The Supply of the Medical Radioisotope Tc-99m/Mo-99

Recent Shortages Call for Action in Developing a Domestic Production Capability

presented to the
American Nuclear Society
Trinity Section

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Outline

- Mo-99 Usage and Production
- The Current Shortage Crisis and Future Status
- History of Mo-99 Production in the US and the World
- Congressional Action Update
- Proposed Domestic Production Concepts
- The SNL Concept
  - Is There a Possibility for a New Mexico Production Facility?

Recent Headlines

Shortage Of Isotopes Hits Clinical Tests

U.S. Dependent On Other Countries After Sandia Labs' Plan Scrapped

- *Albuquerque Journal*
August 13, 2009

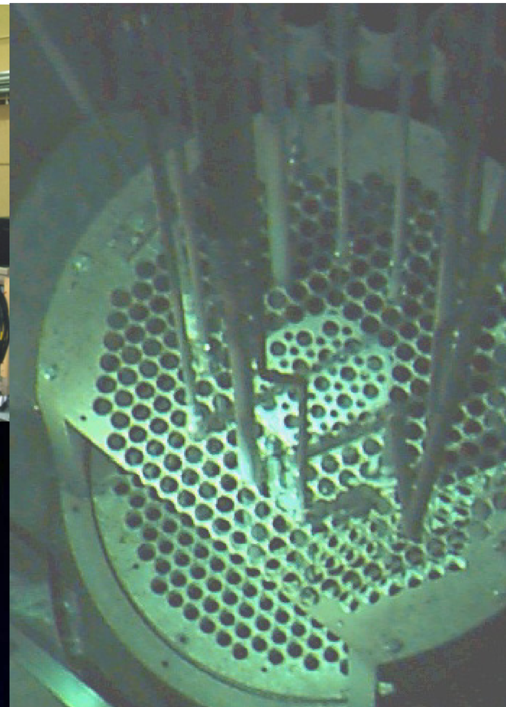
Canada's isotope production reactor will stay down until early 2010. …Since the National Research Universal (NRU) reactor is one of the main producers of radioisotopes for medical applications, its extended outage, which began on May 15 following the discovery of a small leak of heavy water, has led to worldwide shortages of medical isotopes, particularly molybdenum-99.

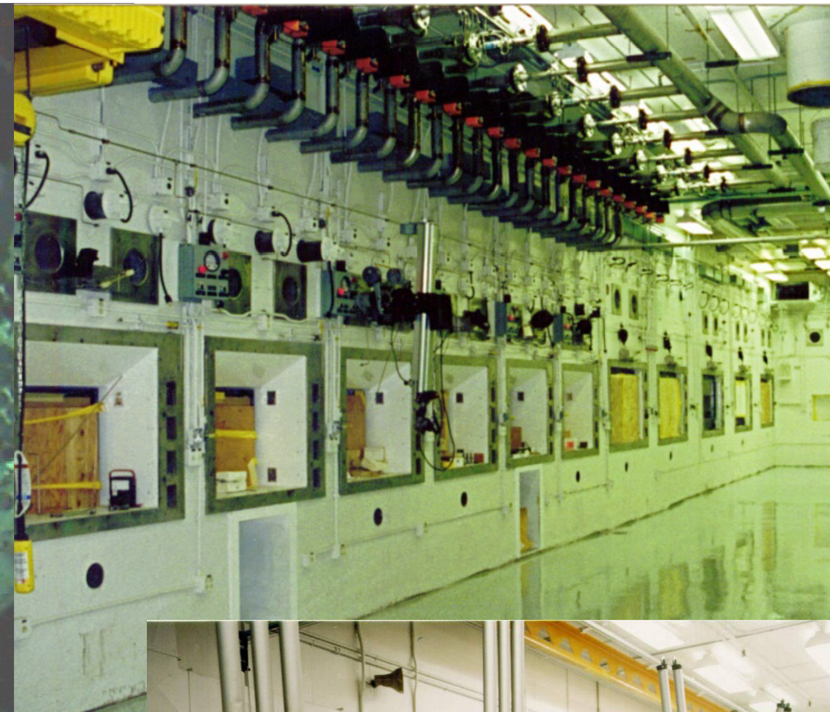
-*Nuclear News*
September 2009

AECL has pulled the plug on the MAPLE reactors project after failing to get the units into production after 12 years of development. …According to AECL, the decision will not have an impact on the supply of medical isotopes…

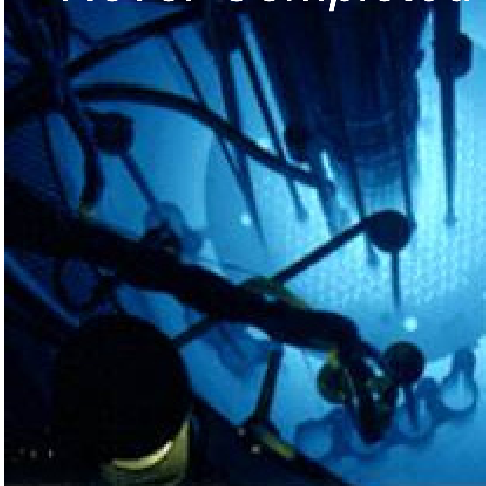
-*Nuclear News*
June 2008

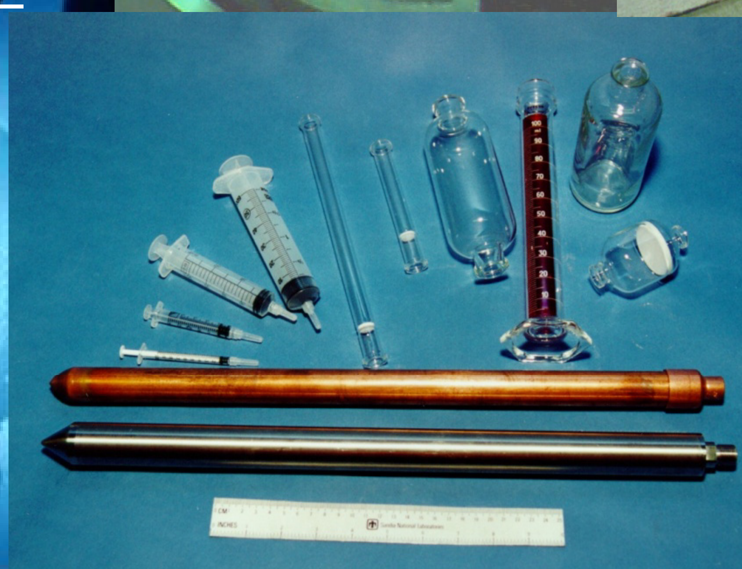
SNL Backup Supply?

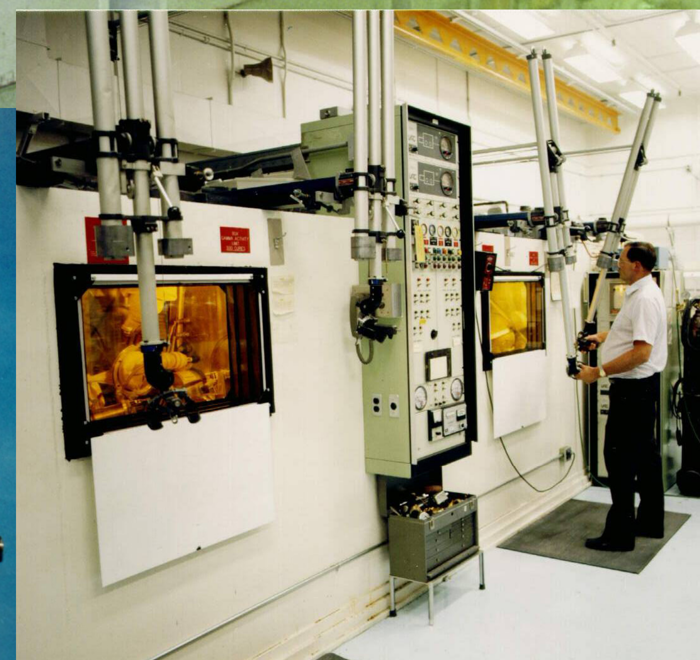




Sandia and Los Alamos were supposed to provide a backup supply for Mo-99 – *Never Completed*







Mo-99/Tc-99m Usage

Technetium-99m (Tc-99m) is the radioactive daughter product of molybdenum-99 (Mo-99). Tc-99m has a short half life (6 hrs) and emits a low-energy gamma ray (140 keV). It is readily "tagged" to a pharmaceutical that transports it to the location of interest in the body.

Technetium-99m (Tc-99m) is the primary medical radioisotope used today for performing diagnostic imaging procedures.

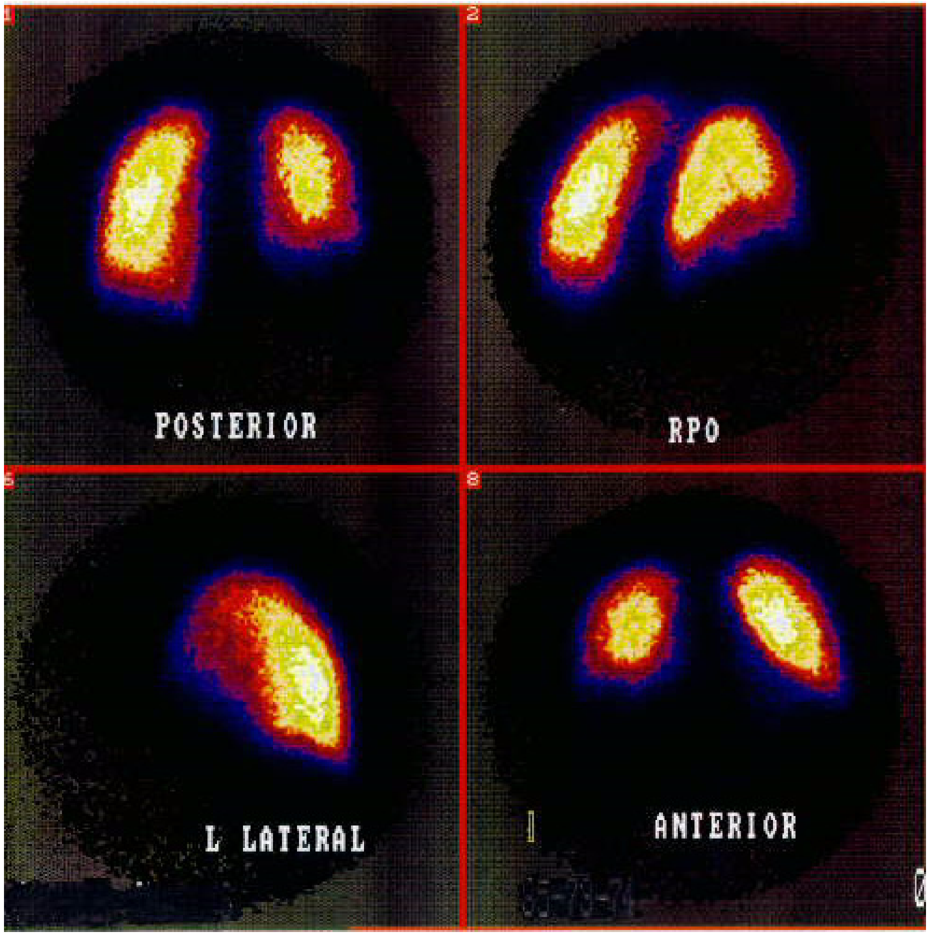
Tc-99m imaging can be performed on the skeleton, blood, intestines, brain, heart, thyroid, lungs, liver, gallbladder, kidneys, and muscles. It is used to detect stress fractures, blood flow abnormalities, tumors, and organ function abnormalities.

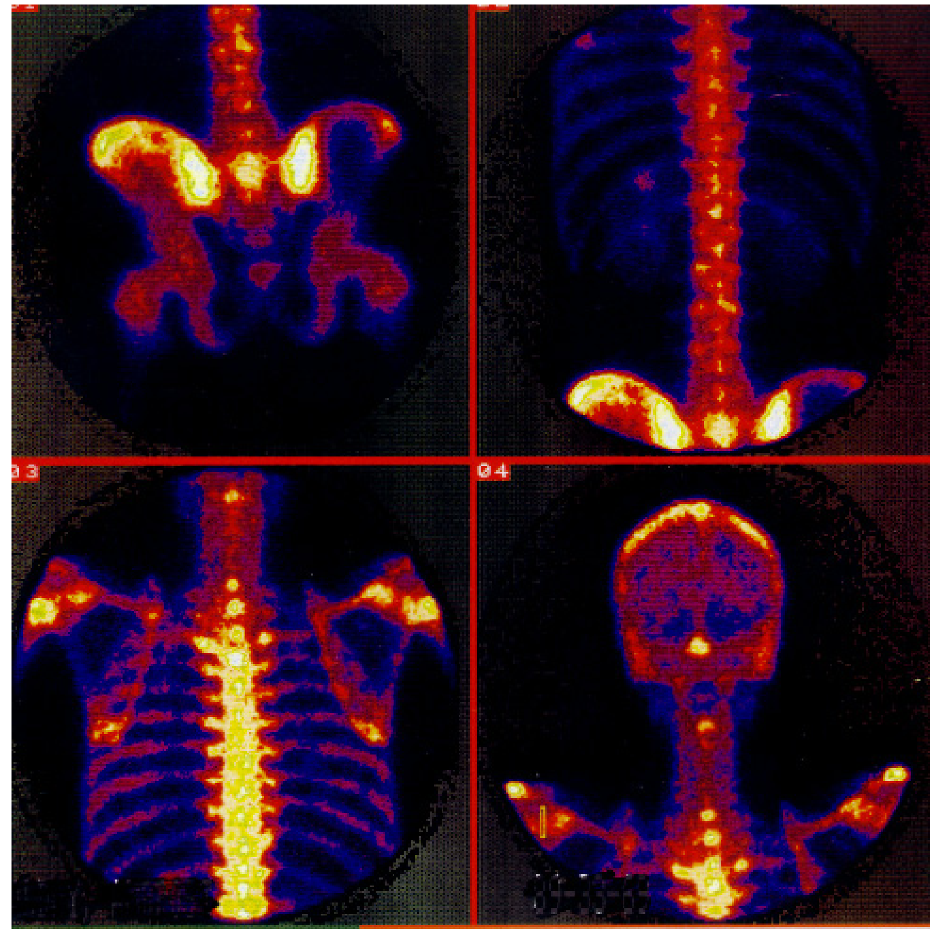
85% of all medical radioisotope procedures use Tc-99m. Tc-99m is used in more than 30 radiopharmaceuticals. About 50,000 Tc-99m-based diagnostic procedures are performed in the US every day, or about 13 million per year.

Usage is growing at 5-10% per year.

If you have ever gone into the hospital for a radio-imaging procedure, chances are you were given Tc-99m.

Tc-99m Lung and Skeletal 2-D Images





Alternatives to Mo-99/Tc-99m

Tc-99m is not the only radiopharmaceutical that can be used for imaging.

Positron Emission Tomography (PET) is also very useful – especially in determining the location and size of tumors.

PET uses a cyclotron to produce a positron-emitting, short-lived radioisotope (e.g. F-18, $T_{1/2}$= 109 minutes) that is then tagged to a pharmaceutical.

Advantages:

- Higher resolution and better 3-D images than Tc-99m due to use of coincidence counting (two 0.511MeV gammas given off in directly opposite directions).

Disadvantages:

- Short lived radioisotopes
  - Generated and used on-site or within a very limited range
  - Patient / Staff / Imaging Machine / Cyclotron timing must be well coordinated
  - No unplanned imaging
  - Cyclotron maintenance and unplanned outages
- Cyclotron is expensive to buy and operate.
- Imaging more expensive - insurance companies and Medicare reluctant to pay

Tc-99m will most likely remain the workhorse in the radio-imaging industry for many years to come.

Whole Body F-18 3-D Image

See Wikipedia – Positron Emission Tomography

For 3-D images of PET

Mo-99/Tc-99m Distribution

Tc-99m is made from the radioactive decay of Mo-99 "Moly-99."
Mo-99 is what is actually distributed from the processing facility to the radiopharmaceutical company.

The Mo-99 is shipped on a regular basis (several times a week) to the radiopharmaceutical company from the processing facility in a few hundred milliliters of solution within a shielded DOT container.

At the radiopharmaceutical company, Mo-99 is "loaded" onto an alumina column. The column, with other hardware and a shield, form the "Moly Generator," "Generator," or "Cow."

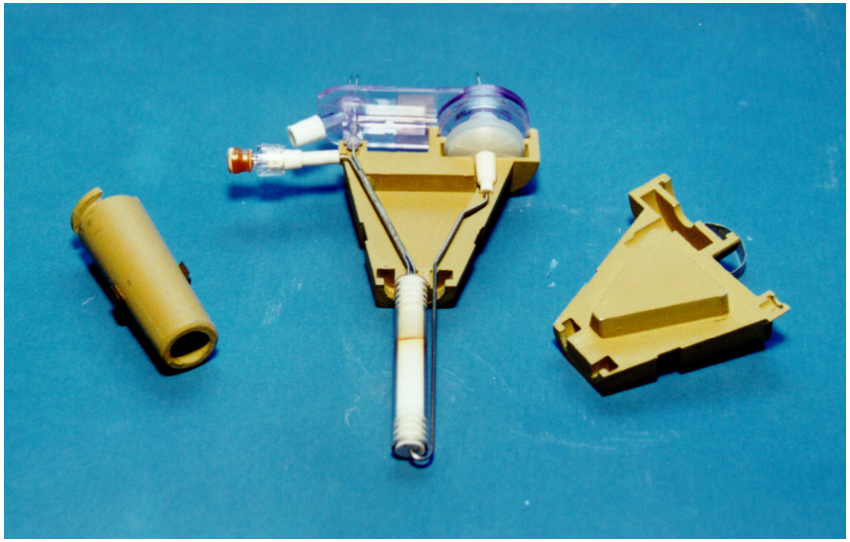
The generator is sent to the hospital radiopharmacy. The Mo-99 decays ($T_{1/2}$= 2.75 days) to Tc-99m ($T_{1/2}$= 6.0 hours). The Tc-99m can be "eluted" or "milked" from the generator using a solution. The Tc-99m is then used to form the radiopharmaceutical that is given to the patient. Images of the organ of interest are taken in time.

After the Mo-99 generator has decayed to a sufficiently low level, the generator is sent back to the radiopharmaceutical company for reuse.

Mo-99/Tc-99m Generator

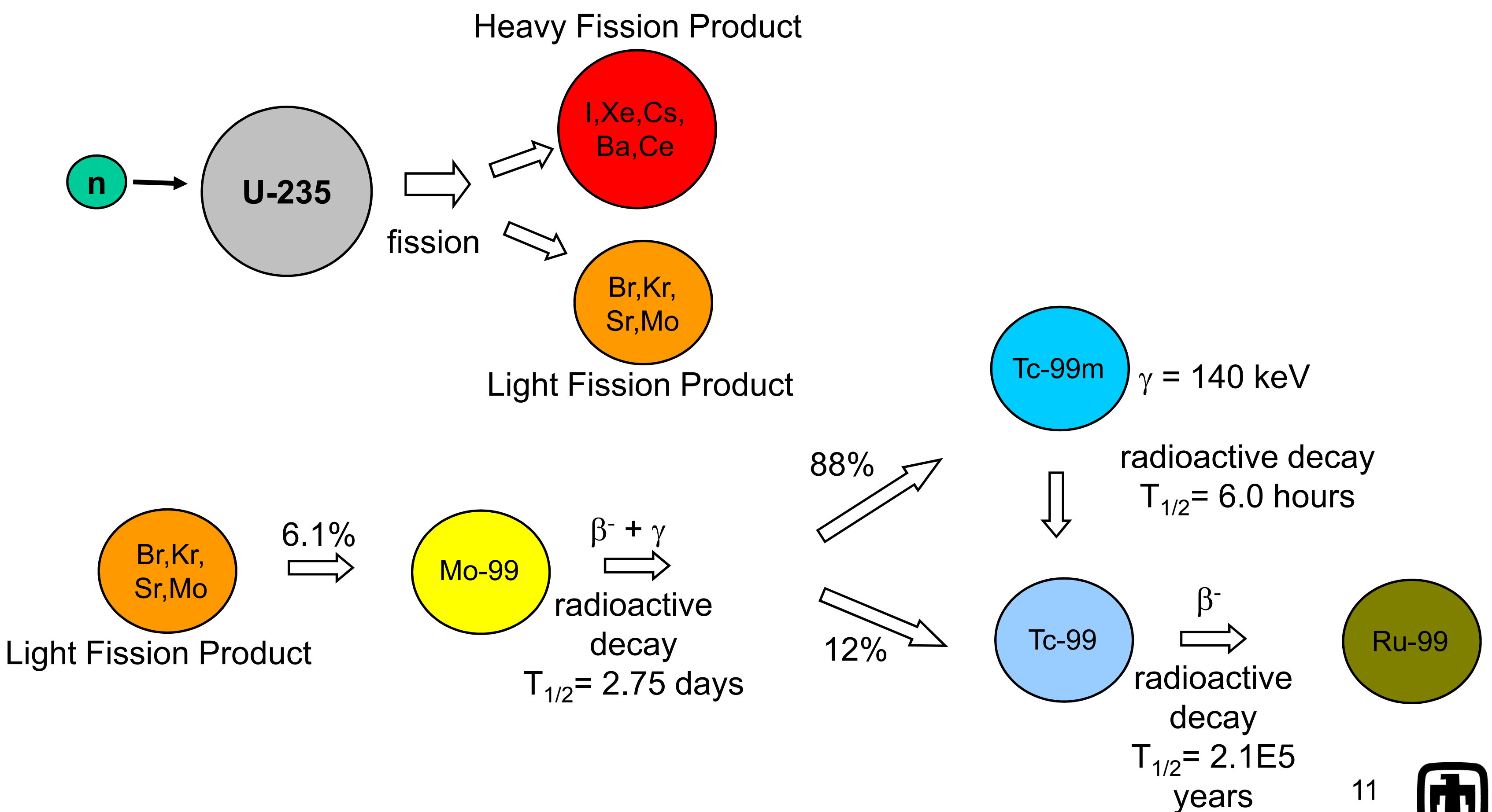
Major US Pharmaceutical Companies:

- Covidien (Tyco) / Mallinckrodt - Missouri
- Lantheus (Brystol-Myers Squibb) - Massachusetts



Mo-99/Tc-99m Production Using Fission

Although Mo-99 can be made by neutron activation of Mo-98, or other exotic accelerator techniques, the world's supply is made by fission of U-235 – "fission moly." Fission moly allows for a high production quantity and a high specific activity.



Mo-99 Demand

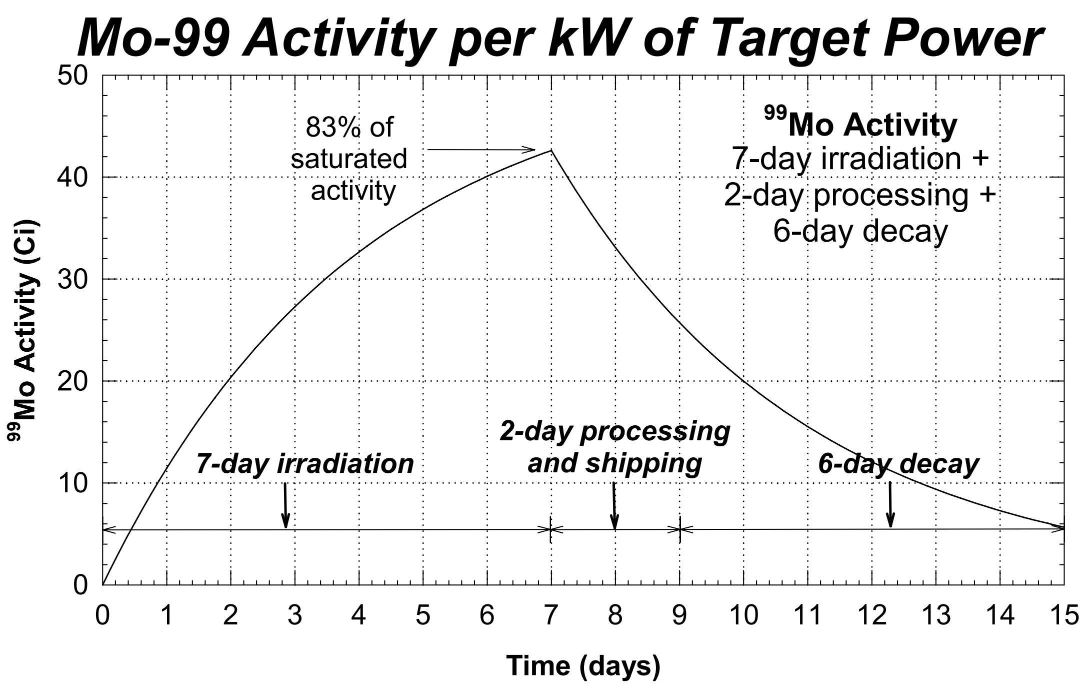
Current US demand for Mo-99 is ~6,000 $Ci_{6\text{-day}}$

World demand (excluding US) is ~6,000 $Ci_{6\text{-day}}$

Demand is growing at a rate of 5-10% per year

Price of Mo-99 is ~$470/ $Ci_{6\text{-day}}$

Revenue from the US demand of Mo-99 = ~$150M/year



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Mo-99 Production Requirement to Meet US Demand

What is the fission power requirement in the targets to meet the current US demand for Mo-99 at ~6,000 $Ci_{6\text{-}day}$?

$$Saturated\ Activity = A_\infty = Production\ Rate$$

$$A_\infty = P(kW) \cdot f(fis/kW \cdot s) \cdot \gamma(^{99}Mo/fis) \cdot C(Ci/dis/s)$$

$$A_\infty = 51.1\ Ci\ ^{99}Mo / kW$$

$$Activity\ for\ t_i\ irradiation = A(t_i) = A_\infty \cdot (1 - e^{-\lambda t_i})$$

$$7 day\ irradiation \Rightarrow A(7 day) = 0.83 \cdot A_\infty = 42.4\ Ci\ ^{99}Mo / kW$$

$$Activity\ after\ t_d\ decay = A(t_d) = A_\infty \cdot (1 - e^{-\lambda t_i}) \cdot (e^{-\lambda t_d})$$

$$2 day\ decay \Rightarrow A(2 day) = 0.60 \cdot A(t_i) = 25.4\ Ci\ ^{99}Mo / kW$$

$$2 day\ decay \Rightarrow A(6 day) = 0.22 \cdot A(t_i, 2 day) = \underline{5.6\ Ci\ ^{99}Mo / kW}$$

$$\lambda = ln(2)/T_{1/2} = 0.252\ /day$$

Mo-99 Production Requirement to Meet US Demand

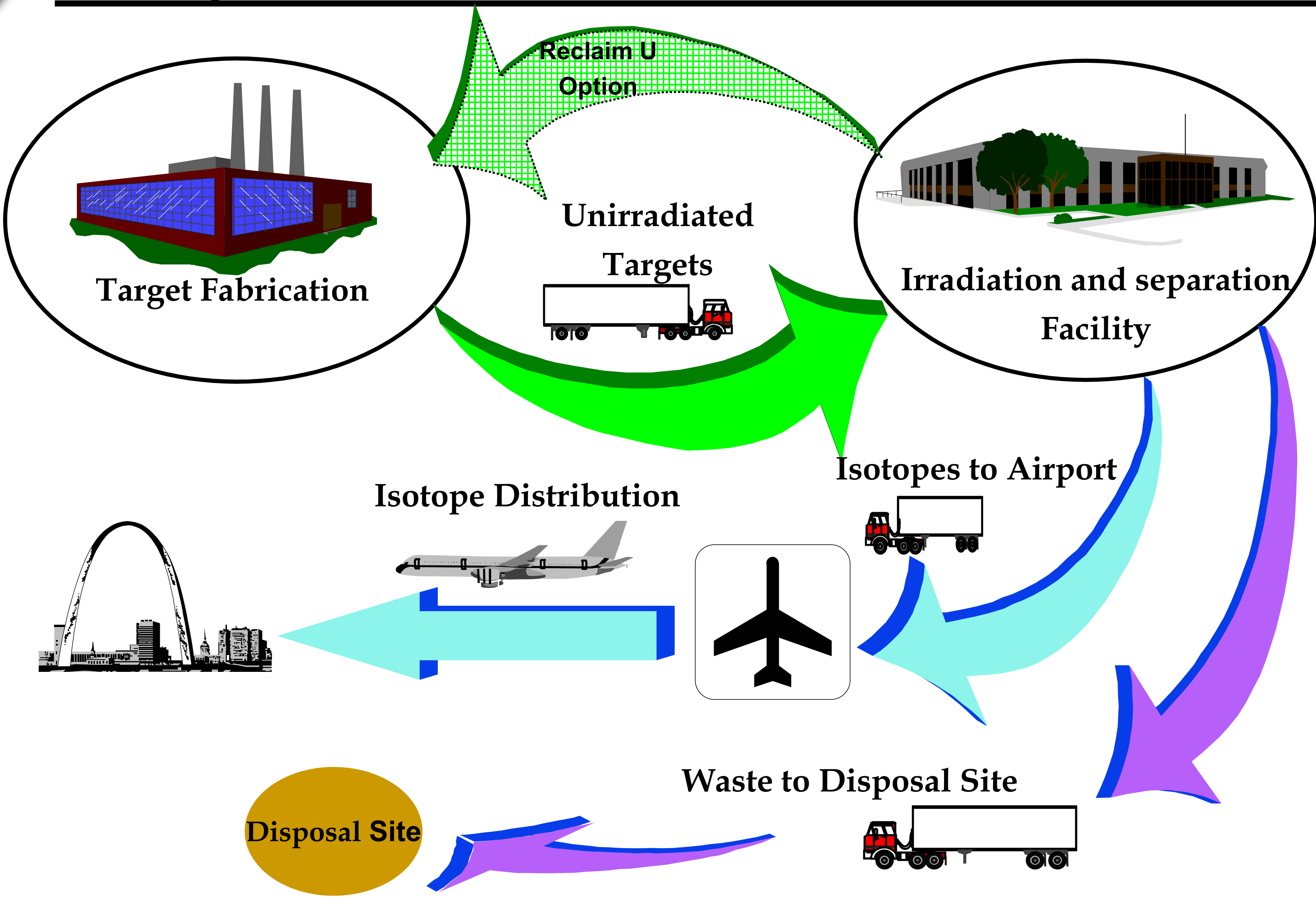
$$Fission\ Power\ Reqd. \Rightarrow P(kW) = 6000\ Ci_{6day} / 5.6\ Ci\ {}^{99}Mo / kW$$

$$\boxed{P(100\%\ US\ demand) = 1070\ kW\ \ target}$$

$$P(50\%\ US\ demand) = 535\ kW\ \ target$$

$$P(20\%\ US\ demand) = 214\ kW\ \ target$$

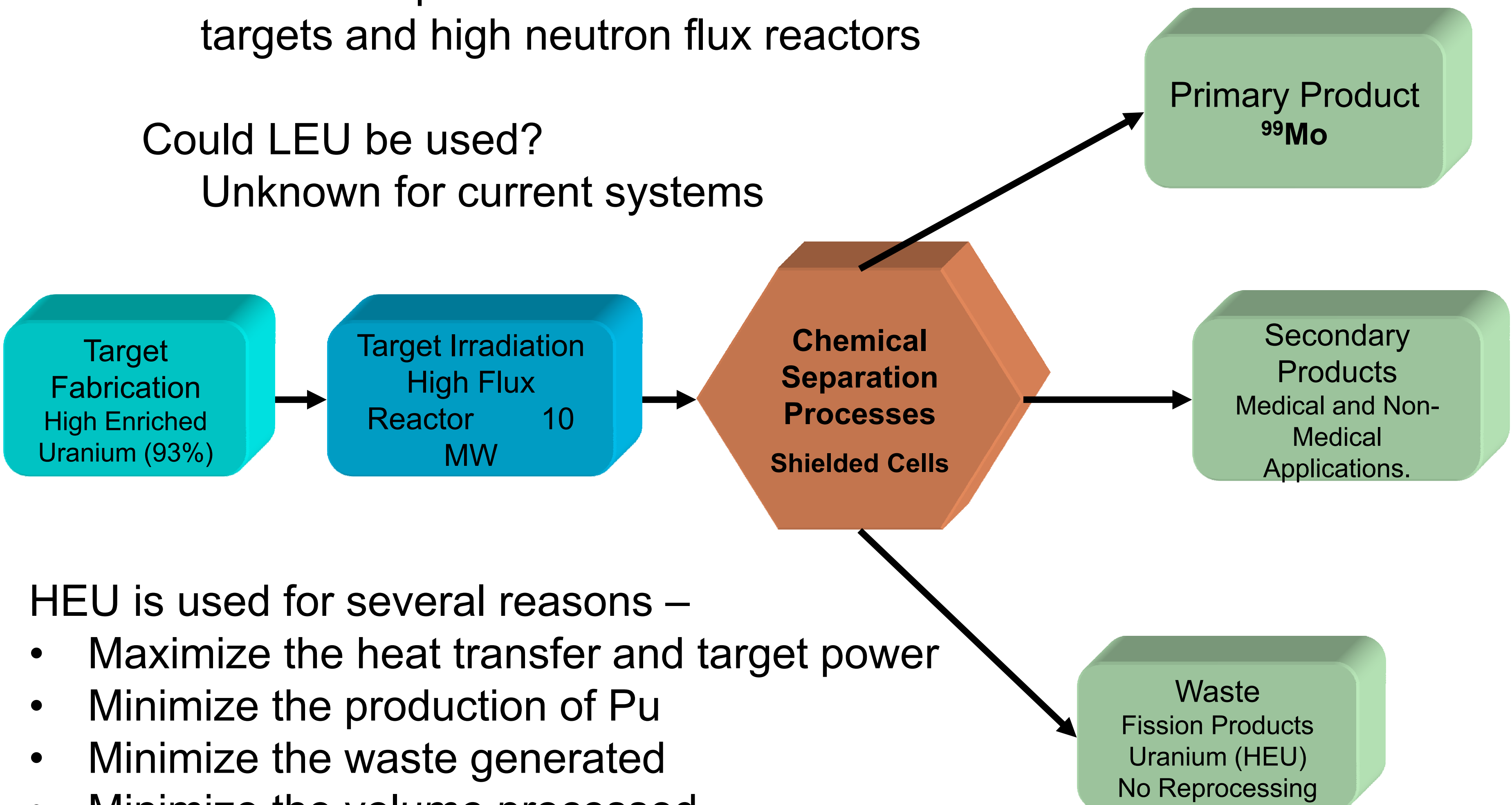
Transportation Links in the Production Process



Processing Steps – Current

Current world production uses HEU in the targets and high neutron flux reactors

Could LEU be used?
Unknown for current systems



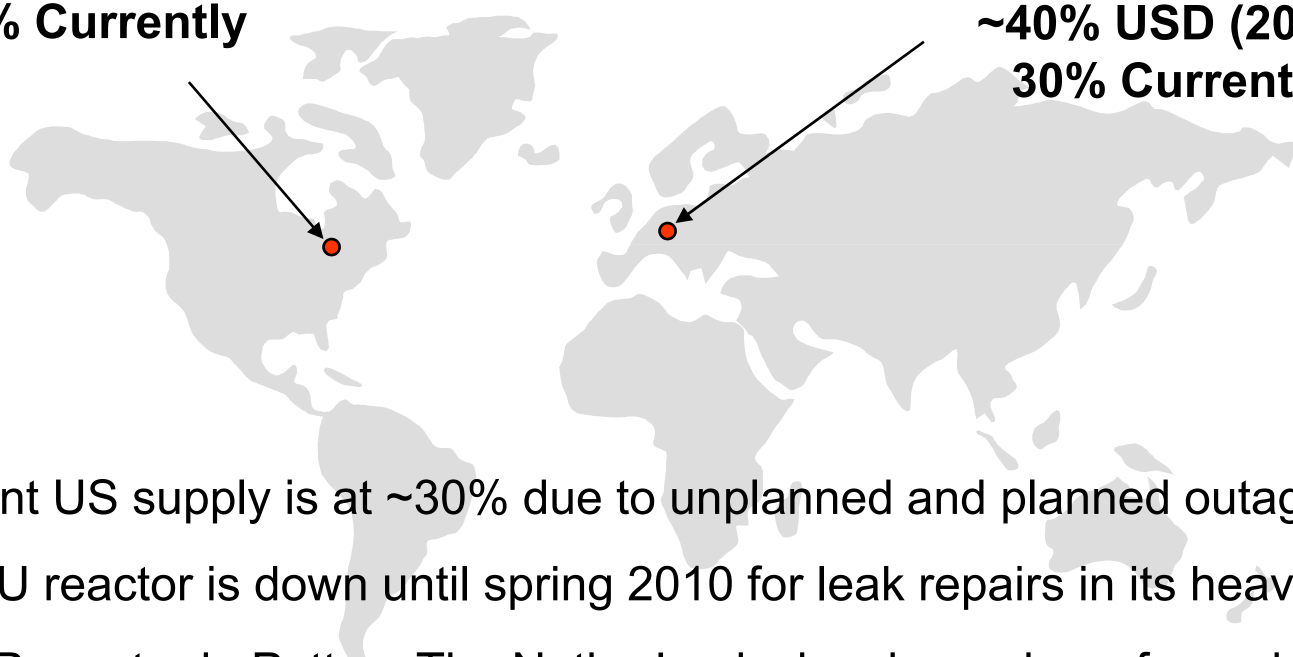
HEU is used for several reasons –

- Maximize the heat transfer and target power
- Minimize the production of Pu
- Minimize the waste generated
- Minimize the volume processed
- Maximize the product purity

US Supply of Mo-99

AECL/Nordion
NRU
~60% USD (2008)
0% Currently

Consortium of Belgium,
The Netherlands, French reactors
Processing by IRE (Belgium) and
Covidien (Petten)
~40% USD (2008)
30% Currently



The current US supply is at ~30% due to unplanned and planned outages

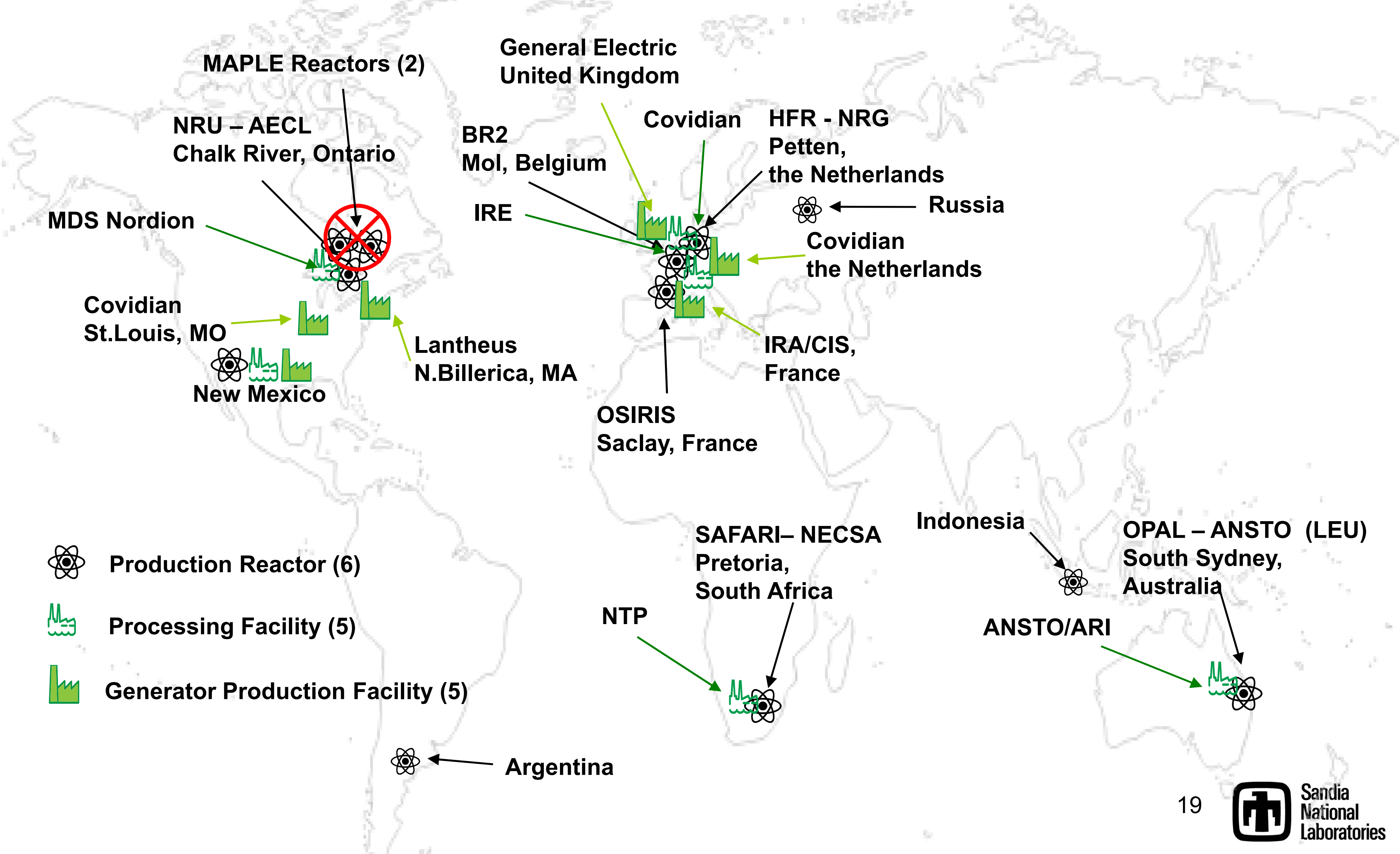
- NRU reactor is down until spring 2010 for leak repairs in its heavy water tank
- HFR reactor in Petten, The Netherlands, has been down for maintenance this past summer. It is scheduled to go down in spring 2010 for major repairs of the primary cooling system (26 weeks).

Mo-99 Shortages and Supply Vulnerabilities

- Mo-99 Cannot be stockpiled - all gone in two weeks
- There have been several planned and unplanned outages at the production sites
  - NRU reactor is down until spring 2010 for leak repairs in heavy water tank
  - HFR will be down for 26 weeks in spring 2010
- The current reactors are old (50 years)
- The current reactors are subsidized by their governments
- The current reactors do not have commercial production of radioisotopes as their only mission
- All current reactors use HEU targets - Pressure to use LEU targets and fuel
- There is no domestic supply – no backup supply – a backup supply was to exist at SNL in the 1990s using LANL fabricated targets
- The MAPLE reactors will not be operated in Canada
- There are no large scale plans to build new facilities abroad
  - Possibly one in The Netherlands (2016)

World ^{99}Mo Production Sites

The U.S. demand for ^{99}Mo is ~6,000 six-day Ci per week.
The world demand (excluding U.S.) is ~6,000 six-day Ci per week.



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Mo-99 Supply Solution

The only serious and lasting solution is an LEU-based domestic reactor/processing facility dedicated to ensuring a robust US supply. The reactor system should be:

- Designed exclusively for commercial Mo-99 production
- Designed to use LEU fuel and targets
- Operational at low power and passively safe
- Drawing upon proven technology with little research effort
- Economically viable/profitable

There is currently a bill in the US House (HR3276) to provide $160M over 5 years to develop a domestic supply of Mo-99 using LEU fuel.

The radiopharmaceutical companies are interested and have much to gain – or lose. They have invested some of their own resources, but to date have not committed to building a new reactor/hot cell facility.

Mo-99 Supply History

1980s – Canada (AECL/MDS Nordion) and a domestic source (Cintichem, Inc. – Tuxedo, NY) supplying Mo-99 to US.

1989 – Cintichem reactor and processing facility shutdown due to operational issues. Facilities decommissioned.

Early 1990s – Canada only supplier; some labor relations issues. Congressional action mandates DOE to develop a domestic backup supply.

1991 – DOE purchases the right to the Cintichem process, equipment, and the Drug Master File (DMF) for the production of Mo-99, I-131, Xe-133, and activation isotope I-125.

1991 – DOE identifies Omega West Reactor (OWR) and the CMR at LANL as proposed backup supply facility.

1992 – Leak discovered in OWR primary coolant pipe. Ultimately leads to the shutdown of OWR.

1996 – DOE selects Annular Core Research Reactor (ACRR) and the HCF at SNL to become backup facility. LANL to fabricate targets. EIS prepared and ROD signed.

1998 – Canada (AECL/MDS Nordion) petitions Clinton administration to discontinue development of a backup supply. Canada is building two new 10 MW reactors (MAPLE 1 & 2) that will adequately supply the world.

Mo-99 Supply History (cont)

1998 – SNL/LANL modification efforts cease with ~80% completion of HCF.

Late 1990s – Mallinckrodt invests in European Consortium to produce significant quantities of Mo-99.

Early and Mid 2000s – NRU operating in Canada and European Consortium providing virtually the world's supply. No major interruptions occur.

2008 – AECL cancels the MAPLE reactors after a investing ~$500M over a 12 year period. Major problem is a positive reactivity feedback coefficient at power.

2009 – NRU develops problems including a leak in its heavy water tank. HFR also develops a leak in its primary coolant piping that will take a half year to fix in 2010.

2009 – US congress proposes isotope production bill to establish a domestic supply of Mo-99 using HEU - $160M over five years.

2009 – US continues to push for targets to be LEU

The US finds itself in the same situation it was in during the 1990s. We are relying on foreign sources for a critical medical radioisotope without enough backup suppliers.

Mo-99 Domestic Supply Concepts

- Modification of existing facility (Fission Moly)
  - University of Missouri (MURR)
    MURR is a 10 MW research reactor. They want to build a hot cell facility ($70M) and irradiate 20% HEU targets in reflector region of core. Could produce 20 to 50% USD.

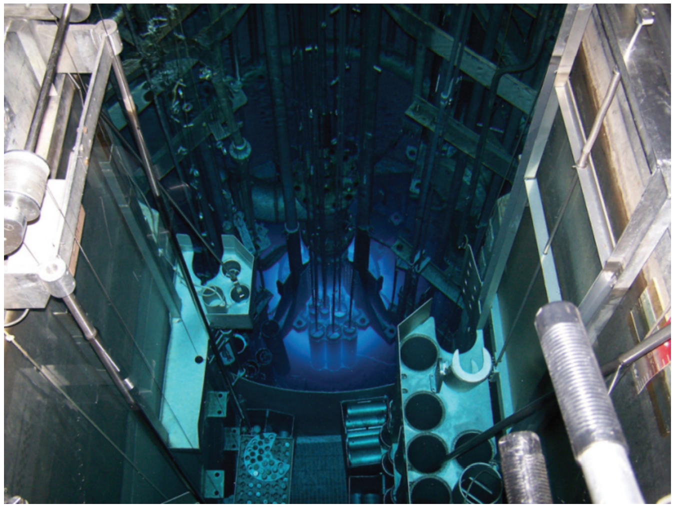
- Build new facility (Fission Moly)
  - Babcock and Wilcox solution reactor concept
    A uranyl nitrate 20% enriched solution that is operated as a reactor at ~200kW. Liquid is processed in a batch mode to remove Mo-99. Could produce ~20% USD.

  - SNL Medical Isotope Reactor Concept
    A small passively safe reactor where the 20% enriched UO2 fuel pins are also the targets. Operates at ~2 MW and could produce 200% USD.

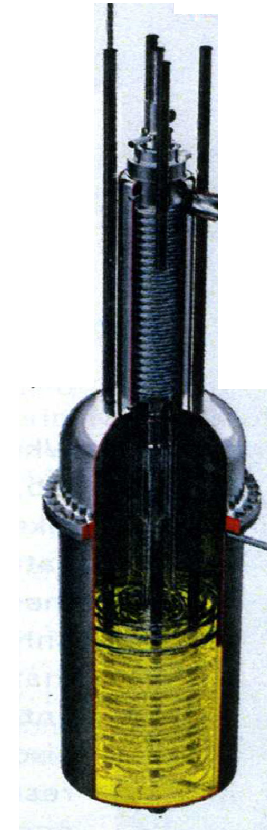
- Accelerator Driven Subcritical Reactor Facilities (Fission Production)

- Non-Fission Production by Accelerator or Reactor

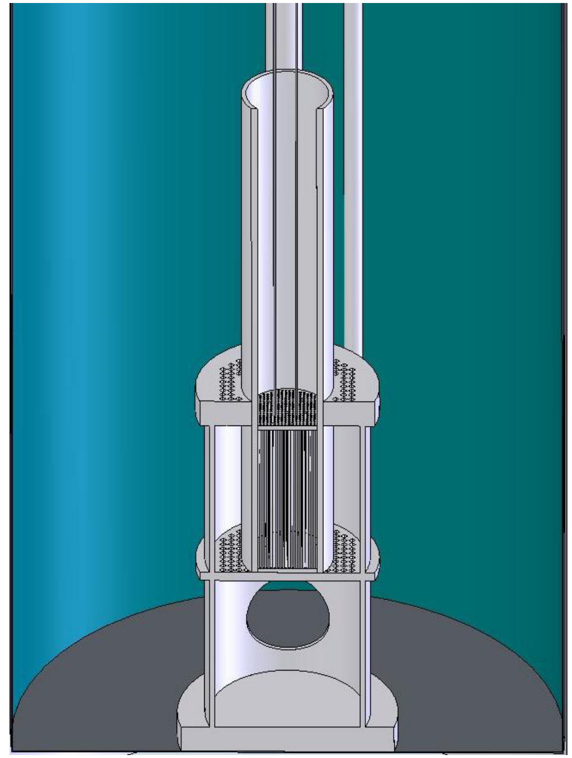
Domestic Supply Reactor Concepts



MURR
10 MW Reactor
Potential 20-50% USD
Weekly batch processing



B&W Solution Reactor
200 kW Uranyl Nitrate Solution Reactor
Potential 20% USD
Weekly batch processing



SNL Pin Reactor
1-2 MW pin core
Potential 100% USD with additional international customer exports
Daily batch processing

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Reactor Concept Issues

MURR

+ Licensed Reactor

+ Reactor Operates 24 hrs/d

+ Reactor Staffed

+ Currently Process Isotopes

- Multi-program

- HEU Fueled

- Irradiation Volume
Target number

- Neutron Flux / Target Power
Flux at target
Target LEU mass
Cooling limitations

- No HCF
Must build new HCF

- Hot Target Handling
Heavily shielded transfer
Remote transfer to cask

- Environmental Impact and Safety Basis Approval
Near campus, stadiums, and golf course

B&W Solution Reactor

+ Low Power

+ Low Fuel Cost

+ Minimum Unprocessed Fuel Waste

+ Minimal Core FP Inventory

- Licensing
No NRC Precedent

- Controllability
Bubble/voiding dynamic reactivity effects

- Hydrogen/Oxygen Generation
Significant quantities generated due to radiolytic decomposition of fission fragments in water

- Product Purity
Buildup of Pu-239 recycled fuel

- Coolability
Cooling of core limited

- Criticality
Liquid fuel processing

- Low Technology Readiness
Liquid fuel processing and Mo-99 product removal

SNL Pin Concept

+ Low Power
non-power reactor (NRC)

+ Proven Technology
Fuel, Pool, Drives, Instrumentation, Cooling, Operability

+ Precedent for NRC

+ Collocated HCF

+ Natural Circulation Cooling
No pumps required for core cooling
Passive shutdown cooling

+ Minimum Unprocessed Fuel Waste

+ Minimal Core FP inventory

- Target Power Uncertain
Maximum target power must be determined

Waste and waste disposal is a common issue for all concepts

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SNL Pin Concept

Goal – simple, passively safe, accessible, proven technology, low cost

In the late 90's SNL investigated a reactor system composed solely of HEU Cintichem targets instead of using a driver reactor core.

An even simpler system results if oxide pins similar to LWR pins replace the Cintichem targets. The pins would be similar to LWR oxide fuel but would be 20% enriched and ~30 cm in length. Reactor core would be ~30 cm in diameter x ~30 cm in length

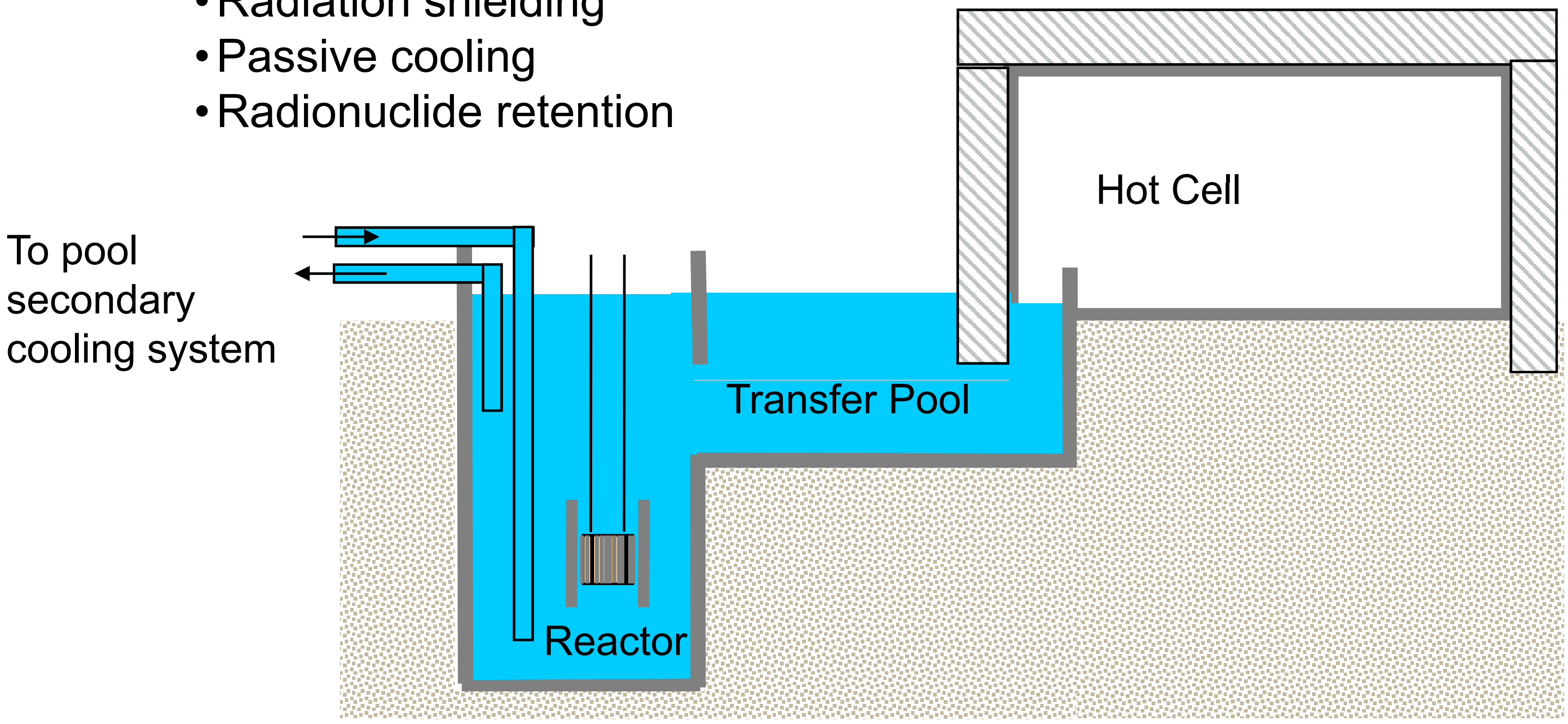
The major advantages include:

- An open swimming pool reactor system
- Current technology uranium oxide pins and targets
- LEU fuel and LEU targets - they are one and the same.
- Interchangeable driver fuel and targets – minimize driver fuel and FP inventory
- Target pitch selected to give:
  - -Negative temperature and void reactivity coefficient (power coefficient)
  - -Minimum core size
- Natural convection cooling of the core. Pool is cooled using heat exchanger.
- Low power ~2 MW
- Passively safe – no backup power supply or shutdown cooling requirements
- Simple control system that is easy to operate
- Water channel connecting reactor pool to co-located hot cell
- Can provide well over 100% USD
- Can be shown to be cost effective

SNL Reactor Pool Layout

Swimming Pool Concept provides:

- Accessibility
- Radiation shielding
- Passive cooling
- Radionuclide retention



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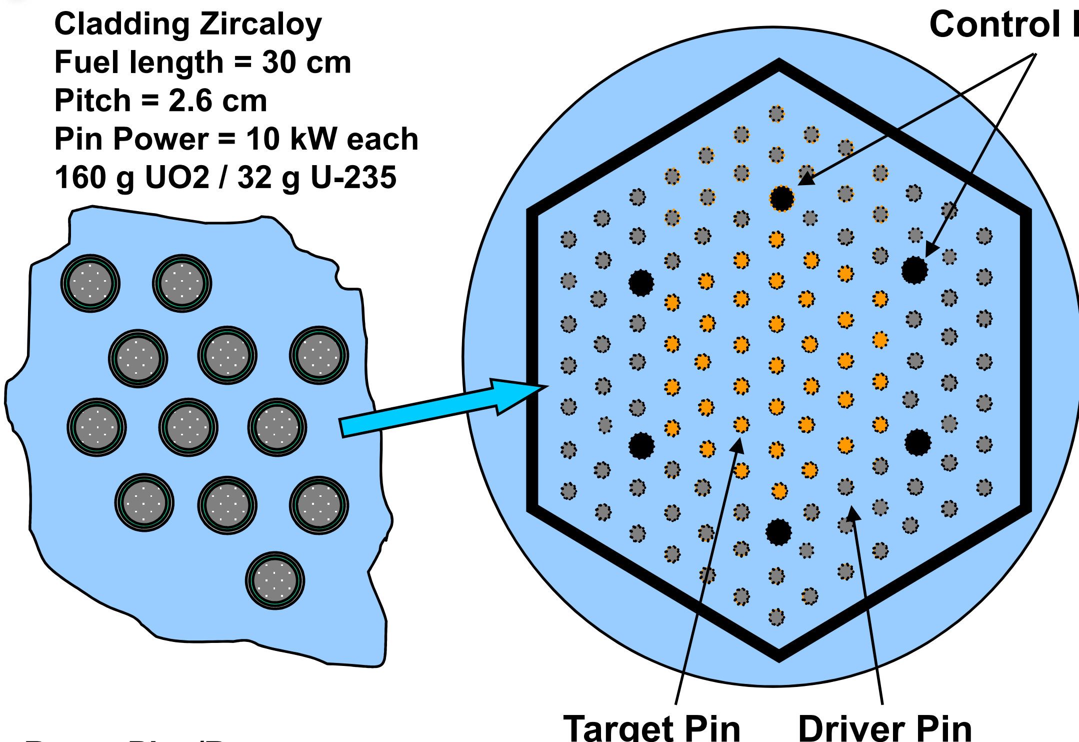
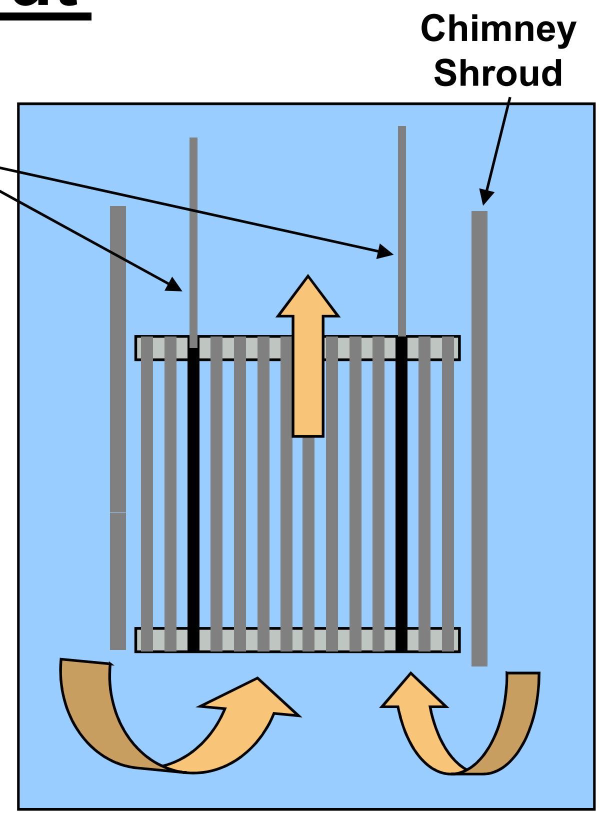
Example Core Layout

Oxide Fuel 20%enr OR = 0.413 cm
Cladding Zircaloy
Fuel length = 30 cm
Pitch = 2.6 cm
Pin Power = 10 kW each
160 g UO2 / 32 g U-235



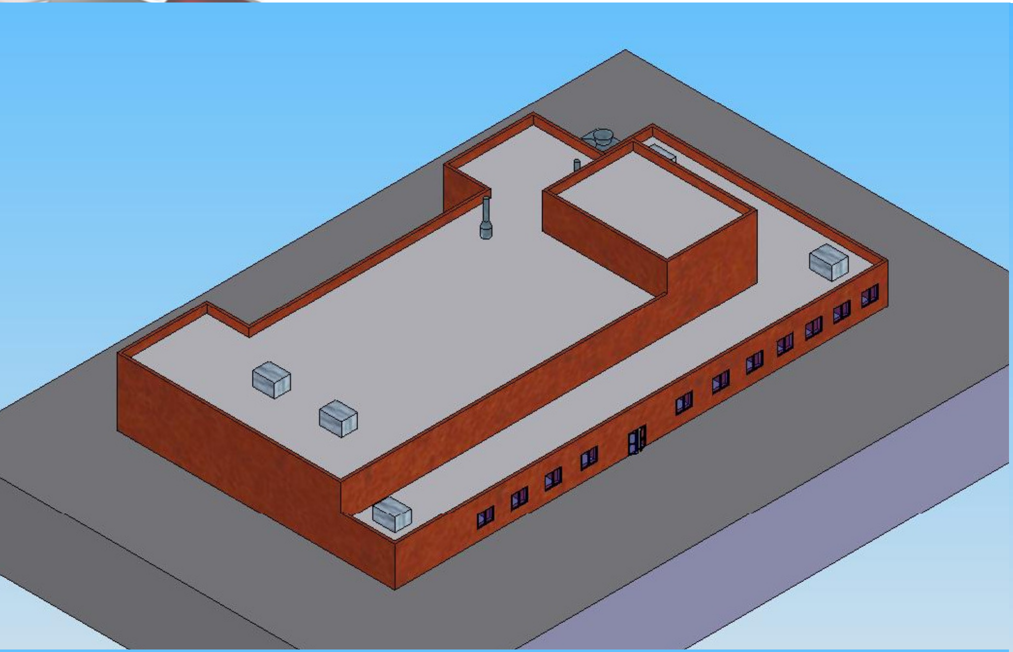


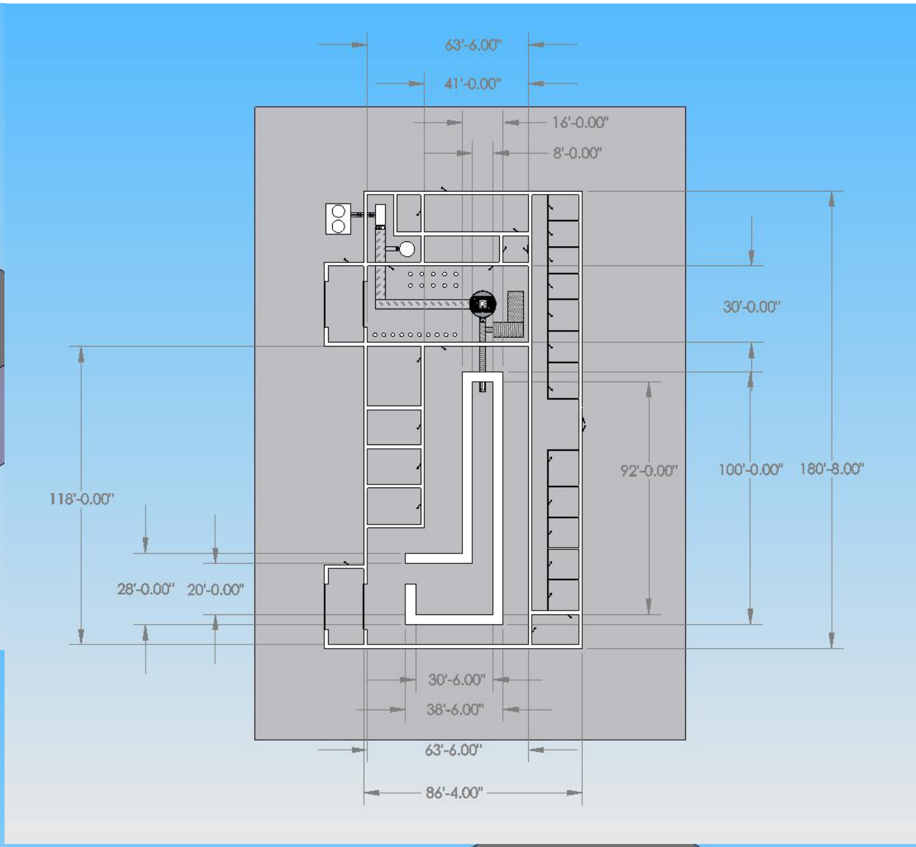
Natural Circulation for Fuel/Target Cooling

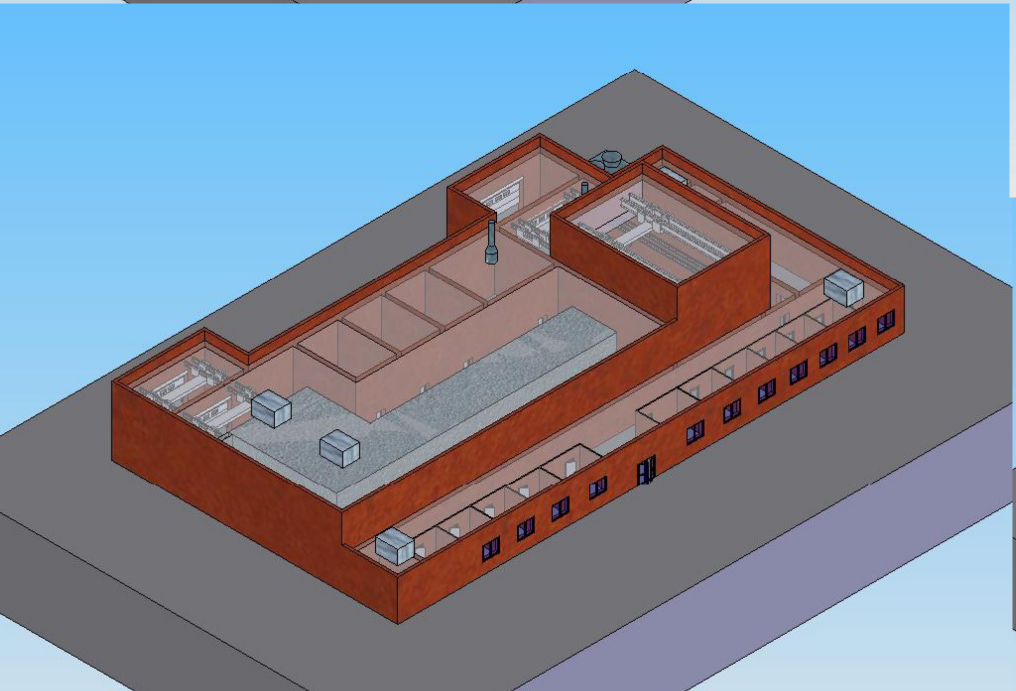
Row	**Pins/Row**
1	1
1	6
2	12
3	18
5	24
6	30
7	36
Total	**127**

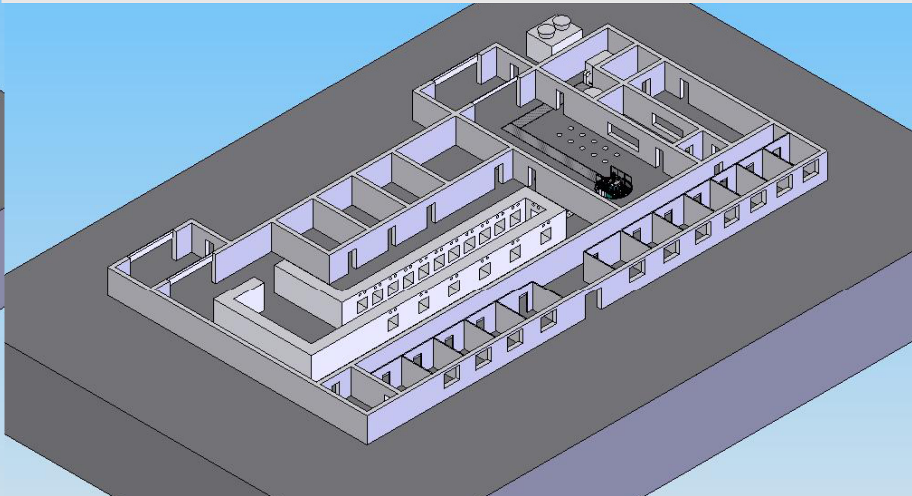
The arrangement shown meets 100% of U.S. demand
Target region is increased for > U.S. demand
Target region is decreased for less than U.S. demand
i.e., number of targets can be adjusted to meet production level desired

Conceptual Facility Layout









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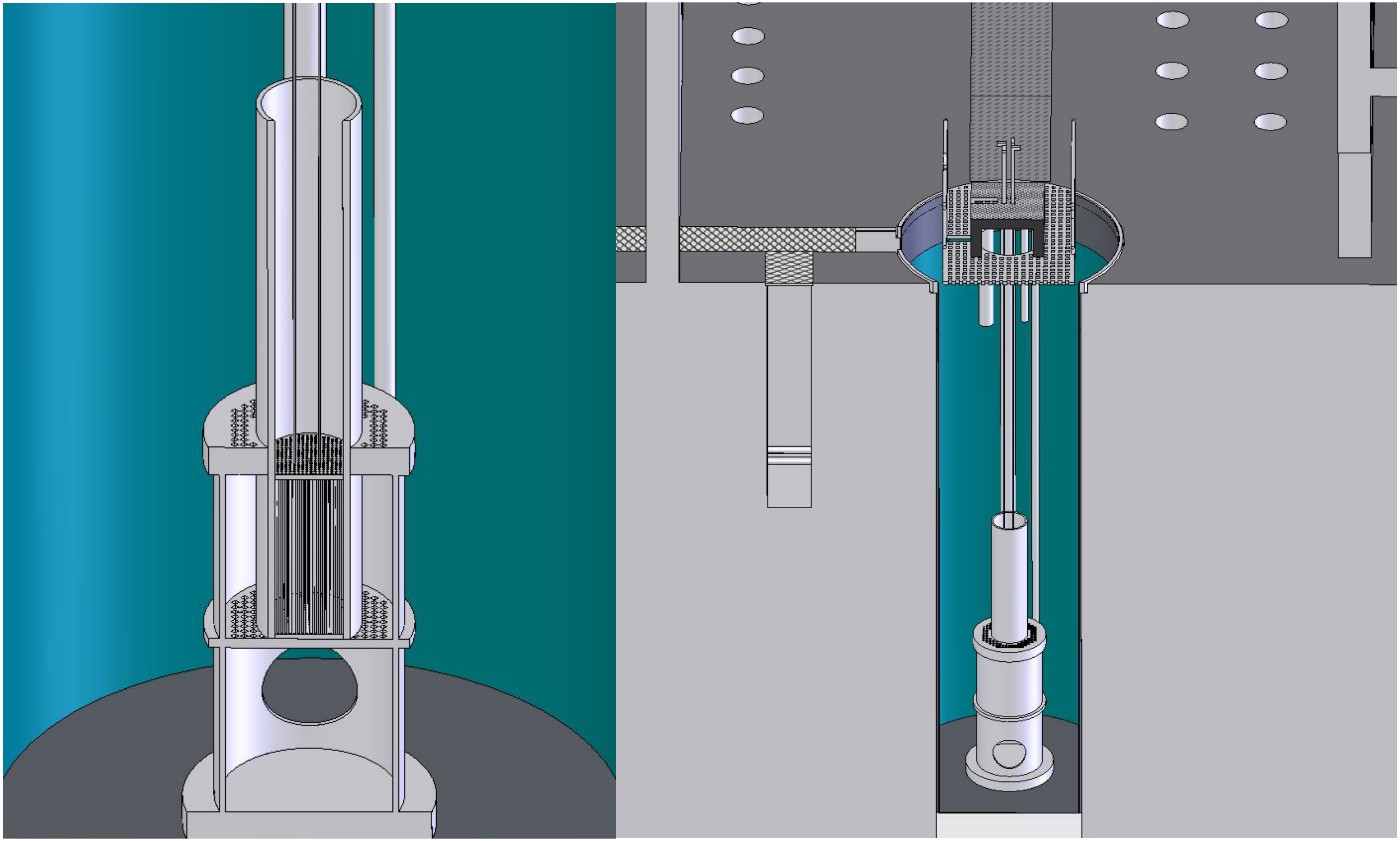

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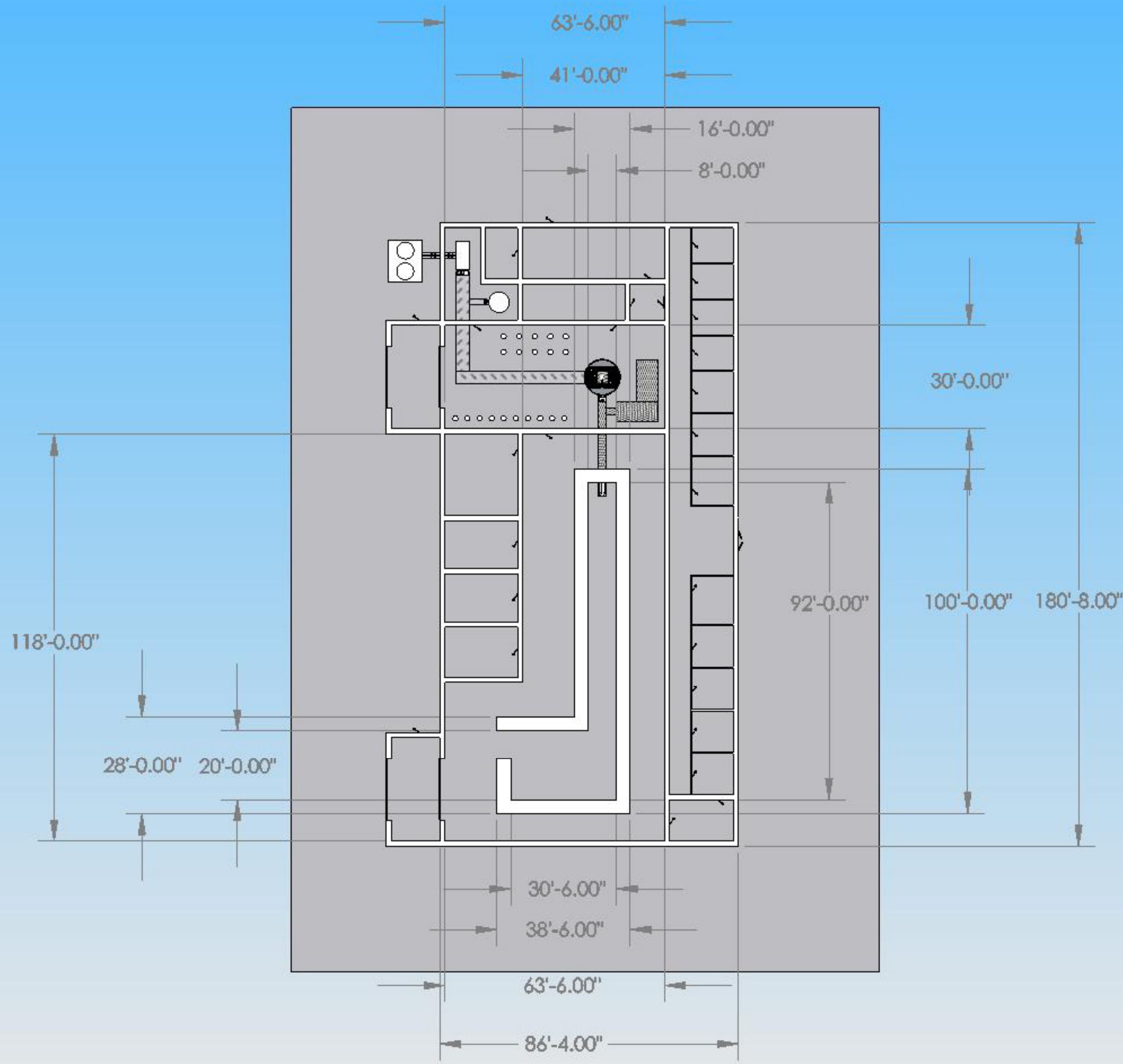

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Summary

- The US is currently in the same situation with its Mo-99 supply that it is with its oil. It is totally dependent on foreign sources.
- Even if supply issues are resolved by end of 2010, all reactors still use HEU fuel for targets. There will still not be a domestic supply.
- Attempts in the past to develop a domestic backup supply have failed.
- Congress is taking action to develop a domestic source using LEU fuel. It will take time to develop.
- We propose a simple, small, passively safe, ~2 MW, LEU-fueled reactor using proven technology oxide pins for targets and fuel - fine tuning the reactor physics can improve performance. At any given time the number of targets can be adjusted to meet production goals. In effect, the reactor is entirely fueled with targets, all of which could be dedicated to ^{99}Mo production, if necessary.
- The swimming pool concept couples well to hot cell, minimizing worker dose and possible release during transport. The low power leads to low radionuclide inventory and low burn-up in reactor driver pins.

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