



**University of Missouri
and
MU Research Reactor Center**

DOE Isotope Workshop

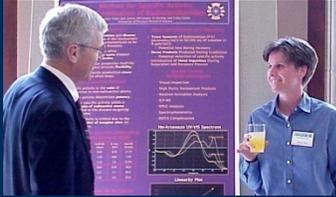
August 2008



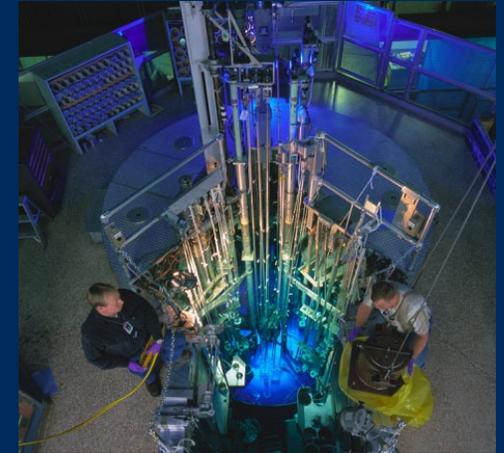
University of Missouri Research Reactor Center

MURR... An MU Pride Point

As a Unique National Resource



Facts & Figures



- October 1966 -- First Reactor Start-up
- At 10 megawatts, MURR is the largest university research reactor
- 2006 -- Relicense application submitted for 20 more years of operation
- Facility operates 24 hours/day; 6 ½ days per week; 52 weeks a year
- It's the People that matter most:
 - Faculty & Staff: - 150; Joint Appointments – 10; Joint MURR funded MU staff - 6
- Students – Learning while helping!
 - Part-time student employees – 26
 - Additional students with unescorted access to MURR – 20



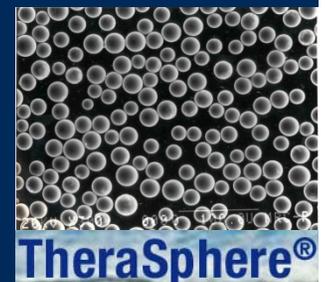
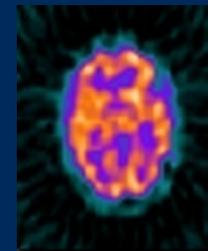
University Research Reactors (Power \geq 1 MW)

Facility	Power (MW)
University of Missouri-Columbia	10
Massachusetts Institute of Technology	5
University of California – Davis	2
Rhode Island Nuclear Science Center	2
Oregon State University	2
University of Texas – Austin	1
North Carolina State University	1
Pennsylvania State University	1
Texas A&M University	1
University of Massachusetts – Lowell	1
University of Wisconsin	1
Washington State University	1

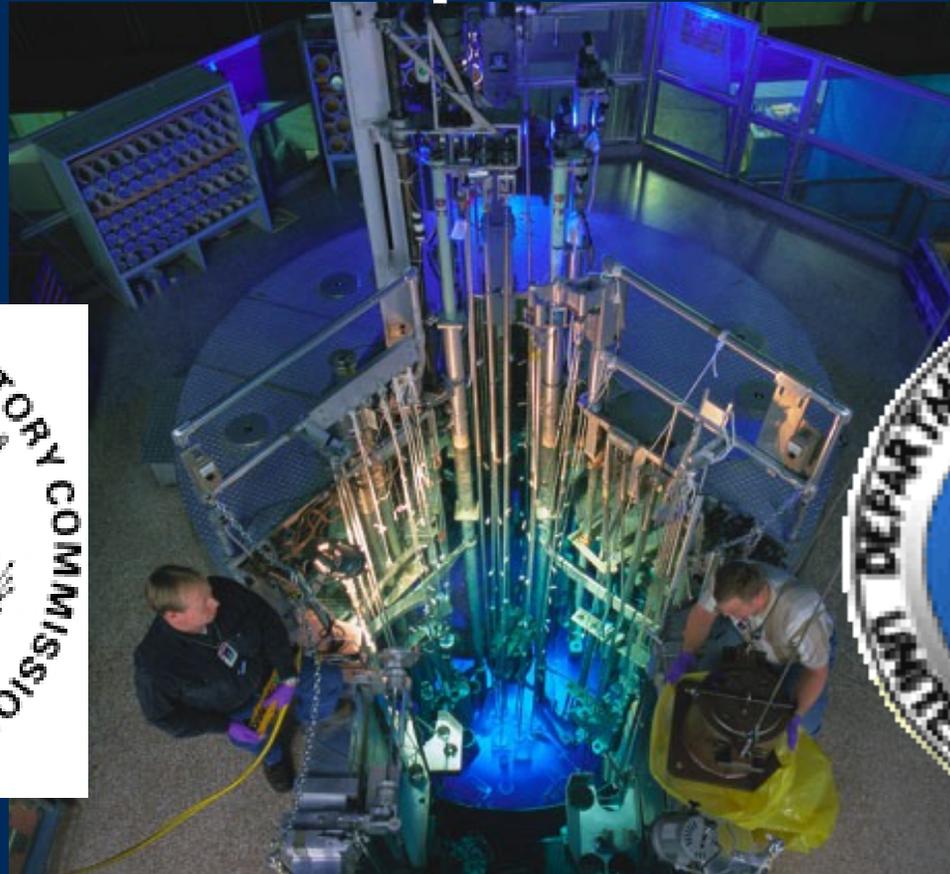
University of Missouri - MU Research Reactor Center

A 25-year history of successful and innovative radiopharmaceutical R&D and collaborations with industry....

- **Ceretec™** (with Tc-99m), a diagnostic used to evaluate cerebral blood flow in patients & label white blood cells
- **Quadramet®** (with Sm-153), a therapeutic for treatment of pain associated with metastatic bone cancer
- **TheraSphere®** (with Y-90), a glass microsphere used to treat patients with inoperable liver cancer
- Cs-131 brachytherapy seeds to treat prostate cancer
- Gd-159 and Ho-166 for research in skeletal targeted radiopharmaceuticals
- Ir-192 brachytherapy seeds to treat solid tumors
- Lu-177 and Pm-149 for receptor-targeted radiopharmaceuticals (support 30 research and clinical trials)
- P-32 and P-33 biomedical radiotracers
- Se-75 biomedical radiotracers



MURR Core Competencies include Strong Record of Regulatory Compliance



U.S. Food and Drug Administration



MURR Core Competencies include International Shipping



In 2007, MURR made
>1000 shipments
including to 14 countries



Associated
COURIERS, INC.



AIR  **NET**

MURR Core Competencies include Volume Radiochemical Processing

Hot Cells

Designed with Versatility in Mind



1st Application...

200 Ci batches of Ho-166

Designed for 500 Ci Batches

P-33 Hotcell Facilities



Lu-177

Weekly producing 40 Ci batches

Potentially capable of 1000's Ci per week

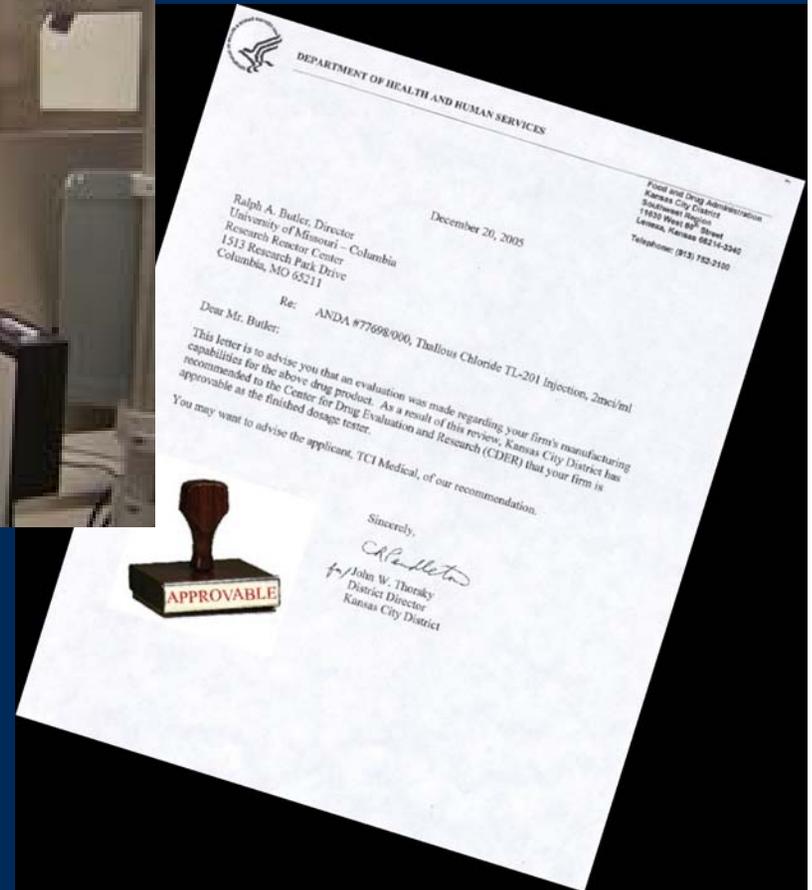


FDA Approvable Facilities... cGMP & GLP Programs



MURR Evolving Competencies

Target FDA-approvable cGMP and GLP Programs



MURR Produced Isotopes

43 Isotopes of 37 Elements Shipped in 2006

As-76	Hg-197; Hg-203	S-35
Au-198	Ho-166	Sb-122; Sb-124
Ba-135m	Ir-192	Sc-46
Ca-45; Ca-47	K-42	Se-75
Co-60	La-140	Sm-153
Cr-51	Lu-177	Sn-125
Cs-134	Na-24	Sr-89
Eu-154	P-32; P-33	Tb-161
Fe-55	Pm-149	Tl-204
Fe-59	Rb-86	Y-90
Gd-159	Re-186	Yb-169; Yb-175
Ge-71	Rh-105	Zn-65
		Zr-95; Zr-97

Sole US supplier

Radiopharmaceutical Research

Currently developing a suite of *carrier free lanthanides* to work in conjunction with *selective targeting agents* to locate and treat cancer.

Ln	$t_{1/2}$	β_{\max}	E_{γ} (I_{γ})	Avg Range (cell diameter)
^{177}Lu	6.7 d	0.5 MeV	208 keV (11%)	20
^{166}Ho	1.1 d	1.8 MeV	286 keV (3%)	60
^{149}Pm	2.2d	1.1 MeV	81 keV (6%)	120

Metal-Ligand
Conjugate



Organic
Linker



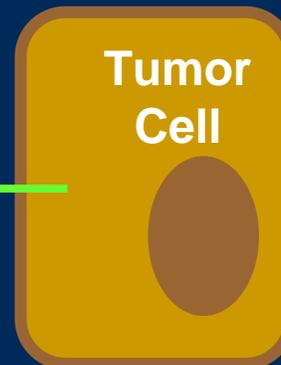
Biomolecule



Receptor



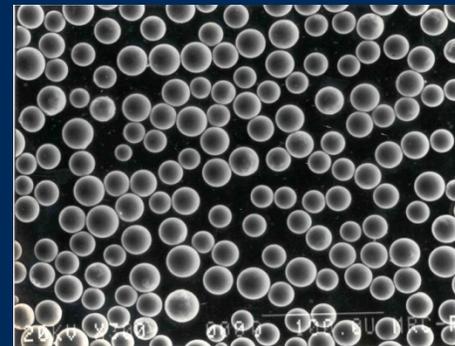
Tumor
Cell



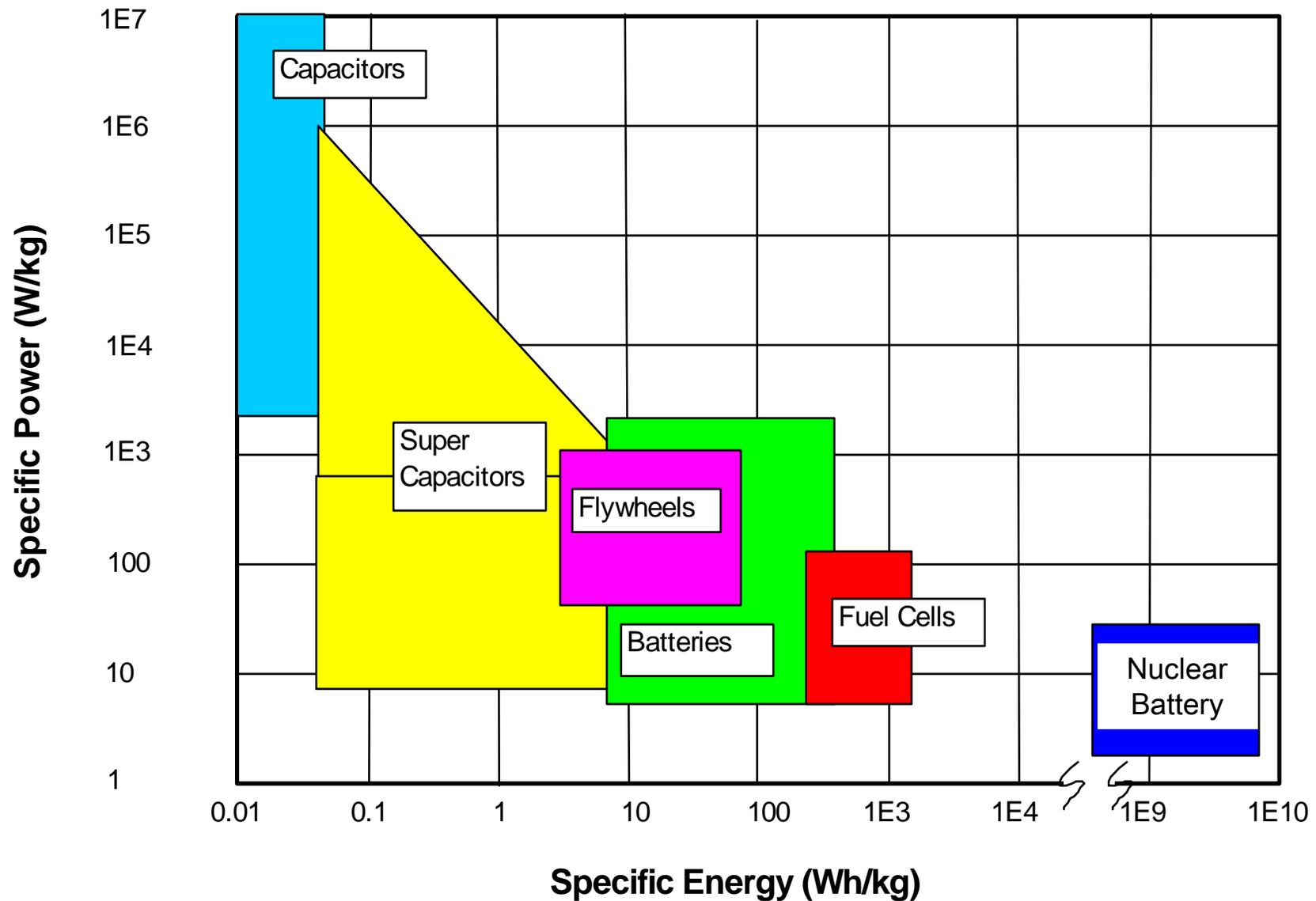
Radiopharmaceutical Research

A History of Success

- Focus on Cancer
 - Sm-153 Quadramet[®]
 - Y-90 TheraSpheres[®]
- Real Patients Demand Our Safe Reliability



Radioisotope Micropower Sources Ragone Plot



Potential Isotopes for Radioisotope Micropower Source Applications

Radioisotope	E_{avg} (keV)	Half-life (years)	Maximum BOL activity (TBq/cm ³)	Maximum BOL source power (mW/cm ³)	Particle range in source (μm)	“Realistic” BOL P_{out} (μW/cm ²)
¹⁴⁷ Pm	61.8	2.6	247	2448	9.6	141.1
²¹⁰ Po	5304	0.38	1566	1.3E6	1	1.4E4

β source

- 100% isotope enrichment
- $\eta_{\text{conv}}=10\%$, $\eta_{\text{source}}=30\%$
- source thickness=2 x beta range

α source

- 100% isotope enrichment
- $\eta_{\text{conv}}=10\%$, $\eta_{\text{source}}=90\%$
- source thickness=1 μm

Examples of Current Collaborations with Industry

- Pm-147 and 210-Po for nuclear batteries
- Cs-131 brachytherapy seeds to treat prostate cancer
- Gd-159 and Ho-166 for research in skeletal targeted radiopharmaceuticalls
- Ir-192 brachytherapy seeds to treat solid tumors
- Lu-177 and Pm-149 for receptor-targeted radiopharmaceuticals (support 30 research and clinical trials)
- P-32 and P-33 biomedical radiotracers
- Se-75 biomedical radiotracers
- Sm-153 for Quadramet
- Y-90 for Theraspheres

Need for Mo-99/Tc-99m

- Tc-99m is used in over 80% of all medical isotope procedures worldwide.
- National need – used ~35,000/day in U.S.
- Use is expected to increase 7% to 10% annually for the next ten years.
- More than 30 different radiopharmaceuticals use Tc-99m for disease detection & organ structure & function.

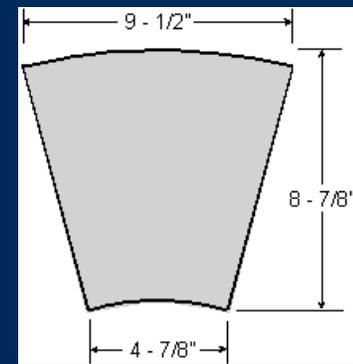
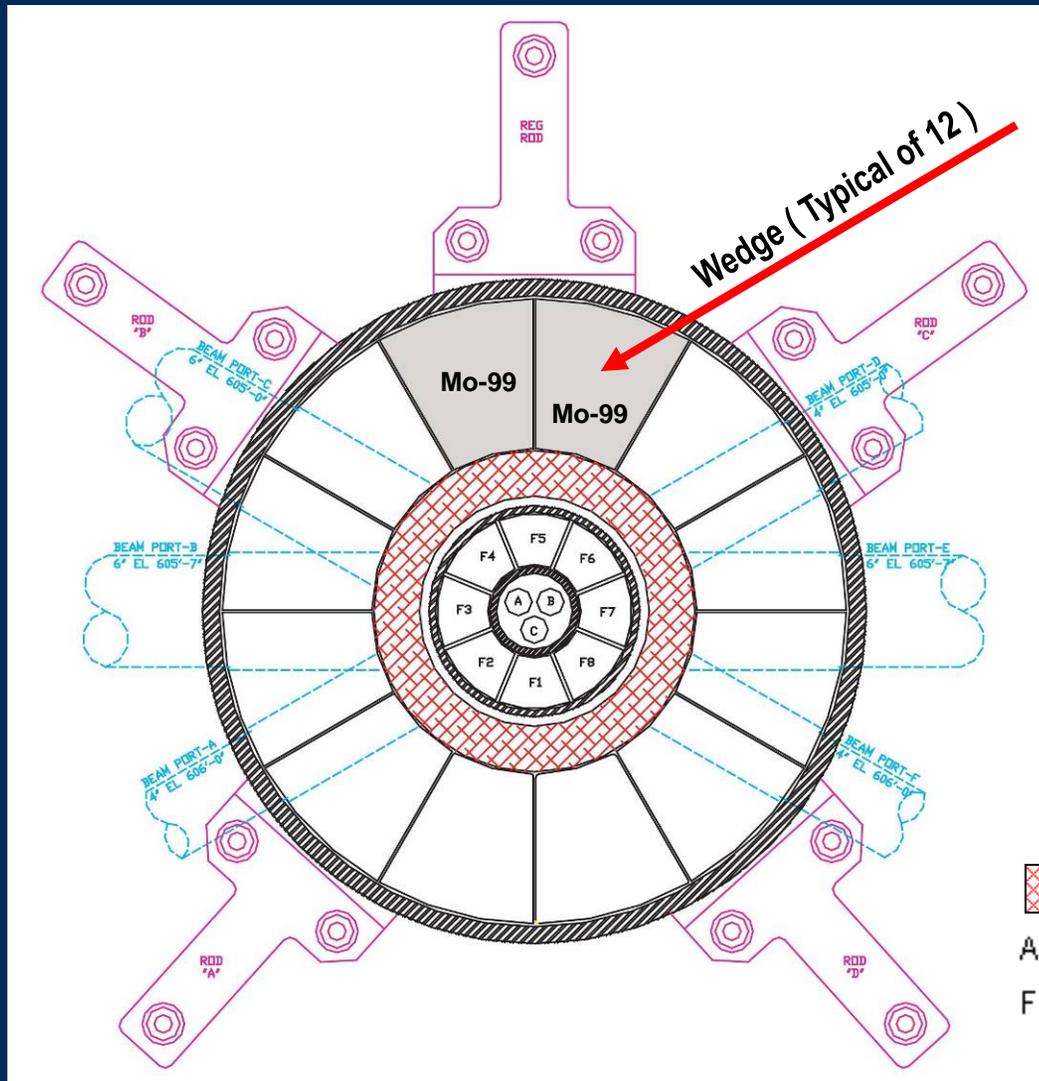
U.S. History of Mo-99 Production

- 1967 - MURR begins production of (n, γ) Mo-99 for Mallinckrodt Nuclear Co.
- 1969 - MURR begins weekly production of Mo-99.
- 1977 - MURR increases Mo-99 production for MediPhysics Inc.
- 1984 - MURR ceases Mo-99 production.
- 1980 - Cintichem, Inc. begins production of fission product Mo-99 and is the single U.S. supplier. .
- 1989 - Cintichem reactor develops leak and is closed.
- 1991 - DOE purchased Cintichem technology, equipment and DMFs for production of Mo-99, I-125, X3-133
- 1991 - DOE identified Omega West Reactor at LANL as proposed backup supply facility and constructs processing facility.
- December 1992 - Omega West Reactor at LANL develops leak and is closed.
- Until 1993, two Canadian reactors, operated by Atomic Energy of Canada Limited (AECL) at the Chalk River site (located about 100 miles from Ottawa, Canada), were available to produce Mo- 99.
- 1996 – DOE selects Annular Core pulse reactor at Sandia National Lab. to become backup supply facility and constructs processing facilities. Project never completed.
- 1998 – Canadian MAPLE reactors were scheduled to open, but remain shutdown today due fundamental design flaw.
- 2008 – Decision made to discontinue work on MAPLE 1 & 2.

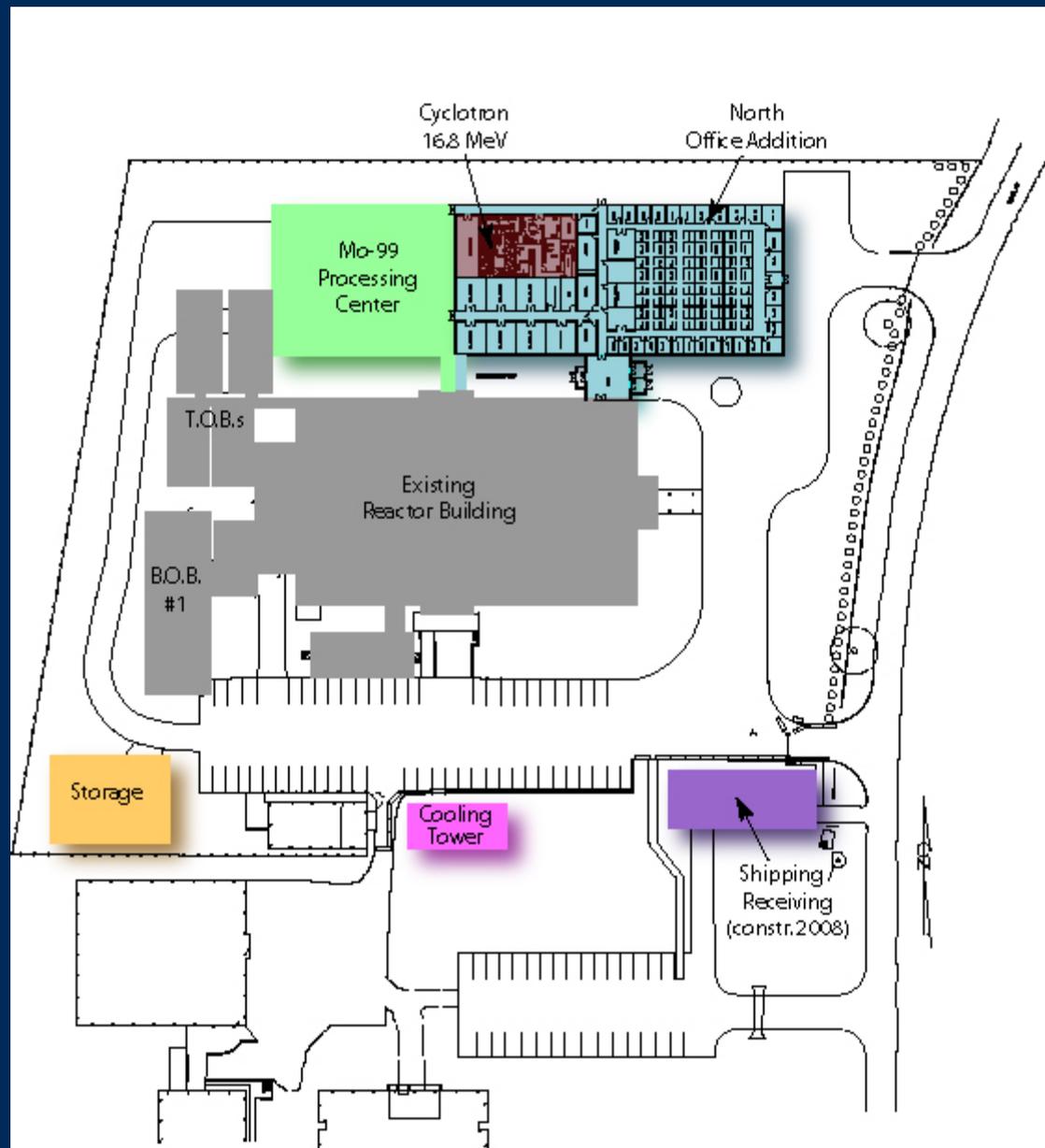
Mo-99 Production at MURR

- Overall objective is to develop the capability to produce Mo-99 from LEU targets.
- Production objective is ~50% of current U.S. weekly demand.
 - Current U.S. weekly demand is estimated to be 6000 six-day Curies (Ci) per week
 - 6000 six-day Ci equates to about 40,000 Ci (End-of-Irradiation), Synonymous with “Out-of-Reactor” Ci
 - Must irradiate / process 40 - 50 targets per week to satisfy ~50% weekly demand.
- Expect turnkey construction project.
 - INVAP (Argentina) has designed & built three facilities.
 - MURR and DOE NNSA are separately funding two different conceptual design by INVAP.

Reactor Plan View



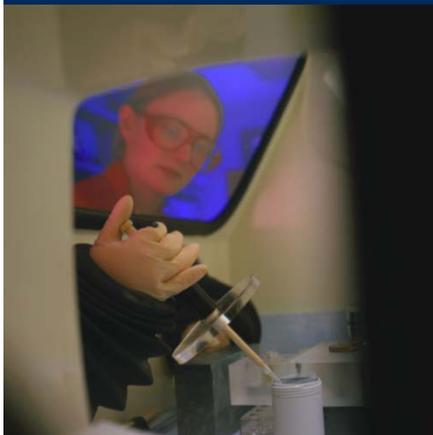
-  - Beryllium Reflector
- A, B, C - Flux Trap
- F1 - F8 - Fuel Elements

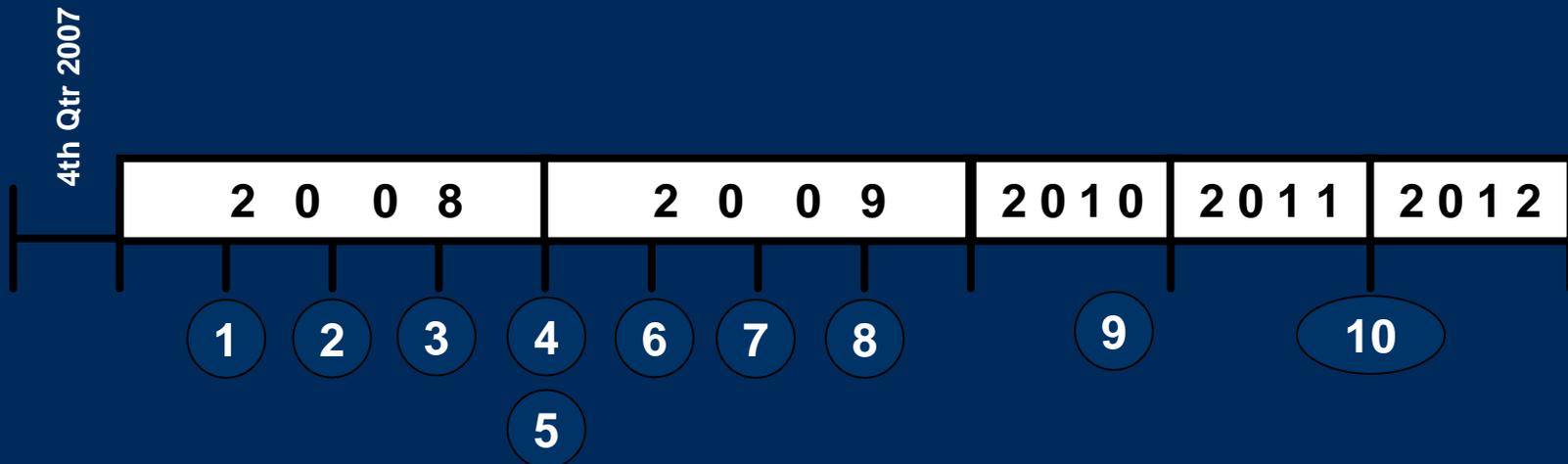


University of Missouri Research Reactor Center

Proof of Concept Summary

- Multiple sample targets are assembled
 - Both Argonne produced LEU foil and KARIE foil
 - Target will be instrumented for temperature
- Multiple cold runs completed with $>94\%$ recovery
- Irradiation/processing of LEU small scale target
 - July/August 2008
 - Awaiting license amendment from U.S. NRC to irradiate 5-gram sample LEU target





Estimated completion

- | | |
|----|---------------------------------------|
| 1 | Proof of concept |
| 2 | Production facility conceptual design |
| 3 | Target design selection |
| 4 | Waste stream studies |
| 5 | Business plan development |
| 6 | Reactor/Irradiation design |
| 7 | Facility design |
| 8 | Materials license application |
| 9 | Construction |
| 10 | Commercial |

University of Missouri – A Unique Set of Resources



Core Competencies

...Education and Training

- **Introduction to Radiochemistry**
 - 40-50 students per year;
largest class in the nation
 - Radiation detection and
radiochemistry labs
at MURR



Host for the 2007 ITAC/SSAC Course

- 35 foreign national participants
- Safeguard exercises using CANBERRA Aquila systems

MU — Preparing the Next Generation

- MU's **Introduction to Radiochemistry** course had 51 students in Academic Year 2006, the highest enrollment in the US



MU — Preparing the Next Generation

- MU has the nation's only National Science Foundation-sponsored Research Experience for Undergraduates (REU) program in Radiochemistry

