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New University Partnership Fortifies Supply of High Specific Activity Se-75 Radiotracer

CONTRIBUTIONS BY DR. DAVID ROBERTSON AND DR. STEVE MORRIS, MURR

A new partnership between the U.S. Department of Energy (DOE) Isotope Program and the University of Missouri Research Reactor Center (MURR®) will ensure that selenium-75 (Se-75), a critical research isotope for understanding the role of selenoproteins, will now be available on a reliable schedule and at a specific activity adequate for sophisticated cell culture and animal experiments. This partnership, finalized in May 2017, establishes MURR as the second official partner under the DOE Isotope Program University Production Network to promote production and availability of high-priority isotopes, and Se-75 is the first reactor isotope to be produced within the network.



Isotope processing at MURR

Once considered a substance even more toxic than arsenic, selenium is now recognized as an essential trace nutrient that is part of the 21st naturally occurring amino acid, selenocysteine, in the genetic code. This micronutrient supports various important cellular functions including protection against oxidative damage. Selenium deficiency contributes to several pathophysiological conditions including heart disease, cancer and inflammation. Selenium also plays a key role in immune function and has been hypothesized to delay the progression of AIDS in HIV-positive patients.

Specifically, the radiotracer Se-75 has been instrumental in teaching us about the selenoproteome and its role in human nutrition and health. This is because only tiny quantities of selenium can be introduced in the physiologically relevant cell culture and animal model studies, and high specific activity Se-75 makes it possible to trace selenoproteins in cells without perturbing the very tiny amount of selenium in the cells. The radiotracer is such a powerful tool as it also allows scientists to probe what happens in a living system when the selenium concentration is lowered to produce a deficient selenium status.

Production of Se-75 began at MURR in the early 1980s following the departure of key suppliers and the realization by researchers that they could use MURR's high flux reactor to fill the market gap for Se-75 with a specific activity high enough for sophisticated cell culture and animal experiments. The new partnership will further solidify the supply of this critical isotope. Following irradiation of enriched Se-74 targets in the Oak Ridge National Laboratory High Flux Isotope Reactor (HFIR), MURR will process the material and add it to their inventory for dispensing. Material produced at the HFIR will have a higher specific activity than what has been produced at MURR. Sales of the resulting isotope will be coordinated through the National Isotope Development Center's (NIDC) Isotope Business Office (IBO).

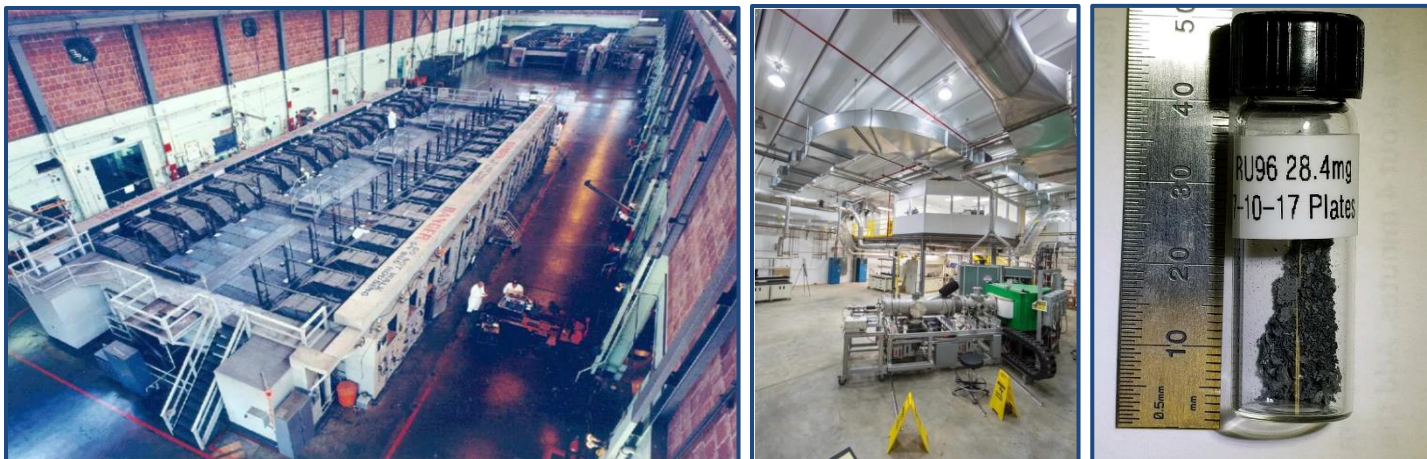
DOE Resumes Enriched Stable Isotope Production at ORNL

In recent months, the NIDC coordinated a shipment for initial quantities of highly enriched ruthenium-96 (Ru-96) to a customer, marking the first time in nearly 20 years that a newly enriched stable isotope has been produced and delivered by the DOE Isotope Program.

Since calutrons at Y-12 National Security Complex were placed into “standby” mode in 1998, the U.S. stockpile of enriched stable isotopes has been dwindling, and consequently, a growing reliance on foreign sources has been building. The need to reestablish domestic production of enriched stable isotope products was recognized by the Nuclear Science Advisory Committee – Isotopes Subcommittee in 2009, and the DOE Office of Nuclear Physics subsequently prioritized several projects to develop electromagnetic and gas centrifuge isotope separator technology at ORNL to address this need.

Starting in FY 2017, production operations commenced with a production campaign for Ru-96 using a newly developed electromagnetic isotope separator, or EMIS, in the Enriched Stable Isotope Prototype Plant (ESIPP). Ru-96, an isotope required for use in an experiment at the Relativistic Heavy Ion Collider at Brookhaven National Laboratory, was no longer in inventory from the U.S. stockpile nor was it available from other sources in the quantity needed. This left the ESIPP as the sole production source for this isotope product.

The NIDC and the DOE Office of Nuclear Physics continues to develop priorities for new production campaigns including development of an expanded plant for enriching kilogram quantities of isotopes. The expanded plant, referred to as the Stable Isotope Production Facility, will be a significant new investment in support of researchers requiring large quantities of enriched stable isotopes not readily available from other sources.

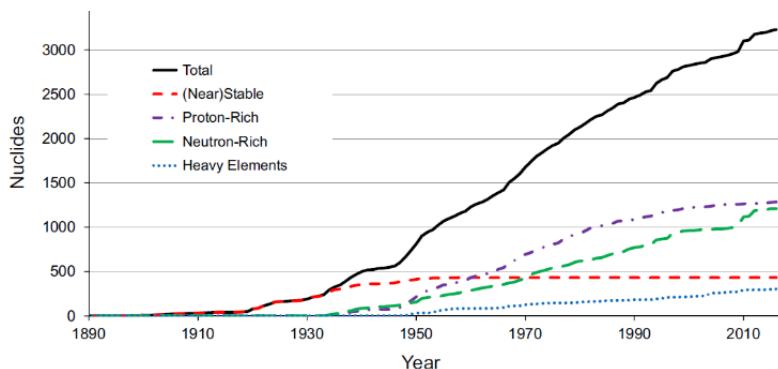


Decommissioned calutron track at Y-12 National Security Complex (left); new ESIPP facility (center); Ru-96 product (right) (Images courtesy of ORNL)

Did You Know...

...that the number of observed nuclides totaled 3,224 at the end of 2016, out of around 7,000 predicted. Included in this list are twelve new nuclides reported in 2016: $4n$, ^{96}In , ^{94}Cd , ^{92}Ag , ^{90}Pd , ^{63}Se , ^{67}Kr , ^{178}Pb , ^{230}Am , ^{234}Cm , and ^{234}Bk .

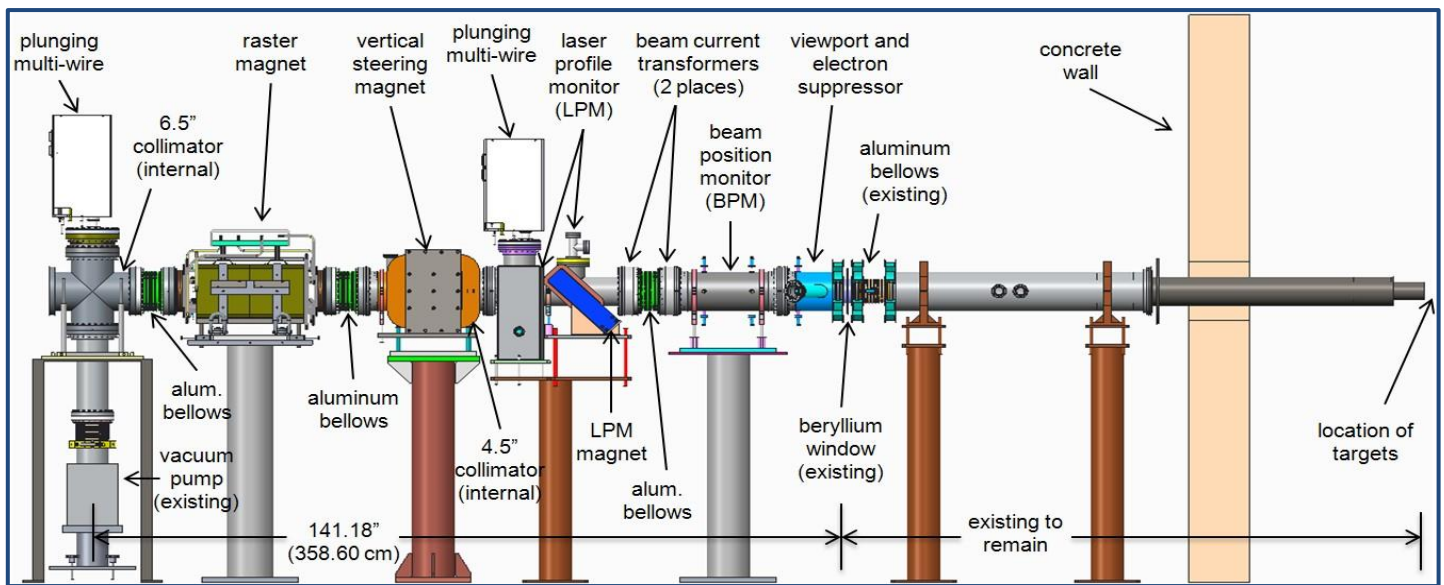
Source: Thoennessen, M. “2016 Update of the Discoveries of Nuclides.” *International Journal of Modern Physics*. April 24, 2017. <https://arxiv.org/pdf/1704.07169.pdf>



National Labs Enhance Facilities, Practices to Boost Isotope Production and R&D Capabilities

For decades, Brookhaven National Laboratory (BNL) and Los Alamos National Laboratory (LANL) have split the lion's share of the nation's high-energy accelerator-based radioisotope production for longer lived isotopes like Sr-82 (half-life = 25 days used in Sr-82/Rb-82 generators for cardiac imaging) and Ge-68 (half-life = 271 days used in Ge-68/Ga-68 generators for cancer imaging). While newer facilities have come on board to help distribute the load, the demand for these critical isotopes and other emerging isotopes is showing no sign of slowing down. Recent upgrades supported by the DOE Isotope Program at BNL and LANL will expand isotope production capabilities, particularly facilitating the development of large-scale production of Ac-225. As an added bonus, these improvements will enhance R&D capabilities for research staff exploring new production and separations techniques.

At BNL, numerous upgrades to the Brookhaven Linac Isotope Producer, or BLIP, have been completed in preparation for large-scale production of key isotopes like Ac-225. Most significant was a \$4.5 million raster system project to “paint” the proton beam in a circular fashion, providing an even distribution of the beam on the BLIP target by spreading out the power density. As a result, beam intensity on BLIP targets has safely increased by 38% (from 125 μA to a maximum of 173 μA) resulting in a commensurate increase in production yields. Additional improvements to BLIP included an extra one-inch of lead shielding applied to existing hot cells, a new high-purity germanium detector with electric cooling installed for daily water sampling, and soundproofing applied to dampen noise created by the new raster system.



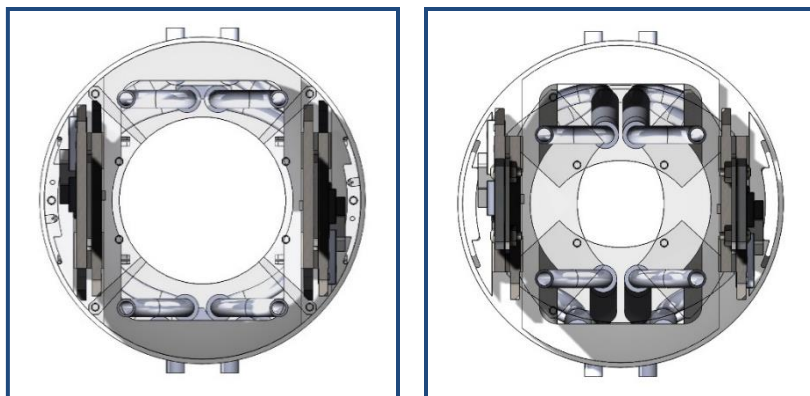
Schematic of BNL's new BLIP raster system (Image courtesy of BNL)

Similarly, LANL has taken a multi-faceted approach toward boosting isotope production capacity in existing facilities, starting with major upgrades to the beam transport system at its Isotope Production Facility (IPF). Specific improvements include the integration of an active and adjustable collimator that enables target optimization (larger aperture used for ultra-high current production, smaller for R&D targets) and an improved raster pattern of up to 100 concentric circles. The larger aperture, with associated distribution of heat over a larger surface, will allow an increase in beam current to 380 μA . LANL also launched a multi-year effort to transition away from RbCl salt targets in favor of Rb metal, removing thermal limits of the salt design. The change allows for an increase in the amount of current on the entire target stack, and, consequently, an increase in the production yields of isotopes. Combined, these IPF improvements have the potential to increase production of all isotopes by 60%.

continued on page 4: “National Labs”

National Labs *(Continued from page 3)*

The combined facility improvements benefit isotopes other than the routinely produced Sr-82 and Ge-68. The DOE Office of Science, Office of Nuclear Physics Tri-Lab Research Effort to Provide Accelerator-Produced Ac-225 for Radiotherapy intends to leverage these critical upgrades to enhance the supply of this critical isotope. The new BNL and LANL capabilities should pave the way for Ac-225 production volumes that meet (or exceed) current annual world supply in 10 days of accelerator operations.



Schematic of new LANL IPF adjustable collimator aperture concept for use in production (left) and R&D (right) target irradiations (Image courtesy of LANL)

Isotope Program Honors Retirees, Welcomes New Staff

Dr. Leonard Mausner – BNL: Dr. Mausner, Senior Scientist and program manager at BNL, retired in July. Throughout his career, he played a critical role in support of the DOE Isotope Program through his conception and implementation of several major facility upgrades at the BLIP, which boosted availability of isotopes used in high-priority research and medical applications. He also helped develop several medical radionuclides used for therapy and diagnosis of life-threatening diseases.

Dr. Brian Rapko – Pacific Northwest National Laboratory (PNNL): Dr. Rapko retired in June after a 25-year career primarily focused on chemical separations, (particularly radiochemical) and in areas of process optimization related to separations flowsheets. Dr. Rapko provided expertise in Sr/Y-90 and U/Th/Ra chemistry and separation and was also part of a team of PNNL scientists that developed the solvent extraction process for separations of Y-90 from Sr-90 that was successfully commercialized and continues to be used today.

Karen Sikes – NIDC Marketing & Communications Manager: Ms. Sikes joined the NIDC team in June, working directly with the Center and the DOE Isotope Program managers to provide comprehensive isotope market information and effective communication support, such as managing the NIDC website, preparing the quarterly NIDC newsletter, monitoring isotope market sectors, and performing detailed analyses on end-product isotope markets and supply chains.

Betty Lane – IBO Project Management Assistant: Ms. Lane joined the IBO in June and is primarily responsible for responding to the broad customer base with price quotations for isotope products and services. Her other responsibilities include collecting end-use data from research applications, and tracking new product requests and isotopes that are not readily available from the Isotope Program for management evaluation. Betty will also be performing administrative duties associated with staff attendance and booth deployment at conferences.



From left to right: Dr. Leonard Mausner (BNL), Dr. Brian Rapko (PNNL), Karen Sikes (NIDC), Betty Lane (IBO)

Oak Ridge and Idaho National Labs Named International R&D Hub by IAEA

The U.S. Department of Energy's HFIR at ORNL and the Advanced Test Reactor (ATR) at Idaho National Laboratory (INL) were officially recognized in September as an International Centre based on Research Reactors (ICERR) by the International Atomic Energy Agency (IAEA). The United States is now one of four countries to receive this prestigious designation, alongside France, Russia, and Belgium.

Both commissioned in the 1960s, HFIR and the ATR each offer a unique appeal to prospective researchers. HFIR, for example, offers the highest flux reactor-based neutron source in the country (up to 2.6×10^{15} neutrons/cm²/sec at 85 MW) and one of the highest steady-state neutron fluxes in the world, which has enabled decades of groundbreaking achievements in heavy element discovery, isotope production, materials irradiation, neutron activation, and neutron scattering. Meanwhile, the ATR is the only U.S. research reactor to offer large-volume, high-flux neutron irradiation in a prototype environment (up to $\sim 10^{15}$ n/cm²/sec at 250 MW), making it a prime candidate for studying the effects of intense neutron and gamma radiation on reactor materials and fuels.

Labs designated as ICERR are encouraged by the IAEA to leverage their unique capabilities and facilities not only to spearhead scientific advancements in fields such as medical radioisotopes, but also to invite other Member States that may lack key infrastructure to use state-of-the-art facilities for joint R&D projects as well as education and training purposes.



U.S. Secretary of Energy Rick Perry accepts ICERR designation and is accompanied by National Laboratory Directors Dr. Thomas Zacharia (ORNL) and Dr. Mark Peters (INL) (Image courtesy of IAEA)

Transportation Working Group Improves Operations, Provides Guidance

The Transportation Working Group has been re-established by the NIDC to address program-wide issues, contribute to strategic planning, and provide guidance to specific isotope projects. Collectively, this group has several years of experience in the routine packaging and shipping of both radioactive and stable isotope products, ranging from exempt quantities up to and including Type B quantities.

Project-specific transportation issues that are currently being addressed include the implementation of a new shielded Type A container for irradiated Th-232 targets for Ac-225 production; revisions to two Type B container certifications to allow for additional radioisotope and/or material-type content; and implementation of a tracking system for returnable Type A containers.

The current membership for the working group (and their corresponding Isotope Program production site) is as follows:

- BNL: Anna Goldberg and Steve Woodburn
- INL: Carla Dwight
- LANL: Lisa Cummins
- ORNL: Keith Raby and Angie McGee
- PNNL: Larry Stuhl
- DOE/HQ: Ethan Balkin
- NIDC: Kevin Felker

We hope to streamline the path to resolution by designating representatives at each site, so please bring any transportation-related issues to their attention as they arise. If you have customer-related transportation issues that require assistance, please contact one of the site representatives or Kevin Felker (NIDC).

Isotope Availability Alerts

| Now Available | Coming Soon | Under Investigation |
|--|---|--|
| <ul style="list-style-type: none"> • Al-26 • Cu-67 • Se-75 • Si-32 • Ti-44 • U-234 • Y-86 | <ul style="list-style-type: none"> • Ba-133 • Sr-89 | <ul style="list-style-type: none"> • C-14 • Gd-153 |

MEDIA ATTENTION

In *Popular Mechanics' It'll Take an Army to Kill the Emperor*, Eva Birnbaum, LANL Isotope Production Facility program manager, explains the massive potential of actinium-225 in targeted cancer therapies and the sense of urgency behind ramping up production. Along with partners at BNL, ORNL, and the NIDC, LANL is participating in the DOE Isotope Program's Ac-225 Tri-Lab Research Effort that leverages the team's unique facilities, capabilities, and expertise to enhance supply of this critical isotope.

FEATURED PUBLICATION

A collaborative research article between staff in LANL's Chemistry Division and ORNL's Nuclear Security and Isotope Technology Division describes a new method for isolating radium isotopes, in high yield and purity, from a proton irradiated thorium-232 matrix in nature.com's **Scientific Reports**.

VISITS

Research staff at ORNL's HFIR and Radiochemical Engineering Development Center recently welcomed Kit Chapman, journalist and comment editor from Chemistry World. Visiting these facilities and conversing with staff aided Chapman in drafting sections of an upcoming publication for Bloomsbury Sigma on the history of superheavy element research and discovery.

FACILITY RECOGNITION

The ATR complex at INL (consisting of the original Materials Testing Reactor, the Engineering Test Reactor, and the Advanced Test Reactor) and the Radiochemical Processing Laboratory at PNNL were both named Nuclear Historic Landmarks by the American Nuclear Society. Congratulations to INL and PNNL on their key contributions to the world of nuclear energy research, security, and safety!

STAFF EXCELLENCE

Congratulations to Suresh Srivastava (BNL) for receiving the 2018 Glenn T. Seaborg Award for Nuclear Chemistry, sponsored by the American Chemical Society (ACS). He will receive this honor in March at the 255th ACS National Meeting in New Orleans, LA.

UPCOMING EVENTS

International Conference on Advanced Applications of Radiation Technology (NICSTAR 2018), March 5-7, 2018, Mumbai, India

18th Radiochemical (RadChem) Conference, May 13-18, 2018, Mariánské Lázně, Czech Republic

2018 American Nuclear Society Annual Meeting, June 17-21, 2018, Philadelphia, PA, USA

SNMMI 2018 Annual Meeting, June 23-27, 2018, Philadelphia, PA, USA



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