



DOE Isotope Program Update July 12, 2021

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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.



Ensure robust domestic supply chains. Reduce U.S. dependency on foreign supply to ensure National Preparedness.

Isotopes are forms of the same element that contain <u>equal numbers of protons</u> but <u>different</u> <u>numbers of neutrons</u> in their nuclei, and hence differ in relative atomic mass but not in chemical properties; in particular, a radioactive form of an element.



DOE Isotope Program Production Sites DOE Mission Essential Function





Started with 6 in 2009





- 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.



Our mission is to support the U.S. Department of Energy Isotope Program as the global leader in the production and distribution of radioactive and enriched stable isotopes that are deemed critical or are in short supply.

About Us

NIDC website homepage

Actinium-225 For Radiotherapy

www.isotopes.gov





ENERGY



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
- Advanced Manufacturing Initiative
- Transformative approaches to targetry to facilitate research and commercial isotope production
- Promoting AI/ML, robotics, automation





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

Biennial FOA's

|--|--|--|--|

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

Custom Designed and Fabricated Biofluidix Printer



Super Heavy Elements and Heavy Element

Chemistry





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 ²⁴⁸Cm, (>95%)



²⁵⁴Es, 0.5 μg experiments on fission mechanisms



 ²⁴⁴Pu, 15 mg
>99% reaction mechanism studies







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 alphaemitters.





non-target normal

tissues.

radiation.



Ac-227 Production Development



- DOE is only world-wide producer of Ac-227.
- DOE continues to place high priority on Ac-227 production
- Making investments in building 3047 to assure continued reliable production
- Assuring sufficient staffing during COVID-19
- Pursuing a new radioisotope processing facility for significantly increased capabilities
- Pursuing additional hydraulic tubes for HFIR to increase target irradiation capability









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Alpha Emitters of Interest for Therapy

adionuclide	Half-life	
²²⁵ Ac	10 d	
²¹¹ At	7.2 h	
²¹² Bi	60 m	
²¹³ Bi	46 m	
²¹² Pb	10.6 h	
²²³ Ra	11.43 d	2300
²²⁶ Th	31 m	
²²⁷ Th	18.7 d	

- 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.

Isotope Program



Actinium-225 Production



- World leaders in production of alpha-emitters
- ORNL extracts Ac-225 from Th-229 recovered from U-233: 1,200 mCi per year
- Thorium cow fully subscribed: no new customers
- Projection of Ac-225 demand assuming multiple, approved Ac-225 and Bi-213 drugs and robust clinical R&D programs could be in the range of hundreds of Ci per year
- DMF submitted for Thorium product



Chemistry and QA team members at a recent Ac-225 Tri-Lab Effort workshop





Accelerator production of Ac-225 (10 d)

- ²³²Th(p,spallation)²²⁵Ac
- First supply of accelerator-produced Ac-225 in the world: now in routine production
- DMF submitted, cGMP production initiated
- Ramping up to >1 Ci batches; focus o production frequency and volume in support of clinical trials
- Challenge to meet demand
- Parent of Bi-213 (46 m)

Additional production in development (no Ac-227)

- Cyclotron production/ BNL: ²²⁶Ra(p,2n)²²⁵Ac
- Phototransmutation/ANL: ²²⁶Ra(γ,n)²²⁵Ra(β)²²⁵Ac
- Reactor production/ORNL: ${}^{226}Ra(3n,\gamma){}^{229}Th(\alpha){}^{225}Ac{}^{10}$

U.S. DEPARTMENT OF
ENERGYOffice of
Science134Ce and 134La;
Promising PET imaging Isotopes

Isotope Program

U.S. Department of Energy



- Demonstrated the production, purification, and potential application of cerium-134. This isotope decays into lanthanum-134, an isotope useful for positron emission tomography (PET) imaging.
- The results show that cerium-134, through its lanthanum-134 decay product, could serve as a diagnostic partner for medical treatments based on actinium-225 or thorium-227.







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	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
•	HSA Tin-117m	Theranostic radiopharmaceutical (Te-119m)
•	Thorium-227	Cancer therapy
•	Thorium-228/Radium-224 Gen	Th-228 supplied as generator for Ra-224 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





FY 21 NIH Appropriation urges NIH to "explore novel applications for radiopharmaceuticals and leverage next-generation advanced manufacturing techniques for isotope production being made by DOE-funded research universities and national laboratories."

Further, the Department [DOE] is directed to provide a plan ... to develop a consortium of research universities to apply advanced manufacturing techniques to radioisotope production, including automation, digitalization, artificial intelligence, fabrication, and state-of-the-art characterization instrumentation."

New FOA for "Accelerating Medical Isotopes": interface of DOE and NIH. Solicitated research to facilitate, streamline, and accelerate the translation of novel radioisotopes and their associated chelating agents and linker/ligands, for both diagnosis and treatment, from the laboratory bench to evaluation for potential usage in clinical and preclinical trials.



Isotope Program

July 23 is Closing Date *DE-FOA-0002532*





Isotope	Usage
actinium-225 (accelerator routes <u>only</u>) and bismuth-213	Treatment of infectious processes as well as cancers using alpha particles.
astatine-211	Treatment of infectious processes as well as cancers using alpha particles.
bromine-76, 77	Bromine-76 is a PET imaging isotope, while bromine-77 offers the advantage of therapeutic low-energy Auger and Coster-Kronig electrons. Potential uses include imaging and therapy of infectious processes as well as cancers.
cerium-134	PET imaging analogue for alpha-emitting isotopes
cobalt-55	Longer half-life PET imaging agent often used to study slower biological processes. (e.g., effects of stroke and Traumatic Brain Injury (TBI))
Copper-67	Theragnostic agent for treatment of cancer and infectious disease.
iridium-192	High dose-rate brachytherapy for treatment of tumors.
iron-52	Radiotracer for early stage medical and biological processes.
lead-212/bismuth-212 (gen)	Treatment of infectious processes as well as cancers using alpha particles.
manganese-52	PET imaging agent.
rhenium-186	Theranostic isotope for diagnostic imaging and treatment.
scandium-43,44,47/titanium-43,44,47	Imaging and therapy of infectious processes as well as cancers. Sc-43 and Sc-44 are PET imaging isotopes, while Sc-47 is a therapeutic β -emitter.
selenium-72/arsenic-72(gen)	PET imaging agent.
Strontium-89	Bone pain palliation.
tellurium-119m/antimony-119 (generator)	Treatment of infectious processes as well as cancers using low-energy Auger and Coster-Kronig electrons.
tin-117m	Therapeutic isotope for various joint diseases using low-energy Auger and conversion electrons.
uranium-230/thorium-226 (gen)	Treatment of infectious processes as well as cancers using alpha particles.
vanadium-48	PET imaging agent.
tungsten-188	beta emitter for treatment of infectious processes and cancer.
yttrium-86	PET imaging agent.
yttrium-88	substitute for Y-90 as a therapeutic isotope.





The DOE Isotope Program is small program with a huge impact

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

We play essential role in ensuring federal agencies have isotopes needed for mission completion

Strongly integrated into medical community

Date (1:00pm EST)	Isotope
August 3 rd	Ac-225
August 10th	At-211
August 17 th	Pb-212
August 24 th	Cu-67











Table 1: List of routes to produce Ac-225

Facility	Projectile	Nuclear Reaction	Comment
Reactor	Thermal	²²⁶ Ra(3 <u>n,g</u>) ²²⁹ Ra	ORNL funded
	neutrons	→ ²²⁹ Ac→ ²²⁹ Th	1g ²²⁶ Ra produces 15 mCi ²²⁹ Th per year
		²²⁸ Ra(n,g) ²²⁹ Ra	1g ²²⁶ Ra produces 7 mCi ²²⁹ Th per a 26-day
		\rightarrow^{229} Ac \rightarrow^{229} Th	irradiation
Accelerator	Electrons	²²⁶ Ra(g,n) ²²⁵ Ra→ ²²⁵ Ac	ANL – pursue funding
	Low energy	²²⁶ Ra(p,2n) ²²⁵ Ac	BNL pursue - funded
	particles	²²⁶ Ra(a,n) ²²⁹ Th	
		²²⁶ Ra(p,pn) ²²⁵ Ra→ ²²⁵ Ac	Talys xsections ~120 mb at 80→40 MeV
		²³² Th(p,x) ²²⁹ Th	ORNL pursued in the past – difficult –
			publication pending
	High energy	²³² Th(p,x) ²²⁵ Ac	DOE funded route will not be included
	protons	232 Th(p,x) 225 Ra \rightarrow 225 Ac	
	High energy	²²⁶ Ra(n,2n) ²²⁵ Ra→ ²²⁵ Ac	
	neutrons		
Hot Cell Facility	N/A	²²⁹ Th decay to ²²⁵ Ac	²³³ U processing