U.S. DEPARTMENT OF ENERGY

Isotope Program
U.S. Department of Energy

DOE Isotope Program Update
January 12, 2021

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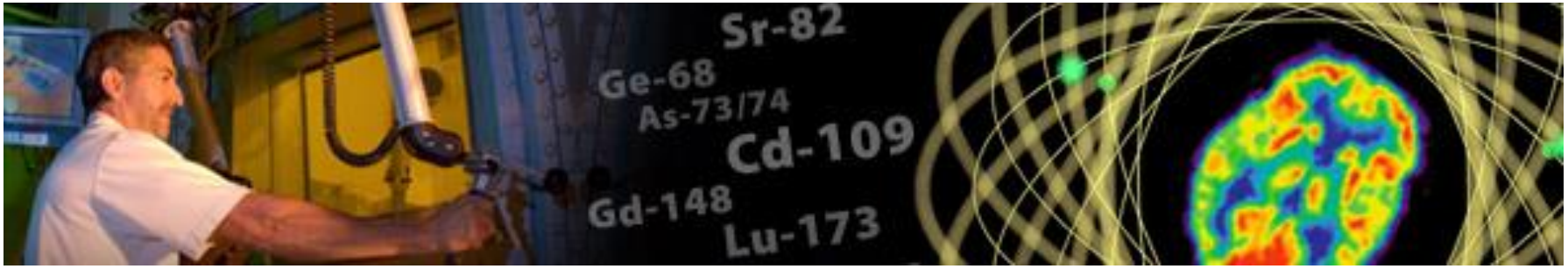
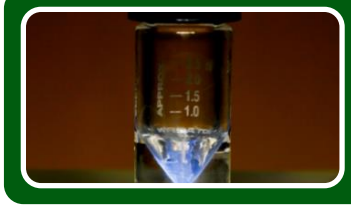


DOE Isotope Program Mission



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 to ensure National Preparedness.

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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.

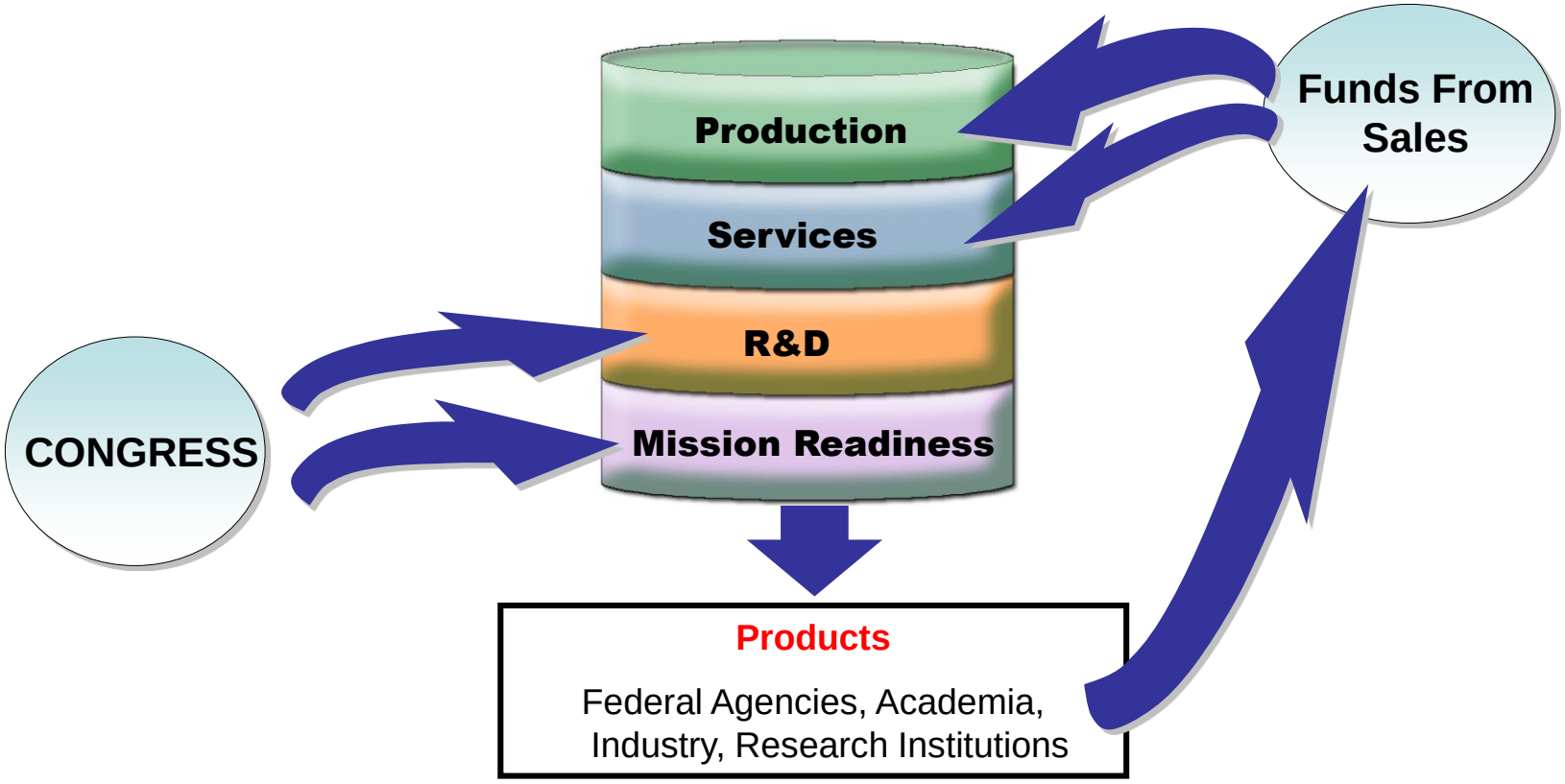
- Public Law 101-101 (1990), as modified by Public Law 103-316 (1995) created the Isotope Production and Distribution Program Fund (called a revolving fund) and allows prices charged to be based on costs of production, market value, U.S. research needs and other factors.
  - **Commercial isotopes at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

- DOE Isotope Program is the only Mission Essential Function in the Office of Science.
  - **Continued to operate during COVID-19 lab shutdowns**

- **DOE IP not responsible for Mo-99 (NNSA), Pu-238 (NE) and SNM for weapons (NNSA)**

Isotope Program Resources

- 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

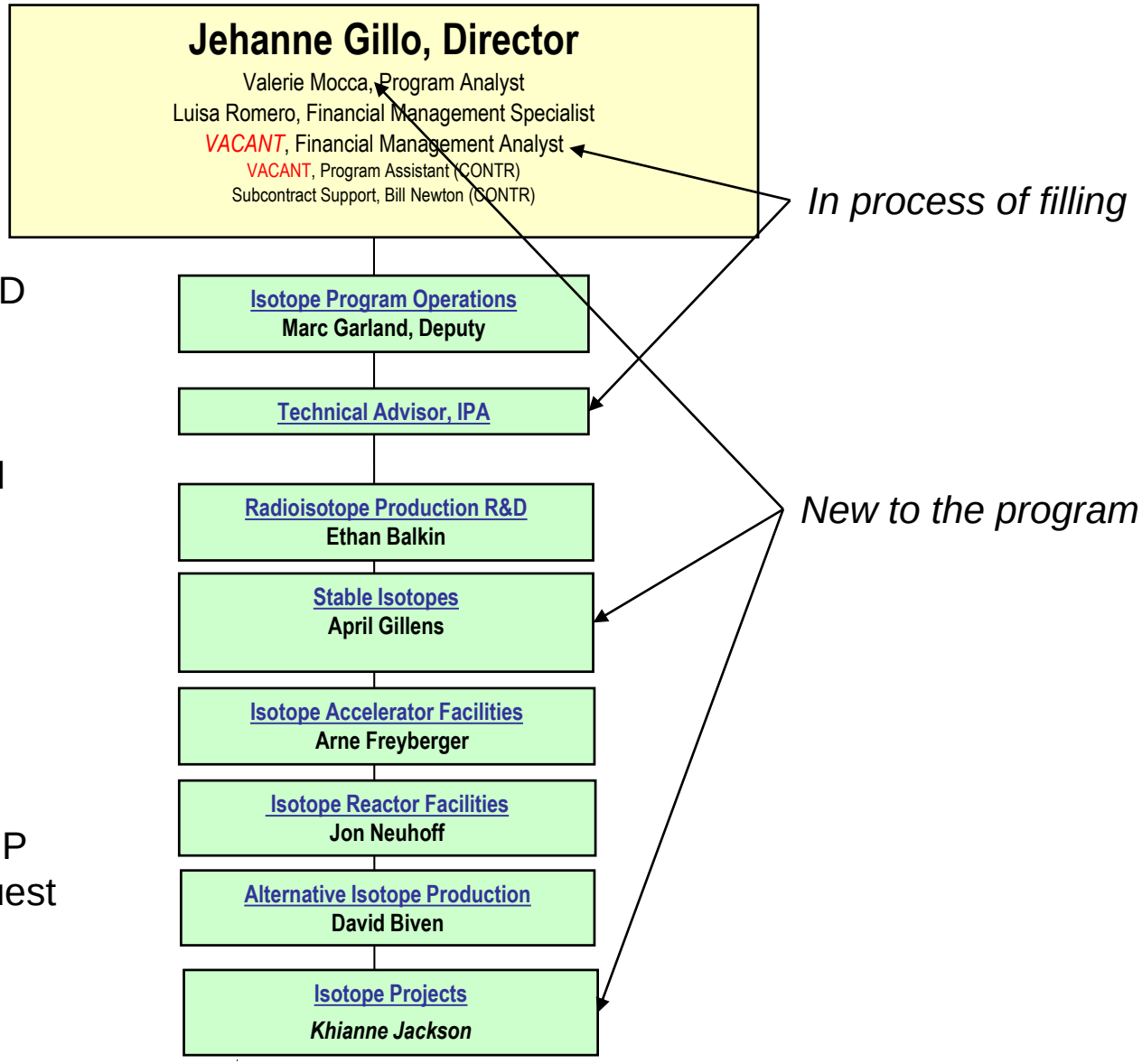


Office of Isotope R&D and Production
SC-24.3

New Office of Isotope R&D established during SC reorganization in 2020

- Shows support for and priority of the DOE IP
- Only SC Mission Essential Program – continued operations during COVID

In FY 2022 Budget DOE IP has separate budget request



Strong communication with and impact on stakeholders

- White House Working Groups
- Inter-agency Working Groups
- Community Users Working Group (medical)
- Professional Society Meetings and Councils
- Commercial stakeholder meetings twice a year
- Annual Industrial Survey
- Annual Federal Workshops and Survey
- Sponsorship of workshops, symposium at conferences

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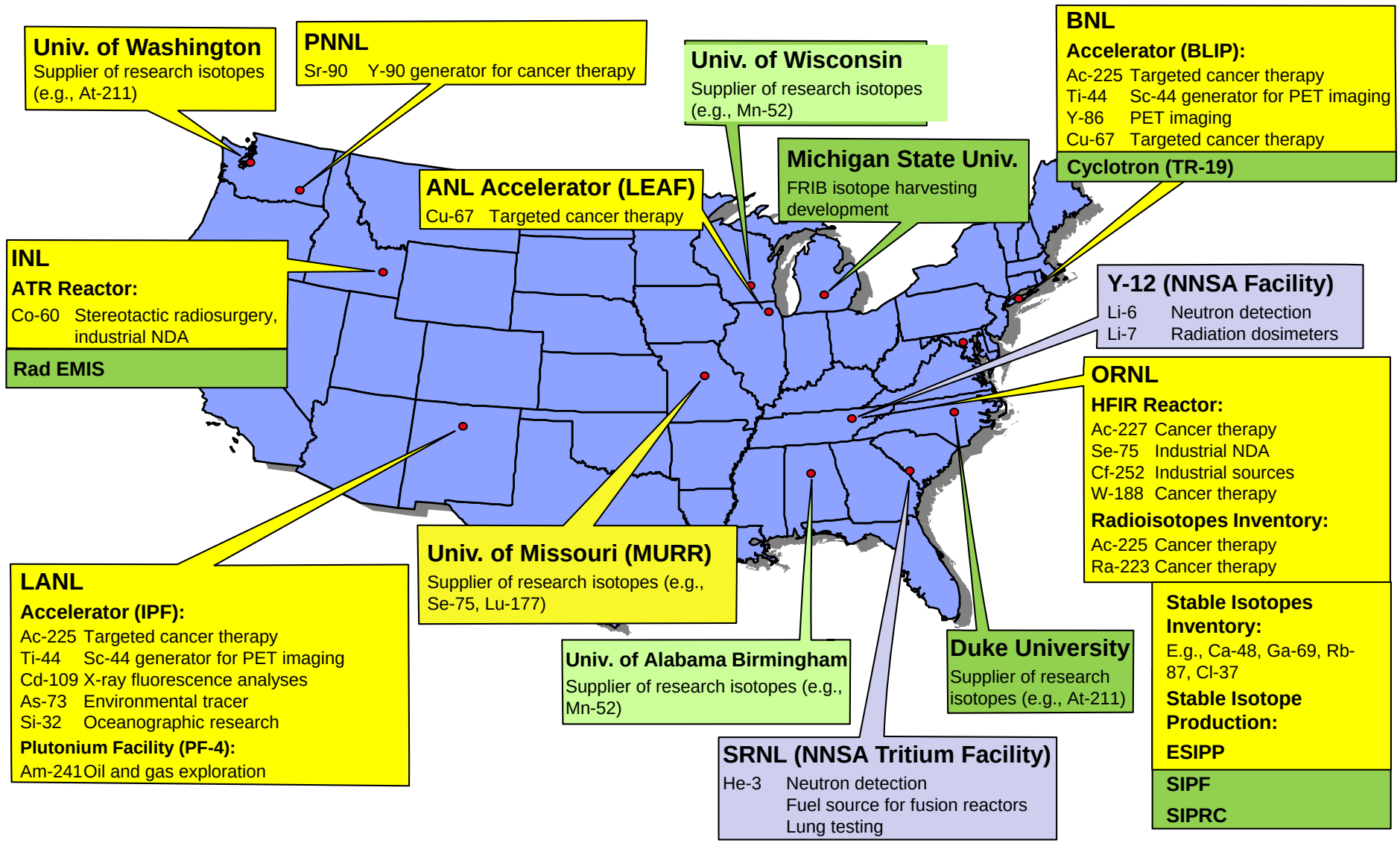
DOE Isotope Program Production Sites

Isotope Program
U.S. Department of Energy



Production Capabilities in IP

Facility	Location	Type	Capability	Sample isotopes
BLIP	BNL	Accel	160 μA protons on target	Ac-225, Sr-82, Ge-68, Be-7, Cu-67, Y-86, Zn-65, Fe-52, Rb-83
IPF	LANL	Accel	Diversion of 100 MeV proton beam to target station	Ac-225, Sr-82, Ge-68, Na-22, As-73, Se-72, Y-88, Si-32, Cd-109
Plutonium Facility	LANL	Proc	Am-241 from Pu-244 waste stream	Am-241
LEAF	ANL	Accel	20 kW beam power in the 30-40 MeV energy range	Cu-67, Sc-47
UW Cyclotron	UW	Accel	50 MeV multi-particle, variable energy cyclotron	At-211
Isotope FRIB	MSU	Accel	Harvesting from accelerator	^{211}At & ^{226}Th via ^{211}Rn and ^{230}U; ^{47}Sc via ^{47}Ca, ^{44m}Sc
NNSA Tritium Facility	SRS	Stockpile	Extract He-3 from tritium stockpile	He-3
Y-12	Y-12	Stockpile	Processing and dispensing	Li-6, Li-7
PNNL	PNNL	Hot cells	Processing and dispensing from stockpile	Sr-90
ORNL	ORNL	Hot cells	Processing capabilities	Ac-225, Ra-223
HFIR	ORNL	Reactor	85 MW; average thermal neutron flux of 2.3 X 10^{15} n/cm^2-s	Ac-227, Cf-252, Se-75, Ni-63, W-188, Lu-177, Th-227, Ra-223, Pb-212/Bi-212, Th-229
ATR	INL	Reactor	250 MW; average thermal neutron flux 1 X 10^{15} n/cm^2-s	Co-60
MURR	UMO	Reactor	10 MW; peak neutron flux 6.0 X 10^{14} n/cm^2-s	Se-75, Lu-177
ESIPP, SIPF, SIPRC	ORNL	Stable	Gas Centrifuge, Electromagnetic Separation	Ru-96, Xe-129, Yb-176, Mo-98, Mo-100 etc

Teal (8/14) shows new facilities since program came to NP – 2009

FY 2021 adding Duke University Cyclotron, INL Rad EMIS for Nuclear Forensics, University of Alabama and University of Wisconsin

DOE Isotope Program
Select Highlights of FY2020

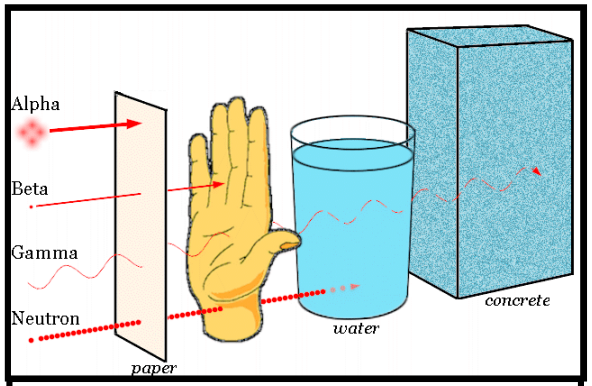
- Drug Master File (DMF) for accelerator produced Ac-225 accepted by the FDA. Ac-225 is promising treatment of metastasized cancers. DMF for Th cow produced Ac-225 submitted in December.
- Provision of Pu-244 for international effort for discovery of element 119. (Produced isotopes for discovery of elements 114, 115, 117, 118.)
- Development of production capabilities for QIS isotopes of interest.
- Added new production site – electron accelerator (LEAF @ANL) and entered market for Cu-67 used for neuroendocrine, brain, etc cancer.
- Cooperated with industry to complete commercialization of Ge-68 used as cancer diagnostic. Now have domestic source.
- Initiated U.S. SIPRC with OPC and TEC funds for large scale enriched stable isotope production.
- Initiated development of FRIB Isotope Harvesting at MSU.
- Proof of principle complete for enrichment of Yb-176, precursor to Lu-177 production for treatment of prostate cancer and mitigates dependence on Russia. Ramping up production capability.
- Upgraded processing facilities at BNL and initiated new processing capability for alpha emitters at LANL.
- Entered market for Am-241 extracted from plutonium waste stream.

Ac-225 in a capsule

DOE IP has provided isotopes for the discovery of elements 114, 115, 117 and 118

The LEAF electron facility is newest addition to DOE IP

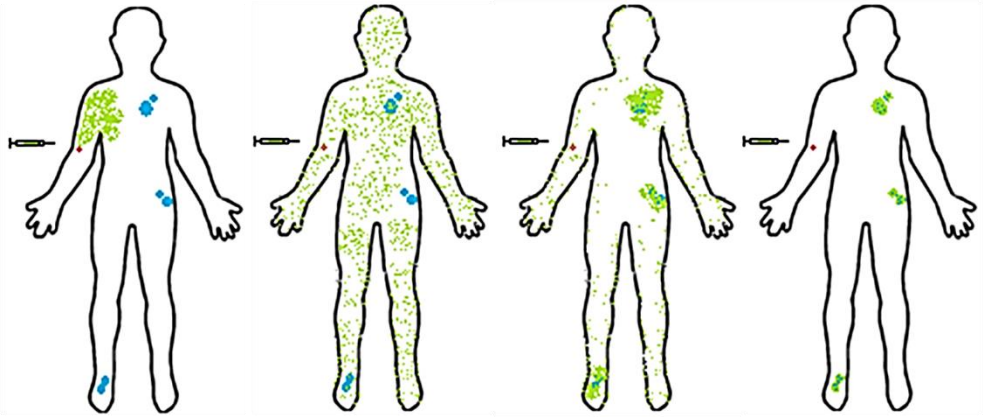
World leaders in alpha-emitter production



Range and effects of alpha, beta, gamma and neutron radiation

The properties of α-emitting isotopes make them well suited for treatment of cancer and infectious disease

The DOE IP is leading globally in the development of production techniques and separation chemistry for alpha-emitters.



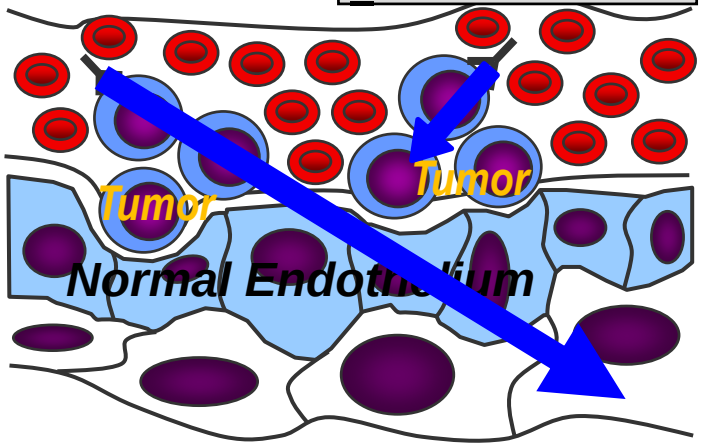
1.The targeted radioligand is administered systemically to the patient.

2.The radioligand distributes throughout the patient.

3.The radioligand localizes and concentrates in target tissues (e.g. tumors) reducing radiation dose to non-target normal tissues.

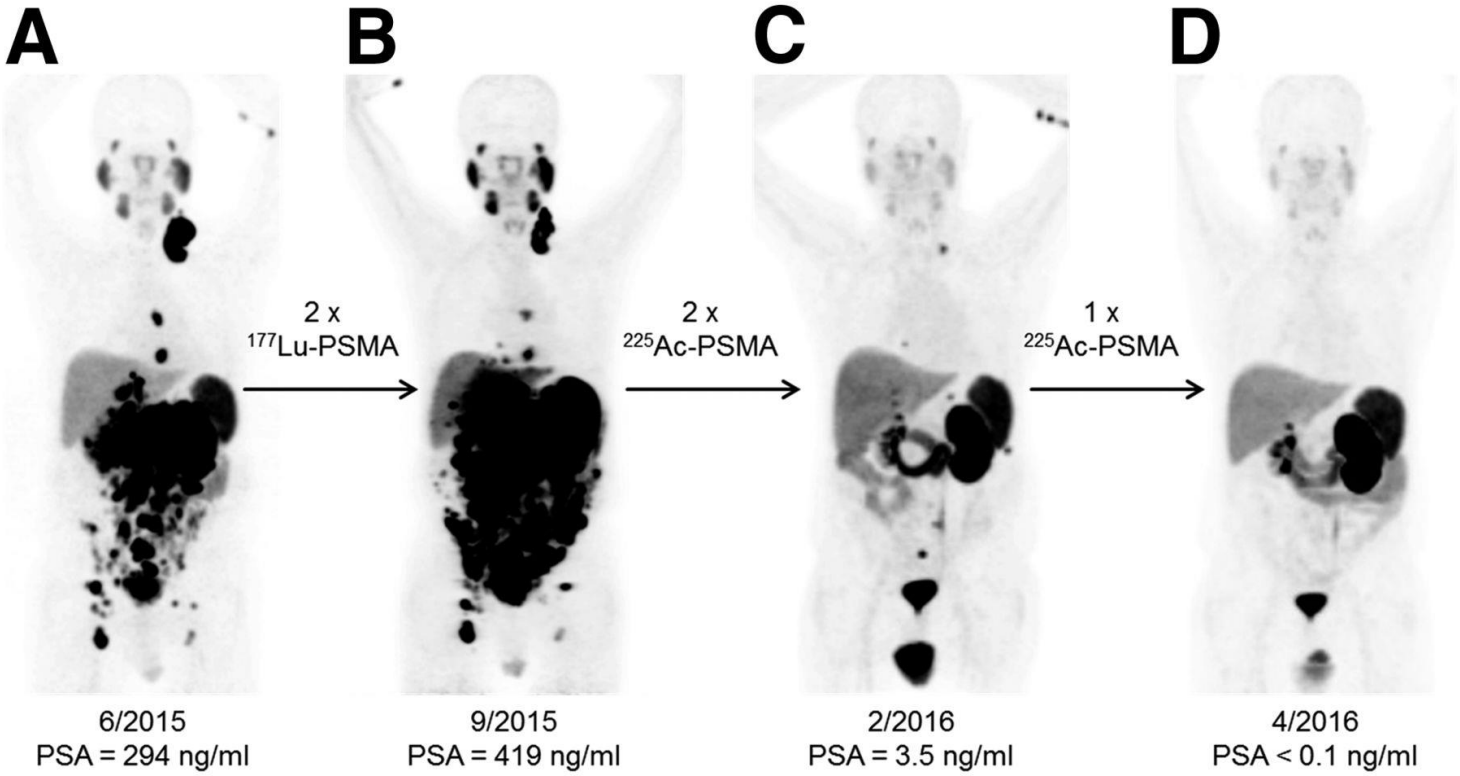
4.The radioligand is retained within the target tissues (tumors) to selectively deliver cytotoxic doses of radiation.

α Particle
5-8 MeV
50-80 µm range
≤ 5 cell diameters



β Particle
0.1-1 MeV
1-10 mm range
~50 cell diameters

Prostate Cancer Therapy



68Ga-PSMA-11 PET/CT scans of patient B. In comparison to initial tumor spread (A), restaging after 2 cycles of β-emitting 177Lu-PSMA-617 presented progression (B). Clemens Kratochwil et al. J Nucl Med 2016;57:1941-1944

Medical Isotopes Routinely Available for Sale

Actinium-225	Th-229 cow and accelerator-based production. Targeted cancer therapy research.
Actinium-227	Ac-227 cow is used to produce very high-purity Ra-223 and Th-227. Ac-227 for Bayer's Xofigo® for cancer therapy.
Arsenic-73	Radiotracer
Astatine-211	University of Washington is currently supplying for several preclinical studies and a clinical trial Targeted cancer therapy research.
Bismuth-213	Targeted cancer therapy research
Cobalt-60	Source applications for cancer radiotherapy/radiosurgery
Copper-67	Therapeutic/theranostic applications
Helium-3	Lung imaging
Iron-52	Radiotracer
Lead-212/Bismuth-212 Gen	Ra-224 is the parent of candidates for new therapeutic alpha-emitting radiopharmaceuticals using Pb-212 and Bi-212. Ra-224 generators are produced at ORNL and can be used to provide both Pb-212 and Bi-212.
Lutetium-177 (c.a.)	Carrier-added for therapeutic applications (prostate cancer treatment)
Radium-223	Cancer therapy
Strontium-89	Bone pain palliation
Strontium-90	Source of Yttrium-90 for therapeutic applications
Thorium-227	Cancer therapy
Thorium-228/Radium-224 Gen	Th-228 is being supplied as a generator for Ra-224, which is currently in clinical trials to develop novel treatments for ovarian, colorectal, and various skin cancers such as metastasized melanoma.
Tungsten-188	Generator of Re-188 for therapeutic applications
Yttrium-86	PET imaging
Yttrium-88	PET diagnostic/theranostic applications
Zinc-65	Tracer in metabolic studies

Medical Isotopes Under Development

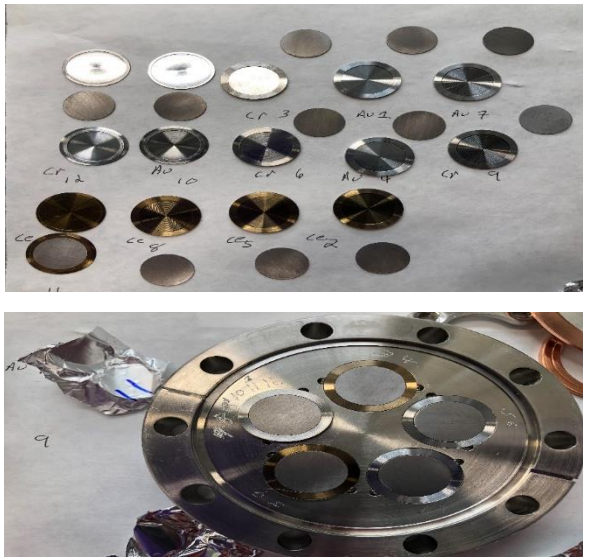
Bromine-76	PET imaging agent
Bromine-77	SPECT imaging agent
Cerium-134	*Positron-emitting analog for alpha emitters*
Lutetium-177 (n.c.a.)	Therapeutic applications
Manganese-52g	PET diagnostic applications
Molybdenum-98/100	Stable isotope enriched samples for Mo-99 production evaluation
Niobium-90	PET diagnostic applications
Platinum-191/193m/195m	Diagnostic applications
Rhenium-186	Diagnostic applications
Scandium-43	PET imaging agent/theranostic applications
Scandium-47	Therapeutic/theranostic applications
Selenium-72/Arsenic-72	Generator for PET diagnostic applications
Tellurium-119m	Sb-119 generator for therapeutic applications
Titanium-44/Scandium-44	*Generator for PET diagnostic/theranostic applications*
Uranium-230/Thorium-226	Generator (alpha therapeutic agent)
Xenon-129	Stable isotope enrichment under development for lung imaging
Ytterbium-176	Stable isotope enrichment under development for Lu-177 (n.c.a.) production

Isotope Production R&D

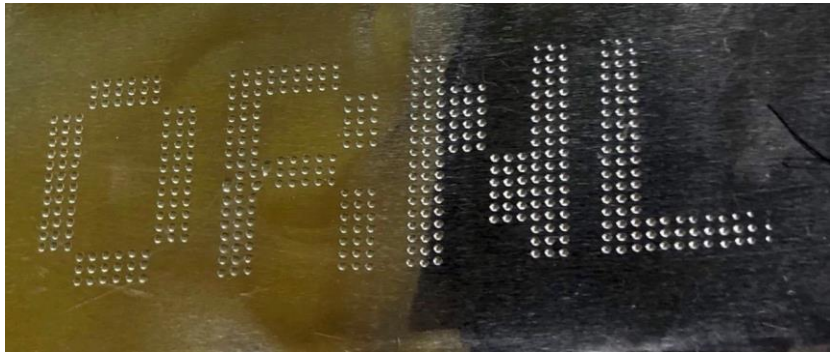
Transmutation and nuclear data (neutrons, charged particles, high energy gamma photons)

- Targetry (thermal hydraulics, materials, particle transport modeling)
- Processes for recovery and purification of radioisotopes; remote handling/automation
- Mass-separation for enriched stable isotopes and HSA radioactive isotopes

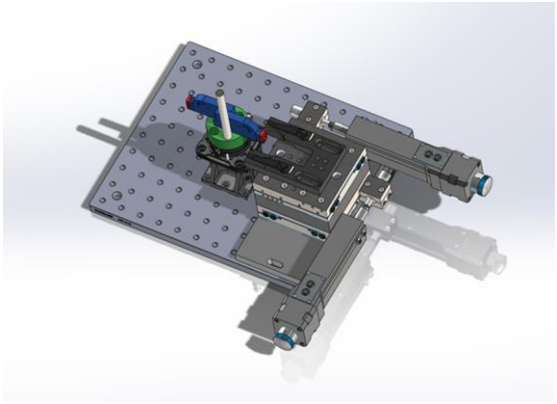
- ➢ SC Fundamental Science to Transform Manufacturing Initiative
- ➢ Transformative approaches to targetry to facilitate research and commercial isotope production



Preparation of parts for initial thermal bonding studies to inform next-gen LANL target design (top) all parts with various coatings (bottom) materials packaged for shipment for thermal pressing



Inkjet printing of Targets: Successful Printing of Bitmap Patterns: 50 nL drops of water on aluminum



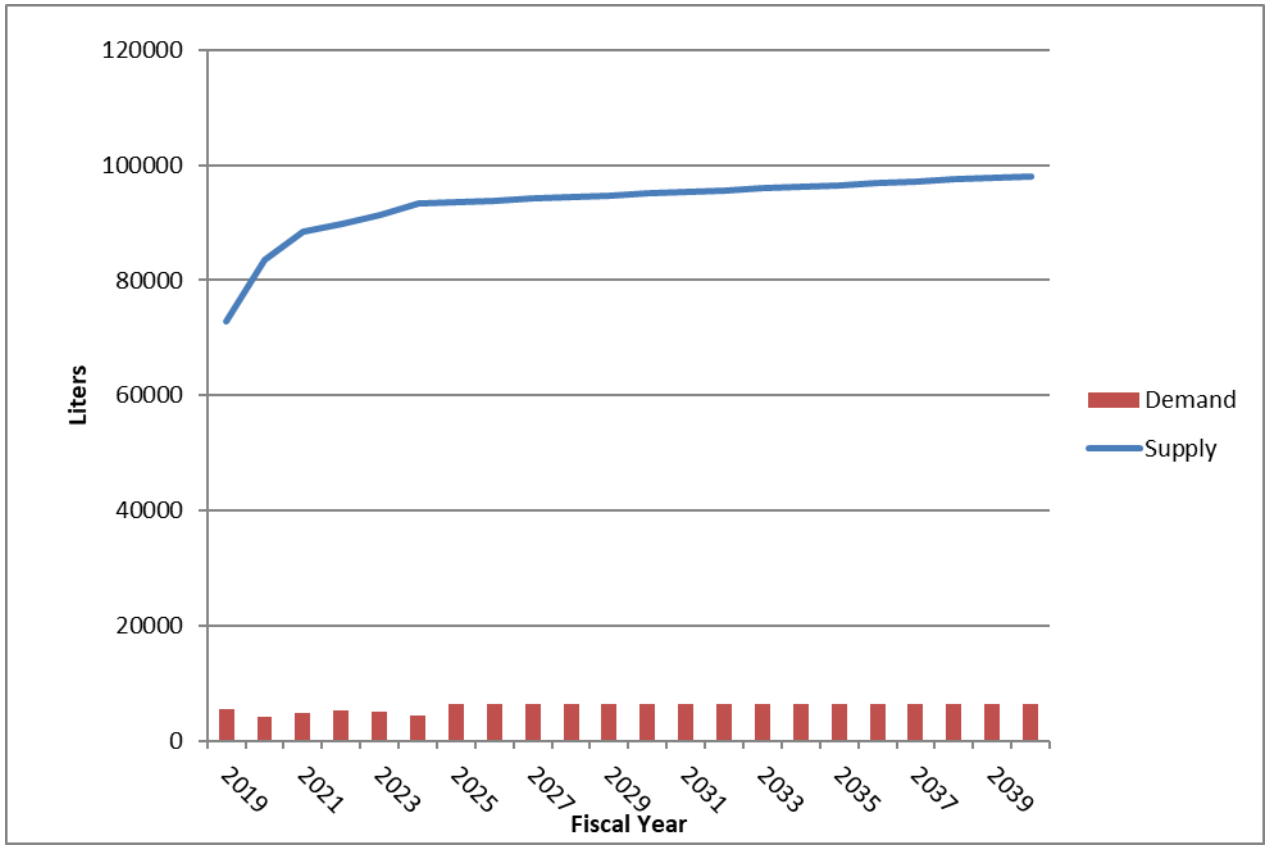
Custom Designed and Fabricated Biofluidix Printer

Mitigating Foreign Dependence

Isotope	Application	DOE IP Mitigation Plan
Am-241 (Russia)	Oil/gas exploration; moisture gauges; smoke detectors	Established production at LANL.
Ba-133 (Russia)	Gamma radiation source	Established production at HFIR*
C-14 (Russia)	Radio labeling	Demonstrated production capability at HFIR*
Cd-109 (Russia)	Medical instrumentation calibration, medical imaging	Established production at HFIR*
Ce-139 (Russia)	Calibration source	Established accelerator route at LANL IPF.
Cf-252 (Russia)	Oil/gas exploration, reactor fuel rod scanning, reactor startup	Re-established U.S. production at HFIR in 2009/2010.
Co-57 (Russia, Europe)	Calibration sources for medical devices	Domestic commercial production
Co-60(Russia)	Cancer therapy machines	Re-established U.S. production at ATR in 2014.
Fe-55 (Russia)	X-ray diffraction sources for industry	Established production capability at HFIR*
Ge-68 (Russia)	Medical device calibration, cancer imaging	Transferred production to domestic industry
Gd-153 (Russia)	osteoporosis detection, process control	R&D at HFIR ongoing
Ir-192 (Russia, Belgium,Neth)	Industrial Gamma radiography	Completing target design for HFIR and ATR*
Kr-85 (Russia)	Radioactivity calibration standard; biological tracer	Options being investigated
Po-210 (Russia)	Anti-static devices	MURR can meet U.S. demand.
Pm-147 (Russia)	Radioisotope power sources, beta emitter for thickness gauges	Established capability at HFIR*
Sr-82 (FR, RU, S Africa, Canada)	Cardiac imaging	Transferred production to domestic industry
Sr-90 (Russia)	Cancer therapy	Processing ongoing at PNNL. Entered market.
U-234 (Russia)	Flux monitor for nuclear power plants	Processed material. Entered market.
W-188 (Russia)	Cancer treatment	Re-established U.S. production at HFIR. Entered market.
Y-88 (Russia)	Weapons physics, stockpile stewardship	Established accelerator production at LANL IPF. Entered Market
Enriched stable isotope production (Russia, Netherlands)	Variety of applications	Re-established enriched stable isotope production in U.S.
He-3 (Russia)	Neutron detectors, cryogenics	R&D to increase He-3 input annually into inventory

He-3 Status

- Isotope Program plays a lead role in Interagency He-3 Working Group- reports to White House National Security Staff. 14 Federal agencies.
- Mitigation and prioritization efforts on behalf of IAG have successfully addressed He-3 shortage.
- The current supply is anticipated to currently meet Federal agency needs.
- Seeing increase in He-3 for cryogenics for QIS



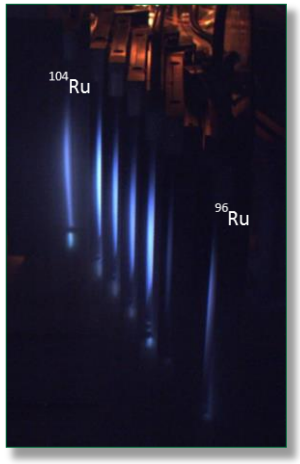
Enriched Stable Isotopes

- Y12 Calutrons produced 250 stable isotopes through 1998.
- DOE Isotope Program manages the Nation's inventory of stable isotopes.
- Inventory decreasing; 11 out of 250 has been exhausted.
- Stable isotopes used in medicine, nuclear criticality, feedstock for radioisotope production, QIS, high precision atomic clocks.
- Growing U.S. dependence on imports (Russia, URENCO).

Stable Isotope Enrichment and Distribution

- **Re-established enriched stable isotope production in the United States – ESIPP - 2017**
  - Electromagnetic separation and gas centrifuge
    - Ru-96, Mo-98, Mo-100, Yb-176
    - Complete and operate new design EMIS for heavier elements

- **Stable Isotope Production Facility MIE**
  (TPC = $27M, PD4=FY24)
  - Leveraged by NNSA
  - Kg GC through-put capability
  - Basic research, applications, industry
  - Xe-129 for polarized lung imaging
    - Complete and operate classified machine shop for GC



- **U.S. Stable Isotope Production and Research Center**
  - CD-0 Approved January 4, 2019
  - ~ $230M TPC; CD4 ~ FY 2028
  - Additional EMIS and gas centrifuge capability
  - Mo-100, Mo-98, Si-28, Yb-176, Er-168, etc

- **QIS initiative**
  - Simulations, GC design and test stands

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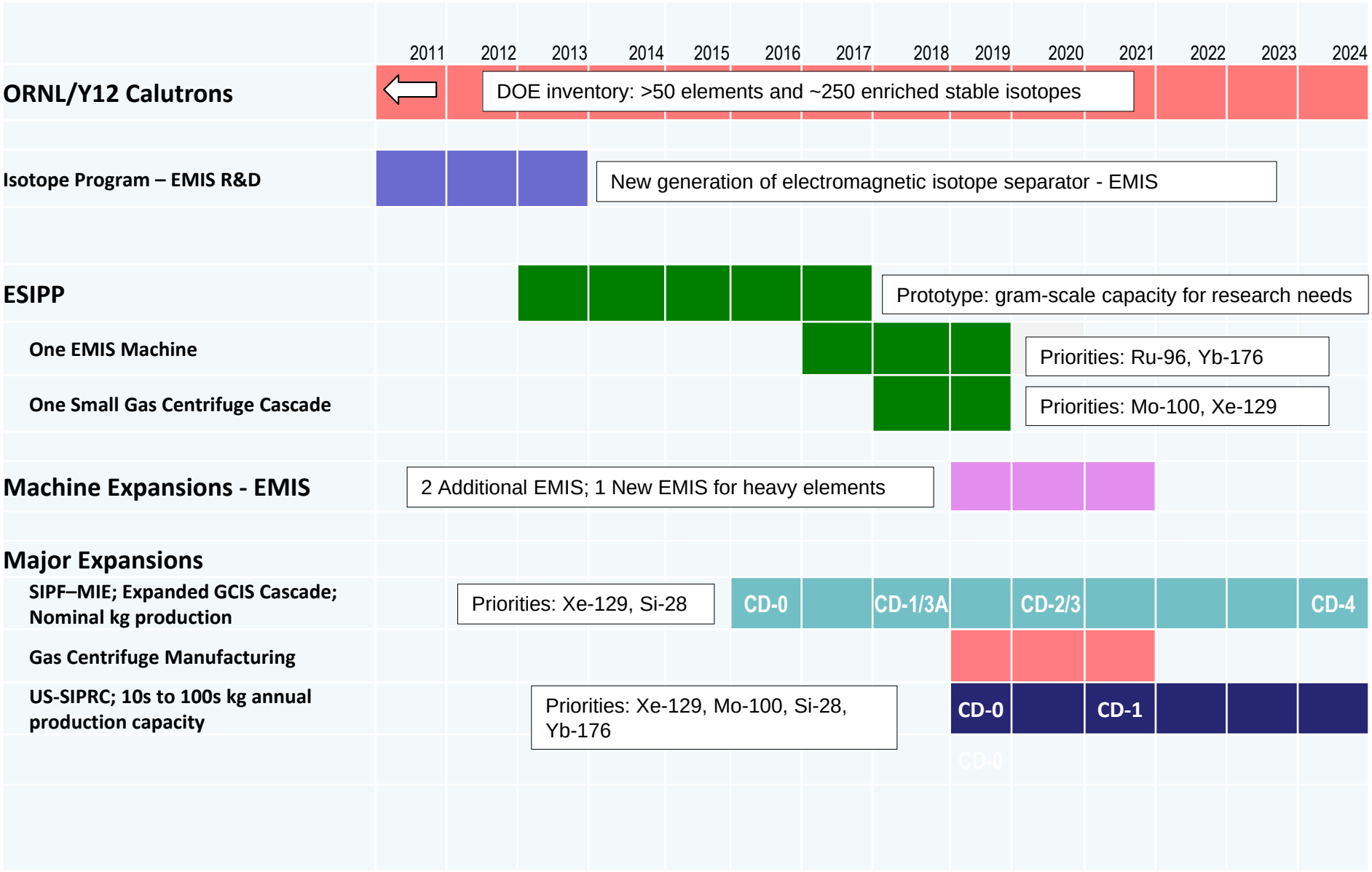
Isotope Enrichment at a Glance



Evolving Watchlist

A table of isotopes was shown at the workshop which is OUO. If you would like to see this list, please contact me directly. If you know of an isotope which meets any of the criteria below and should be on our watchlist, please contact me.

Inventories typically only for domestic use with federal priority

- Critical feedstock for high priority isotope
- At capacity
- Low inventory/supply
- Emerging technology
- Temporary or permanent supply constraints

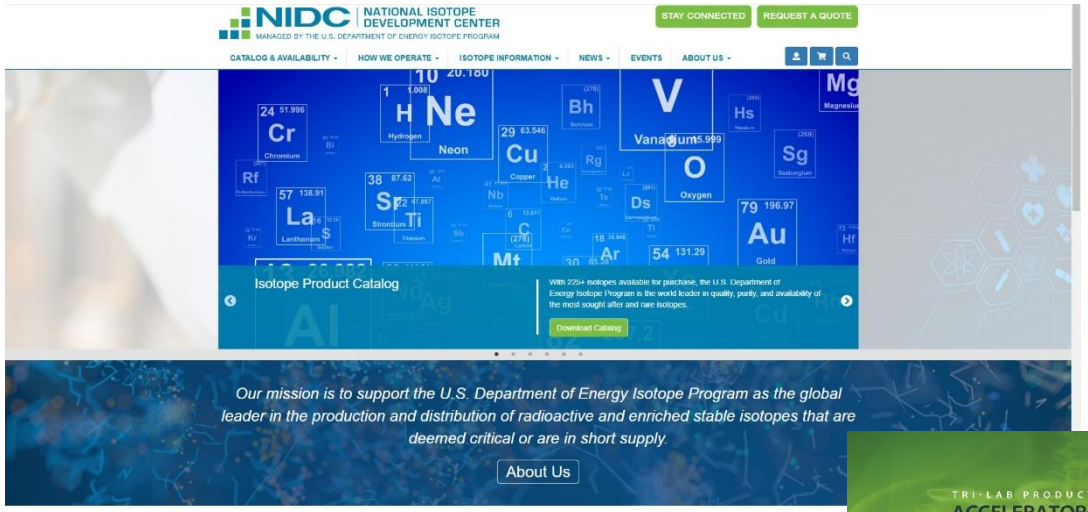
National Isotope Development Center

- 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.

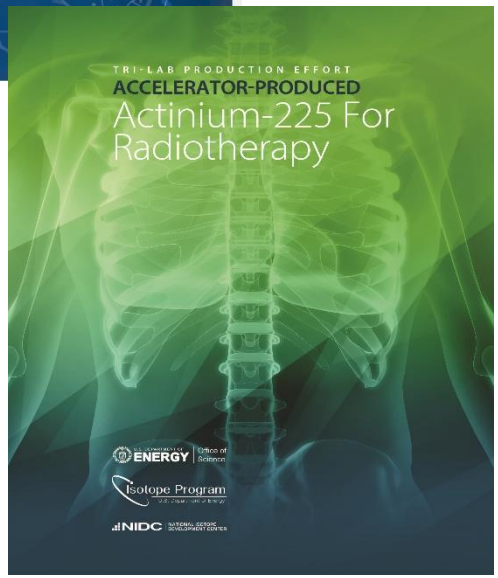
- All contractual discussions with customers.

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

- www.isotopes.gov



NIDC website homepage



NIDC brochure

Summary

The DOE Isotope Program is a modest program with a significant impact.

World leaders in developing novel isotope production approaches and bringing rare and critical isotopes to the global community.

We provide a service. Produce isotopes important for federal missions.

Encourage federal stakeholders to submit surveys.

- Will loop back around to agency
- Will consider commercial availability
- Will consider production timeline
- Will consider R&D to develop capability
- Will look at overall supply chain and peak demands

We will start looping back to agencies upon completion of individual surveys for a more timely response.