Nuclear Science Advisory Committee
Isotopes Subcommittee

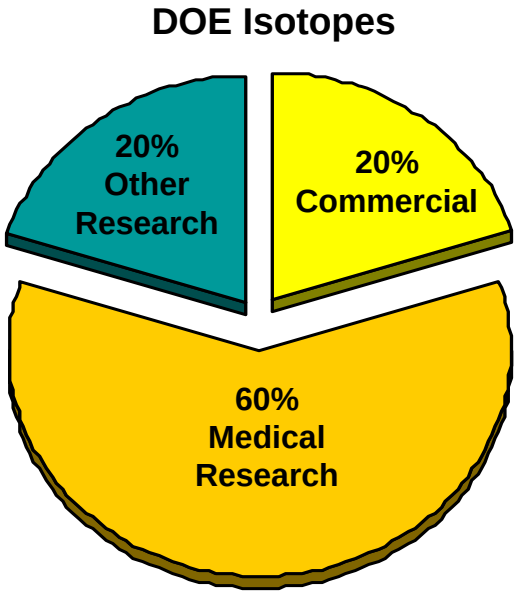
Co-chairs
Ani Aprahamian
Donald Geesaman

Status Report on the 2nd Charge

2 March 2009
NSAC Meeting

Mission of DOE's 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.
- Over 190 customers in FY 2008
- Over 560 shipments in FY 2008
- Ten customers provided over 85% of sales



Bulletin of the Atomic Scientists

Making domestically produced medical isotopes a national priority

By Edwin S. Lyman | 18 December 2008

Despite the clinical importance of medical isotopes, used in an estimated 18 million procedures per year in the United States alone, the world's supply is increasingly unreliable due to antiquated reactors. At one point in August, all five of the most important medical isotope-producing reactors, all located outside of the United States, were inoperable. The simultaneous shutdowns resulted in supply interruptions, causing a rationing of medical procedures in some areas. Problems are likely to persist for months because one of the largest reactors requires significant repairs.

But the reliance on old reactors causes more than just supply problems; it also poses safety and security dangers. Small-sized medical isotope reactors aren't required to have the same extensive safety and security features (i.e., robust containments and armed guards against terror attacks) that larger nuclear power plants have, leaving them vulnerable to accidents or sabotage that could endanger nearby communities by releasing significant quantities of radioactive iodine and other hazardous radionuclides into the environment.

Health

NAS report

Wealth

$200M business

Note, at present, the Isotopes Program does not produce Mo-99

Security

NAS report

NUCLEAR MEDICINE'S DOUBLE HAZARD

Imperiled Treatment and the Risk of Terrorism

Cristina Hansell

This article examines the production of metastable technetium-99 (Tc-99m), the world's most important radiopharmaceutical, focusing on reliability of supply and risks of nuclear terrorism. Only four producers manufactured about 95 percent of the world's Tc-99m; a closure of any of them could cause worldwide shortfalls. Moreover, all four employ highly enriched uranium in their production process, in a form relatively easy to convert into the metal needed for a nuclear bomb.

Example: 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
- Omnibus language mandates a study of one of these

David Robertson of the University of Missouri Reseach Reactor's View of the U.S. History of Mo-99 Production

- 1967 - MURR begins production of (n, γ) Mo-99 for Mallinckrodt Nuclear Co.
- 1969 - MURR begins weekly production of Mo-99.
- 1977 - MURR increases Mo-99 production for MediPhysics Inc.
- 1984 - MURR ceases Mo-99 production.
- 1980 - Cintichem, Inc. begins production of fission product Mo-99 and is the single U.S. supplier. .
- 1989 - Cintichem reactor develops leak and is closed.
- 1991 - DOE purchased Cintichem technology, equipment and DMFs for production of Mo-99, I-125, X3-133
- 1991 - DOE identified Omega West Reactor at LANL as proposed backup supply facility and constructs processing facility.
- December 1992 - Omega West Reactor at LANL develops leak and is closed.
- Until 1993, two Canadian reactors, operated by Atomic Energy of Canada Limited (AECL) at the Chalk River site (located about 100 miles from Ottawa, Canada), were available to produce Mo- 99.
- 1996 – DOE selects Annular Core pulse reactor at Sandia National Lab. to become backup supply facility and constructs processing facilities. Project never completed.
- 1998 – Canadian MAPLE reactors were scheduled to open, but remain shutdown today due fundamental design flaw.
- 2006 – MURR initiates efforts to become supplier of Mo-99
- 2008 – Decision made to discontinue work on MAPLE 1 & 2.

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 form of a strategic plan for the NIPA Program.

FY09 Omnibus bill

"Within this amount, $24,000,000 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 technicium-99."

Is the change from Isotope Production and Applications Program to Research Isotope Production and Applications program significant?

"technicium" does not exist!

NSACI Subcommittee

Ercan Alp Ph.D.
Argonne National Laboratory

Ani Aprahamian Ph.D. (co-chair)
University of Notre Dame

Robert W. Atcher Ph.D.
Los Alamos National Laboratory

Kelly J. Beierschmitt Ph.D.
Oak Ridge National Laboratory

Dennis Bier M.D.
Baylor College of Medicine

Roy W. Brown
Council on Radionuclides and Radiopharmaceuticals, Inc

Daniel Decman Ph.D.
Lawerence Livermore National Laboratory

Jack Faught
Spectra Gas Inc.

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Argonne National Laboratory

Kenny Jordan
Association of Energy Service Companies

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Los Alamos National Laboratory

Lee L. Riedinger Ph.D.
University of Tennessee

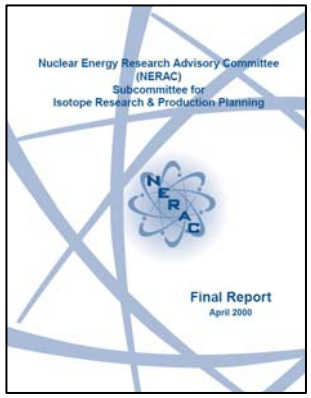
Thomas J. Ruth Ph.D.
TRIUMF

Robert Tribble Ph.D.
Texas A&M University/
Susan Seestrom Ph.D.
LANL – ex officio

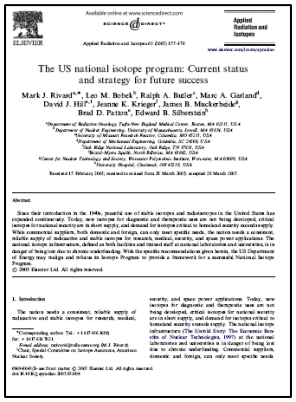
Roberto M. Uribe Ph.D.
Kent State University

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

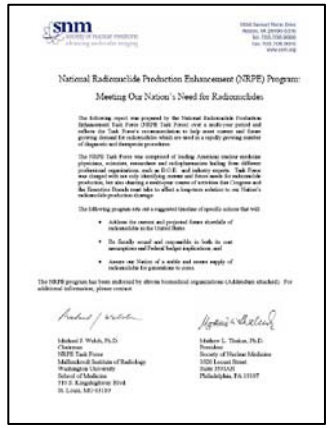
DOE-NE Expert Panel 1999



NERAC 2005

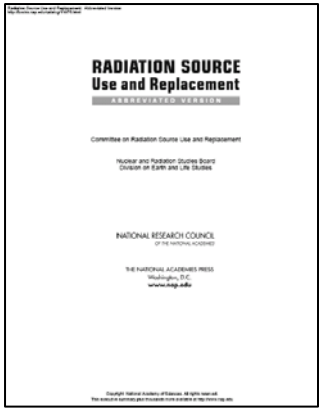


ANS 2005

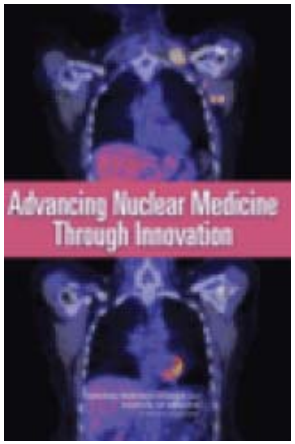


SNM 2005

NCI 2008

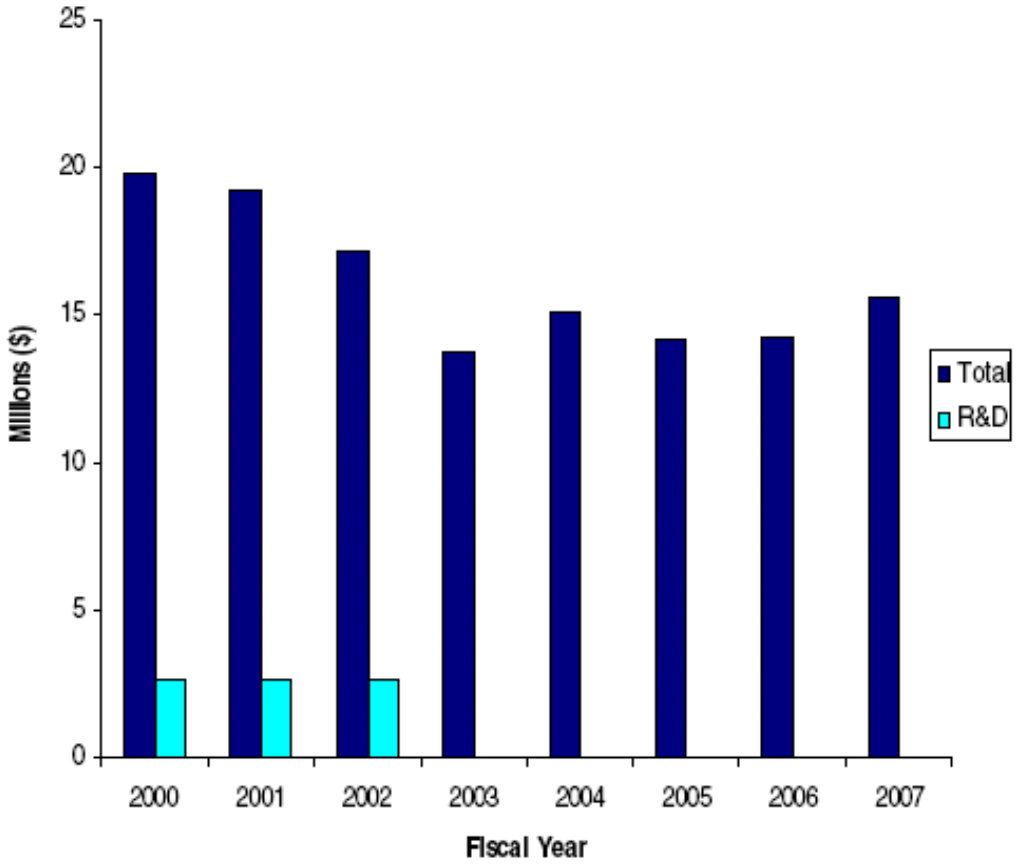


NAS 2008



NAS 2007

Some part of this is decreasing funding



Annual Appropriations for the Department of Energy-Office of Nuclear Energy's (DOE-NE) Isotope Program, 2000-2006 ($ in millions) SOURCE: Data provided by DOE-NE.

From 2007 NAS report

Another large part is the complexity of the mission and diffuseness of the resources - I

The program is highly leveraged by using existing facilities whose primary operations are supported by other DOE program offices or outside of DOE. Often other programs require non-optimum schedule for isotope production.

Economies of scale: If one large customer pulls out, there can be major cost implications for the remaining customers. Cf-252

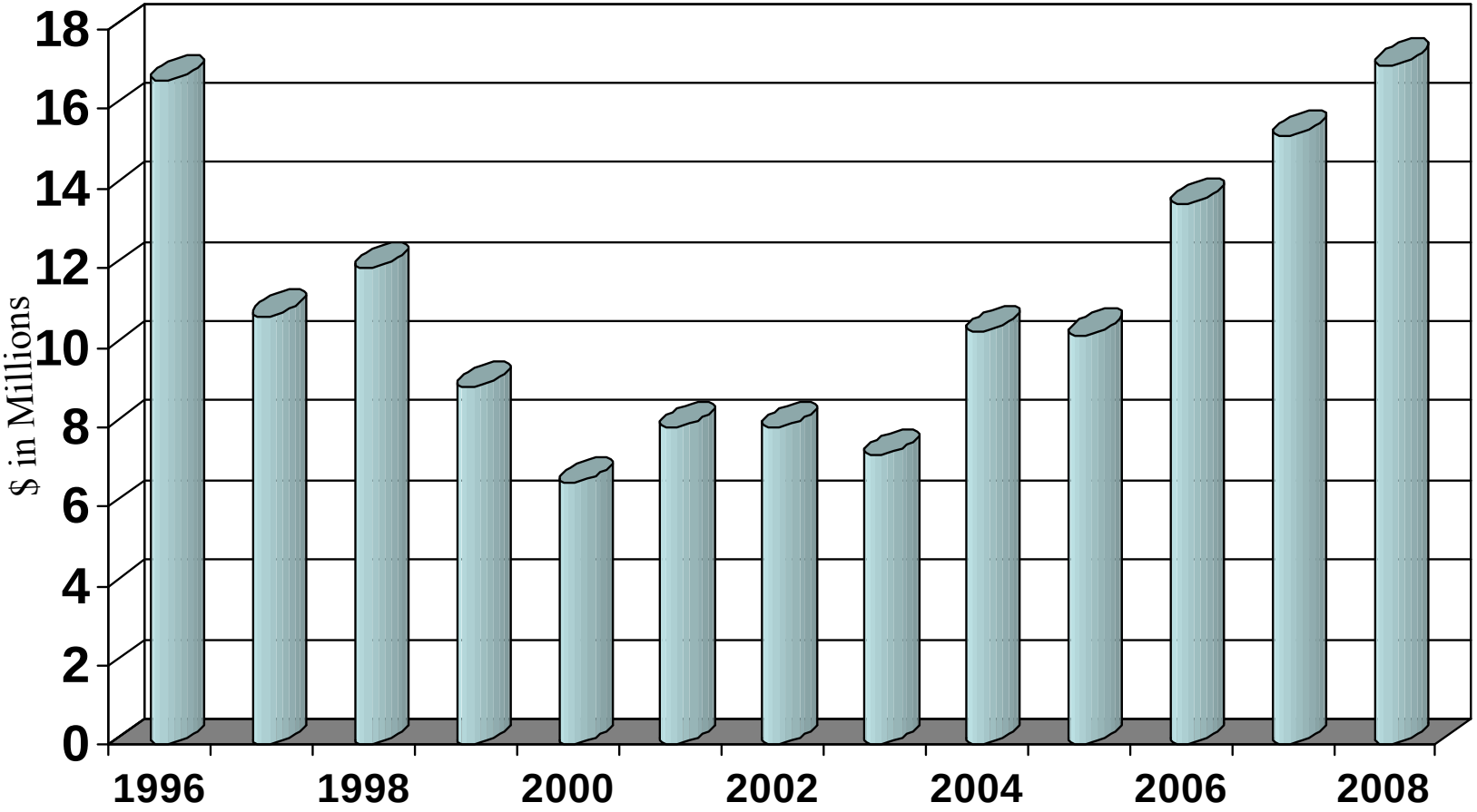
Priorities between fields and applications are difficult to set.

Much of the research involves moving money from one branch of the federal government to another (vs model of "free beam time" at national user facilities).

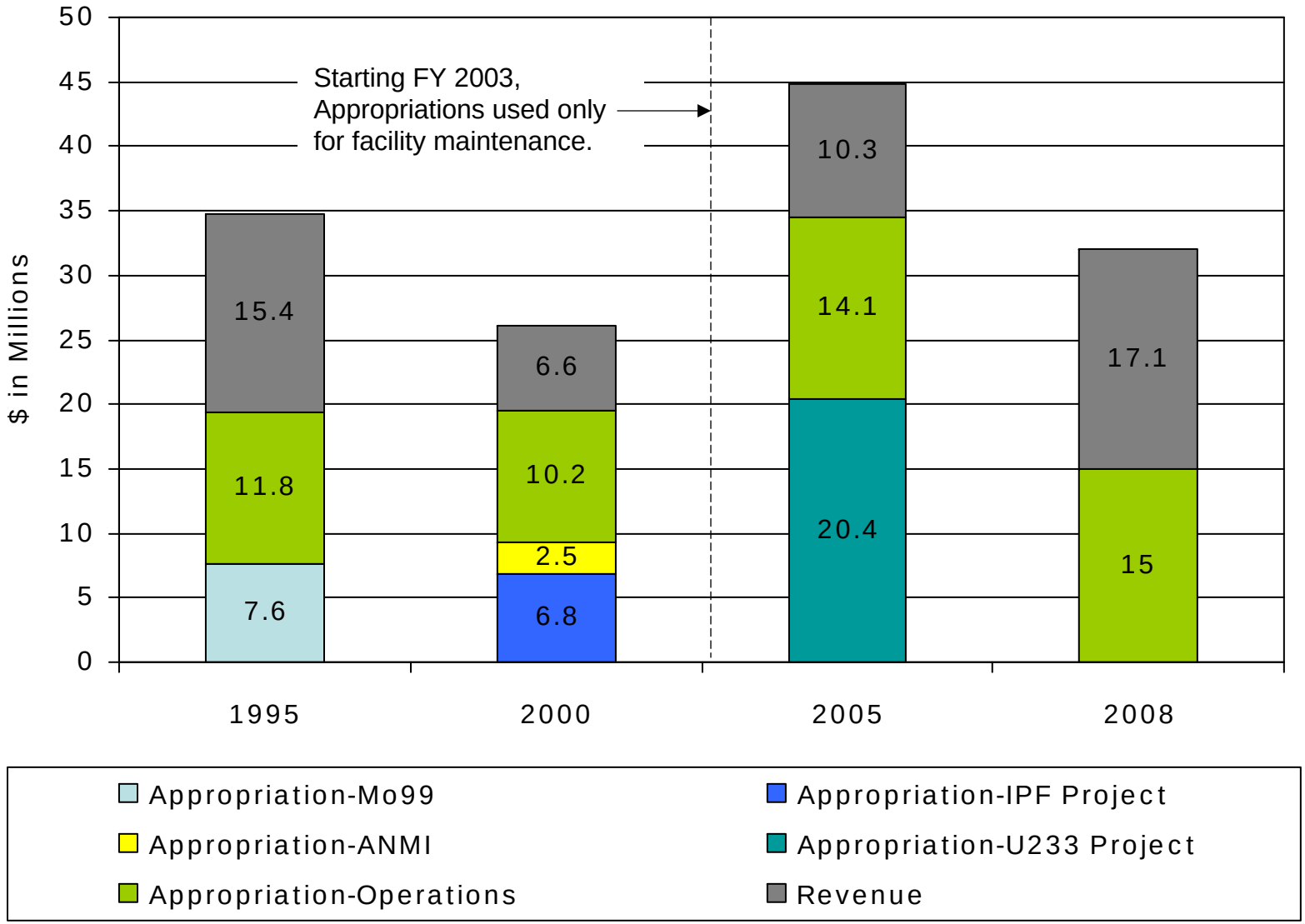
Over time a number of initiatives in the isotope program have been started and then stopped.

There are important national security issues involved: NDD, HEU/LEU, Disposing of "waste" which could be milked for valuable isotopes.

Total budget= Appropriations plus Sales
Fiscal Years 1998 – 2008
Sales Revenue Trend



Fiscal Years 1995 - 2008 Resources



Another large part is the complexity of the mission and diffuseness of the resources - II

Should the program support repeat customers with a regular supply or new applications?

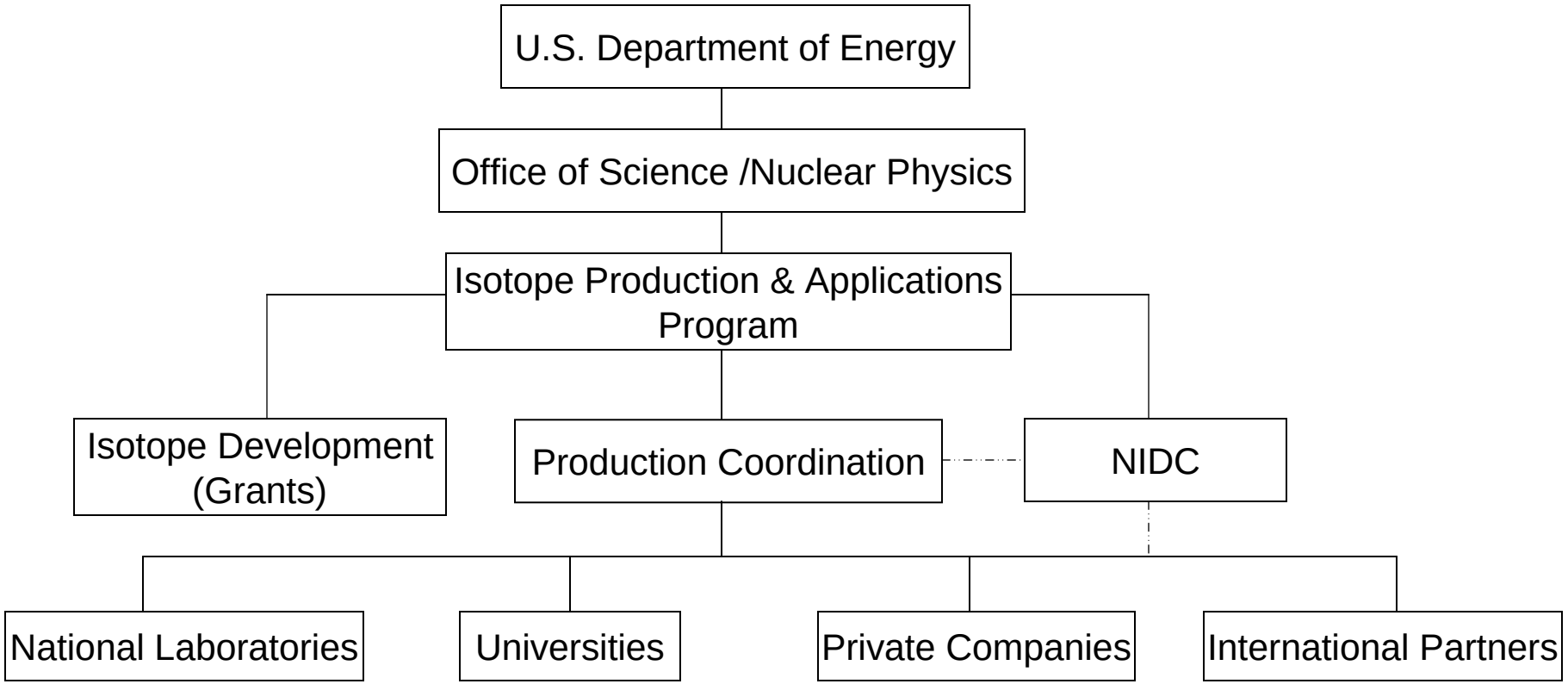
When can the government compete with commercial suppliers and foreign suppliers?

Foreign suppliers are, in many cases, subsidized by governments or capitalizing on previous government stocks.

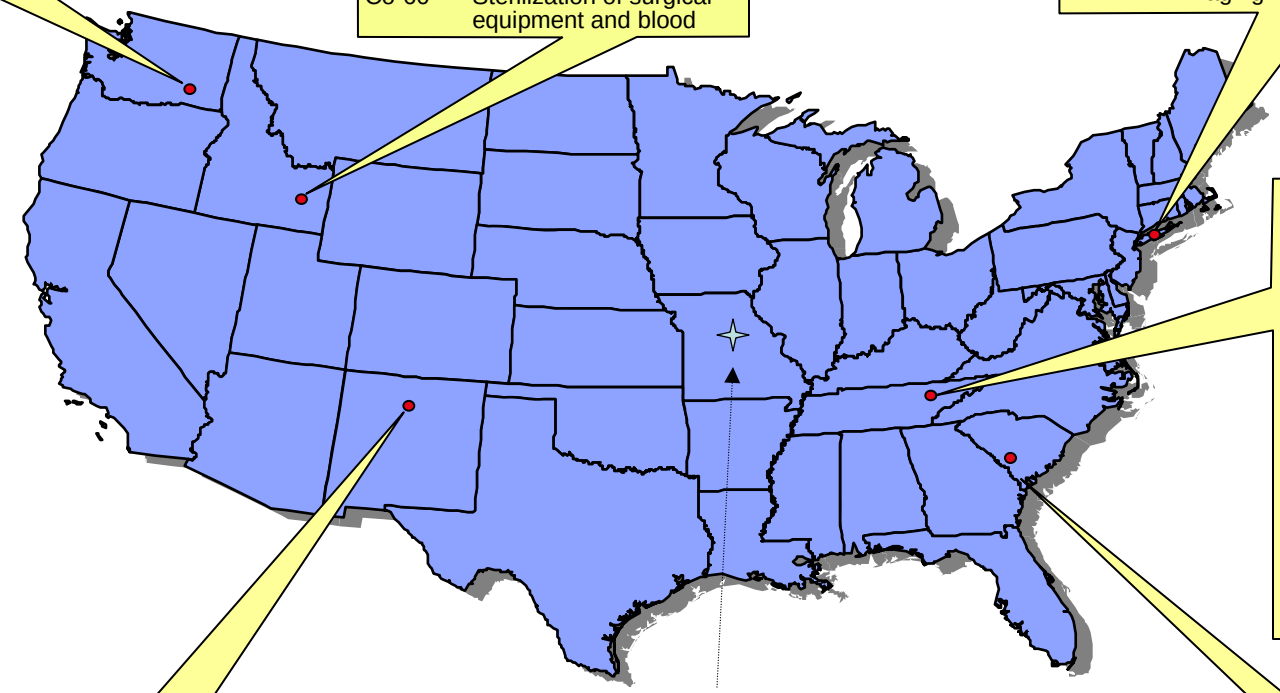
> **OECD NEA Workshop 29-30 Jan 2009:**
> **“In addition, questions were raised regarding the long-term validity of the current economic model where the security of supply relies mainly on government–run reactors which charge only marginal costs for their irradiation services”**

As DOE-NP considers managing the program, they want an emphasis on communications with all interested parties and a visible and open process.

Program Structure



Current DOE Production Sites



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

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

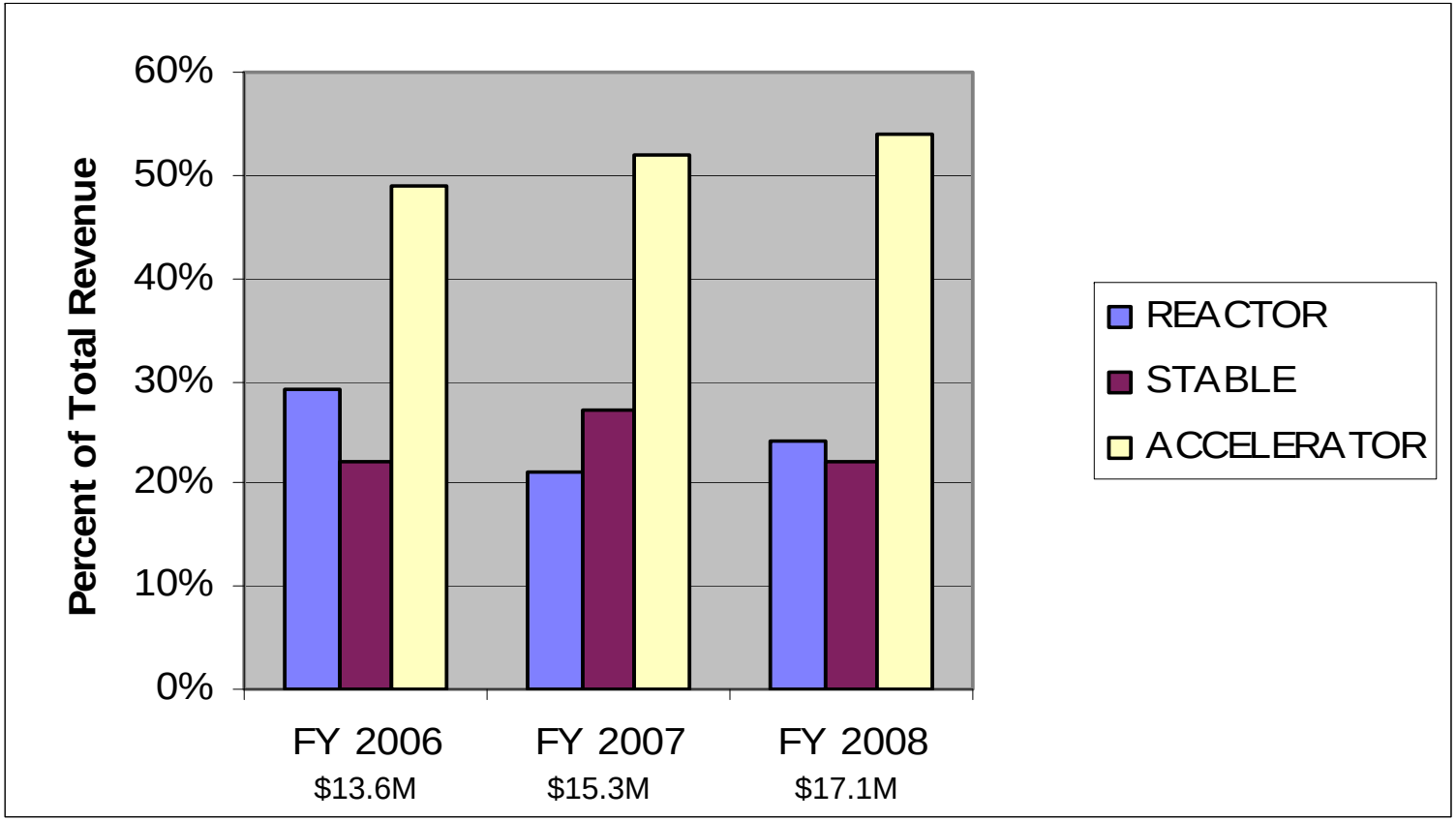
Sr-82 – Rb-82 gen used in cardiac imaging

Am-241 – Oil well logging

Savannah River – Tritium Facility:

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

Fiscal Years 2006 – 2008 Production Categories



Notes: Includes Technical Services; Stable includes He-3

Program Authority

- Atomic Energy Act of 1954, sections 31,53,54, and 81.
  - Prices are based on an equitable basis to provide reasonable compensation to the government and will not discourage the use of or the development of sources of supply independent of DOE, and will encourage research and development.
- Department continues to adhere to the procedures and criteria expressed in the Federal Register, Tuesday, March 9, 1965, with respect to determinations involving its withdrawal and re-entry into commercial markets
  - Single source or Foreign producers may be acceptable
  - Prices are reasonable and consistent
  - Withdrawals or petition

Program Authority (cont'd)

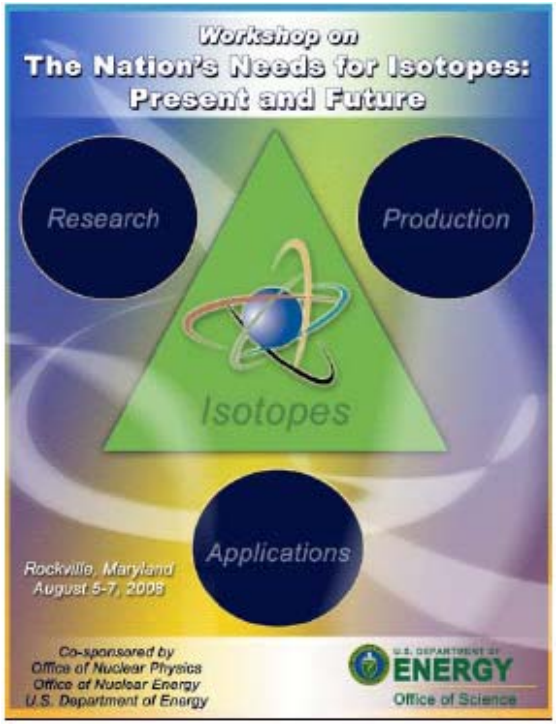
- Public Law 101-101, as modified by Public Law 103-316 created the Isotope Production and Distribution Program Fund (a revolving fund) and allow prices charged for products and services to be based on production costs, market value, U.S. research needs and other factors.
- Prices for commercial isotopes are based on full cost.
- Prices for research isotopes are based on direct cost for the entire batch.
- *Currently, the pricing policy for research isotopes is being reconsidered (Isotopes program office statement).*

Office of Nuclear Physics has been very proactive

- August Workshop on The Nation's Need for Isotopes: Present and Future

- Working group with NIH to define needs
  - NCI Produced list of expected needs for next few years
- Restart Cf-252 production
- Isotope charges to NSAC

All in a period where the legal transition of oversight was still in limbo



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
April/May 2009	Write report on second charge
June-July 2009	Meeting to finalize 2nd report???
15 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

General Issues

- Definition of research isotope
- Definition of commercial isotope
- Are there issues that are off the table?
  - Yes: weapons issues, t and Pu
  - NNSA currently leads for Mo-99
- How to do hand-off to industry effectively?
    - Examples where early commercialization was not sustainable
- Remember Mike Holland's mantra – show me current resources are used efficiently and effectively before considering upgrades.

Outline

Executive Summary
I. Introduction and History of the DOE Isotopes program
Success stories
II. Uses
A Biology, Medicine and Pharmaceuticals
B. Physical Sciences and Engineering
C. Security and other Applications
D. How to continuously stay on top of needs?
Recommendations
III. Scope, current status and challenges
IV. Stable isotope capabilities – Research and Commercial
Recommendations
V. Accelerator based isotope capabilities - Research and Commercial
Recommendations
VI. Reactor Based isotope capabilities - Research and Commercial
Recommendations
VII R&D for production and use
Recommendation
VIII Operation of the Program
Recommendation
IX. Trained manpower and education
Recommendation
X. Budget Scenarios
XI. Summary

Scope, Status, Impact

Opportunities and impact

Scope, Status, Impact

Existing and planned capabilities

Robustness of program

Optimum and CE budget

Working Groups, Leaders

- Program Operation – Riedinger
- Stable isotope production – Bier
- Accelerator based capabilities - Peterson
- Reactor Based capabilities- Beierschmitt
- R&D needed- Ruth
- Education- Aprahamian
- Budgets – Geesaman

- Biology, Medicine and Pharmaceuticals – Atcher
- Physical Sciences and Engineering- Alp
- Security and other Applications- Decman

March Meeting Straw Schedule

	March 25	March 26	March 27
800		Stable Isotope Options	
900	**Open Session** Presentations IAEA Other speakers Summary of past reports	R&D required	Recommendations
1000		Program Operations	Break-out if needed
1100			
1200	**Closed meeting**		
1300	General Issues	Education	Budgets
1400	Accelerator Options	General Discussion	
1500		Breakout	Plans to complete report
1600		Coordinated Strategy	
1700	Reactor Options	Budgets	finis
1800		Constant effort budget	

Schedule to Complete

- Groups have draft recommendations and rationale ready to present at March meeting
- 1 April DFG delivers interim report on 2nd charge – simply snapshot of recommendations
- 24 April – Drafts of each chapter
- 15 May – First draft of entire report to committee
- 31 May – Comments to DFG
- 10 June – Second draft to committee and decision on another meeting
- Mid-July- Submit to NSAC
- Late July ?? NSAC meeting to consider

Questions and Suggestions

A lot of people are looking over our shoulders on these issues
- Other research communities
- Commercial users
- Commercial suppliers
- Doctors and Patients
- Other government users including national security
- Congress

We need to do our best to get it right.

We welcome all suggestions.