DOE Isotope Program Overview
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The DOE Office of Science (SC) is fully committed to fostering safe, diverse, equitable, and inclusive work, research, and funding environments that value mutual respect and personal integrity. Effective stewardship and promotion of diverse and inclusive workplaces that value and celebrate a diversity of people, ideas, cultures, and educational backgrounds is foundational to delivering on the SC mission. The scientific community engaged in SC-sponsored activities is expected to be respectful, ethical, and professional.

The DOE SC does not tolerate discrimination or harassment of any kind, including sexual or non-sexual harassment, bullying, intimidation, violence, threats of violence, retaliation, or other disruptive behavior in the federal workplace, including DOE field site offices, or at national laboratories, scientific user facilities, academic institutions, other institutions that we fund, or other locations where activities that we support are carried out.

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As SC continues to identify opportunities to improve our policies, practices, and communications to advance diversity, equity, and inclusion in furtherance of our core values and mission, updated policies, procedures, and resources will be posted here on an ongoing basis.
Produce and/or distribute radioactive and stable isotopes that are in short supply; includes by-products, surplus materials and related isotope services

Maintain the infrastructure required to produce and supply priority isotope products and related service

Conduct R&D on new and improved isotope production and processing techniques which can make available priority isotopes for research and application. Develop workforce.

Reduce U.S. dependency on foreign supply
Isotope Program Authority, Resources, Goals

- Isotope Program in DOE has sole authority to produce isotopes for sale and distribution – labs may not embark on isotope production on their own.

- Public Law 101-101 (1990), as modified by Public Law 103-316 (1995) created the Isotope Production and Distribution Program Fund (called a revolving fund) and allows prices charged to be based on costs of production, market value, U.S. research needs and other factors.
  - Commercial isotopes at full-cost recovery; research isotopes at reduced prices.

- Anticipate isotope demand for federal missions, research and U.S. industry
  - Increase availability of isotopes in short supply
  - Mitigate potential shortages
  - Develop new production and processing techniques of isotopes currently unavailable
  - Reduce U.S. dependencies on foreign supply

- DOE IP not responsible for Mo-99 (NNSA), Pu-238 (NE) and SNM for weapons (NNSA)
- Isotope Program operates under a **revolving fund** and is audited annually.
- Program costs are financed by two resources: **appropriation and revenue**.
  - Appropriation supports mission readiness and R&D program
  - Revenue supports production and distribution of isotope

CONGRESS

DOE
Nuclear Physics

Production

Services

R&D

Mission Readiness

Funds From Sales

Products

Federal Agencies, Academia, Industry, Research Institutions
Most recent NSAC Report released July 20, 2015

Recommendations:

- Significant increase in R&D funding
  - Continue R&D on alpha-emitters (Ac-225, At-211)
  - High specific activity theranostic isotopes
  - Electron accelerators for isotope production
  - Irradiation materials for targets

- Complete stable isotope capability

- Increase in infrastructure investments and operating base
  - Isotope harvesting at FRIB
  - Separator for radioactive isotopes
    - Several programs looking at actinide EMIS
    - Potential needs for medical and research isotopes
  - BLIP intensity upgrade and second target station
  - IPF intensity, stability and energy upgrades

- Continue integration of university facilities
Recognized growing interests in radionuclides

**Section 5.5 Availability of Radionuclides**

**Recommendation 1.** Improve domestic radionuclide production. To alleviate the shortage of accelerator- and nuclear reactor- produced medical radionuclides needed for research, a dedicated accelerator and upgrade to a nuclear reactor should be considered.

**Recommendation 2.** Review enriched stable isotope inventory and evaluate domestic supply options if needed. The current inventory of enriched stable isotopes is decreasing and there is growing concern that the aging calutrons cannot be operated cost-effectively to meet demand if reopened. The **DOE** should evaluate the option of a domestic enriched isotope supply source to ensure availability for medical research.
Strong communication with stakeholders

- OSTP High Activity Sources Subcommittee (GARS)
- OSTP Subcommittee on Critical Materials
- Interagency He-3 Working Group
- DOE/NIH Working Group
- Mo-99 Stakeholders Working Group
- NRC Sealed Sources Working Group
- BLM He-4 Interagency Working Group
- Pb-212 Users Working Group
- At-211 Users working Group
- Council on Radionuclides and Radiopharmaceuticals
- Society of New Medicine and Molecular Imaging
- Commercial stakeholder meetings twice a year
- Annual industrial survey
- Annual Federal Workshops and survey
- Conference workshops, symposium
- Certified Reference Materials Working Group
- CRM Np-236 Sub working group
- New Brunswick Lab Interagency Working Group
- DOE Nuclear Materials Advisory Board
- Mark 18 Interagency Working Group
- IN Nuclear Materials Information Program
- Li-7 Intra-agency Working Group
- U-233 Intra-agency Working Group
DOE Isotope Program Production Sites
The Department of Energy NIDC (includes the Isotope Business Office located at Oak Ridge National Laboratory) coordinates the distribution of all DOE isotope products and services available from DOE facilities.

All contractual discussions with customers.

Responsibilities in transportation, Q&A, public relations (website, newsletter, booth), cross-cutting technical topics, marketing strategy and assessments.

Customers maintain technical discussions with sites.

www.isotopes.gov
Brookhaven National Laboratory Brookhaven Linac Isotope Producer (BLIP)
- BLIP beam line directs protons up to 160 μA intensity to targets; parasitic operation with nuclear physics programs for more cost effective isotope production.

Los Alamos National Laboratory Isotope Production Facility (IPF)
- Diversion of 100 MeV proton beam to target station.
- Irradiates targets while LANSCE operates for NNSA.

Argonne National Laboratory Low Energy Accelerator Leaf Facility (LEAF)
- 50 MeV/25 kW electron linear accelerator
- Newest addition to program
Idaho National Laboratory Advanced Test Reactor (ATR)
- Office of Nuclear Energy is steward
- High Specific Activity Co-60 for medical applications
- Developing Ir-192 for industrial radiography

Oak Ridge National Laboratory High Flux Isotope Reactor (HFIR)
- Office of Basic Energy Science is steward
- Radiochemical Engineering Development Center (REDC) – extensive processing capabilities
- Next HFIR cycle in November 2019
Y-12 National Security Complex
- Li-6 (neutron detection)
- Li-7 (dosimeters)

Pacific Northwest National Laboratory
- Radiochemical Processing Laboratory
- Process Automation

Savannah River Site (SRS)
- He-3 extraction from NNSA tritium
- Developing new sources He-3

Facility for Rare Isotope Beams (FRIB)
- New accelerator for the study of nuclear structure and astrophysics
- Implementing isotope harvesting capabilities
Unique capabilities and expertise
- R&D on isotope production
- Workforce development
- Cost-effective
- Regional networks
- Examples: UW, UCD, TAMU, PENN, Duke, UW-M, Wash.U, UAB, Univ. of MO/MURR

University of Washington and MURR produce isotopes for the DOE Isotope Program
Stable Isotope Enrichment and Distribution

- Isotope Program manages the Nation’s inventory of stable isotopes

- Have re-established enriched stable isotope production in the United States – ESIPP - 2017
  - Electromagnetic separation and gas centrifuge
  - Production started 2017 – 500 mg of Ru-96 for RHIC
  - Xe-129, Mo-98, Mo-100, Yb-176

- Stable Isotope Production Facility MIE – under construction
  - Leveraged by NNSA
  - Kg through-put capability
  - Basic research, applications, industry
  - Quantum Information Science

- U.S. Stable Isotope Production and Research Center
  - CD-0 Approved January 4, 2019
  - $150 – 200M TPC
  - Additional EMIS and gas centrifuge capability
DOE IP has provided isotopes for the discovery of elements 114, 115, 117 and 118.

Also provide isotopes for Heavy Element Chemistry such as Am-243, 248Cm, 249,251Cf, 249Bk, Es & Fm.

Now searching for Elements 119 and 120.

9 mg of $^{248}$Cm, (>95%)

$^{254}$Es, 0.5 μg experiments on fission mechanisms

$^{244}$Pu, 15 mg >99% reaction mechanism studies
Mitigation of U.S. Dependence on Foreign Sources

**Sr-90 for cancer therapy**
- Just entered market
- Processed at PNNL

**Cf-252 for well logging, industrial applications**
- **Maintaining supply of 97% of domestic market**
- Working with industrial consortium
- Long term contract in place; provision for research quantities

**Am-241 for oil-gas exploration**
- Re-established production capability in U.S.
- Extraction from plutonium waste stream at LANL

Other examples:
- Ba-133, C-14, Cd-109, Co-57, Fe-55, Gd-153, Ir-192
Bayer drug Xofigo® treats prostate cancer and severe pain from bone metastases; approved in 48 countries.

Active ingredient Ra-223 from limited global supplies of existing Ac-227.

Recover Ra-226 from waste medical devices secured by the DOE IP and diverted from a radioactive waste landfill. Ra-226 targets irradiated in HFIR.

Chemically separate and purify the Ac-227 created during irradiation – shipped to Bayer in Norway where they extract Ra-223 which decays into Ac-227 and ships it around the world for immediate use as a cancer therapy.

After 2 years of R&D, scale up to full production in 2017.

10-year production contract signed with Bayer end of 2017.
- High priority for NIH for decades
- Since 2009, IP is world leader in R&D
- ORNL extracts Ac-225 from Th-229 recovered from U-233: 1,200 mCi per year - entire U.S. supply and more than half the worldwide supply.
- Supply cannot support adequate clinical trials or therapy
- IP has developed accelerator production route- full scale production can meet clinical and therapy demands
- Accelerator production started 2017

- Completed Stage 1: 5-50mCi/B
- Stage 2: Jan 18: 10-100mCi/B; already 150mCi
- Stage 3: 100-1000mCi/B
- IP strategy includes other production routes- reactor production of Th-229, extraction of Th-229 from legacy U-233, low-energy cyclotron production, and electron accelerator production demand.
- PRODUCT AVAILABLE NOW
### Alpha Emitters of Interest for Therapy

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-life</th>
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<tbody>
<tr>
<td>$^{225}$Ac</td>
<td>10 d</td>
</tr>
<tr>
<td>$^{211}$At</td>
<td>7.2 h</td>
</tr>
<tr>
<td>$^{212}$Bi</td>
<td>60 m</td>
</tr>
<tr>
<td>$^{213}$Bi</td>
<td>46 m</td>
</tr>
<tr>
<td>$^{212}$Pb</td>
<td>10.6 h</td>
</tr>
<tr>
<td>$^{223}$Ra</td>
<td>11.43 d</td>
</tr>
<tr>
<td>$^{226}$Th</td>
<td>31 m</td>
</tr>
<tr>
<td>$^{227}$Th</td>
<td>18.7 d</td>
</tr>
</tbody>
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- For the past ten years, alpha emitters have been the highest priority for the DOE Isotope Program.
- The DOE Isotope Program is producing or developing production of all of these isotopes.
Other Medical Isotopes Routinely Available for Sale

- $^{177}$Lu: therapeutic applications
- $^{67}$Cu: therapeutic/theranostic applications
- $^{86}$Y: PET diagnostic/theranostic applications
- $^{88}$Y: radiotracer
- $^{52}$Fe: radiotracer
- $^{72}$As, $^{72}$Se: PET diagnostic/theranostic applications
- $^{89}$Sr: bone pain palliation
- $^{90}$Sr: source of $^{90}$Y for therapeutic applications
- $^{188}$W: generator of $^{188}$Re for therapeutic applications
Medical Isotopes Under Development

- $^{177}$Lu nca for therapeutic applications
- $^{67}$Cu hsa for therapeutic/theranostic applications
- $^{72}$Se/$^{72}$As generator for PET diagnostic applications
- $^{77}$As therapeutic/theranostic applications
- $^{52}$Mn PET diagnostic applications
- $^{90}$Nb PET diagnostic applications
- $^{191/193m/195m}$Pt diagnostic applications
- $^{186}$Re diagnostic/theranostic applications
- $^{47}$Sc therapeutic/theranostic applications
- $^{119m}$Te $^{119}$Sb generator for therapeutic applications
- $^{111}$Ag therapeutic applications
- $^{134}$Ce positron-emitting analog for alpha-emitters
- $^{44}$Ti/$^{44}$Sc generator for PET diagnostic/theranostic applications
- $^{129}$Xe enrichment under development for use in lung imaging
- $^{176}$Yb enrichment under development for Lu-177 production
- $^{98,100}$Mo samples for $^{99}$Mo production evaluation
The DOE Isotope Program is a service oriented program

Objective is to fill gaps not make a profit

We consider constraints in supply chains, dependence on foreign supply, novel isotopes

We want to know what you need for medical applications
NP reorganized the DOE Isotope Program

- Restructured and increased the federal organization
- Created the National Isotope Development Center
- Created R&D Program – competitive, base
- Developed priorities for research & production
- Scrubbed production costs of isotopes
- Increased portfolio of isotope production sites
  - University sites
  - Addition of other DOE/NNSA sites
- Investments in infrastructure
- Development of new capabilities
- Increased availability of research isotopes and made more affordable
- Introduced peer review into mode of operations
- Improved business operations
- Improved communication, visibility with stakeholders
- Improved marketing strategy and demand forecast
- Improved public outreach and workforce development
Increased Availability of Isotopes (1)

- **Ac-225:** Developed large-scale accelerator production capability, therapeutic medical applications research
- **Ac-227:** Developed reactor-based production, therapeutic medical applications research
- **Am-241:** Established domestic production capability
- **At-211:** Funding production development at multiple sites to establish nationwide availability
- **Ba-133:** Reactor production. Used as gamma radiation reference source. Removed Russian dependency.
- **Bk-249:** Produced 22 mg target for the discovery of element 117; produced 26 mg for further super-heavy element research
- **Cd-109:** Developed reactor production routes, radioanalysis
- **Cf-249:** Heavy element chemistry research
- **Cm-243:** Acquired curium with a high Cm-243 content for research applications
- **Cm-248:** Developed recovery process for high purity Cm-248 for research applications
- **Cf-251:** Super-heavy element research
- **Cf-252:** Re-established production in FY 2009; industrial applications
- **Co-60:** Re-established domestic production with new target design; cancer therapy (Gamma Knife®), industrial applications
- **Cu-64:** Medical diagnostic imaging applications
- **Cu-67:** Cancer therapy research; new electron accelerator production route
- **Es-254:** Provided for SHE nuclear science and heavy element chemistry research
- **He-3:** MRI imaging of lung function for pediatric apps; strict government controls mitigated shortage
- **Heavy water:** PET imaging instrumentation; Acquired supply
Increased Availability of Isotopes (2)

- **Li-6:** Production of metal form for neutron detector isotope sales
- **Li-7:** Reserve for nuclear power industry to mitigate potential shortage
- **Lu-177:** Added new production capability at MURR
- **Np-237:** Inventory for dispensing bulk quantities and capability to fabricate reactor dosimeters
- **Pb-212/Bi-212:** Therapeutic medical applications research
- **Ru-96:** Nuclear Physics research
- **Se-72/As-72:** Developed production capability for Se-72 for As-72 generator; medical diagnostic imaging
- **Si-32:** Oceanographic and climate modeling research; replenished depleted inventory
- **Sr-89:** Developed reactor production capability; palliation of bone pain associated with metastases
- **Sr-90:** Developing reserve to mitigate US dependence on foreign sources; therapeutic apps
- **Th-227/Ra-223:** Established Ac-227 cows for Th-227 and Ra-223, therapeutic medical applications research
- **Th-232:** New source available for distribution
- **Th-228:** Recovered from Ac-227 production to supply Ra-224 for Pb-212/Bi-212 generators
- **Ti-44:** Developed accelerator production capability for medical imaging
- **U-233:** Recovered and purified mass-separated U-233 for research applications
- **U-234:** Neutron flux monitors
- **W-188:** Established routine reactor production for therapeutic medical applications
- **Y-86:** Established production capability for medical diagnostic imaging applications
- **Zr-89:** Funded development of production at universities; medical diagnostic imaging applications
Isotopes under Development

- **As-72/77**: Exploring reactor and accelerator production for theranostic medical applications
- **C-14**: Ramping up to full scale production
- **Cm-248**: Process Mark 18 targets
- **Co-57**: University production development
- **Heavy water**: Supporting new production techniques
- **Ho-163**: Demonstrated technical feasibility of production; if interest would need to scale up production
- **Ir-192**: Multi-lab target design team; mitigate foreign dependence
- **Li-7**: Developing new production capability: reactor operations, physics research
- **Lu-177 HSA**: Large Scale processing/production capability
- **Mo-98/Mo-100**: Conducting validation runs
- **Mn-52**: PET diagnostic applications
- **Nb-90**: PET diagnostic applications
- **Np-236/Pu-236**: Ongoing R&D for accelerator-based production for security reference materials
- **Pa-231**: Purifying 100 mg for applications such as fuel cycle research
- **Pm-147**: Technical feasibility established; ramping up to full scale processing capability
- **Pt-191/193m/195m**: Exploring accelerator production; theranostic medical applications
- **Re-186**: Exploring accelerator production; theranostic medical applications
- **Se-72**: Accelerator production for Se-72/As-72 generator
- **Sc-47**: Exploring accelerator production; theranostic medical applications
- **Si-28**: Consider EMIS and centrifuge production of Si-28 for computing and electronic applications
- **Sr-89**: Investigating economic feasibility of reactor production; palliation of bone pain associated with metastases
- **Te-119**: Accelerator production for Te-119/Sb-119 generator; technical feasibility established
- **Th-229**: Developing reactor production route for Ac-225
- **U-230/Th-226**: Medical applications; technical feasibility established
- **Xe-129**: Polarized lung imaging
- **Yb-176**: Stable production capability for production of Lu-177
- **Zn-62/Cu-62**: Funding production development for generators for medical diagnostic imaging applications