Production of Medical Radioisotopes at Oak Ridge National Laboratory

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TRTR/IGORR 2023 – University of Maryland

June18-22, 2023

US Government sponsored radioisotope production work is supported by various organizations depending upon the isotope

Isotope Program
U.S. Department of Energy

National Nuclear Security Administration

DOE Isotope Program

- ^{252}Cf
- ^{225}Ac
- ^{227}Ac
- ^{75}Se
- ^{63}Ni
- ^{249}Bk
- ^{14}C

NASA/DOE-NE

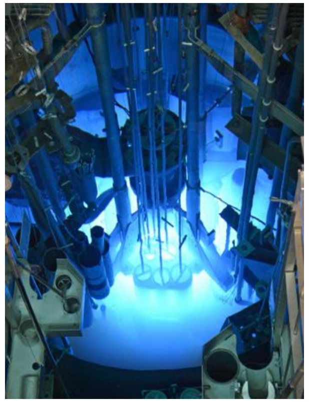
- ^{238}Pu

NNSA

- ^{99}Mo
- Uranium
- Lithium

Sites supporting the DOE Isotope Program

Isotope Program
U.S. Department of Energy



MURR - Missouri

ATR - Idaho

HFIR - Tennessee

University of Washington Cyclotron
Supplier of research isotopes (e.g., At-211)

PNNL
Sr-90 Y-90 generator for cancer therapy
Np-237 Research

INL Reactor (ATR)
Co-60 Stereotactic radiosurgery, industrial NDA

Argonne National Laboratory
Accelerator (LEAF):
Cu-67 Targeted cancer therapy

Brookhaven National Laboratory
Accelerator (BLIP):
Ti-44 Sc-44 generator for PET imaging
Y-86 PET imaging
Cu-67 Targeted cancer therapy
Ac-225 Targeted cancer therapy

Michigan State Univ. (FRIB)
Development of isotope harvesting (e.g., Mg-28, Si-32, Ca-47)

Y-12 (NNSA Facility)
Li-6 Neutron detection
Li-7 Radiation dosimeters

Oak Ridge National Laboratory
HFIR:
Ac-227 Cancer therapy
Se-75 Industrial NDA
Cf-252 Industrial applications
W-188 Cancer therapy
Radioisotopes Inventory:
Ac-225 Targeted cancer therapy
Ra-223 Targeted cancer therapy
Stable Isotopes Inventory:
E.g., Ca-48, Ga-69, Rb-87, Cl-37
Stable Isotope Production
E.g., Ru-96, Yb-176

Los Alamos National Laboratory
Accelerator (IPF):
Ac-225 Targeted cancer therapy
Ti-44 Sc-44-68 generator for PET imaging
Cd-109 X-ray fluorescence analyses
As-73 Environmental tracer
Si-32 Oceanographic research
Na-22 Sodium tracer and positron source
Plutonium Facility:
Am-241 Oil and gas exploration

University of Missouri (MURR)
Supplier of research isotopes (e.g., Se-75, Lu-177)

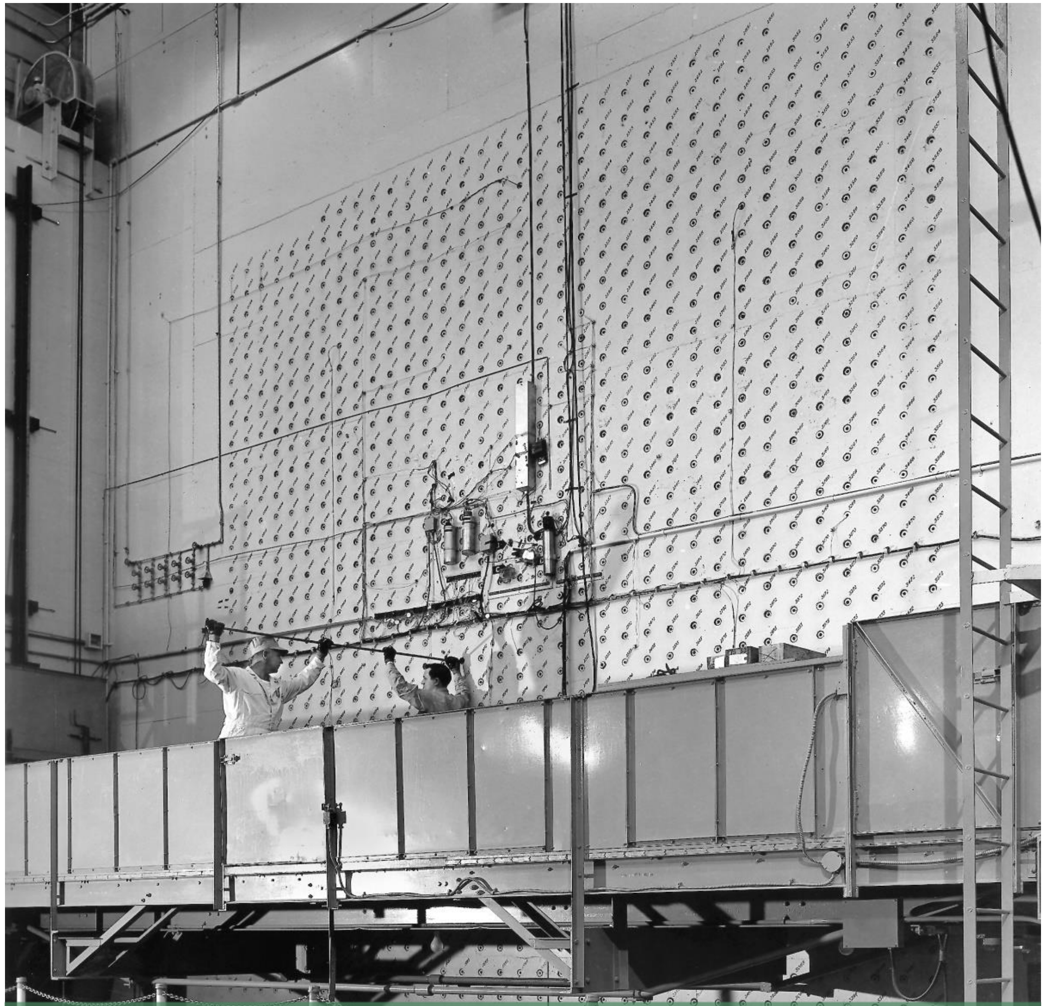
Savannah River National Laboratory (NNSA Tritium Facility)
He-3 Neutron detection
Fuel source for fusion reactors
Lung testing

Medical radioisotopes originated from ORNL

In 1946, ORNL sent the first official shipment of a medical radioisotope, carbon-14, to a hospital—Barnard Free Skin and Cancer Hospital in St. Louis

Members of the management team of the then-Clinton Laboratories review the site in 1946. Shown are Frederick Seitz, Director James Lum, Research Director Eugene Wigner, and Alexander Hollaender. Image credit: Monsanto

The small container of carbon-14 was use for research in cancer studies and was the first peaceful isotope produced from the Manhattan Project.



Workers in the Graphite Reactor use a rod to push fresh uranium slugs into the reactor's concrete loading face

ORNL produced Radioisotopes

- ^{227}Ac
- ^{252}Cf
- ^{225}Ac
- ^{133}Ba
- ^{63}Ni
- ^{75}Se
- ^{228}Th
- ^{249}Bk
- ^{257}Fm
- ^{89}Sr
- $^{254/253}$Es
- ^{117m}Sn
- ^{224}Ra/^{212}Pb
- ^{188}W/^{188}Re
- ^{166m}Ho
- ^{223}Ra/^{227}Th
- ^{170}Tm*
- ^{229}Th*
- ^{147}Pm
- ^{238}Pu
- ^{191}Os
- ^{60}Co
- ^{177}Lu
- ^{192}Ir
- ^{195m}Pt
- ^{229}Th
- ^{14}C
- ^{210}Pb
- ^{85}Kr

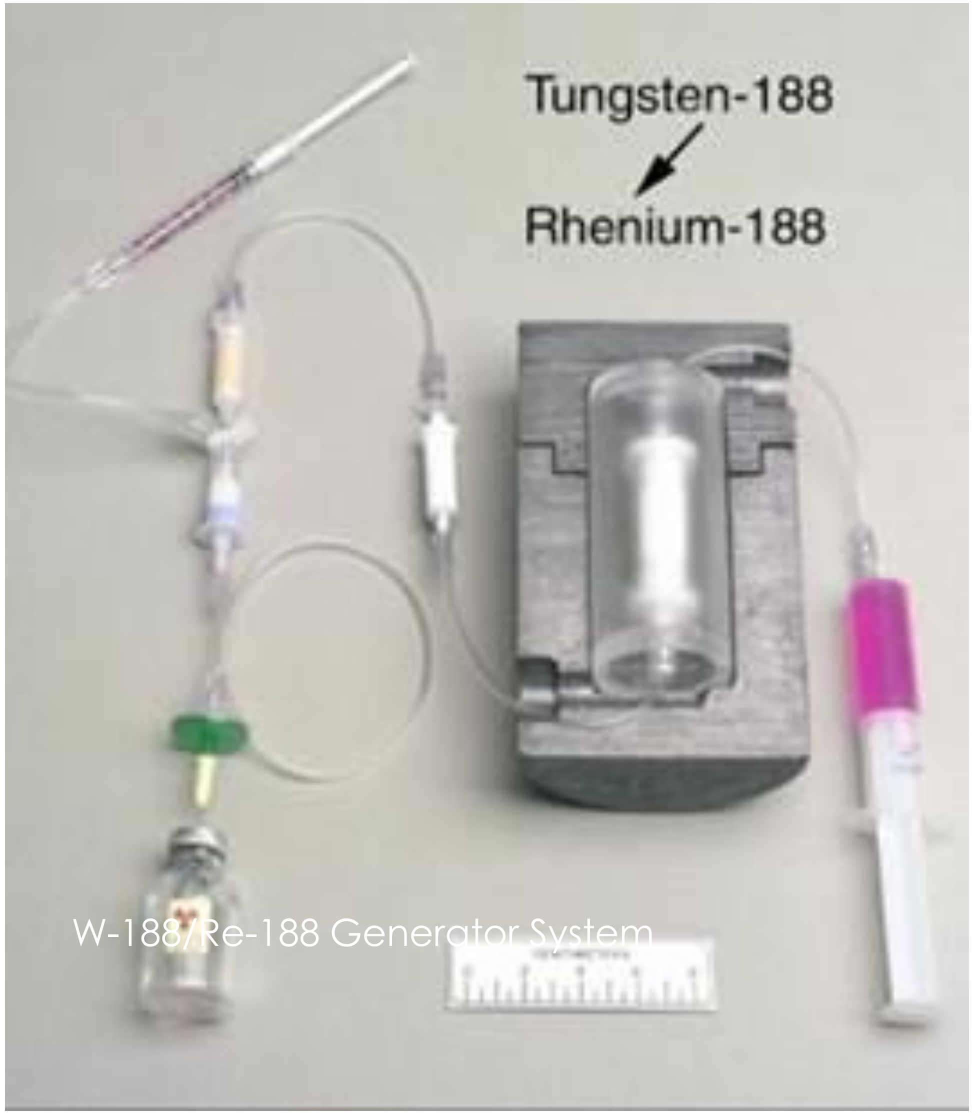
ORNL also dispenses high-purity ^{238,239,240,242,244}Pu, ^{237}Np, ^{243}Am, ^{99}Tc, ^{209}Po, ^{233,234,235,238}U, and ^{244,248}Cm from inventory

In production
Production ready
Under development

The production of these radioisotopes is made possible because of the High Flux Isotope Reactor and hot cell processing capabilities at ORNL

W-188 is the parent of medical radioisotope Re-188

- Re-188 is a high energy beta-emitting radioisotope ($t_{1/2}$ = 17h)
- The high energy allows for penetration and destruction of targeted tissues
- Low-energy, low-intensity gamma emission is effective for imaging
- Chemically similar to Tc-99 for ease of preparation and targeting
- Available at high specific activity via W-188 generators
- Being studied for Bone Pain Palliation as well as Hematological and Solid Tumors

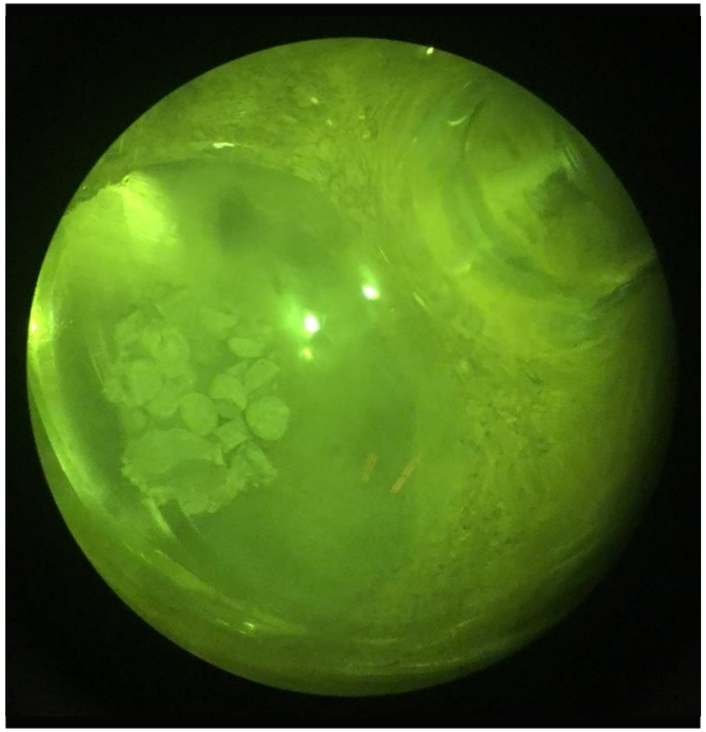


W-188/Re-188 Generator System

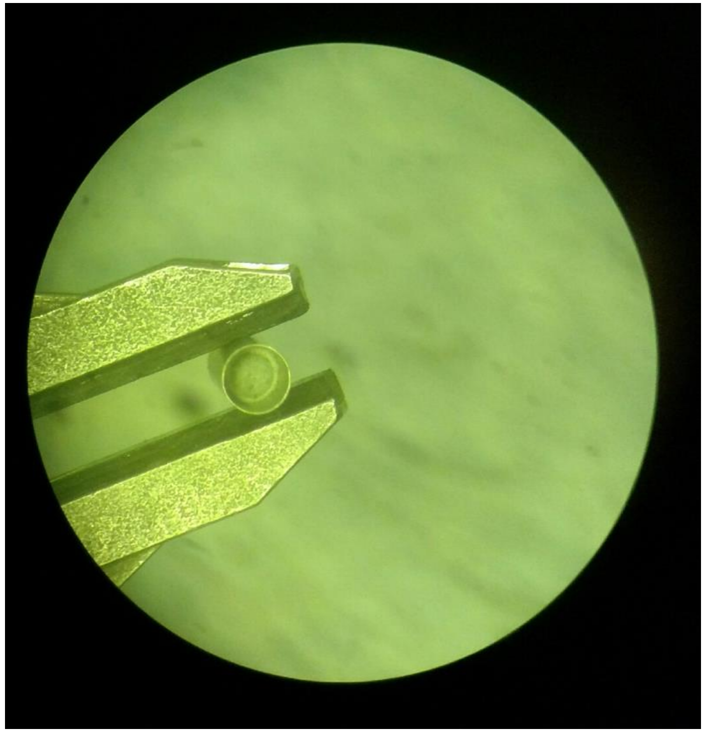
Sr-89 ($t_{1/2}$ = 50.6 d) Production (beta-emitter)

^{89}Sr-produced in HFIR from highly enriched ^{88}Sr and intended for bone pain palliation

Anion exchange column



Irradiated pellets



Irradiated pellets

OAK RIDGE National Laboratory

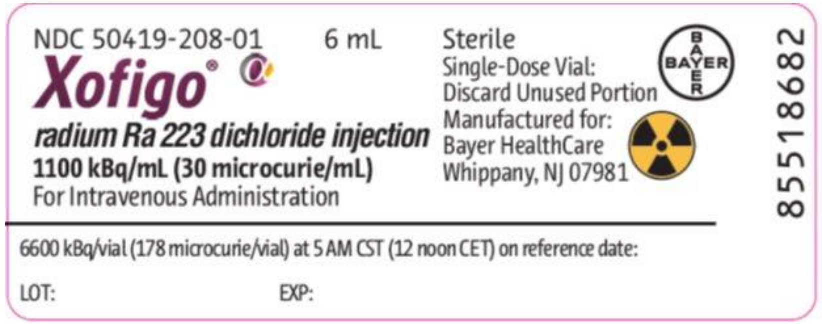
Sn-117m treats arthritis in dogs

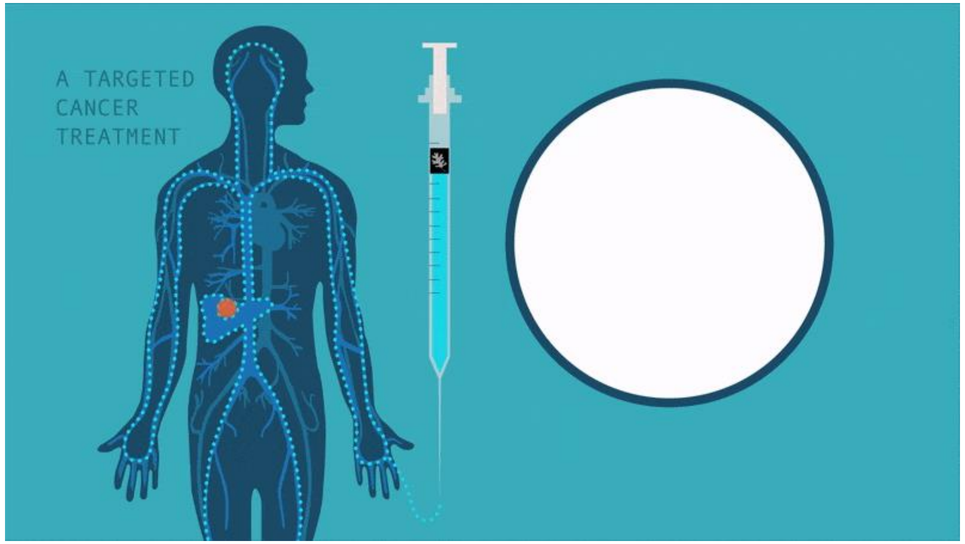
- Sn-117m decays via internal conversion with a half life of 13.6 d
- Decays to inert tin and is removed via the lymphatics
- Emits a 159 keV gamma for imaging purposes
- Discrete radiation range, with minimal dose to others
- Could someday be considered for humans

Introducing
Synovetin OA™

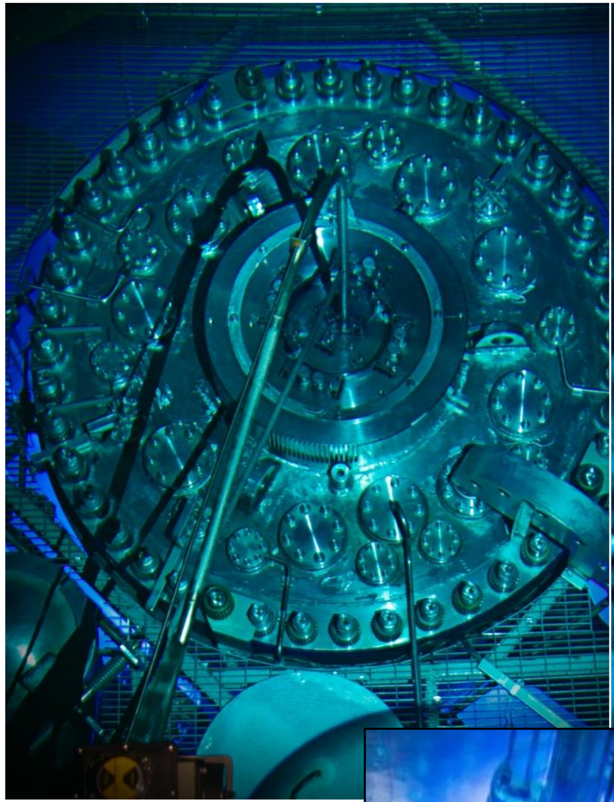
Alpha-emitting isotopes can directly target tumor sites

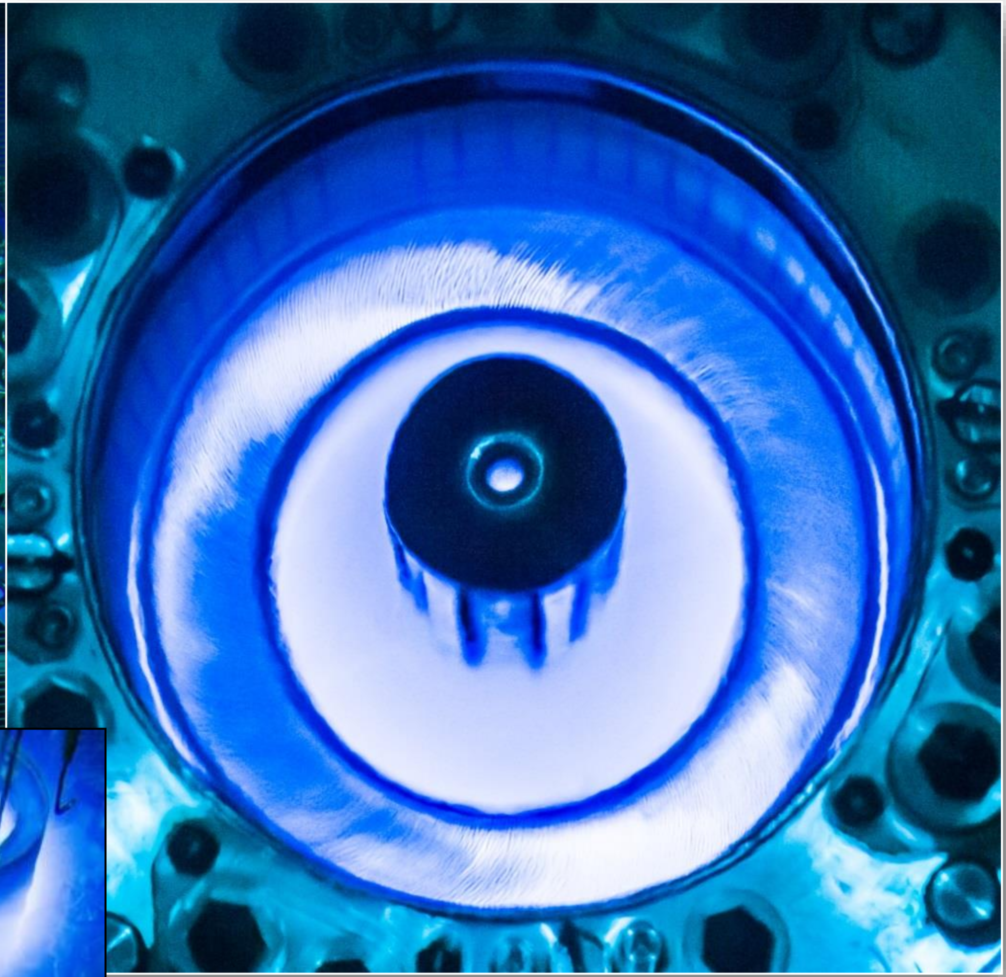
- **Ac-227** is the parent isotope of ^{223}**Ra** ($t_{1/2}$ = 11.4 d), the active pharmaceutical ingredient in Xofigo®
  - Radium has similar chemical behavior to Ca and travels to the bones where it attacks bone metastases, providing pain relief and potentially life extension
  - Higher LET than Sr-89, a beta emitter with similar applications
- **Ac-225** has desirable decay characteristics for targeted alpha therapy
  - Emits 5-8 MeV from 4 α particles, cell kill possible with 1 hit
  - 10-day half-life for effective handling logistics
  - Targeting vector required
  - Significant recoil
- **Pb-212** is similar to Ac-225, with a shorter half-life
  - More challenging handling logistics, higher dose rate





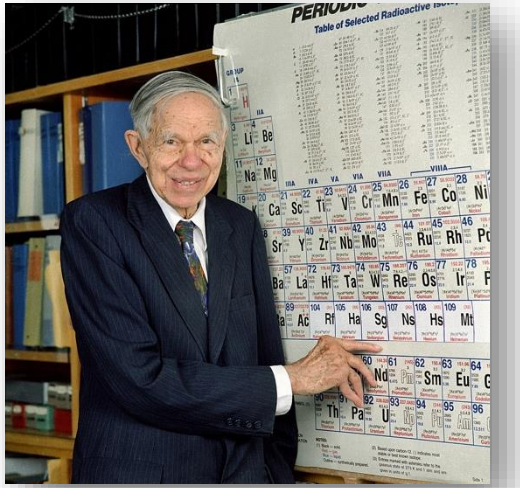
HFIR is our workhorse for isotope production





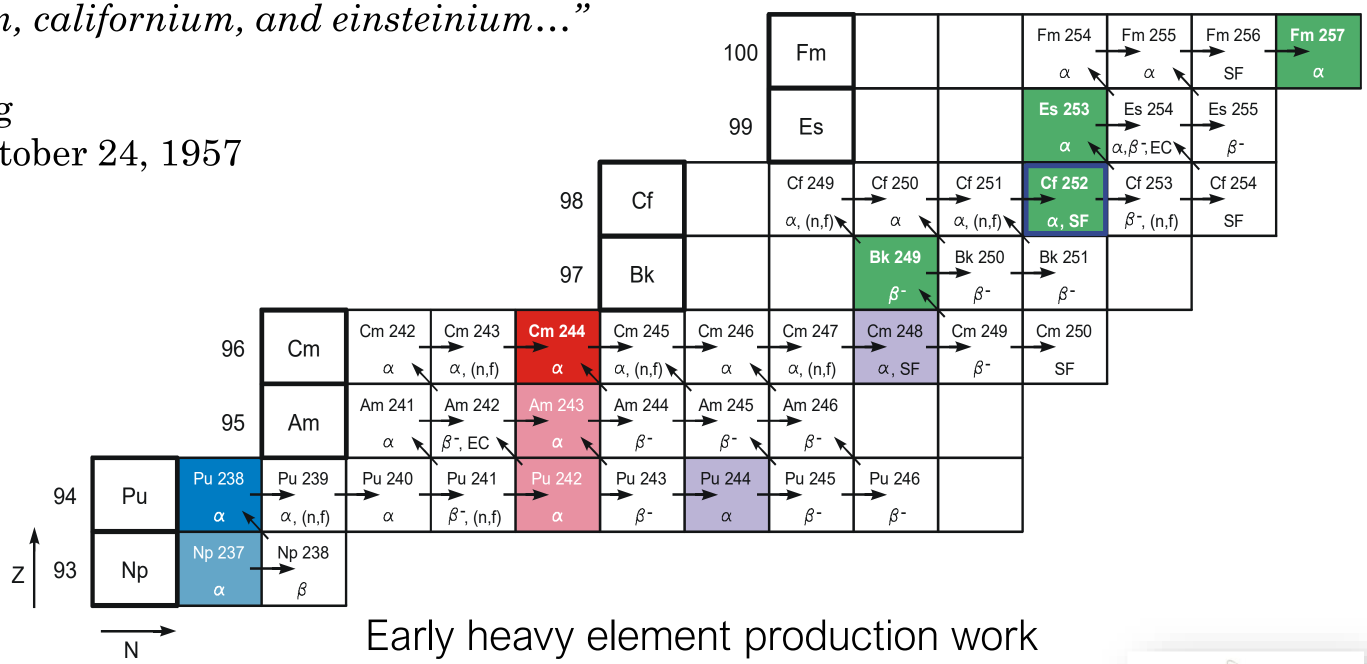
- **85 MW Thermal Power**
- **Peak Thermal Flux = 2.5 E 15 n/cm^2-sec**
- **Peak Fast Flux = 1.2 E 15 n/cm^2-sec**
- **Light water moderated and cooled**
- **Beryllium reflected**
- **Fuel: AL clad U_3O_8 plates – 9.4 Kg $_{235}U$**
- **Control – concentric cylinders of EuO**
- **Cycle length: 24.5 days (85 MW operations)**

Purpose-built for heavy element production

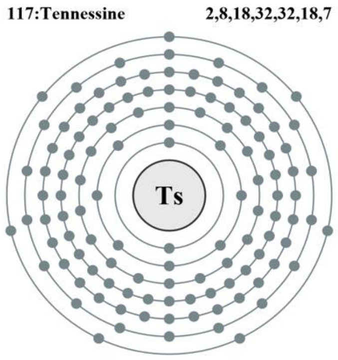


"The field of new transuranium elements is entering an era where the participating scientists in this country cannot go much further without some unified national effort… The future progress in this area depends on substantial weighable quantities (say milligrams) of berkelium, californium, and einsteinium…"

G. T. Seaborg
Berkeley, October 24, 1957



Glenn Seaborg and his colleagues discovered 10 new elements including plutonium. Additionally they identified more than new 100 isotopes. Glenn was the leading advocate for building HFIR as an isotope production reactor to support heavy element research.

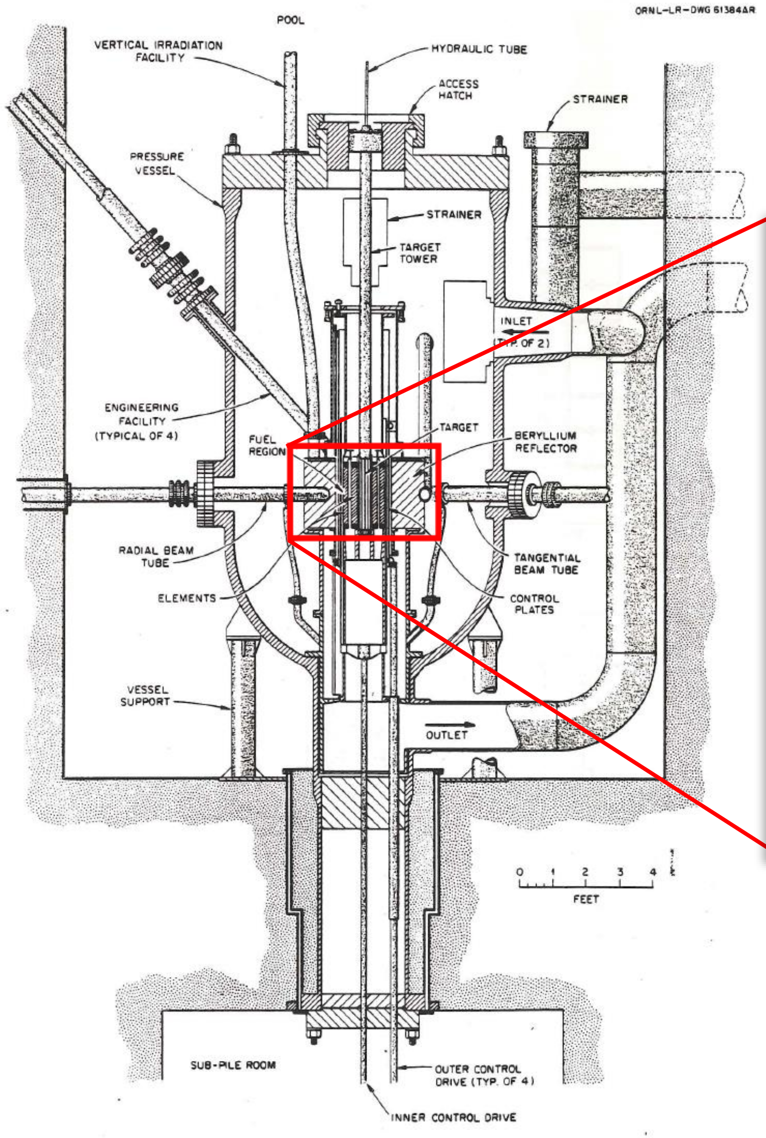


Element 117 – Tennessine was discovered using ^{249}Bk from HFIR

Early heavy element production work led to the commercial sale of ^{252}Cf. HFIR supplies 70% of the world's demand for ^{252}Cf, which is used as a reactor startup source, and radiography, for the coal and oil industry. HFIR operation forms an irreplaceable cornerstone of this billion dollar industry.

^{252}Cf source

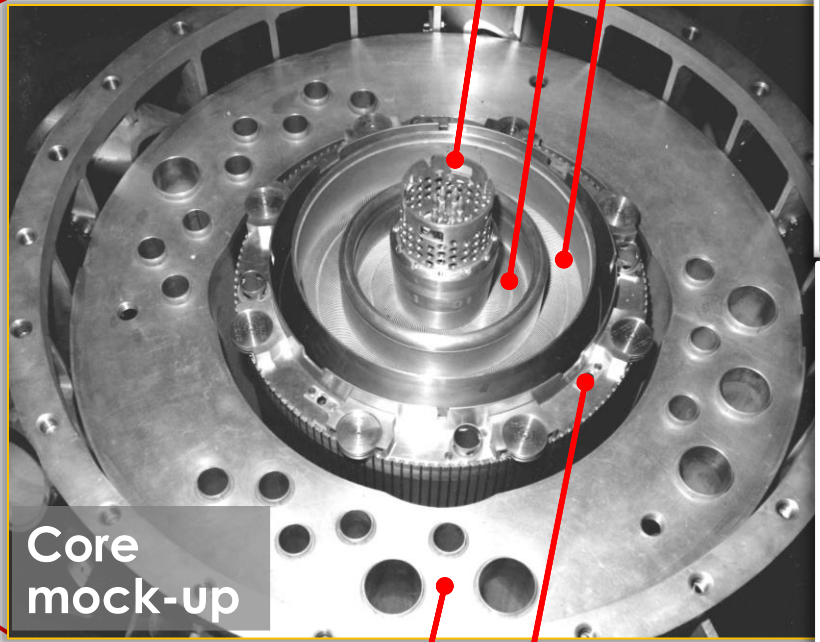
HFIR's high flux is due to its fuel and flux trap type design



Outer fuel element (OFE)

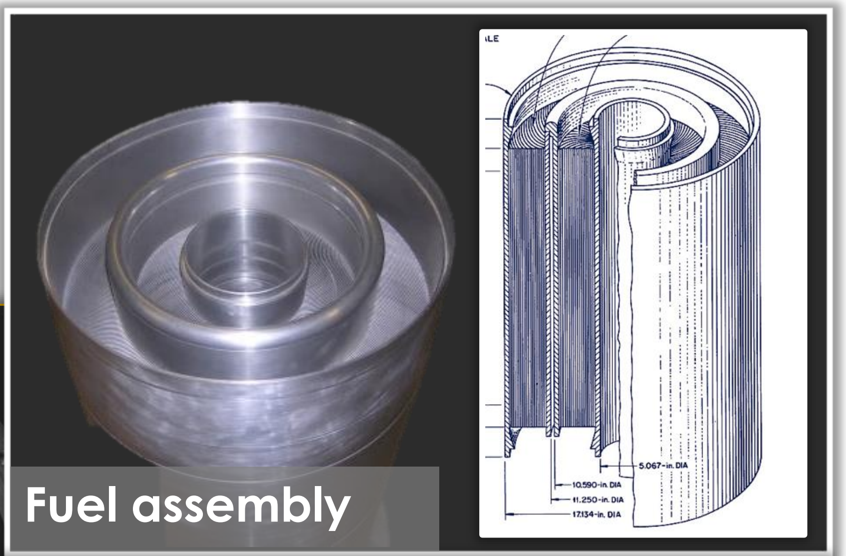
Inner fuel element (IFE)

Target basket

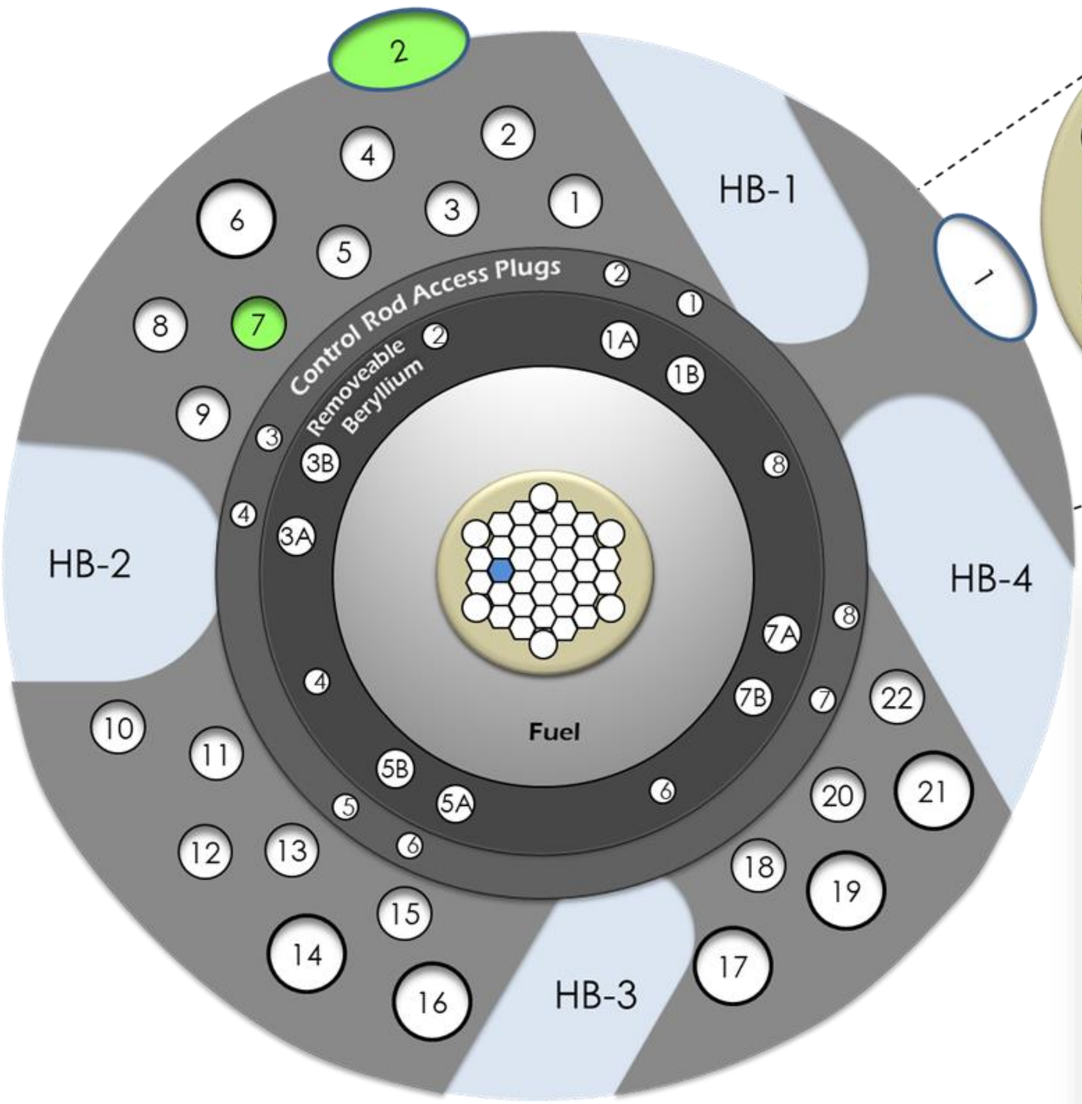
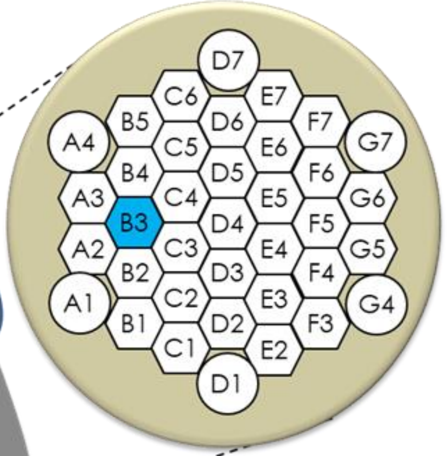


Beryllium

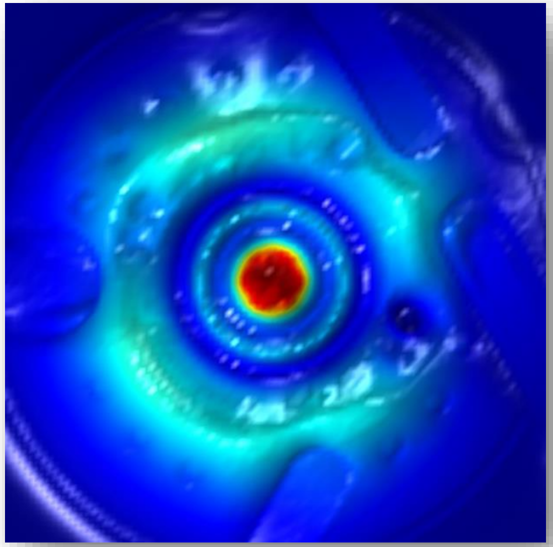
- Permanent (20 year life; replace in 2024)
- Removable



Irradiation capsule/experiment requirements are rigorous

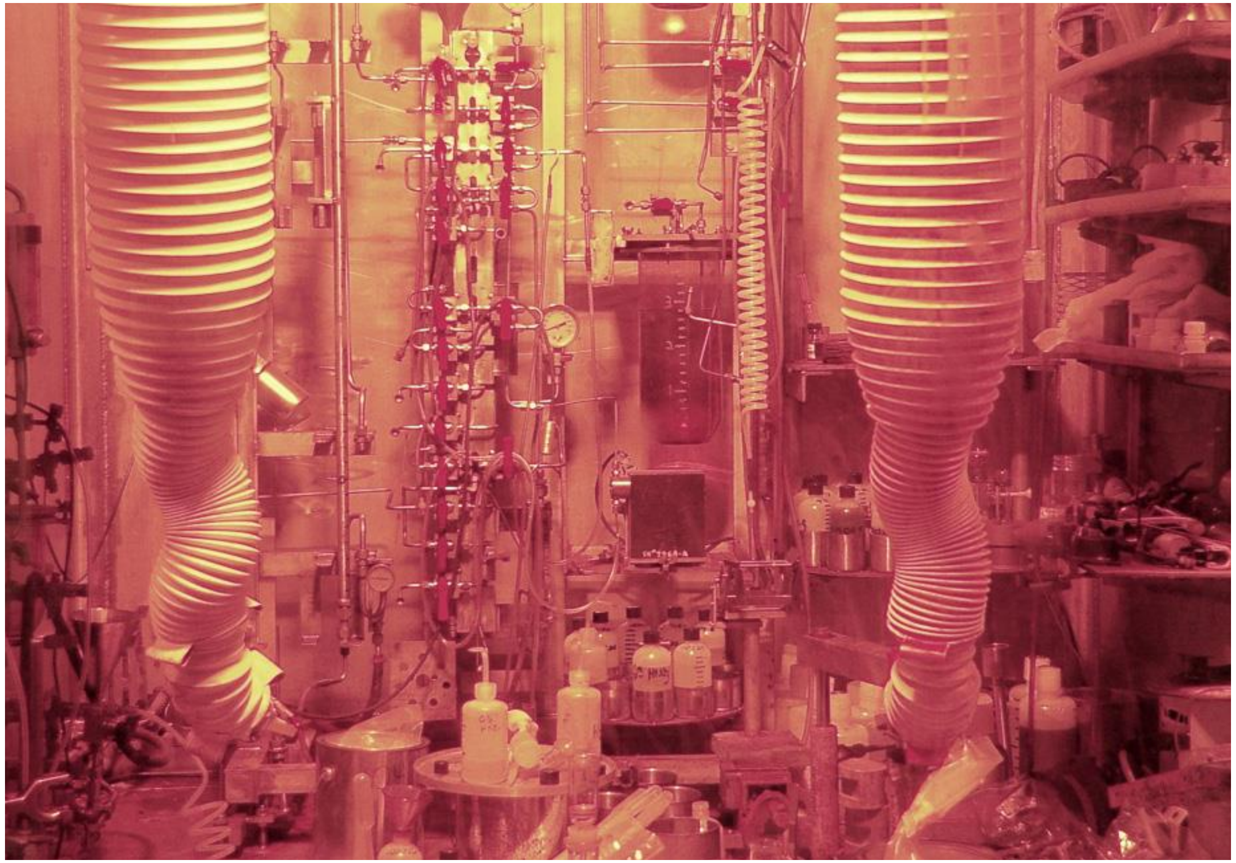
HFIR Mid-place cross-section



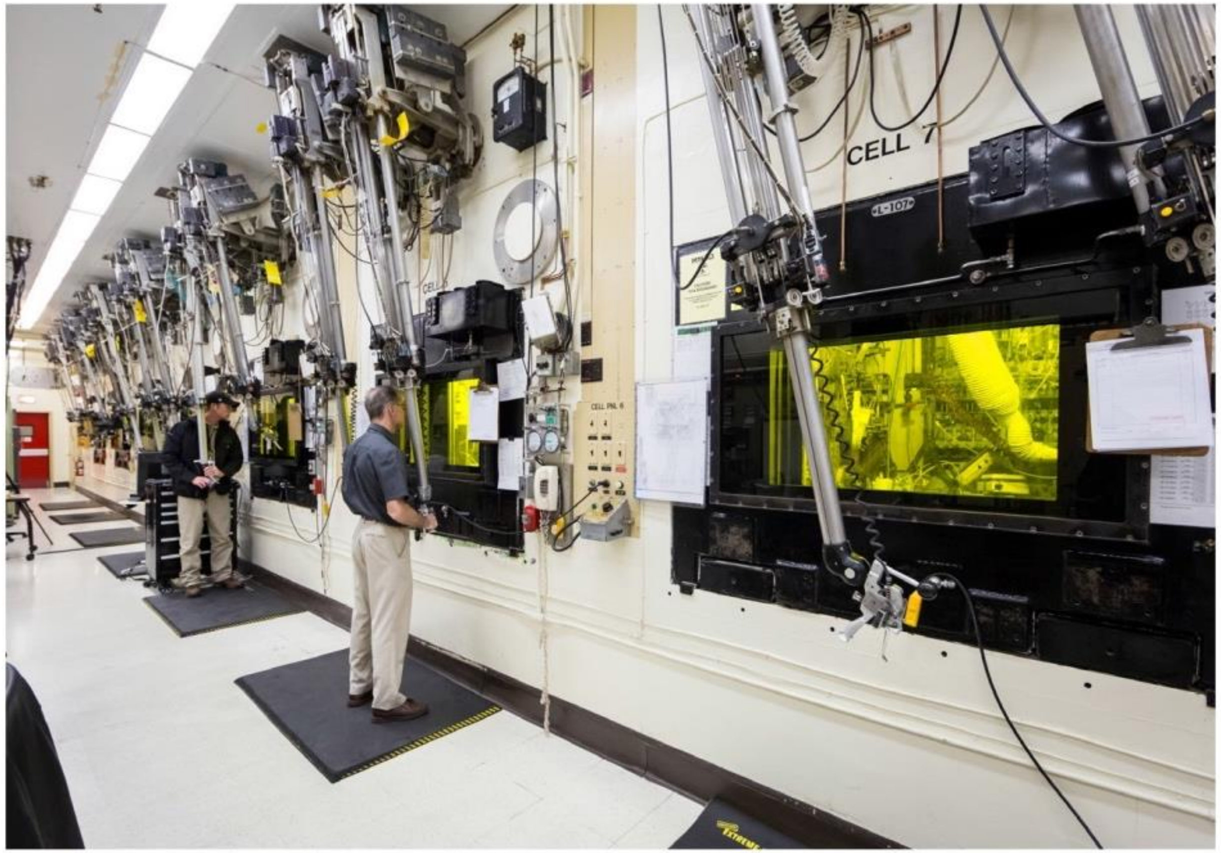
3D Thermal neutron flux surface plot of the HFIR core

- Neutronic core interactions
  - Flux tilt, cycle-length reduction, etc…
- Capsule heat removal
- Target material/cladding interactions
- Target material performance
  - Expansion, growth, compound formation, fission gas release, etc…
- Capsule integrity
  - Material certification, weld qualification, internal/external pressure capacity

Radioisotope chemical separation and purification have grown from the heavy element production program



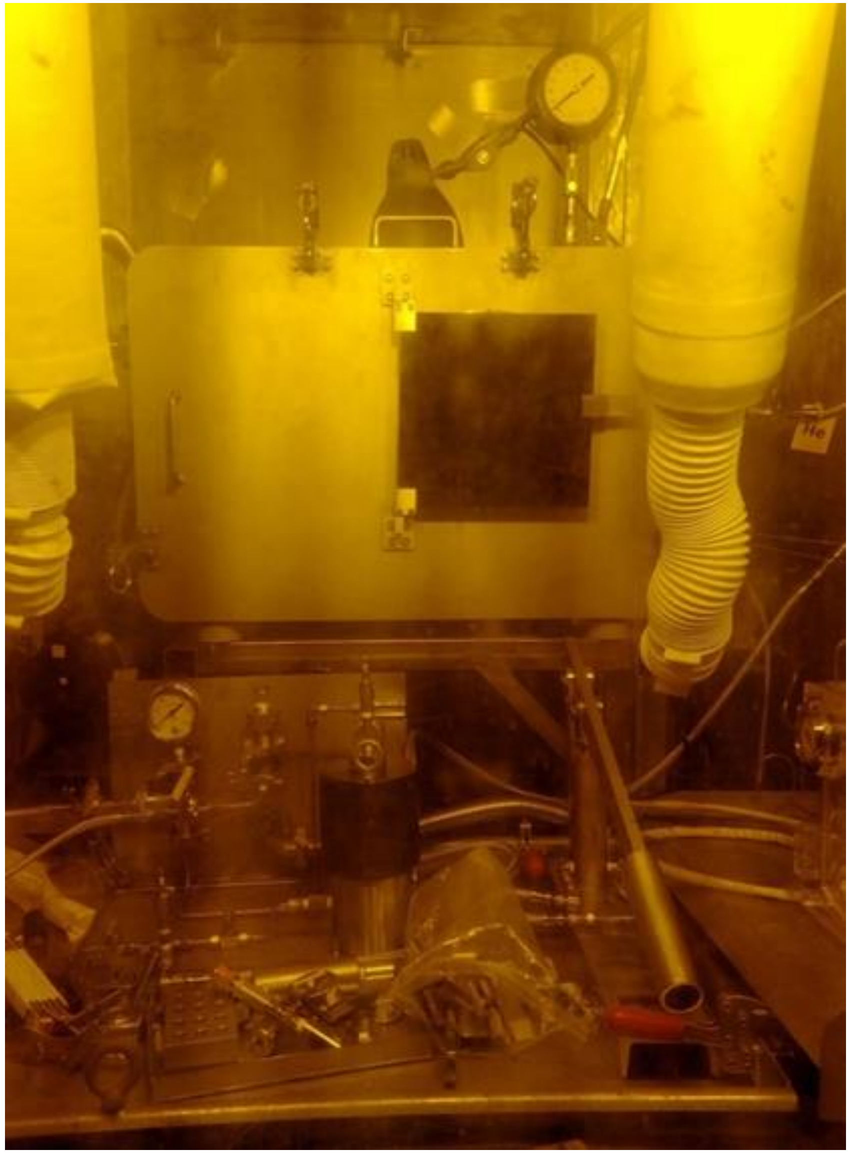
Main dissolution hot cell in the Radiochemical Engineering Development Center (REDC)



REDC hot cells are used for curium target fabrication/assembly and irradiated Pu-238 and Cf-252 target dissolution, separation and purification.

ORNL's hot cells and gloveboxes enable unique isotope production

- Hot target fabrication has history at ORNL
  - ORNL has multiple hot cells with this capability.
  - Most are irradiated in smaller rabbit capsules.
  - Some use HFIR hydraulic tube (less than 25d irradiation), while others require multiple cycle irradiations.

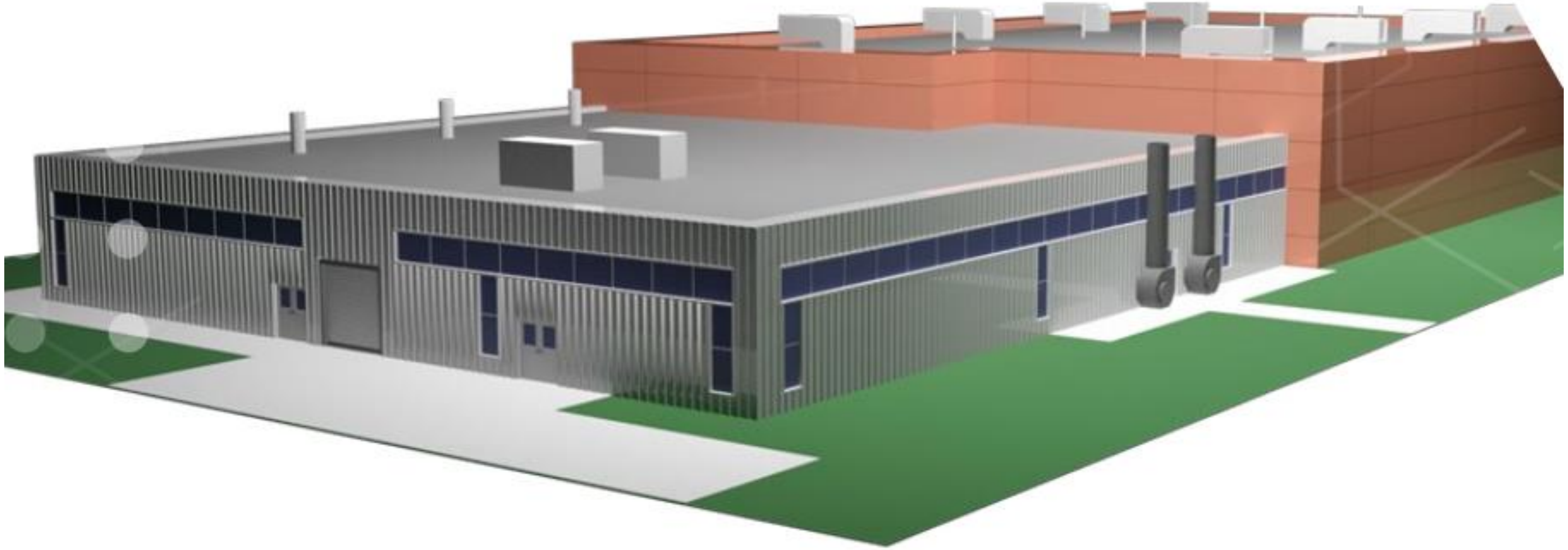


Assembly and welding of ^{226}Ra targets in an ORNL hot cell

Radioisotope Processing Facility (RPF) is a funded project that enables new isotope production plus expanded hot cell and glovebox processing capacity.

Proposed new isotopes possible through RPF

Iridium-192	**Strontium-90**	**Lutetium-177 (cGMP)**
Gadolinium-153	**Strontium-89 (cGMP)**	**Carbon-14**
Thorium-229	**Promethium-147**	**Phosporus-33**



Thank you!