Nuclear Science Advisory Committee
Isotopes Subcommittee

Co-chairs
Ani Aprahamian
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A Strategic Plan for the Isotope Development and Production for Research and Applications Program

Presentation to NSAC
5 November 2009

Charges to NSAC

Charge 1:

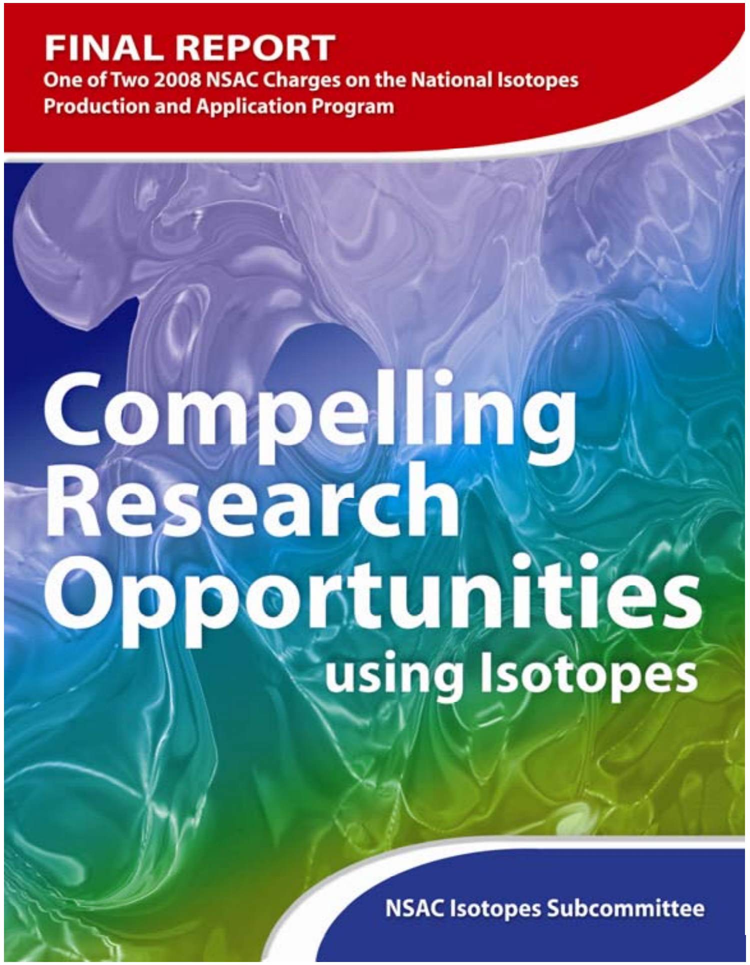
As part of the NIPA Program, the FY 2009 President's Request includes $3,090,000 for the technical development and production of critical isotopes needed by the broad U.S. community for research purposes.

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.

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



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

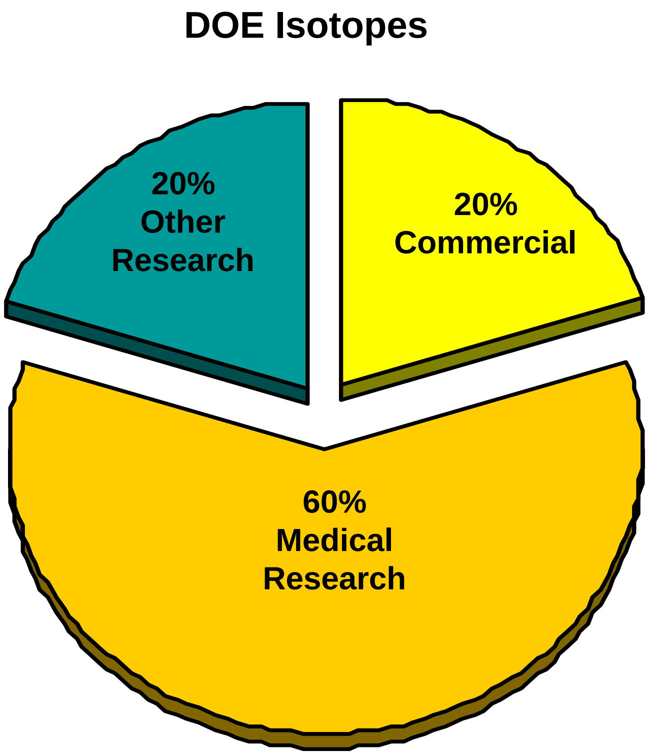
Charge 2 Continued:

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.

The DOE Isotope 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 of isotopes – not for end-use
- Over 190 customers in FY 2008
- Over 560 shipments in FY 2008
- Ten customers provided over 85% of sales



- FY08 Appropriations: $15.0M, FY09: $24.9M, FY10: $19.2M
- FY08 Sales: $17.2 M

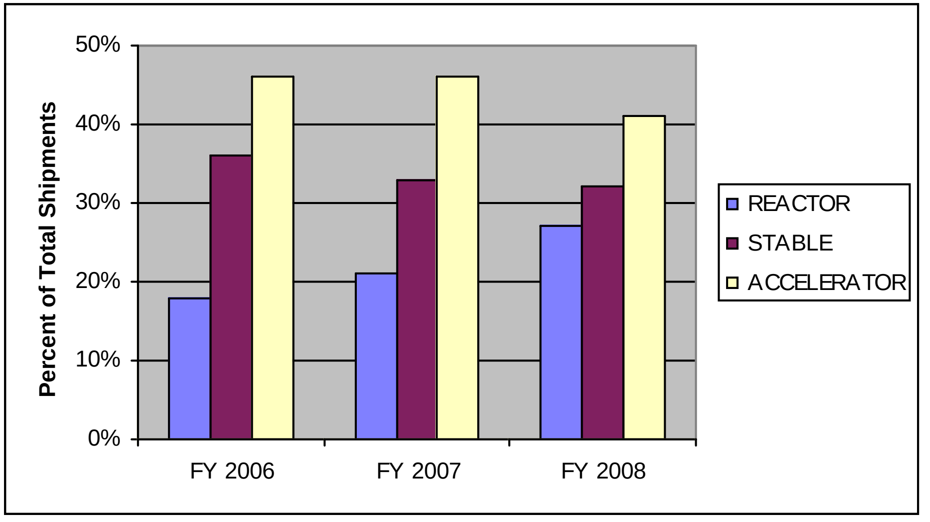
For Some Isotopes, the Federal Responsibility Has Been Assigned Elsewhere

- Weapons-related isotopes: tritium, plutonium (for example for thermoelectric generators)
- Reactor fuels, highly enriched uranium
- Mo-99, the generator for the isotope most commonly used in medical procedures – DOE/NNSA as part of Strategic Threat Reduction Initiative
  - We will return to this later

Sources of Isotopes

- Accelerators – BLIP, IPF, universities, commercial
- Reactors – HFIR, ATR, universities (MURR, Davis…)
- Isotope Separators – No DOE facilities.

  US commercial production of light isotopes (B, C, O) in metric ton ranges by distillation, chemical exchange and thermal diffusion.
  - Forecast high volume uses
    - Double beta decay
    - Li for new reactor concepts
    - He-3 for NNSA and DHS neutron detectors
    - Target material to produce radioisotopes
    - Beams of rare isotopes



- Stockpiles of long-lived or stable isotopes
  - Pool of separated isotopes from Calutrons
    - Actual value ?????
    - Audited value based on sales \$3.5M (~ 1.0 M\$/year, 7% of sales)
  - Lots of precious and nasty stuff from reactor burn-up

DOE Production Sites

Past and potential future participants

Pacific Northwest:

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:

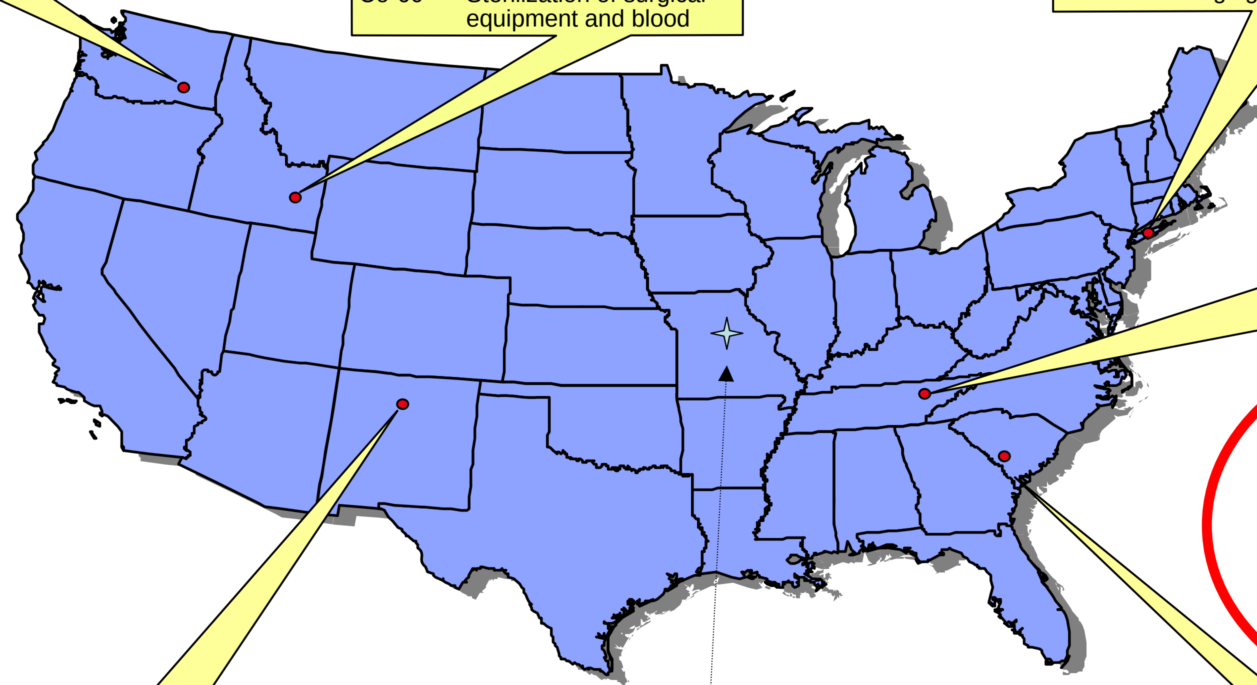
Top 10 stable isotopes sold over the last 5 years:

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 with IDPRA stewardship responsibilities

Savannah River – Tritium Facility:

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

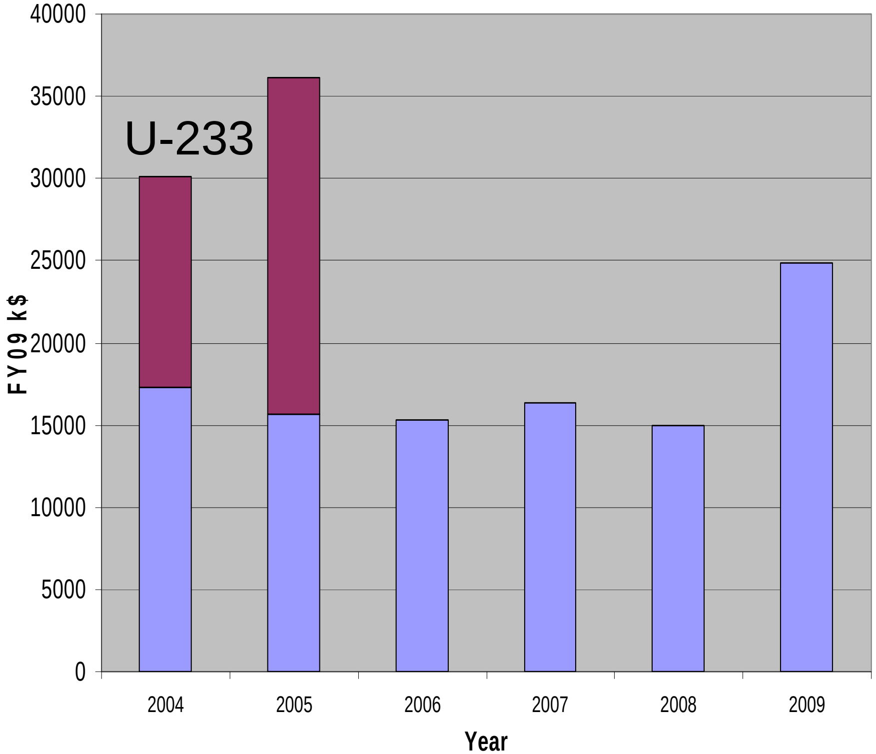
IDPRA acts as sales broker

Budget History in FY09$

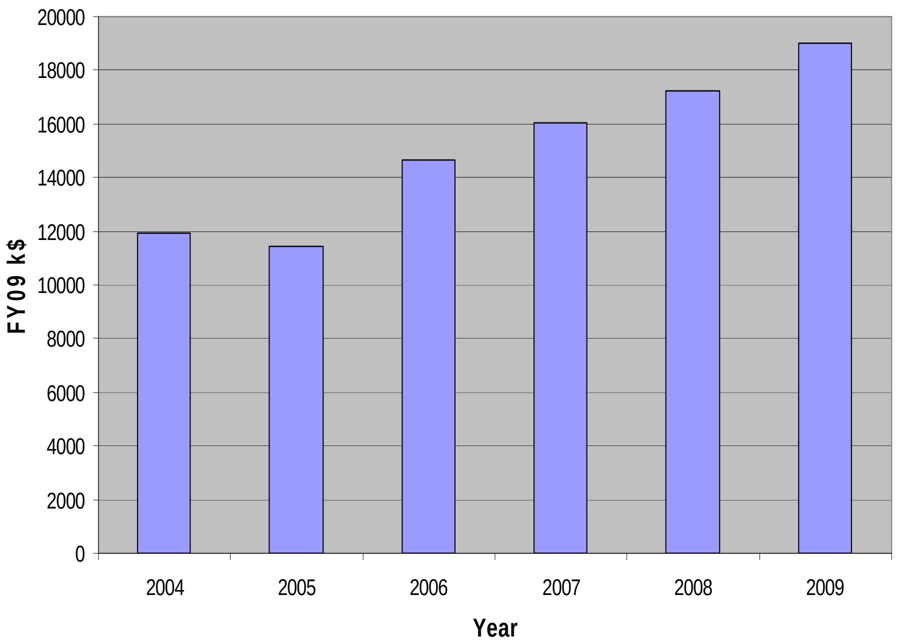
Table 11.3: FTE support at the national laboratories by the appropriation and by sales revenue.

	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

Appropriations



Sales



Challenges

- Program serves many federal agencies and commercial customers.
- Nature of demand can change dramatically as research and commercial needs change.
- Requires broad and expensive infrastructure, with significant continuous costs to be mission ready and deal with ES&H implications.
- Requires highly skilled teams and there are currently shortages of expertise.
- To use in human patients, FDA requires meeting and adhering to current Good Manufacturing Practices.
- Program leverages major investments by other parts of DOE, but then is subject to changing mission priorities affecting operating schedules or facility closures.
- Many radioactive isotopes have a short shelf life. Patient treatment may require continuous access.
- May invest in a promising application, but if it fails to perform as expected, demand may collapse.
- If successful, demand may increase many-fold.
- Once a commercial supplier is available, DOE must leave market.
- If a major customer pulls out, price for all other users can increase dramatically.

Challenges

- Foreign suppliers, in some case subsidized by governments or capitalizing on previous government stocks can artificially determine the price.
- If governments subsidize research isotopes for their own researchers, U.S. research community can be put at a significant disadvantage.
- Non-proliferation issues must be balanced with isotope use issues.
- Isotope separation technology could possibly be used by rogue states to create weapons, nuclear or radiological. State of the art may be classified.
- Benefits of maintaining stockpiles for isotope harvesting must be balanced with risks (environmental risks or risks of diversion) of maintaining isotopes in temporary storage facilities.
- If demand exceeds supply, who decides who gets it, especially if there are national security needs.
- At present, for costing purposes, “Research” and “Commercial” are defined based on the isotope, not the intended use.

All in all, it is clear this is a very difficult business model. Commercialization has been confined to a limited number of isotopes with high-volume and regular demand. It often fails!

NSACI Subcommittee

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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	2nd Report submitted to NSAC
27 July 2009	NSAC comments
27 August 2009	Revised report submitted to NSAC

Major NSAC Comments in July

- There was general support for the recommendations

NSAC Requests

- Give priority ordering for recommendations
- Interchange the order of recommendations on workforce development and new capabilities
- Small rewording changes of recommendations to allow DOE flexibility to optimize response – place specific suggestions in accompanying text
- Make discussion of workforce development recommendation more targeted to isotope production
- Add a few more sentences of justification in the executive summary
- Reduce some of the detail in the discussion of the program operations and laboratories requests for funding.

There were a number of small wording corrections and refinements.

All of these, to the extent solid information is available, have been addressed in the revised report.

There was also significant NSAC discussion of putting this report in the context of the rest of the Nuclear Physics program and budget. This is clearly outside the charge and expertise for NSACI and no such changes were made. It may be appropriate for NSAC to comment on in the cover letter.

Example of Potential Increases in Demand for Ac-225/Bi-213 and the Risk of Successful Trails

Current source is ^{229}Th milked at ORNL providing 100 mCi every two months. We also get our ^{225}Ra from the same place. This treats five patients for Acute Myeloid Leukemia and could treat 30 patients per year. ^{225}Ac/^{213}Bi are under investigation for other cancers and for HIV treatment.

Table 3.A.2: Estimated annual usage of ^{225}Ac and/or ^{213}Bi based on known needs. Estimates can vary by ±50% depending on whether the approved treatment is with ^{225}Ac or ^{213}Bi [NO08].

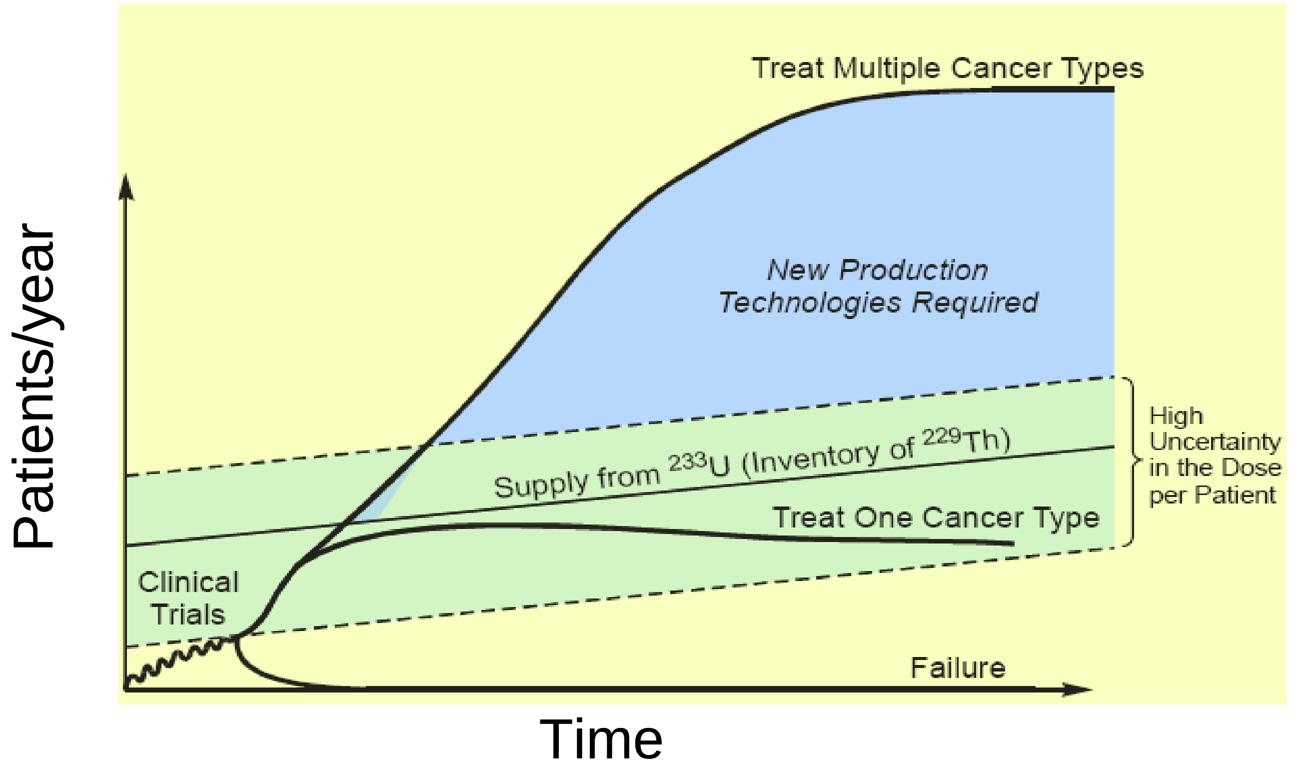
Year	**Amount(mCi)**	**Program**
2009	1600	Clinical trails (1 multi-center)/R&D support
2010	3100	Clinical trails (2 multi-center)/R&D support
2011	4600	Clinical trails (2 multi-center)/R&D support
2012	7400	Clinical trails (3 multi-center)/R&D support
2013	15000	One approval; Clinical trials (2 multi-center)/ R&D support
2014	50000+	Two approvals; Clinical trials/R&D support

Recent disappointing results for cancer trails with Bi-209. Does not mean alpha therapy is not valued. NCI is switching to Pb-212 obtained from Ra-224 and direct use of Ac-225. In the short term, Ra-224 seems to be more available.

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. Tried and failed.

Current 0.5-0.6 Ci/yr
Perhaps 20M$ for 3 Ci/yr, but
Congress has mandated disposal



In the News - Mo-99

Health

NAS report

Security

NAS report

Wealth

$200M business

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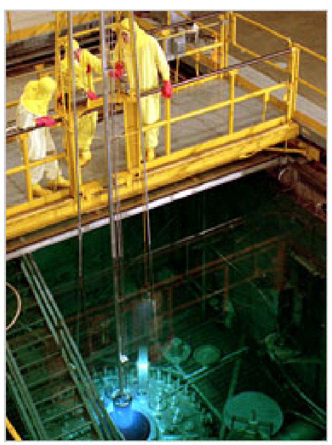
WASHINGTON — A global shortage of a radioactive drug crucial to tests for cardiac disease, cancer and kidney function in children is emerging because two aging nuclear reactors that provide most of the world's supply are shut for repairs.

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

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
- Over past year, emphasis has changed from non-proliferation to reliable supply

NSACI Subcommittee 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.

Success Story – ^{82}Sr

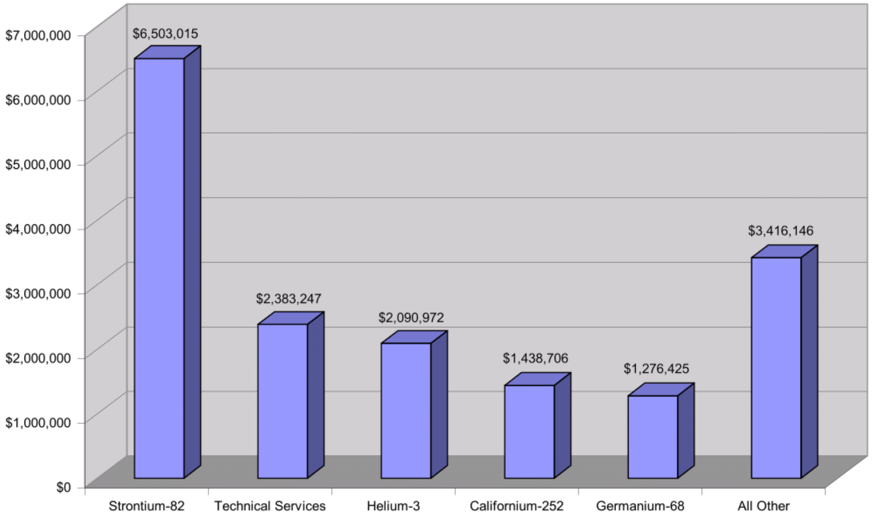
- ^{82}Sr - ^{82}Rb used in clinical positron emission tomography for cardiac perfusion studies. ^{82}Sr has a 25 day half-life. 100 mCi generator supports 240 patients

- 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

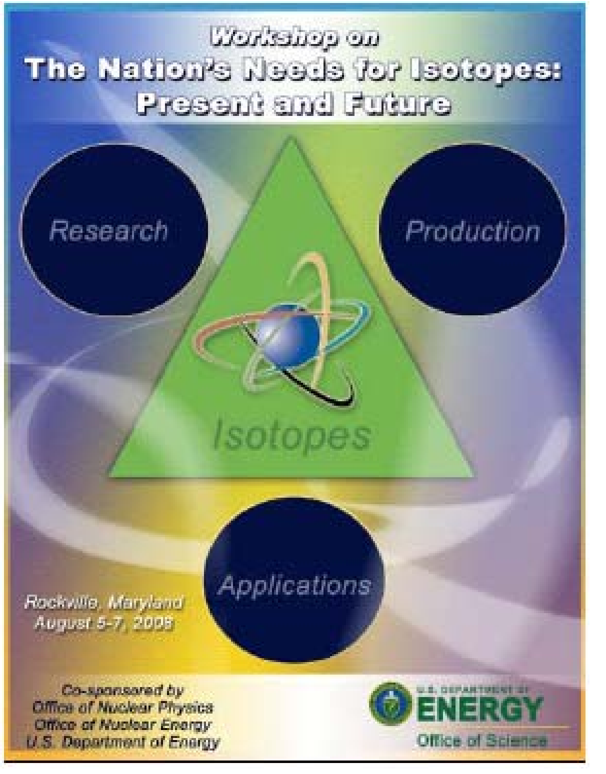
In Many Cases DOE-ONP Has Already Started Down This Path

- **Communication, Communication, Communication**
  - August 2008 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



Isotope Initiatives under ARRA

<u>Research and Development on Alternative Isotope Production Technique ($4.617 Million)</u>

- 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

<u>Enhanced Utilization for Isotope Facilities ($10 Million) to better meet the needs of the nation for isotopes in short supply to industry and basic research</u>

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

<u>Applications of Nuclear Science and Technology Initiatives ($19.4 Million + base funding)</u>

- **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

All contribute to training the scientific and technical workforce the U.S. needs

Recommendations – The Present Program (in priority order)

I.1: Maintain a continuous dialogue with all interested federal agencies and commercial isotope customers to forecast and match realistic isotope demand and achievable production capabilities.

For the isotope program to be efficient and effective for the nation, it is essential that isotope needs be accurately forecast. 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: Coordinate production capabilities and supporting research to facilitate networking among existing DOE, commercial, and academic facilities.

In the short term, increased isotope production and the availability of new research isotopes require more effectively exploiting the available production facilities including resources outside those managed by the program. This will require both research and development to standardize efficient production target technology and chemistry techniques and flexible funding mechanisms to direct production resources most effectively.

Recommendations – The Present Program

I.3: 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.

Research and development may significantly expand the production efficiency and capacity of the program. It is also an important path to expanding the skilled isotope production workforce and retaining the most creative people in the program.

I.4 Devise 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.5: Encourage the use of isotopes for research through reliable availability at affordable prices.

Many research applications, and especially medical trials, cannot proceed without a dependable source of isotopes. At the same time, DOE should reexamine its pricing policy for research isotopes to encourage U.S. leadership in isotope-based research.

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

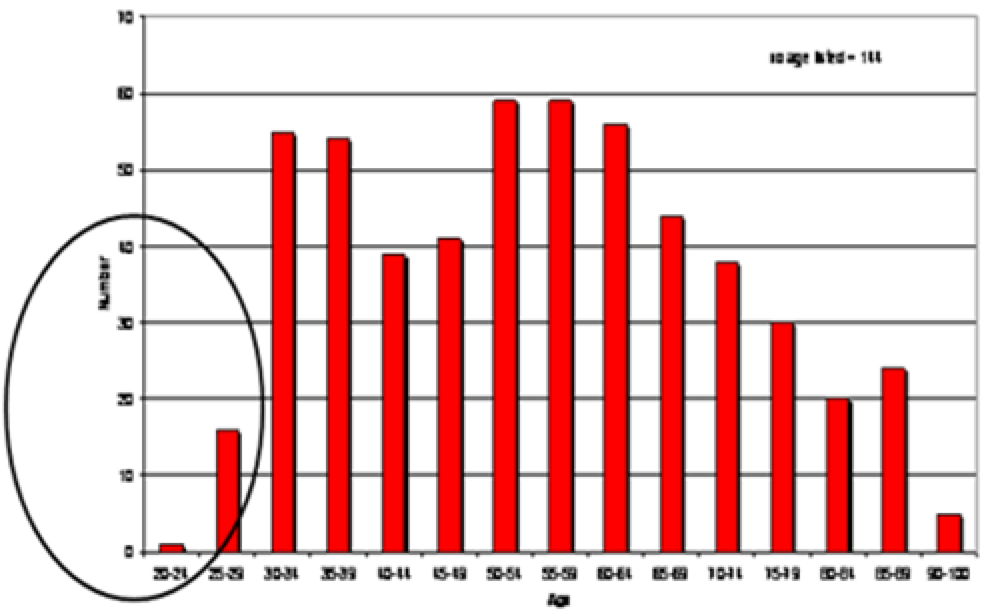
- **Identify and prioritize transportation needs through establishing a transportation working group.**
- **Initiate a collaborative effort to develop and resolve the priority issues (i.e., certification of transportation casks).**

Recommendations – Highly Trained Workforce (of priority similar to I.3- R&D)

II: 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 areas relating to isotope production and applications is a widely documented concern. This recommendation is focused on the needs of the IDPRA program, itself. The relative priority of this recommendation is comparable to that for a sustained R&D program, with which it is closely linked.

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

Recommendations – Major Investments

III.1: Construct and operate an electromagnetic isotope separator facility for stable and long-lived radioactive isotopes.

It is recommended that such a facility include several separators for a raw feedstock throughput of about 300-600 milliAmpere (10-20 mg/hr multiplied by the atomic weight and isotopic adundance of the isotope). This capacity will allow yearly sales stocks to be replaced and provide some capacity for additional production of high-priority isotopes.

III.2 Construct and operate a variable-energy, high-current, multi-particle accelerator 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. Given the uncertainties in future demand, this facility should be capable of producing the broadest range of interesting isotopes. Based on the research and medical opportunities considered by the subcommittee, a 30-40 MeV maximum energy, variable energy, high-current, multi-particle cyclotron seems to be the best choice on which to base such a facility.

Stable Isotopes in Short Supply or Exhausted from ORNL Pool

	Years remaining	Isotope	Years remaining
Gadolinium-154, 2nd Pass	2.5	Zirconium-94	18.5
Gallium-69	3.7	Barium-137	19.0
Nickel-62	3.9	Samarium-149	19.6
Osmium-187	5.2	Gadolinium-157	0.2
Lutetium-176	5.5	Platinum-195	12.0
Ruthenium-99	6.3	Gadolinium-157, 2nd Pass	0.0
Osmium-186	7.5	Lead-204, 2nd Pass	0.0
Barium-136	7.6	Lead-207, 2nd Pass	0.0
Neodymium-150	7.9	Ruthenium-96	0.0
Mercury-204	10.2	Samarium-150, 2nd Pass	0.0
Cadmium-106	10.7	Tantalum-181	0.0
Mercury-202	11.5	Vanadium-51	0.0
Palladium-106	12.6	Tungsten-180, 2nd Pass	0.0
Silver-109	14.3		

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 approximately scaled 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

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 28 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, (^{225}Ac).

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 no longer be available (due to termination of primary DOE missions of the host facilities) a higher energy accelerator must be considered.

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	Lower priority now
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

Budget Recommendations

-- requires increases starting from constant effort budget of $19.9M (FY09) which was a $4.9M increase over FY08

- Base of funds for research and development: ~10% of operating budget
- Additional funds to maintain infrastructure: ~10% of operation budget
- Stabilize funding for key personnel : ~25% increase of manpower on appropriations
- Funds for workforce development: ~5% of operating budget

ARRA funds allows these to be phased in to 2012.

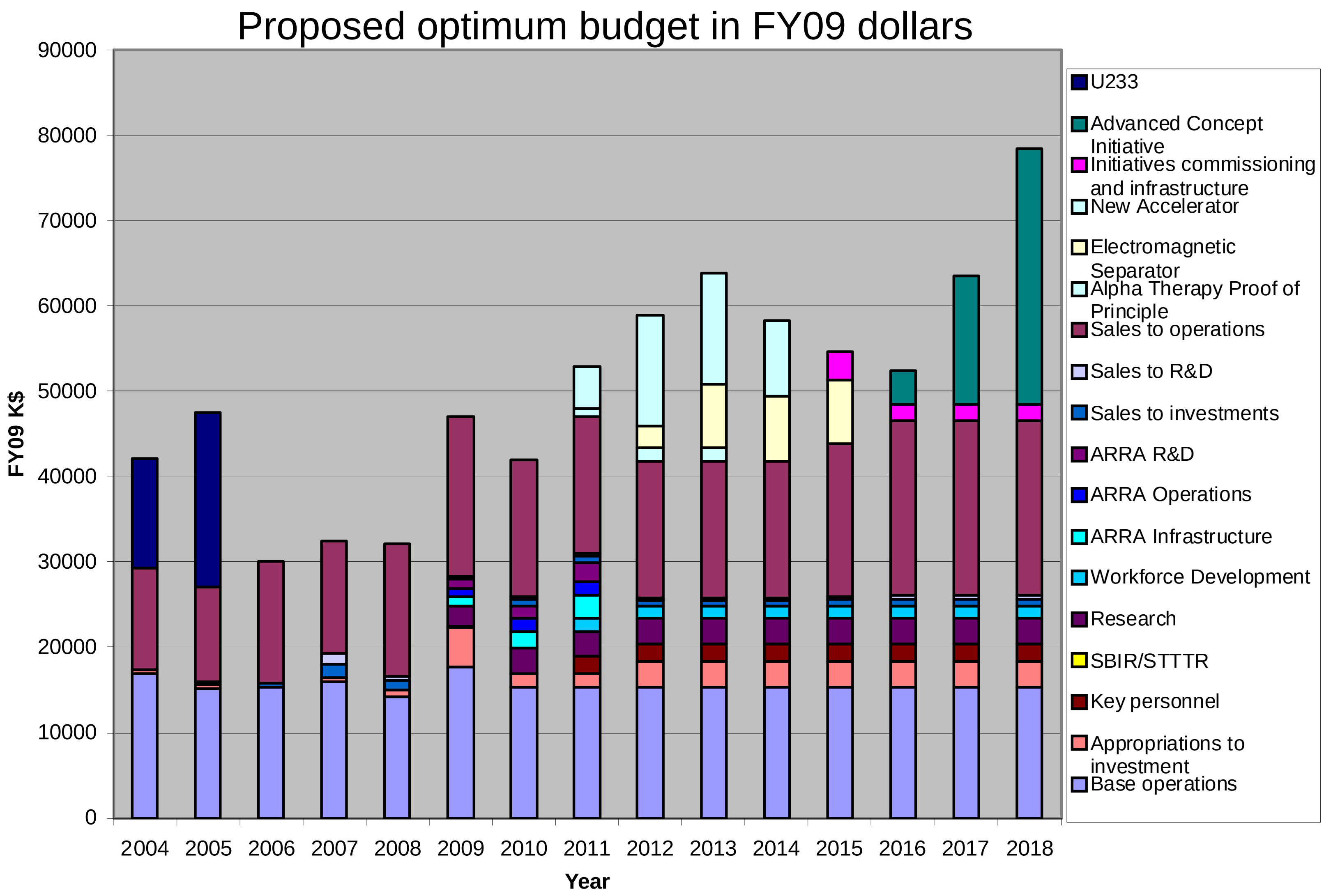
This corresponds to appropriations of ~$25M (FY09) ~ FY09 appropriation

Initiatives

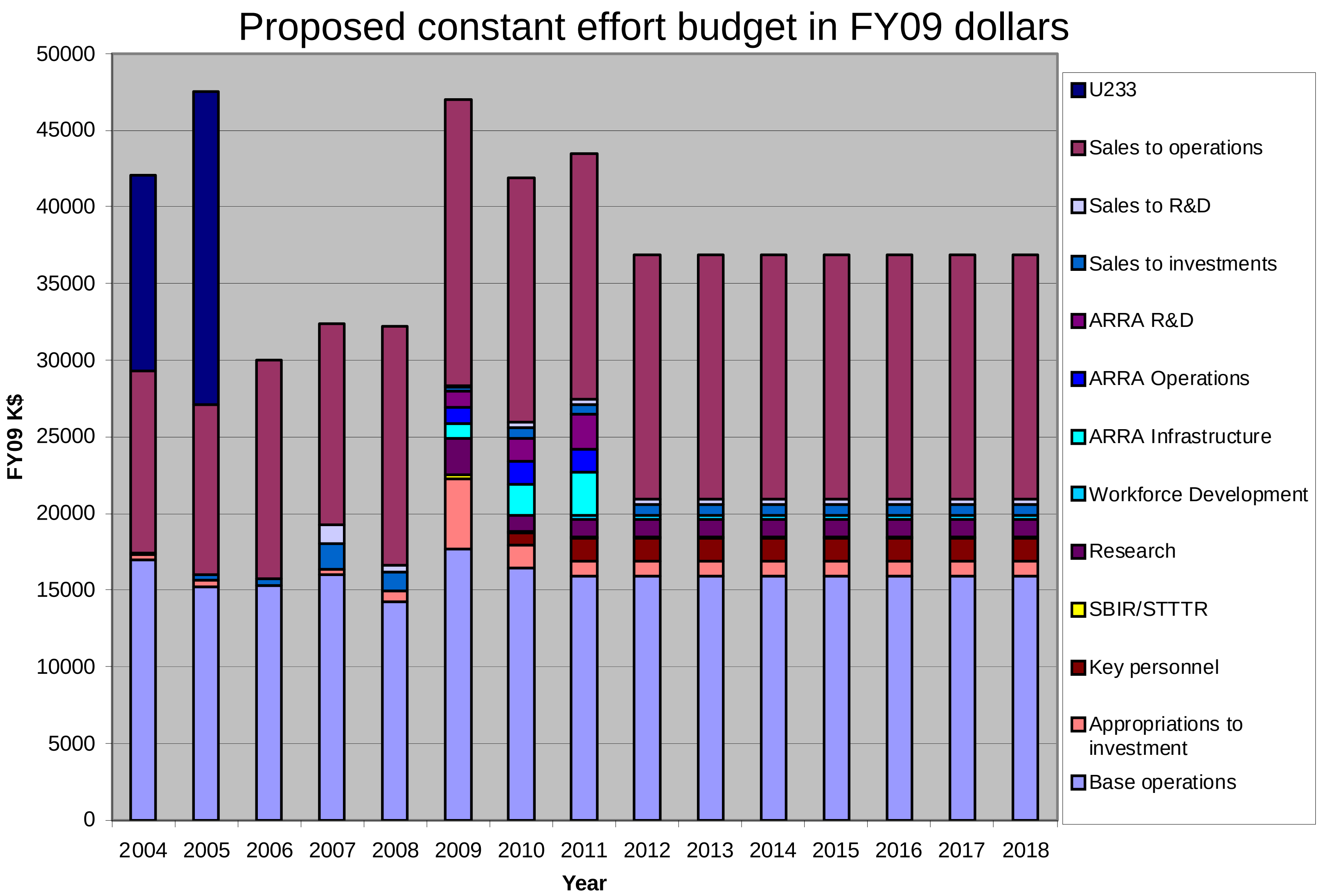
- Proof of principle for increased production of alpha emitters: $4M
- New accelerator and associated infrastructure: $40M
- Electromagnetic separation facility: $25M
- Plan for major future facility to address significant increase in demand:

  ~50M starting in 2016

Budget Scenarios



Budget Scenarios



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. We do not believe that constant effort funding would be a wise choice for the future.**

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

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

Case Study -- Californium-252

- Widely used neutron source, including for research, national security, and prompt gamma neutron activation analysis of coal, cement, explosive detection and well logging.

- Only two locations capable of production, HFIR at ORNL and Research Institute of Atomic Reactors in Dimitrovgrad, Russia

- In spring of 2007, a major customer, NNSA, withdrew from the market. Ongoing sales could not support the significant up-front costs to prepare the production targets during the 1-2 years required from initiation until sources are available for sales.

- In 2009, DOE entered a contract with industry partners. They bought a “seat license” providing a significant fraction of the up-front costs, ensuring sole access to HFIR-produced Cf-252, which the exception of a small amount (4.5 mg over 4 years for research use (in large part CARIBU). The supply is now assured, but likely at an increase in cost.

Helium-3 (0.00014% natural abundance)

Helium-3 is obtained from the decay of tritium obtained from the maintenance and dismantlement of nuclear weapons.

Prior to 2001, supply exceeded demand.

Since 2001, demand greatly exceeded supply and the stockpile is almost depleted.

SRNL has an MOU to supply isotope program 10000 liters per year for the next five years.

DOE/NNSA and DHS projects needs for neutron detectors of 150000 liters within next five years.

Under study by an interagency working group.

No ready supply solution, unless we can recover it from CANDU power reactors in Canada. If you project you need He-3, buy it now.

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

You want ^{211}At

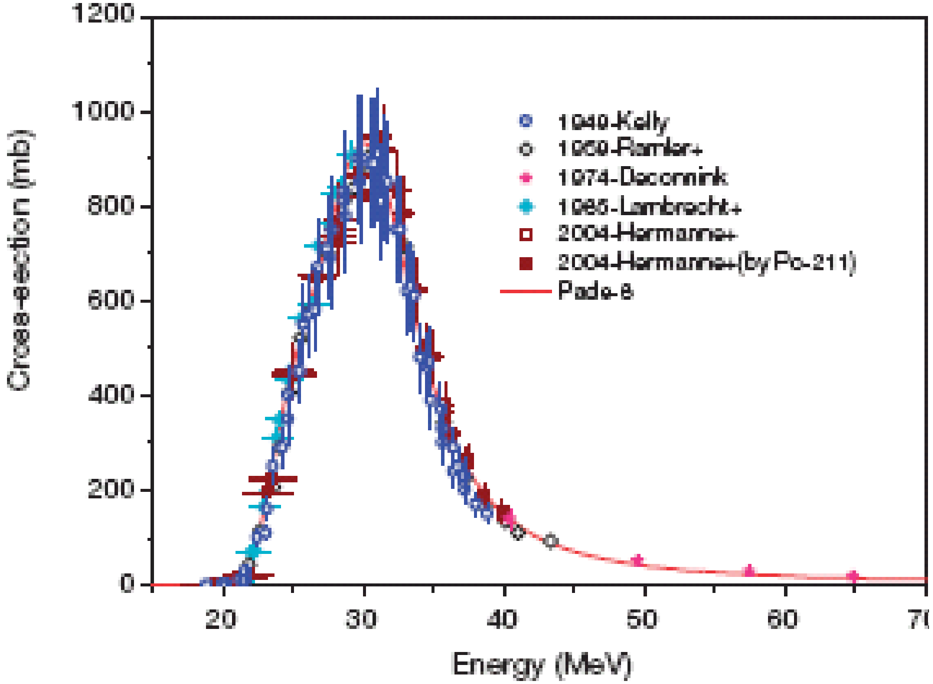


FIG. 2.4.2. Excitation function for the $^{209}Bi(\alpha, 2n)^{211}At$ reaction.

and not ^{210}At

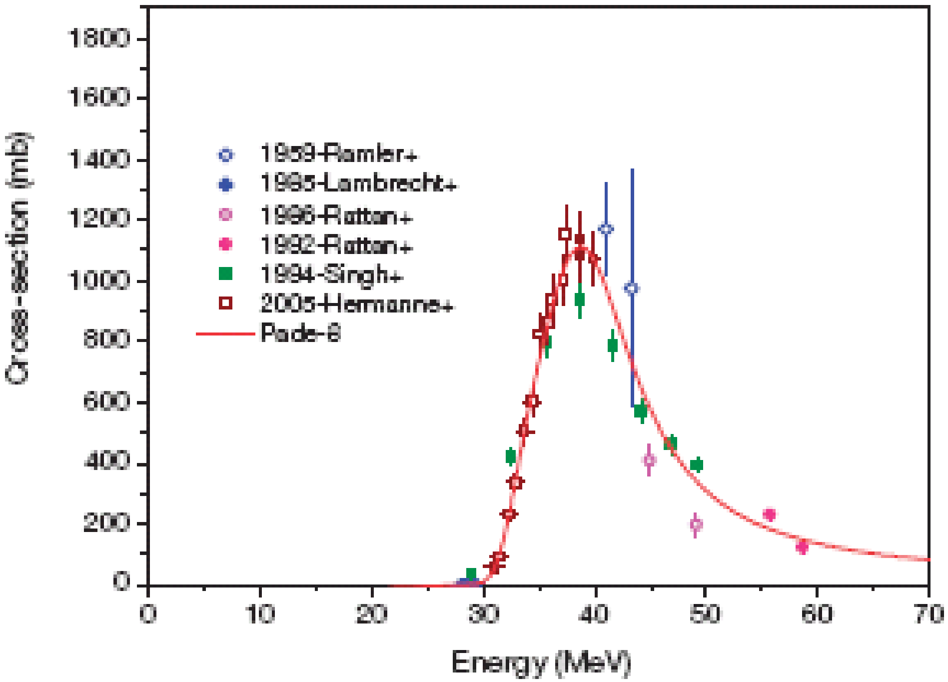


FIG. 2.4.3. Excitation function for the $^{209}Bi(\alpha, 3n)^{210}At$ reaction.

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

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 identify compelling research opportunities 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
IDPRA

Atomic Energy Act -1954

The Atomic Energy Commission was directed to insure the continuing conduct of research and development and training activities in a number of areas including nuclear processes and the utilization of radioactive material for medical, biological and health purposes.

Prices were to be based on an equitable basis to provide reasonable compensation to the government, to not discourage the use of or development of sources of supply independent of the DOE, and to encourage research and development.

This led to an explosion in the uses of isotopes. Essentially all the National Labs participated in isotope production efforts. Isotopes were cheap (relatively)!

1990- Energy and Water Appropriations Act - Public Law 101-101- Two Great Changes

“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.” [No distinction between commercial sales and research]

An Isotope Production and Distribution Program Fund was established, and appropriations and revenues received from the sales of isotopes and related services were credited to this account to be available for carrying out these purposes without further appropriation.

This is quite rare in federal agencies. A “slush” fund to merge appropriated moneys and sales.

Impact of the Pricing Structure of Public Law 101-101

Prices went up

Researchers could not afford isotopes

Foreign competition priced isotopes just below DOE prices, further reducing sales

Operating facilities could not recoup costs and were closed

Y-12/ORNL Calutrons were shut down in 1998. While they are officially on “stand-by”, the cost of restart, especially in today’s regulatory climate is prohibitive.

No U.S. source for many isotopes. Dependent on foreign producers

1995 Public Law 103-316

“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)”

But every year the President’s budget request contains language similar to that in the 2009 request.
“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 shall be priced such that the customer pays the cost of production. The DOE will continue to sell commercial isotopes at full-cost recovery.”

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

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.

FY09 Budgets

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		ORNL Upgrades	296	1796	
Totals			19900	24900	32

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

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.

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.