D for development and production
- Over 190 customers in FY 2008
- Over 560 shipments in FY 2008
- Ten customers provided over 85% of sales





A Change in Management was Proposed in the President's FY09 Budget Submission

The Fiscal Year (FY) 2009 President's Request Budget proposes to transfer the Isotope Production Program from the Department of Energy (DOE) Office of Nuclear Energy to the Office of Science's Office of Nuclear Physics and rename it the Isotope Production and Applications Program. In preparation for this transfer, NSAC was requested to establish a standing committee, the NSAC Isotope (NSACI) sub-committee, to advise the DOE Office of Nuclear Physics on specific questions concerning the National Isotope Production and Applications (NIPA) Program. NSACI will be constituted for a period of two years as a subcommittee of NSAC. It will report to the DOE through NSAC who will consider its recommendations for approval and transmittal to the DOE.

The Subcommittee is asked to establish the priority of research isotope production and development, and to recommend a long-term strategic plan for the NIPA Program.

DOE has renamed it the Isotope Development and Production for Research and Applications Program

FY09 Omnibus bill: DOE-ONP Budget

"Within this amount, $24,900,000 is provided for the Research Isotope Production and Applications program, and within these funds $5,000,000 is provided for the Research Isotope Development and Production Subprogram to develop and implement a research strategy consistent with the National Academy of Sciences study entitled "State of the Science of Nuclear Medicine." Consistent with the cost-sharing requirements of Public Law 101-101, the Department is directed to develop a cost recovery strategy to ensure the long term viability of the isotope production program. The Department is directed to complete a study of the feasibility of using the University of Missouri Research Reactor to supply up to half the U. S. demand for feedstock medical imaging compounds in the form of molybdenum-99 and technetium-99."

NSACI Subcommittee

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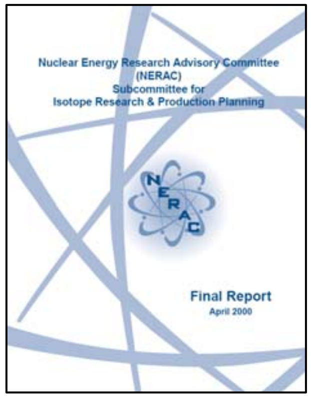
Susan Seestrom Ph.D.
LANL – ex officio

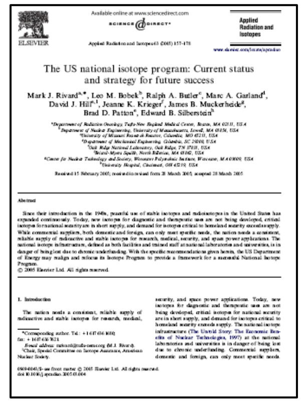
Roberto M. Uribe Ph.D.
Kent State University

A lot of people are on record saying things are not working as well as they would like

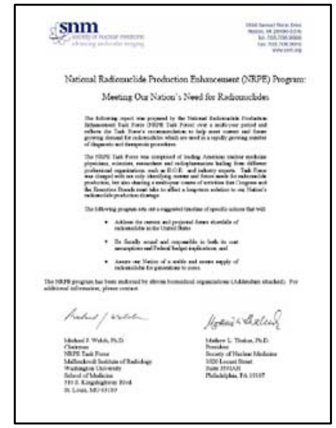
DOE-NE Expert Panel 1999



NERAC 2005

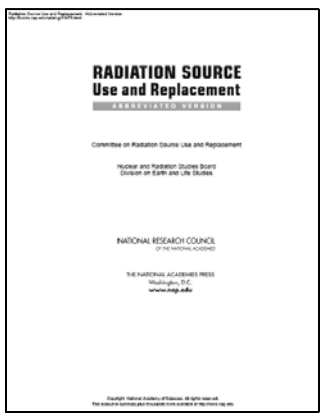


ANS 2005

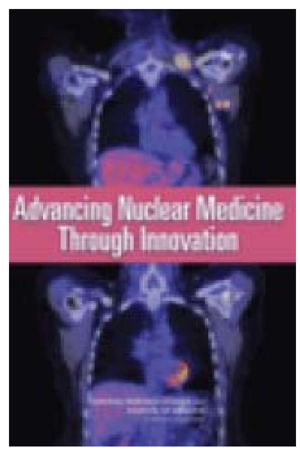


SNM 2005

NCI 2008



NAS 2008



NAS 2007

- Some of this is decreasing funding through 2008.
- Another component is the complexity of the mission and the current reliance on shared resources.

Current DOE Production Sites

Past and potential future participants

Richland:

Sr-90 – Y-90 gen for cancer therapy

Idaho – ATR:

Ir-192 – Industrial non-destructive analysis

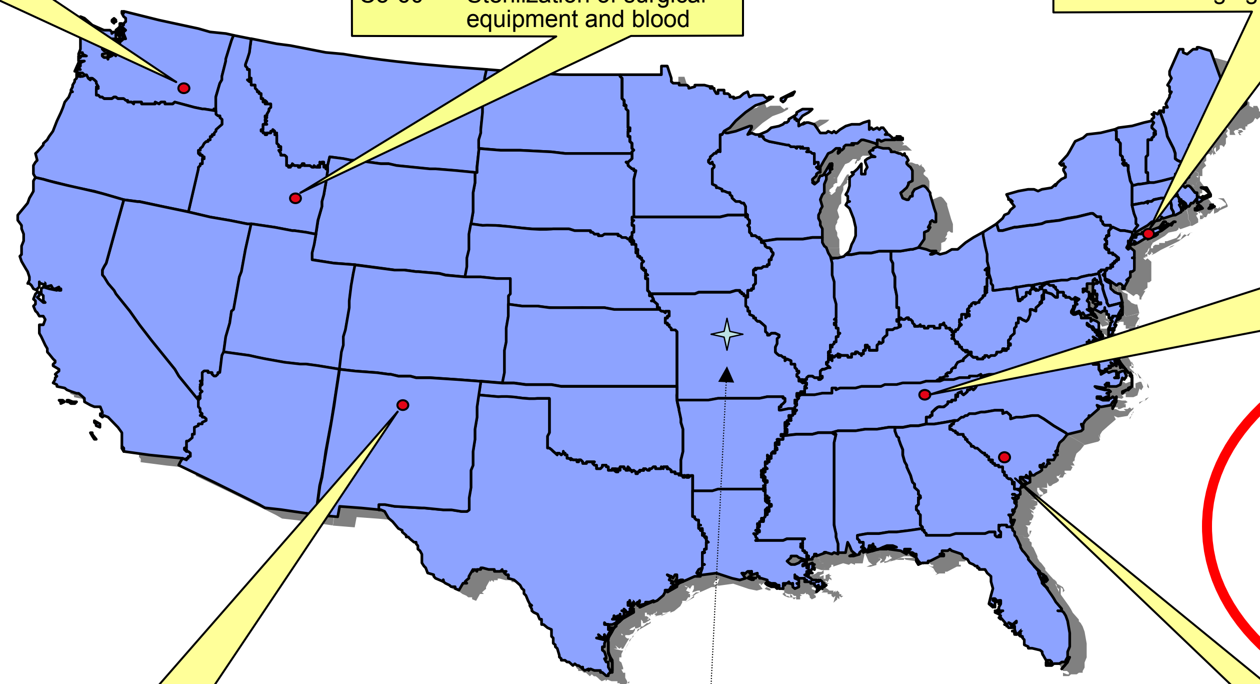
Co-60 – Sterilization of surgical equipment and blood

Brookhaven – BLIP:

Ge-68 – Calibration sources for PET equipment; Antibody labeling

Sr-82 – Rb-82 gen used in cardiac imaging

NP



BES

Oak Ridge – HFIR:

Se-75 - Industrial NDA; Protein studies

Cf-252 - Industrial source

W-188 - Cancer therapy

Stable Isotopes Inventory:

Top 10 stable isotopes sold over the last 5 years:

Ca-48, Ga-69, Rb-87, Cl-37, Pt-195, Nd-146, Sm-149, Ru-99, Zr-96

Inventory:

Ac-225 - Cancer therapy

Ni-63 - Explosives detection

Columbia – MURR:

Memorandum of Understanding for potential collaboration

Los Alamos – LANSCE/IPF:

Ge-68 – Calibration sources for PET equipment; Antibody labeling

Sr-82 – Rb-82 gen used in cardiac imaging

Am-241 – Oil well logging

NNSA/ BES

Facilities operated By IDPRA

Savannah River – Tritium Facility:

He-3 – Neutron detection
– Fuel source for fusion reactors
– Lung testing

IDPRA acts as sales broker

FY09 Budgets

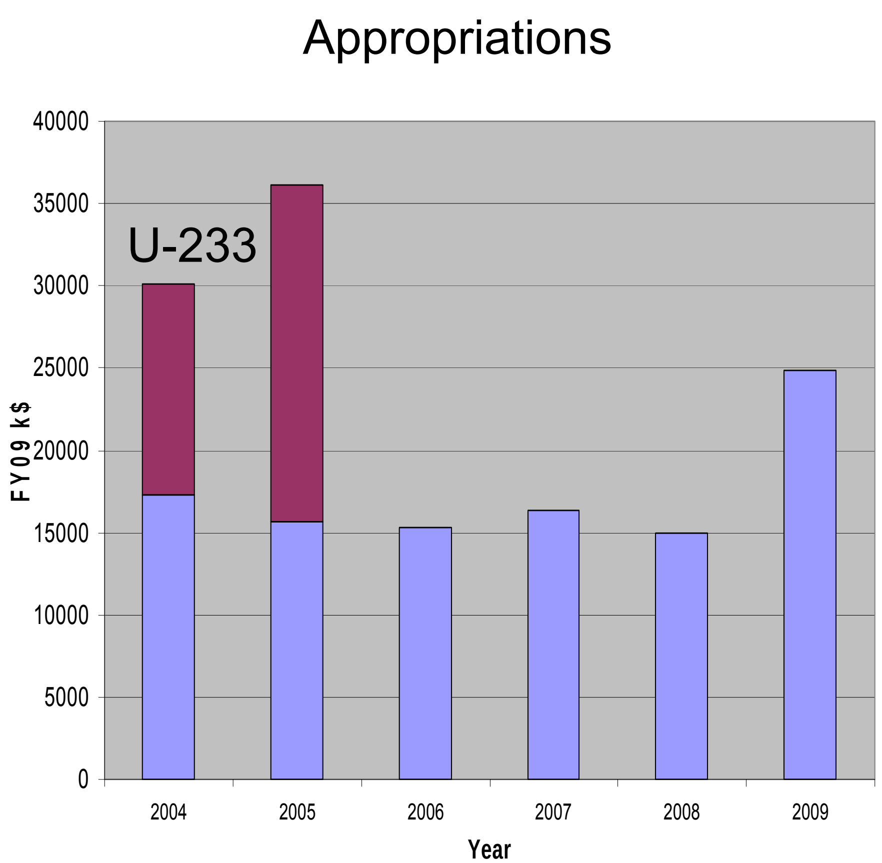
Table 11.2: FY09 President's Budget request and appropriated funding for the isotope program in FY09 and the FTE's funded at each laboratory by the appropriation (rounded to nearest FTE).

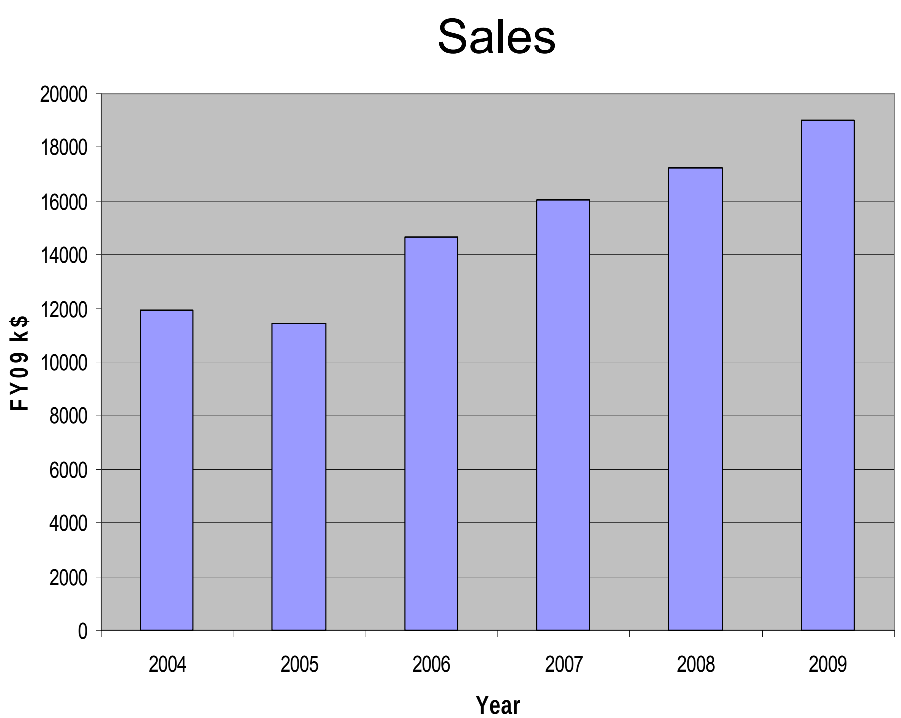
Lab	Total	Item	FY09 k$ Pres. request	FY09 k$ appropriated	FTEs
		Research Development and Production	3090		
		Research Development and Production - Production (estimate)		2430	
		Research Development and Production - Research (estimate)		2430	
		Other Research - SBIR/STTR	90	200	
		Associated Nuclear Support - including University Operations	750	870	
LANL	4640	IPF Operations/ LANL Hot Cells	3650	3650	12
		IPF Upgrades	990	2490	
BNL	3470	BLIP Operations/ BNL Hot Cells	3200	3200	8
		BNL Upgrades	270	270	
ORNL	7860	ORNL Hot Cells - Radioisotopes	3800	3800	3
		ORNL Chemical and Material Laboratories - Stable Isotopes	3764	3764	9
		ORNL Upgrades	296	1796	
Totals			19900	24900	32

Budget History in FY09$

Table 11.3: FTE support at the national laboratories by the appropriation and by sales revenue.

	Total	Appropriation	Sales
ORNL	24.4	12.0	12.4
LANL	20.0	12.0	8.0
BNL	9.0	7.6	1.4
INL	0.2		0.2
PNNL	1.2		1.2
SRS	1.5		1.5





Charges to NSAC

Charge 1:

As part of the NIPA Program, the FY 2009 President's Request includes $3,090,000 for the technical development and production of critical isotopes needed by the broad U.S. community for research purposes.

NSACI is requested to consider broad community input regarding how research isotopes are used and to identify compelling research opportunities using isotopes.

The subcommittee's response to this charge should include the identification and prioritization of the research opportunities; identification of the stable and radioactive isotopes that are needed to realize these opportunities, including estimated quantity and purity; technical options for producing each isotope; and the research and development efforts associated with the production of the isotope. Timely recommendations from NSACI will be important in order to initiate this program in FY 2009; for this reason an interim report is requested by January 31, 2009, and a final report by April 1, 2009.

Charges to NSAC

Charge 2:

The NIPA Program provides the facilities and capabilities for the production of research and commercial stable and radioactive isotopes, the scientific and technical staff associated with general isotope development and production, and a supply of critical isotopes to address the needs of the Nation. NSACI is requested to conduct a study of the opportunities and priorities for ensuring a robust national program in isotope production and development, and to recommend a long-term strategic plan that will provide a framework for a coordinated implementation of the NIPA Program over the next decade.

The strategic plan should articulate the scope, the current status and impact of the NIPA Program on the isotope needs of the Nation, and scientific and technical challenges of isotope production today in meeting the projected national needs. It should identify and prioritize the most compelling opportunities for the U.S. program to pursue over the next decade, and articulate their impact.

A coordinated national strategy for the use of existing and planned capabilities, both domestic and international, and the rationale and priority for new investments should be articulated under a constant level of effort budget, and then an optimal budget. To be most helpful, the plan should indicate what resources would be required, including construction of new facilities, to sustain a domestic supply of critical isotopes for the United States, and review the impacts and associated priorities if the funding available is at a constant level of effort (FY 2009 President's Request Budget) into the out-years (FY 2009 – FY 2018).

Charges to NSAC

Charge 2 Continued:

Investments in new capabilities dedicated for commercial isotope production should be considered, identified and prioritized, but should be kept separate from the strategic exercises focused on the remainder of the NIPA Program.

An important aspect of the plan should be the consideration of the robustness of current isotope production operations within the NIPA program, in terms of technical capabilities and infrastructure, research and development of production techniques of research and commercial isotopes, support for production of research isotopes, and current levels of scientific and technical staff supported by the NIPA Program. We request that you submit an interim report containing the essential components of NSACI's recommendation to the DOE by April 1, 2009, and followed by a final report by July 31, 2009.

NSACI Subcommittee Plan to meet our charges

Aug. 5-7, 2008	DOE ONP/ONE Workshop on The Nation's Need for Isotopes: Present and Future
August 8, 2008	Charge to NSAC
Nov. 13-14, 2008	Organizational meeting
	Publicize our charges and seek community input
Dec. 15-16, 2008	Get input from government agencies
Jan. 13-15, 2009	Input from customers,
	Ideas for production research R&D
	Research priorities recommendations
Jan. 31, 2009	First charge interim report submitted to NSAC
Feb. 10-11 2009	2- day Meeting to hear plans for facility and infrastructure improvements
Mar. 2, 2009	NSAC Meeting to consider report on 1st charge
Mar 25-27, 2009	3 day meeting
	Decide on recommendations for Long Range Plan
1 April 2009	Interim report for 2nd charge submitted by NSAC
23 April 2009	NSAC accepts report on 1st charge and transmits it to DOE
20 July 2009	Final report submitted to NSAC

Federal Agencies Contacted

Air Force Office of Scientific Research, Armed Forces Radiobiology Research Institute, Department of Agriculture, Department of Defense, Department of Energy - Fusion Energy Sciences, Department of Energy- National Nuclear Security Administration - Nuclear Non-proliferation, Department of Energy-Basic Energy Sciences, Department of Energy-Biological and Environmental Research, Department of Energy-Nuclear Physics, Department of Homeland Security, Environmental Protection Agency, Federal Bureau of Investigation, National Cancer Institute, National Institute of Allergy and Infectious Disease, National Institute of Biomedical Imaging and Bioengineering, National Institute of Drug Abuse, National Institute of Environmental Health Science, National Institute of General Medical Science, National Institute of Standards and Technology, National Science Foundation - Directorate for Engineering, National Science Foundation - Directorate for Mathematical and Physical Sciences, National Science Foundation- Directorate for Biological Sciences, Office of Naval Research, State Department, U. S. Geologic Survey

Professional Societies Contacted

Academy of Molecular Imaging, Academy of Radiology Imaging, Academy of Radiology Research, Amercan Association of Physicists in Medicine, American Association of Cancer Research, American Chemical Society, American Chemical Society - Division of Nuclear Chemistry and Technology, American College of Nuclear Physicians, American College of Radiology, American Medical Association, American Nuclear Society, American Nuclear Society - Division of Isotopes and Radiation, American Pharmacists Association - Academy of Pharmaceutical Research and Science (APhA-APRS), American Physical Society, American Physical Society - Division of Biological Physics, American Physical Society - Division of Material Physics, American Physical Society - Division of Nuclear Physics, American Society of Clinical Oncology, American Society of Hematology, American Society of Nuclear Cardiology, American Society of Theuraputic Radiation and Oncology, Council on Ionizing Radiation and Standards, Health Physics Society, National Organization of Test, Research and Training Reactors, Radiation Research Society, Radiation Therapy Oncology Group, Radiochemistry Society, Radiological Society of North America, Society of Molecular Imaging, Society of Nuclear Medicine

Trade Groups contacted

Association of Energy Service Companies

Council on Radionuclides and Radiopharmaceuticals

Gamma Industry Processing Alliance

International Source Suppliers and Producers Association

Nuclear Energy Institute

Written input received -January 2009 http://sun0.phy.anl.gov/pub/geesaman/Jan13-15,2009-Meeting

- American Association of Physicists in Medicine- AAPM
- American Pharmacists Association-APPM-NPPS
- American Physical Society- Division of Material Science
- American Physical Society- Division of Nuclear Physics
- American Society of Clinical Oncology
- American Society for Radiation Oncology
- CIRMS forwards respond to NAS study on source replacement
- DOE-BES Heavy Element Chemistry
- Health Physics Society
- National Organization of Test, Research and Training Reactors
- Nuclear Energy Institute-MURR
- Society for Nuclear Medicine/Amercian College of Nuclear Physicians- SNM/ACNP

NSACI Agenda: February meeting
Facility Capabilities and Initiatives

10 February

9:00	Welcome
9:15	John Pantaleo, DOE NIPA
10:10	David Robertson, MURR
10:50	Break
11:10	Glen Young, ORNL
11:50	Jeff Binder, ORNL
12:30	Lunch
14:00	Leonard Mausner, BNL
14:40	Brad Sherrill, NSCL/FRIB
15:20	Richard Kouzes, PNNL
16:00	Break
16:15	Steve Laflin, International Isotopes
16:55	Ian Horn, NuView
17:35	Hugh Evans, Nuclitec

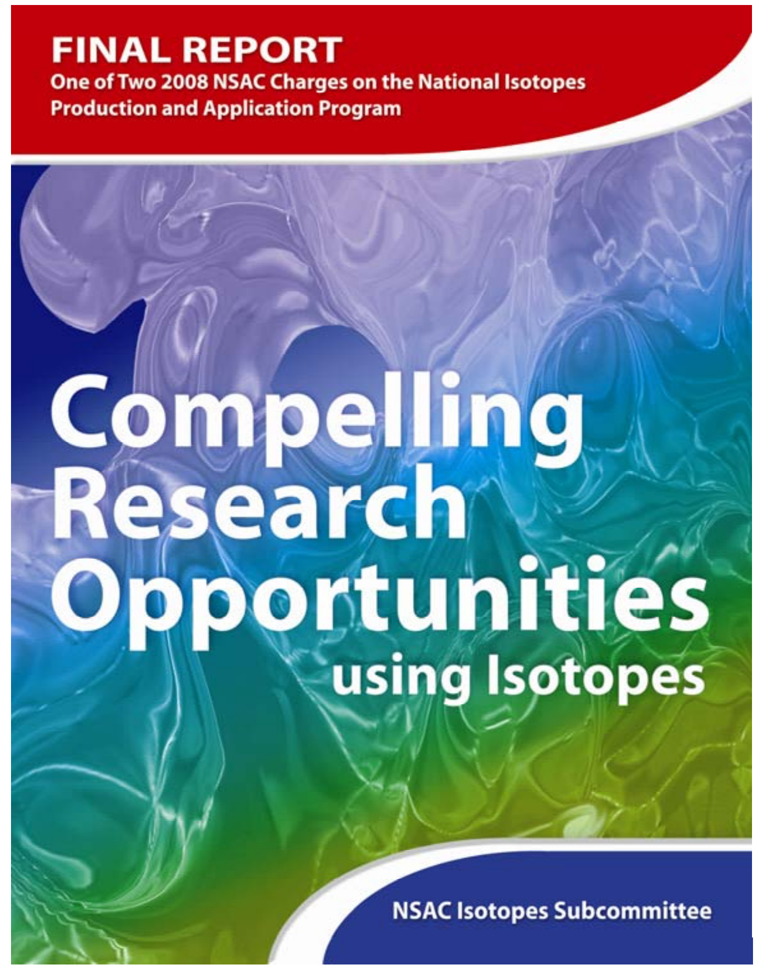
11 February

8:30	Doug Wells, Idaho State University
9:00	Donna Smith, LANL
9:40	Tracy Rudisill, SRNL
10:30	Richard Coats, SNL
11:10	Jim Harvey, Northstar
11:50	Frances Marshall, INL
12:30	Jerry Nolen, ANL
13:10	Lunch
14:00-16:00	Executive Session

We asked the institutions to present their current capabilities their plans. NSACI used this as input and examples without endorsing any individual requests. ONP reviews the operation of each of the DOE facilities as it does all its program elements.

First Report

- Ani Aprahamian led the first report which was accepted by NSAC and transmitted to DOE on 24 April 2009
- Research Divided into
  - Medicine, Biology and Pharmaceuticals
  - Physical Sciences and Engineering
  - National Security and Applications
- Recommendations



Long Range Plan Report Outline

Executive Summary
1. Introduction
2. History of the DOE Isotopes program
3. Uses
   A. Biology, Medicine and Pharmaceuticals
   B . Physical Sciences and Engineering
   C. Security and other Applications

4. Challenges

5. Stable isotope capabilities
6. Accelerator based isotope capabilities
7. Reactor Based isotope capabilities
8. Isotope Harvesting from long-lived stockpilies

9. R&D for production and use
10. Trained Workforce and Education
11, Operation of the Program

12. Budget Scenarios
13. Summary

Charge elements

Scope, Status, Impact

Opportunities and impact

Scope, Status, Impact

Existing and planned capabilities

Robustness of program

Optimum and CE budget

Challenges in Radio-pharmaceuticals

• Initial supply of new isotope suitable for basic characterization –R&D

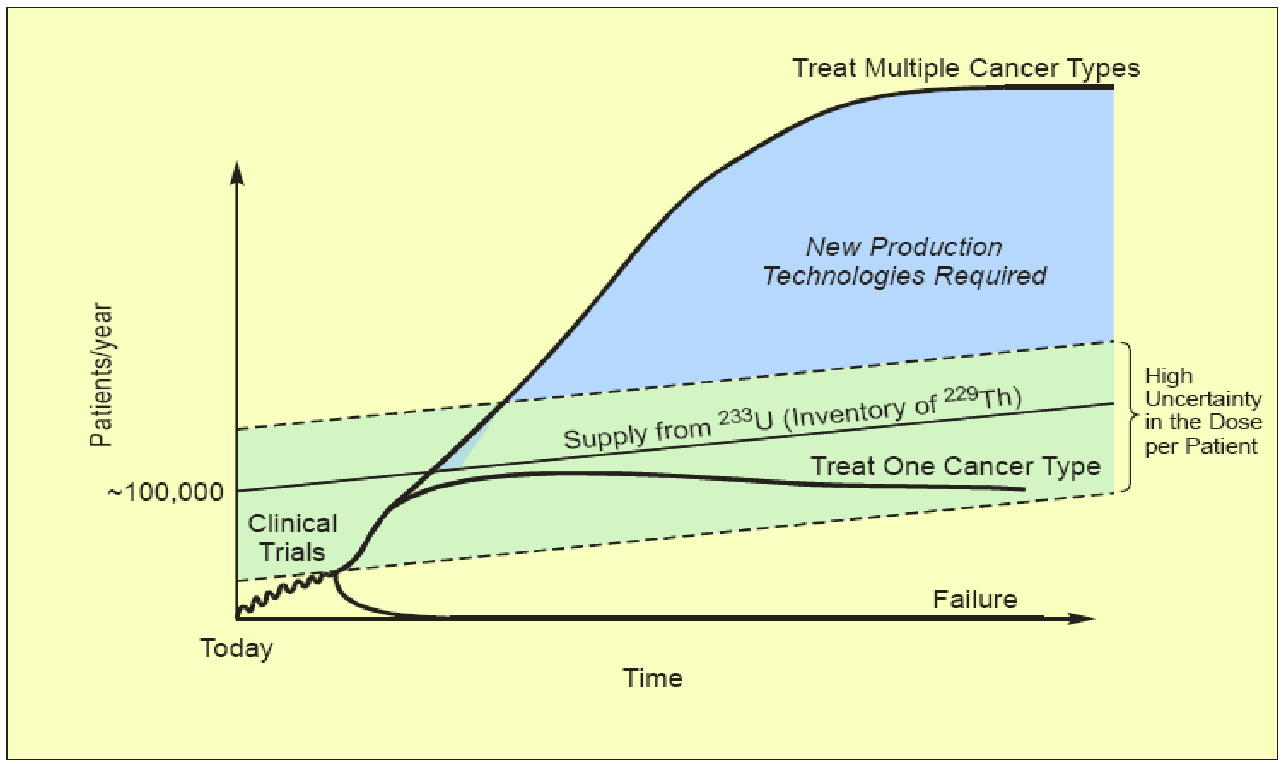
• NIH wants supply to be available before funding research

• Quantities increase as clinical trials proceed. Part of the research is to establish the correct dose

• Need consistent year-round availability. In many cases, can't stockpile

• If trials succeed, quantity needed can increase dramatically. New production techniques may be required – R&D

• If trials fail, demand can shrink dramatically.



• Risk unattractive to commercial producers

Success Story – ^{82}Sr

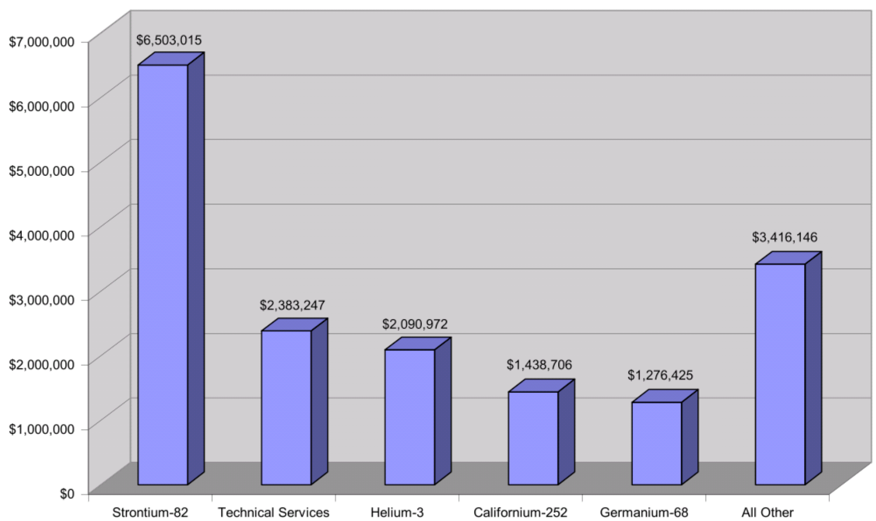
- ^{82}Sr - ^{82}Rb used in clinical positron emission tomography for cardiac perfusion studies

- Requires 70 MeV to produce

- Production and use pioneered by BNL and LANL

- Limited running time at accelerators requires multiple producers for year-round availability.

- Currently isotope with highest sales



Virtual Isotope Center Concept

The Path to an Effective Program

- **Communication, Communication, Communication**

Isotope program has to know what to produce. - Requires forecasts from major customers and funding agencies. The NIH-DOE Working Group is an excellent example.

- **Coordination with outside partners**
  - potential unused capacity
  - coordinate production schedules for required availability
  - can introduce major complications

- **R&D**
  - create more efficient processes (R) and ones that can be shared (D)

- **Transportation**
  - make it more reliable to ship isotopes

- **Skilled workforce**
  - Make sure the ones you have are available
  - Ensure a new generation of isotope production workforce exists

- **Make sure the facilities you have are mission ready** – infrastructure and maintenance

- Where needed production capacity does not exist, **new investment**
  - Dedicated flexible accelerator with year-round availability for isotope production
  - New isotope separation facility

Isotope Demand from NIH-DOE Working Group

Isotope	Half-life	Availability	Comments
Ac-225	10 d	very limited	
At-211	7.2 h	limited, university facility may be able to meet demand	Requires α beam
Bi-213	47 m	requires Ac-225	
Br-76	16 h	not been done	Low energy
Br-77	2.4 d	not been done	Low energy
Cu-64	12.7 h	supply probably ok	
Cu-67	2.6 d	NuView, more needed if large increase	70 MeV required
Ho-166	1.1 d	Could potentially meet demand	HFIR
I-124	4 d	?	Low energy
Lu-177	6.7 d	Can be met during HFIR run cycles	Weekly deliveries
Pb-212	10 h	Limited Commercial	
Re-188	17 h	Limited by HFIR production cycles	
Th-228	1.9 y	Limited - commercial	From U-232
Y-86	14 h	Needs can be met	Low energy
Zr-89	3.3 d	Needs can be met	Low energy

Detailed projections are made for 5 years, but these are considered sensitive

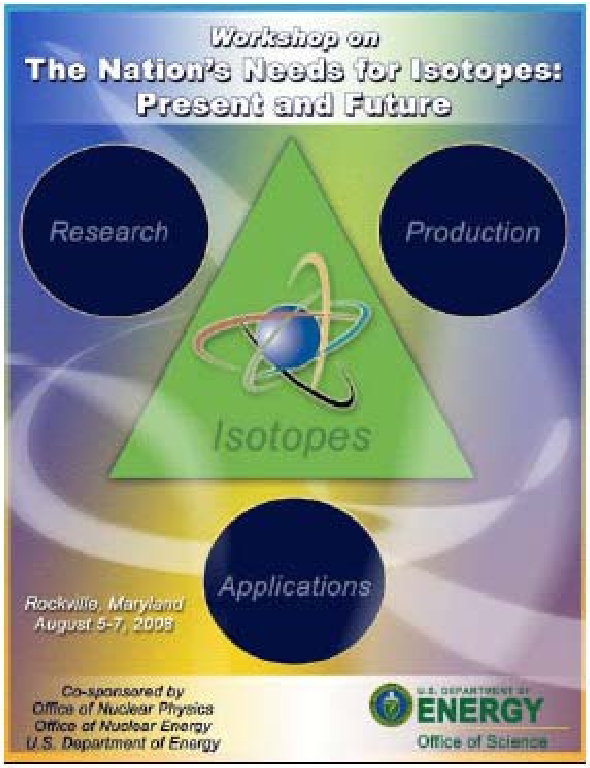
In Many Cases DOE-ONP Has Already Started Down This Path

- **Communication, Communication, Communication**
  - August Isotope Workshop
  - NIH-DOE Working Group
  - Inter-Agency Working Group on ^{3}He
  - Restart of ^{252}Cf production and sales
  - Search for a NIDC Director- new position

- **Coordination with outside partners**
  - Virtual Isotope Center

- **R&D**
  - Significant development and production for research budget line
  - Significant ARRA investment in research

- **Make sure the facilities you have are mission ready and improve their capabilities**
  - Significant investment in FY09 in upgrading infrastructure
  - Significant ARRA funding



Recommendations – The Present Program

I.1: For the isotope program to be efficient and effective for the nation, it is essential that DOE-ONP maintain a continuous dialogue with all interested federal agencies and commercial isotope customers to forecast and match realistic isotope demand and achievable production capabilities.

The DOE-NIH interagency working group is an excellent start for this type of communications in a critical area of isotope production and use.

I.2: We recommend devising processes for the isotope program to better communicate with users, researchers, customers, students, and the public and to seek advice from experts:

—Initiate a users group to increase communication between isotope program management and users on issues of availability, schedules, priorities, and research.

—Form expert panels as needed to give advice on issues such as definition of isotopes as research or commercial in primary usage, new production methods, and needed actions when demand exceeds supply.

—Modernize the web presence for the isotope program to give users an easier way both to learn about properties, availability, production methods, and services, and also to have access to interactive tools that help customers plan purchases and use, researchers to share information and form collaborations, and students and the general public to learn about the important uses of isotopes.

Recommendations – The Present Program

I.3: Encourage the use of isotopes for research through reliable availability at affordable prices.

I.4: Coordinate production capabilities and supporting research to facilitate networking among existing DOE, commercial, and academic facilities.

I.5: Support a sustained research program in the base budget to enhance the capabilities of the isotope program in the production and supply of isotopes generated from reactors, accelerators, and separators.

I.6: Increase the robustness and agility of isotope transportation both nationally and internationally.

Important elements in this program include
—Identify and prioritize transportation needs through establishing a transportation working group.
—Initiate a collaborative effort to develop and resolve the priority issues (certification of transportation casks).

Recommendations – Major Investments

II.1: Construct and operate a ~30-40 MeV variable-energy, high-current, multi-particle cyclotron and supporting facilities that have the primary mission of isotope production.

The most cost-effective option to position the isotope program to ensure the continuous access to many of the isotopes required is for the program to operate a dedicated accelerator facility.

II.2: Construct and operate an electromagnetic isotope separator facility for stable and long-lived radioactive isotopes. This should include several separators for a raw feedstock through-put of about 300-600 milliAmpere (10-20 mg/hr multiplied by the atomic weight and the isotopic abundance of the isotope).

Note typo in version distributed to NSAC
microAmpere→milliAmpere

Why ~40 MeV variable-energy, multi-particle Accelerator?

- The priority is year-round availability of a wide variety of research isotopes. Most research isotopes can be produced at < 40 MeV
- You want excellent beam properties from 15-40 MeV. This is typically hard for cyclotrons to do at less than ½ maximum energy
- Most commercial cyclotrons have alpha energies fixed at the maximum. ^{211}At production requires around 30 MeV. Higher energies produce too much ^{210}At which must be minimized because its decay product binds to bone marrow.
- 40 MeV allows target cooling on both sides.
- Shielding and activation requirements increase significantly for 70 MeV
- Production technology developed is more easily transferred to commercial producers
- Only 6 isotopes require higher energy: ^{82}Sr, ^{68}Ge, ^{28}Mg, ^{32}Si, ^{67}Cu (^{68}Ge).

If 1) a higher energy accelerator could have excellent beam properties at 15-20 MeV, or 2) parasitic operation of the current IDPRA facitlies should not longer be available (due to termination of primary DOE missions of the host facilities) a higher energy accelerator must be considered.

Why ~40 MeV variable-energy, multi-particle Accelerator?

You want ^{211}At

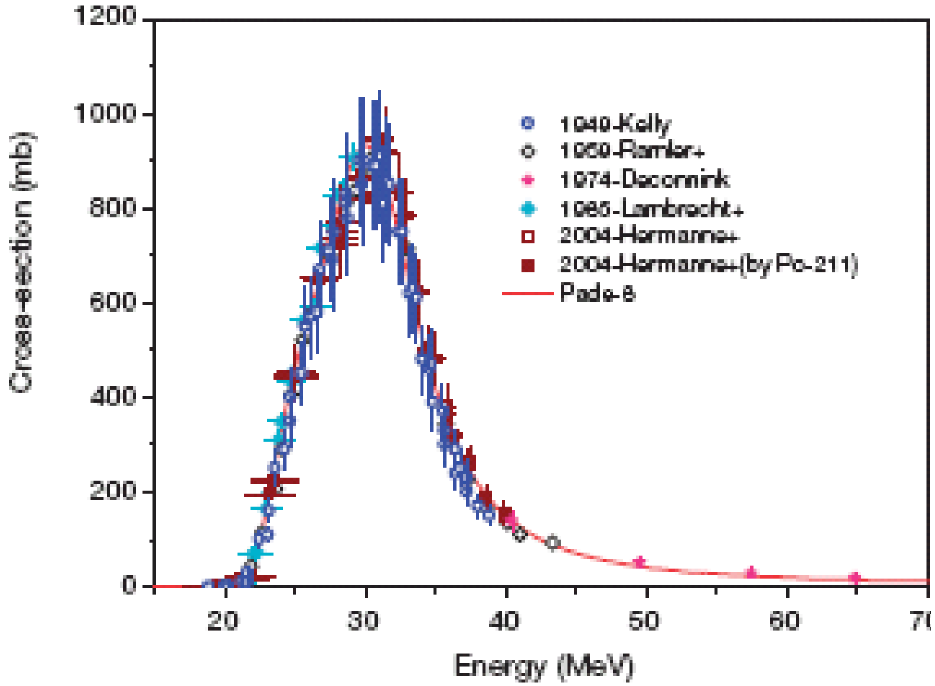


FIG. 2.4.2. Excitation function for the $^{209}Bi(\alpha, 2n)^{211}At$ reaction.

and not ^{210}At

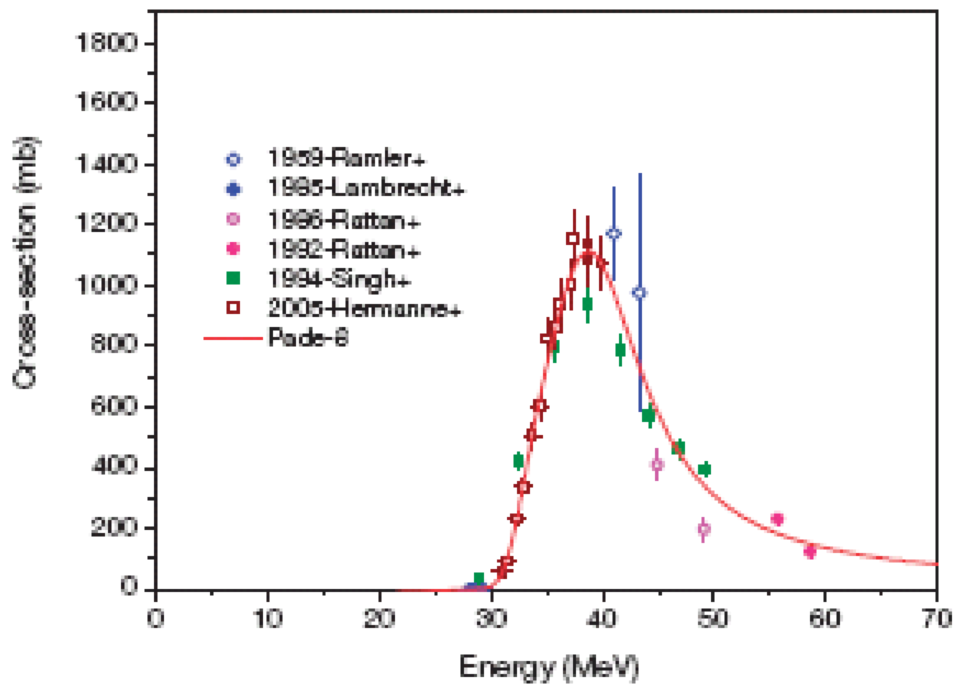


FIG. 2.4.3. Excitation function for the $^{209}Bi(\alpha, 3n)^{210}At$ reaction.

Properties of a modern 70 MeV variable-energy, high-current, multi-particle Accelerator vs an existing cyclotron

Table 1. Main characteristics of the ARRONAX cyclotron.

Beam	Accelerated Particles	Energy (MeV)	Intensity (µA)
Protons	H-	30-70	<350
	HH+	17.5	<50
Deuterons	D-	15-35	<50
α particles	He++	70	<35

U-C Davis Crocker Lab
from their web site

p	1.3-68 MeV	30 µA
d	15-45 MeV	40 µA
α	5-90 MeV	40 µA

Isotope Separators

Only electromagnetic separation currently provides the range of isotopes and enables high purity.

Scaled to capacity of 4 separators similar to Calutrons

- **2 for production**
- **1 in set-up, maintenance or R&D**
- **1 dedicated to radioactive material**

This gives capacity about equal to current sales.

There may be new technology, possibly classified, that may make the capacity possible with fewer devices.

There are security and export control issues with operation of high-throughput separators. This may limit the choice of available sites.

Plasma separation continues to look promising for large quantity, moderate purity applications.

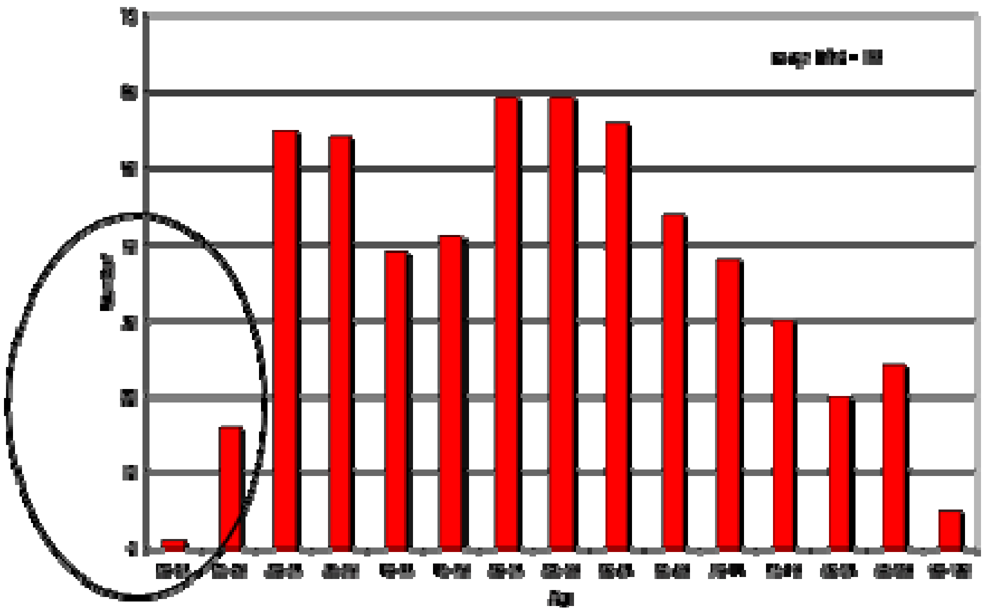
There are other R&D issues to be addressed: ^{3}He, Li

Recommendations – Highly Trained Workforce

III: Invest in workforce development in a multipronged approach, reaching out to students, post-doctoral fellows, and faculty through professional training, curriculum development, and meeting/workshop participation.

The dwindling population of skilled workers in the area of isotope production and applications is a widely documented concern.

American Chemical Society
Division of Nuclear Chemistry and Technology



- NSAC, 2004, Education in Nuclear Science
- NRC, 2007, Advancing Nuclear Medicine through Innovation
- AAAS, APS, CSIS, 2008, Readiness of the U. S. Nuclear Workforce for 21st Century
- APS, AAAS, 2008, Nuclear Forensics: Role, State of the Art, Program Needs

Budget Scenarios

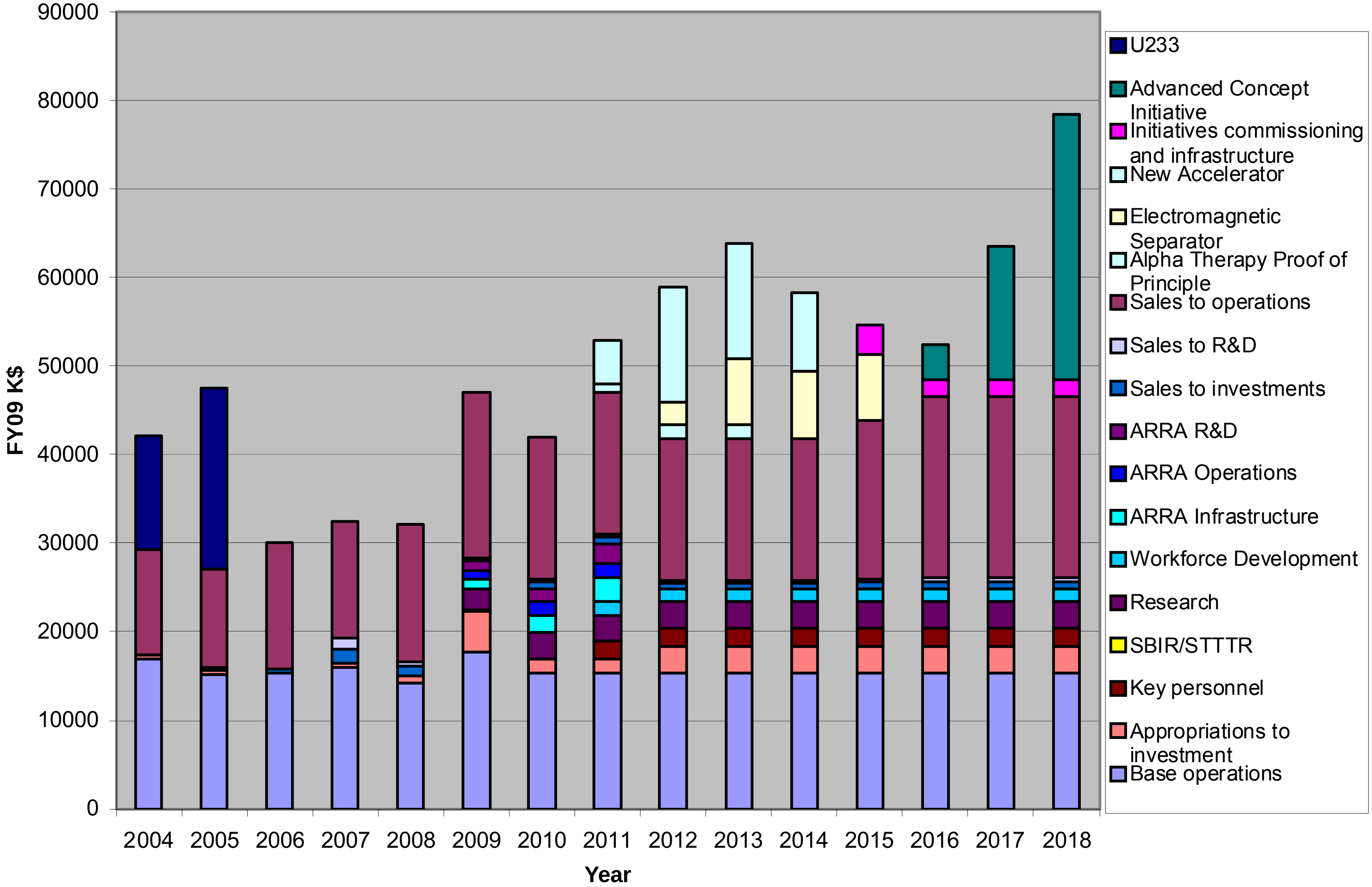
Table 12.1 Adjustments to 2009 President's budget request (in FY09 dollars) to implement recommendations of this report

Program Element	Change in Optimum Budget	Change in Constant Effort Budget
Stabilize Skilled Workforce	+2M	+1.5M
Infrastructure and Maintenance	+1.5M (to 3.0M)	Set at 1.0M
Research and Development	Set at 3.0M	Set at 1.2M
Workforce Development	+1.5M	+0.3M
Sales invested in infrastructure	Maintain at 4%	Maintain at 4%
Sales invested in R&D	Maintain at 2%	Maintain at 2%
Capital Projects		
Pilot Th-229 recovery from U-233	$4M total 2011-2014	←Recognize major issues involved
New Accelerator	$40M total 2011-2014	
New Electromagnetic Separator	$25M total 2012-2015	
Future Initiative	$50M total 2016-2018	←Anticipating increased future demand

The initiatives obviously assume an aggressive schedule.
The initiative costs are estimates and are not based on specific proposals made to the subcommittee. There is the possibility of substantial reductions by effective use of existing resources or public-private partnerships

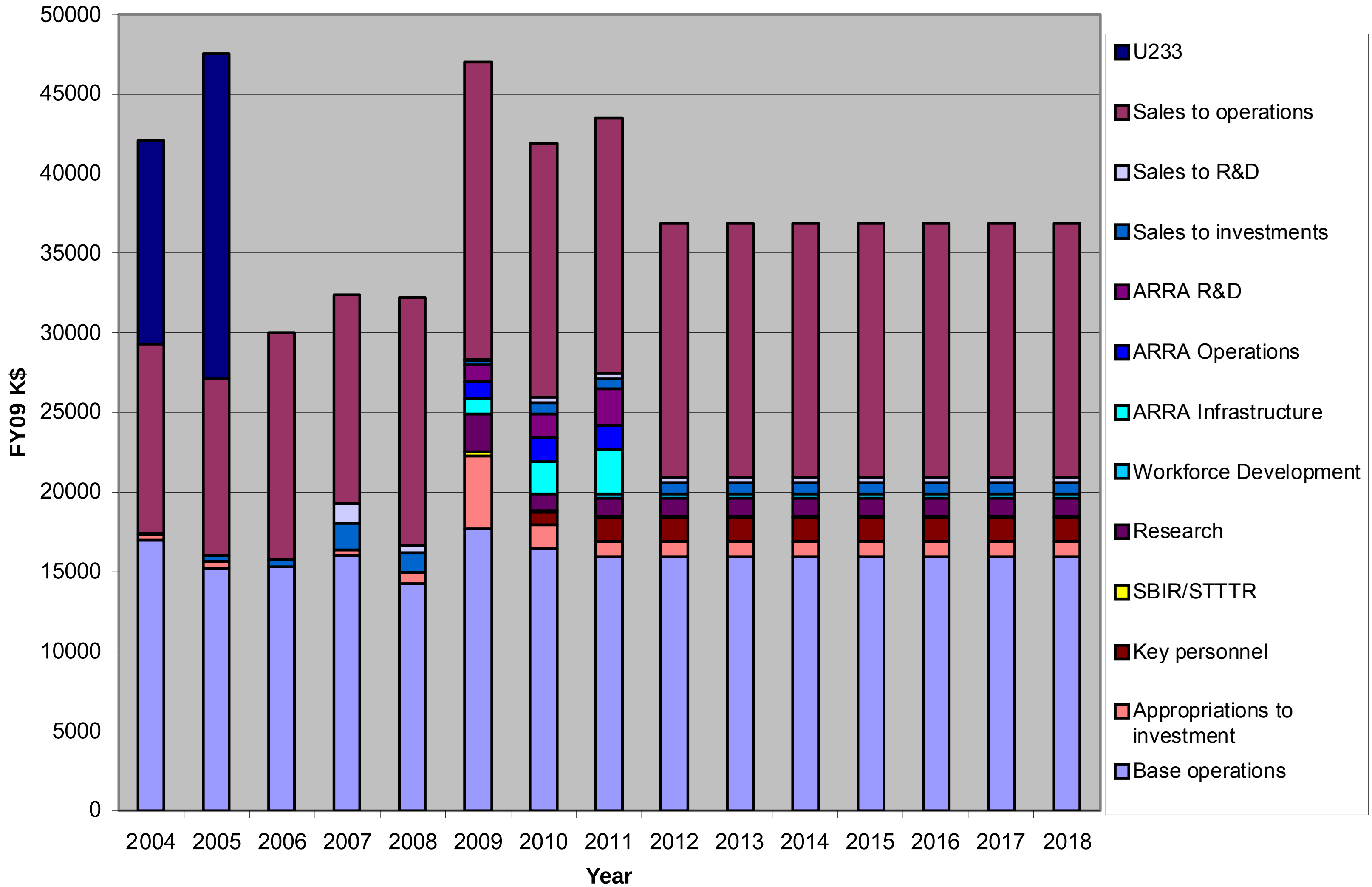
Budget Scenarios

Proposed optimum budget in FY09 dollars



Budget Scenarios

Proposed constant effort budget in FY09 dollars



Isotope Initiatives under ARRA

Research and Development on Alternative Isotope Production Technique ($4.617 Million)

- Utilizes funds from stimulus funding for alternative production techniques initiatives
- Dedicated to the production and development of stable and radioactive research isotopes important for the Nation
- Competitive: labs and universities

Enhanced Utilization for Isotope Facilities ($10 Million)

- $4.425 Million is for BLIP, IPF, HFIR, INL
- $5.575 Million is for investment in infrastructure at national lab facilities

Applications of Nuclear Science and Technology Initiatives ($19.4 Million + base funding)

- **Not specific to isotopes**
- Utilizes stimulus funds and base funds
- Need to be NP research that is beneficial to applications
- Developing technology and scientific approaches of relevance to applications is a strength of the NP program
- Exploit basic nuclear science research and technological of relevance to applications
- Focus on practical technologies for applications such as nuclear energy, nuclear medicine, advanced accelerator and instrumentation techniques, and nuclear security

In the News - Mo-99

Health

NAS report

Security

NAS report

The New York Times

Science

WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

ENVIRONMENT SPACE & COSMOS

Radioactive Drug for Tests Is in Short Supply

By MATTHEW L. WALD
Published: July 23, 2009

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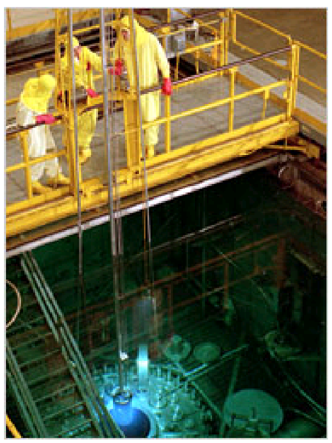
WASHINGTON — A global shortage of a radioactive drug crucial to tests for cardiac disease, cancer and kidney function in children is emerging because two aging nuclear reactors that provide most of the world's supply are shut for repairs.

Enlarge This Image



Oak Ridge National Laboratory

The Oak Ridge National Laboratory produces medical isotopes but does not have equipment to produce technetium-99m.

The 51-year-old reactor in Ontario, Canada, that produces most of this drug, a radioisotope, has been shut since May 14 because of safety problems, and it will stay shut through the end of the year, at least.

Some experts fear it will never reopen. The isotope, technetium-99m, is used in more than 40,000 medical procedures a day in the United States.

Loss of the Ontario reactor created a shortage over the last few weeks. But last Saturday a Dutch reactor that is the other major supplier also closed for a month.

The last of the material it produced is now reaching hospitals and doctors' offices. The Dutch reactor, at Petten, is 47 years old, and even if it reopens on schedule, it will

Wealth

$200M business

Note, at present, the isotopes program does not produce Mo-99

Issue: Mo-99/Tc-99m

Successful outcome of DOE Isotope program – Developed at BNL.

Used in 70-80% of all nuclear medicine procedures

~200M$ in commercial technetium generator sales each year in US

U.S. consumption 5000-7000 6 day Curies per week ($T_{1/2}$=2.75 days)

From NAS study: ~60% from Canada, ~40% from Europe via Mallinckrodt

Translates to ~ 1 MW of continuous fission target power

Based on 7 day target irradiation, daily target removal, & 2 days for processing and shipping

7 day irradiation gives 83% of equilibrium value, 1 day of delay costs 22% of product

Issues

- Reliability of Supply – old reactors are having problems
- Proliferation – Most current production uses highly enriched uranium (HEU)
- Was part of isotopes program portfolio in 1990's
- Currently NNSA has the responsibility, stemming from proliferation issues.
- 2009 NAS report concluded LEU production is feasible and would not increase cost more than 10%
- At least two commercial or public-private partnerships are seeking to solve
- FY09 Omnibus language mandates a study of one of these

Major concern

The supply of ^{99}Mo, the isotope used to generate the radioactive isotope most frequently used in medical procedures, is of great concern. Recent disruptions in international supply demonstrate the vulnerability of the nation's health care system in this area. The nation must address this vulnerability. At the present time, the isotopes program does not produce 99Mo. With the non-proliferation issues associated with the transport and use of the highly-enriched uranium currently used for 99Mo production, DOE/NNSA has the lead responsibility in this area and is actively investigating options for 99Mo commercial production. The subcommittee chose to refrain at this time from inserting itself into the intense activity underway but reiterates the importance of the issue.

Summary

- **The Isotope Development and Production for Research and Applications Program is a major asset for the nation's competitiveness.**

- **It is an essential role for the Federal government.**
    - **unique capital investments**
    - **sensitive technology**
    - **considerable economic risk**
    - **intellectual advances**

- **It should focus on development and production.**

- **It needs to replace lost capabilities – stable isotopes – and be able to provide radioactive isotopes for research year-round.**

- **Following the recent significant pulse of investment, the program could operate on a constant effort budget for a few years. In the long term, this will force the nation to rely heavily on uncertain foreign sources of isotopes.**

Ani and I must express our deep thanks to all the members of the subcommittee, whose wisdom, insight, and hard work created this strategic plan.

Background Material

FY10 Congressional Language

House

Science: The Committee recommends $29.2M, $10.0M above the request, for the Isotopes Development and Production for Research and Applications, University Operations. The Committee is aware that several universities, including the University of California at Davis and Idaho State University, operate facilities with the potential to make important contributions to the nation's supply of medical isotopes. The Committee directs the Department to work with the academic community to most cost-effectively increase the availability of medical isotopes.

NNSA: The Committee has included an additional $10M for university reactors in Office of Science Medical Isotope Production and Applications, University Operations. The Committee directs that activities to support the short term production of critical isotopes in short supply, including Mo-99, be given the highest priority for this funding. The Department should also evaluate the material processing facilities to support this effort

Senate

Within the funds provided, $17.5M is for nuclear medicine medical application research. The Committee emphasizes its commitment to nuclear medicine medical application research at the DOE. All of the additional funds must be awarded competitively in one or more solicitation that includes all sources– universities, the private sector, and Government laboratories. Funding for nuclear medicine application research was previously within the BER program.

Research Priorities: Medicine …

Research Activity	Isotope	Issue/Action
Alpha therapy	^{225}Ac ^{211}At ^{212}Pb	Current sources are limited. One valuable source for ^{225}Ac, extraction of ^{229}Th from ^{233}U may soon be lost.
Diagnostic dosimetry for proven therapeutic agents	^{64}Cu ^{86}Y ^{124}I ^{203}Pb	Used in conjunction with ^{67}Cu therapy ^{90}Y therapy ^{131}I therapy and immune-diagnosis ^{212}Pb therapy The issue is the need for a coordinated network of production facilities to provide broad availability. There is need for R&D for common target and chemical extraction procedures.
Diagnostic Tracer	^{89}Zr	Immune-diagnosis 3.27 d half-life allows longer temporal window for imaging of MoAbs, metabolism, bioincorporation, stemcell trafficking, etc.
Therapeutic	^{67}Cu	Requires specialized high energy production facilities and enriched targets

Research Priorities: Physical Sciences

Research activity	Isotope	Issue/action
Begin new facility to produce and study radioactive beams of nuclei from ^{252}Cf fission, for research in nuclear physics and astrophysics - CARIBU at ANL	^{252}Cf (2.6 yr)	Supply of ^{252}Cf is uncertain; 1 Ci source is needed each 1 ½ year for at least four years.
Measure permanent atomic electric dipole moment of ^{225}Ra to search for time reversal violation, proposed to be enhanced due to effects of nuclear octupole deformation;	^{225}Ra (15 d)	Supply of ^{225}Ra is limited. Need 10 mCi source of ^{225}Ra every two months for at least two years
Create and understand the heaviest elements possible, all very short-lived and fragile. Study the atomic physics and chemistry of heavy elements for basic research and advanced reactor concepts.	^{209}Po, ^{229}Th,^{232}Th, ^{231}Pa, ^{232}U, ^{237}Np,^{248}Cm, ^{247}Bk	Make certain actinides in HFIR and then prepare targets for accelerator-based experiments to make superheavy elements; targets needed are ^{241}Am, ^{249}Bk, ^{254}Es - not available now; need10 - 100 mg on a regular basis; purity is important
Neutron detectors, electric dipole moment measurement, low temperature physics,	^{3}He	Total demand exceeds that available
Isotope dilution mass spectrometers	^{236}Np, $^{236,244}Pu$, ^{243}Am, ^{229}Th	High purity ^{236}Np is not available; others are in limited supply; 10 - 100 mg needed on a regular basis; purity is important
Search for double beta decay without neutrino emission - an experiment of great importance for fundamental symmetries	^{76}Ge	Need to fabricate large detectors of highly enriched ^{76}Ge; U.S. cannot produce quantity needed, ~1000 kg
Spikes for mass spectrometers	$^{202,203,205}Pb$, ^{206}Bi, ^{210}Po	$^{202,205}Pb$ difficult to get in high purity in gram quantities
Avogadro project - worldwide weight standard based on pure ^{28}Si crystal balls	^{28}Si	Concern about future supply and cost of kg of material needed
Radioisotope micro-power source	^{147}Pm,^{244}Cm	Development needed for efficient conversion
Isotopes for Mossbauer Spectroscopy, over 100 radioactive parent/stable daughter isotopes	^{57}Co, ^{119m}Sn ^{67}Ni, ^{161}Dy, …	Some Isotopes only available from Russia, a concern for scientific community

Charge 1: Recommendations

1. **Invest in new production approaches of alpha-emitters with highest priority for ^{225}Ac. Extraction of the thorium parent from ^{233}U is an interim solution that needs to be seriously considered for the short term until other production capacity can become available. (Medicine #1)**

2. **We recommend investment in coordination of production capabilities and supporting research to facilitate networking among existing accelerators. (Medicine #2)**

3. **We recommend the creation of a plan and investment in production to meet these research needs for heavy elements. (Physical Sciences 1-3)**

Charge 1: Recommendations -continued

4. **We recommend a focused study and R&D to address new or increased production of ^{3}He. (Physical Sciences #4)**

5. **Research and Development efforts should be conducted to prepare for the reestablishment of a domestic source of mass-separated stable and radioactive research isotopes. (Physical Sciences 5-8 and 10)**

6. **We recommend that a robust investment be made into the education and training of personnel with expertise to develop new methods in the production, purification and distribution of stable and radio-active isotopes. (All)**

101-101

Energy and Water Development Appropriations Act, 1990 (Engrossed as Agreed to or Passed by House)

ISOTOPE PRODUCTION AND DISTRIBUTION PROGRAM FUND

For necessary expenses of activities related to the production, distribution, and sale of isotopes and related services, $16,243,000, to remain available until expended: *Provided,* That this amount and, notwithstanding 31 U.S.C. 3302, revenues received from the disposition of isotopes and related services shall be credited to this account to be available for carrying out these purposes without further appropriation: *Provided further,* That all unexpended balances of previous appropriations made for the purpose of carrying out activities related to the production, distribution, and sale of isotopes and related services may be transferred to this fund and merged with other balances in the fund and be available under the same conditions and for the same period of time: *Provided further,* That fees shall be set by the Secretary of Energy in such a manner as to provide full cost recovery, including administrative expenses, depreciation of equipment, accrued leave, and probable losses: *Provided further,* That all expenses of this activity shall be paid only from funds available in this fund: *Provided further,* That at any time the Secretary of Energy determines that moneys in the fund exceed the anticipated requirements of the fund, such excess shall be transferred to the general fund of the Treasury.

103-316

Energy and Water Development Appropriations Act, 1995 (Enrolled as Agreed to or Passed by Both House and Senate)

DEPARTMENT OF ENERGY

Energy Supply, Research and Development Activities

- For expenses of the Department of Energy activities including the purchase, construction and acquisition of plant and capital equipment and other expenses incidental thereto necessary for energy supply, research and development activities, and other activities in carrying out the purposes of the Department of Energy Organization Act (42 U.S.C. 7101, et seq.), including the acquisition or condemnation of any real property or any facility or for plant or facility acquisition, construction, or expansion; purchase of passenger motor vehicles (not to exceed 25, of which 19 are for replacement only), $3,314,548,000, to remain available until expended: *Provided,* That the Secretary of Energy may transfer available amounts appropriated for use by the Department of Energy under title III of previously enacted Energy and Water Development Appropriations Acts into the Isotope Production and Distribution Program Fund, in order to continue isotope production and distribution activities: *Provided further,* That the authority to use these amounts appropriated is effective from the date of enactment of this Act: ***Provided further,* That fees set by the Secretary for the sale of isotopes and related services shall hereafter be determined without regard to the provisions of Energy and Water Development Appropriations Act (Public Law 101 -101): *Provided further,* That amounts provided for isotope production and distribution in previous Energy and Water Development Appropriations Acts shall be treated as direct appropriations and shall be merged with funds appropriated under this head.**

FY09 President's Budget Language

The Isotope Program (Isotope Production and Distribution Program Fund) produces and sells radioactive and stable isotopes, byproducts, surplus materials, and related isotope services world wide. The Isotope Program operates under a revolving fund established by the 1990 Energy and Water Appropriations Act (Public Law 101-101), as modified by Public Law 103-316. Each isotope will be priced such that the customer pays the cost of production. The DOE will continue to sell commercial isotopes at full-cost recovery.

The Program's fiscal year appropriation will be received via transfer from the Nuclear Physics program starting in FY 2009. Prior to FY 2009, the direct appropriation was provided via transfer from the Radiological Facilities Management program within the Office of Nuclear Energy. The appropriation is used to maintain and upgrade the infrastructure that is needed to assure continued reliable production, with the production costs borne by the customers. Only funds from the Isotope Production and Application subprogram within the Nuclear Physics program will be expended on the development or production of isotopes.

There is similar language every year in the President's request

Sales revenues

Fig. 11.5: Sales in last five years in as spent dollars, and the listing of the three top sales isotopes each year. The FY09 number is a projection made in April.