ACCELERATOR-DRIVEN PRODUCTION OF FISSION ^{99}MO

Mo-99 2016 Topical Meeting on Molybdenum-99 Technological Development

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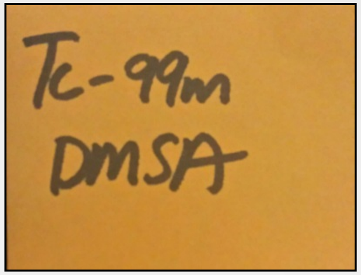
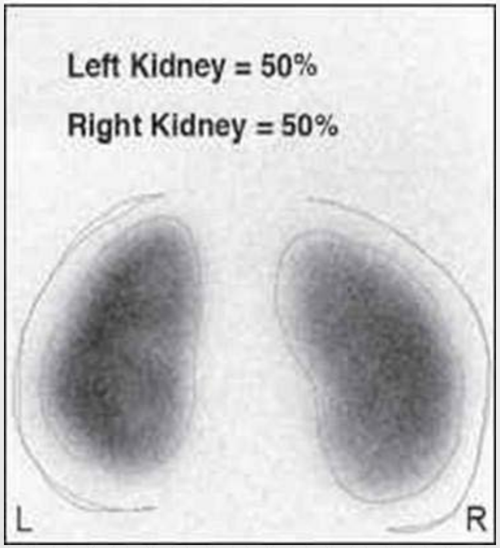
^{99m}TC-DMSA SCAN





SHINE MEDICAL TECHNOLOGIES

- SHINE Medical Technologies is dedicated to being the world leader in safe, clean, affordable production of medical tracers and cancer-treatment elements
- SMT and its partners have developed a system that can produce reactor-grade medical isotopes without a nuclear reactor
- Technology has two key aspects
  - Primary neutrons created by high-output D-T source
  - Neutrons enter an LEU solution where they multiply sub-critically and create medical isotopes
- Initial construction will produce nationally relevant quantities of ^{99}Mo and other medical isotopes (50% of U.S. ^{99}Mo demand)

MINI-SHINE EXPERIMENTS

Electron linac – Irradiate aqueous LEU uranyl sulfate solutions

- Study the effects of fission on target-solution chemistry and radiolytic off-gas generation
- Demonstrate the recovery and purification of ^{99}Mo from an irradiated target solution
- Ship ^{99}Mo product to potential ^{99m}Tc generator manufacturer partners

Phase I - Completed

- Linac operated initially at 35 MeV and 10 kW beam power on the target
- 5 L irradiated with neutrons generated through gamma-n reaction in tantalum target
- Maximum solution power was $\leq$ 0.05 kW/L
- 1.4 Ci ^{99}Mo produced EOB and 1.1 Ci ^{99}Mo shipped to GE Healthcare in the UK (October 2015)

Phase II - Underway

- Experiment will be conducted at 35 MeV beam energy and up to 30 kW beam power
- 20 L will be irradiated with neutrons generated in a depleted-uranium (DU) target
- Maximum solution power will be $\leq$ 0.5 kW/L
- Up to 20 Ci of ^{99}Mo will be produced

PHASE I IRRADIATIONS

Date of Irradiation	^{99}Mo Produced (mCi)	Processing
#1 - 2/23/2015	80*	Yes
#2 - 3/4/2015	330*	Yes
#3 - 4/20/2015	900*	Yes
#4 - 4/26/2015	340*	Yes
#5 - 10/14/2015	460*	Yes
#6 - 10/26/2015	**1400***	**Yes**
#1 - 5/21/2015	200**	No
#2 - 9/27/2015	60**	No
#3 - 10/3/2015	200**	No

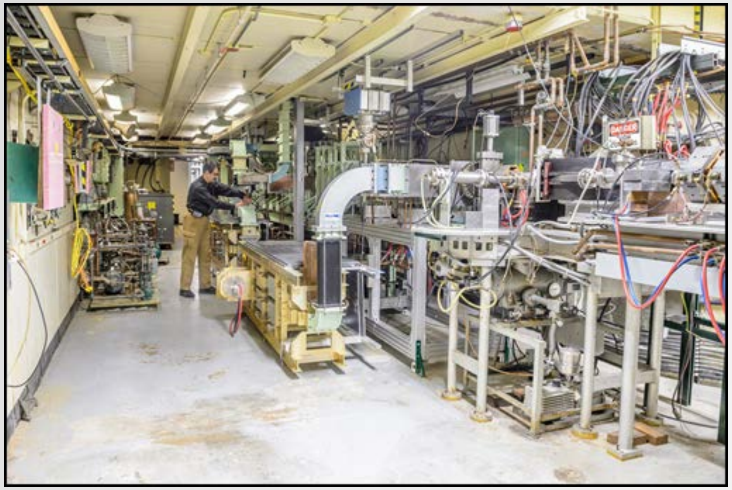
*Based on ^{99}Mo in the product from first titania column

**Based on sample collected after irradiation

- Processing – 2 titania columns and LEU-Modified Cintichem process
- Irradiation times, beam power, and U concentration varied
- #6 Shipment to GE Healthcare

PHASE I SYSTEM COMPONENTS

Electron Linac

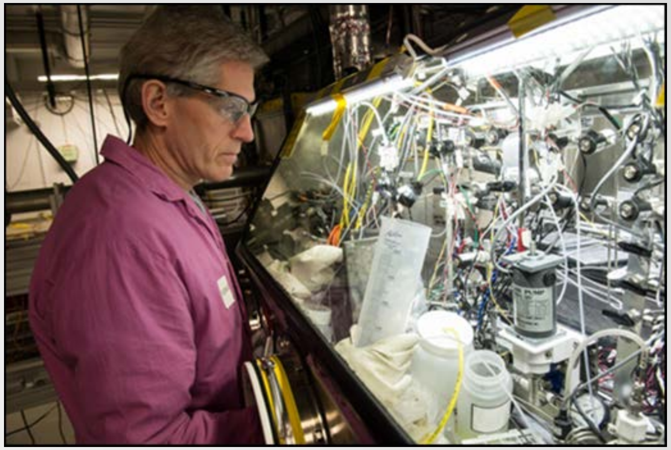


Separation Glovebox

Gas Analysis System

Hot Cell with Manipulators

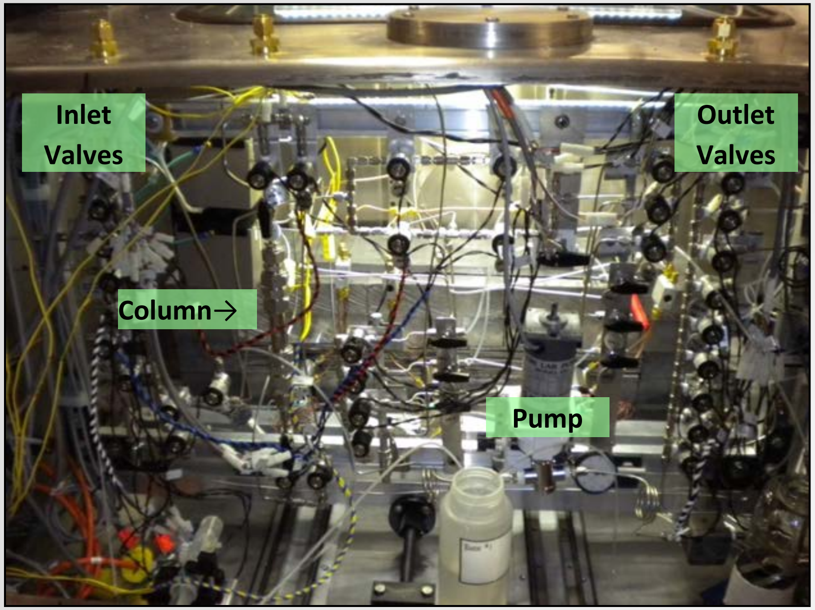
GE SHIPMENT RUN



- 20 hours total irradiation with 17 hours at full power (10 kW)
- EOB 1.4 Ci ^{99}Mo produced
- 1.1 Ci ^{99}Mo shipped to GE Healthcare in the UK

10/27/15 13:35 FedEx picked up ^{99}Mo at Argonne →	**10/28/15 13:52** ^{99}Mo shipment arrived at Stanstead →	**10/28/15 22:00** ^{99}Mo shipment arrived at GE
10/29/15 3:55 ^{99}Mo loaded onto ^{99m}Tc generator →	**10/30/15** ^{99m}Tc tested with 2 radiopharmaceutical kits →	**10/31/15** All kit tests were successful

FIRST TITANIA COLUMN RESULTS



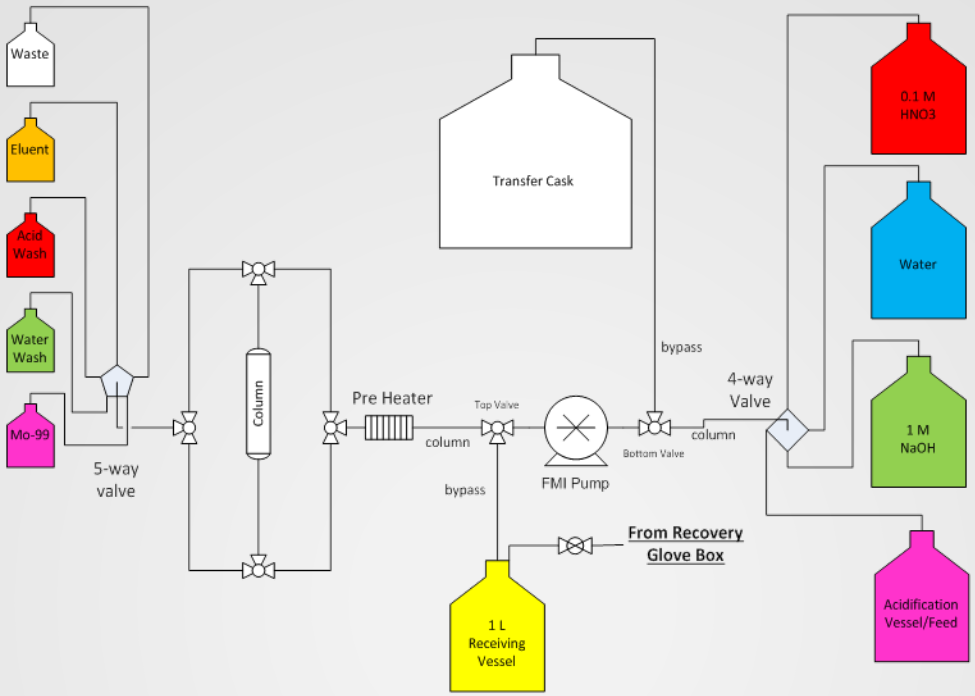
- All operations done remotely with LabView software
- Sachtopore - 110 micron particles and 60 Å pores
- Column size – 2 cm ID x 10 cm L
- Loading and washing – up-flow direction
- pH adjustment and stripping – down-flow direction
- Temperature – 80°C
- Flow rate – 40 mL/min (loading) and 20 mL/min (stripping)
- Total time - ~ 3 hours
- Mo-product sent directly to hot cell for additional processing

- Qualitative results for first titania column
- ^{95}Zr and ^{99}Mo adsorb strongly on titania
- ^{103}Ru, ^{132}I, ^{131}I, ^{136}Cs, ^{137}Cs, ^{132}Te, and ^{127}Sb adsorb fairly well on titania
- ^{237}U, ^{239}Np, ^{140}Ba, ^{147}Nd, ^{151}Pm, ^{143}Ce, and ^{105}Rh adsorb poorly on titania

CONTAMINANTS IN MO PRODUCT FROM RECOVERY COLUMN

- ^{237}U, ^{239}Np, ^{140}Ba, ^{147}Nd, and ^{143}Ce were present in the NaOH wash (pH adjustment) to a small extent – most likely due to residual irradiated LEU solution in the tubing and/or valves
- Main contaminants more likely due to co-elution with ^{99}Mo include ^{103}Ru, ^{131}I, ^{133}I, ^{105}Rh, ^{125}Sn, and ^{127}Sb

SECOND TITANIA COLUMN



- All operations done in a hot cell with manipulators
- Mo-product from 1st titania column acidified to pH 2 prior to loading 2nd titania column
- Sachtopore - 40 micron particles and 60 Å pores
- Column size – 1 cm ID x 1 cm L
- Loading and washing – up-flow direction
- pH adjustment and stripping – down-flow direction
- Temperature – Loading and washing (80°C) and stripping (70°C)
- Flow rate – 16 mL/min (loading) and 4 mL/min (stripping)
- Total time - ~ 2 h 40 min
- Mo product concentrated from ~1 L to 25 mL

CONCENTRATION COLUMN PARTITIONING

Radionuclide	Feed, mCi (1σ, %)	Eluent, mCi (1σ, %)	HNO_3 wash, mCi (1σ, %)	H_2O wash, mCi (1σ, %)	Waste, mCi (1σ, %)	CC product, mCi (1σ, %)	Filter, mCi (1σ, %)
^{95}Zr	7.70E-02 (27)	<3E-02	<1E-03	<3E-04	<4E-04	<5E-02	<4E-04
^{95}Nb	<5E-02	3E-02 (25)	1.8E-03 (16)	<3E-04	<3E-04	<3E-02	<2E-04
^{99}Mo	1.42E+03 (2.7)	2.64E+00 (21)	1.77E-01 (13)	1.46E+00 (2.6)	2.80E+00 (2.7)	1.47E+03 (2.3)	1.95E+01 (2.3)
^{103}Ru	3.18E+00 (2.2)	2.76E+00 (1.9)	3.10E-02 (2.4)	5.20E-03 (3.4)	3.06E-02 (2.0)	3.2E-01 (9.3)	1.75E-01 (1.9)
^{131}I	1.92E+02 (1.9)	1.03E+02 (1.9)	5.34E+00 (1.9)	1.44E+00 (2.0)	8.00E-01 (1.9)	2.81E+01 (2.8)	2.84E+00 (2.0)
^{133}I	3.27E+03 (1.9)	1.77E+03 (1.9)	9.25E+01 (1.9)	2.46E+01 (1.9)	1.33E+01 (1.9)	4.65E+02 (1.9)	4.60E+01 (2.0)
^{136}Cs	9.9E-02 (13)	<2E-02	<8E-04	<3E-04	1.1E-03 (7.6)	3.E-02 (26)	<3E-04
^{105}Rh	7E+00 (21)	4.4E+00 (13)	1.5E-01 (15)	2.4E-02 (20)	<2E-02	1.9E+00 (28)	5E-01 (24)
^{125}Sn	9.19E-01 (28)	<3.50E-01	3.32E-02 (19)	1.23E-02 (19)	5.73E-02 (4.3)	9.88E-01 (26)	8.19E-03 (25)
^{127}Sb	5.43E+00 (3.6)	8E-02 (30)	<3E-03	<1E-03	3.89E-01 (3.1)	3.10E+00 (4.0)	<4E-03
^{91}Sr	<6E+01	1.8E+01 (16)	5.8E-01 (17)	2.0E-01 (20)	2.7E-01 (25)	<1E+01	>12 Halflives
^{135}I	4.91E+03 (2.7)	2.96E+03 (2.3)	1.57E+02 (2.4)	4.05E+01 (2.3)	2.32E+01 (4.6)	7.69E+02 (5.8)	>12 Halflives

- **Activities detected in concentration column fractions calculated at EOB**

LEU MODIFIED CINTICHEM PROCESS

- Acidification of CC strip solution (1 M NaOH)

- ~25 mL of CC strip adjusted with 10 M HNO_3 to ~1 M HNO_3

- Filtration

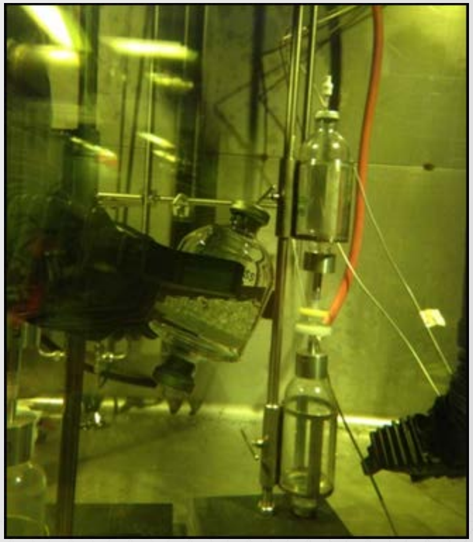
- 40mm 0.3 mm PP filter to collect white precipitate (filter)
- wash with 10 mL of 1 M HNO_3

- Feed into LMC process ~41 mL (RF1)

- Iodine precipitation (NaI+$AgNO_3$)
- Mo carrier, $KMnO_4$, Ru & Rh carrier
- ABO precipitation

- Mo-ABO filtration

- Mo in precipitate washed with 0.1 M HNO_3, FPs in solution (RFW)



LMC RESULTS

Radionuclide	RF-1, mCi (1σ, %)	RFW, mCi (1σ, %)	LMC product, mCi (1σ, %)
^{95}Zr	<5E-02	3.8E-03 (8.8)	4.02E-03 (4.0%)
^{95}Nb	8.8E-02 (11)	1.2E-03 (16)	8.64E-03 (2.2%)
^{99}Mo	1.32E+03 (2.3)	3.06E+00 (3.6)	1.27E+03 (2.3)
^{103}Ru	2.0E-01 (14.5)	1.58E-01 (1.9)	4.40E-03 (3.1)
^{131}I	2.01E+01 (3.0)	9.02E+00 (1.9)	5E-03 (26)
^{133}I	3.37E+02 (1.9)	1.46E+02 (1.9)	5.53E-02 (2.9)
^{125}Sn	8.9E-01 (19)	5.88E-01 (3.7)	<3E-03
^{127}Sb	2.89E+00 (4.9)	3.29E+00 (3.2)	<6E-04

- ^{99}Mo CC Feed – 1420 mCi
- ^{99}Mo CC Product – 1470 mCi
- ^{99}Mo LMC Feed- 1320 mCi
- ^{99}Mo LMC Product – 1270 mCi
- ^{99}Mo Recovery – 89.4%
- All gamma counting results have error of +/- 5%

PURITY SPECIFICATIONS MET

- ^{99}Mo produced at Argonne loaded on GE Healthcare’s Drytec™ ^{99m}Tc generator
- ^{99m}Tc product successfully tested with GE Healthcare’s Myoview™ and Ceretec™ radiopharmaceutical kits

GE Healthcare

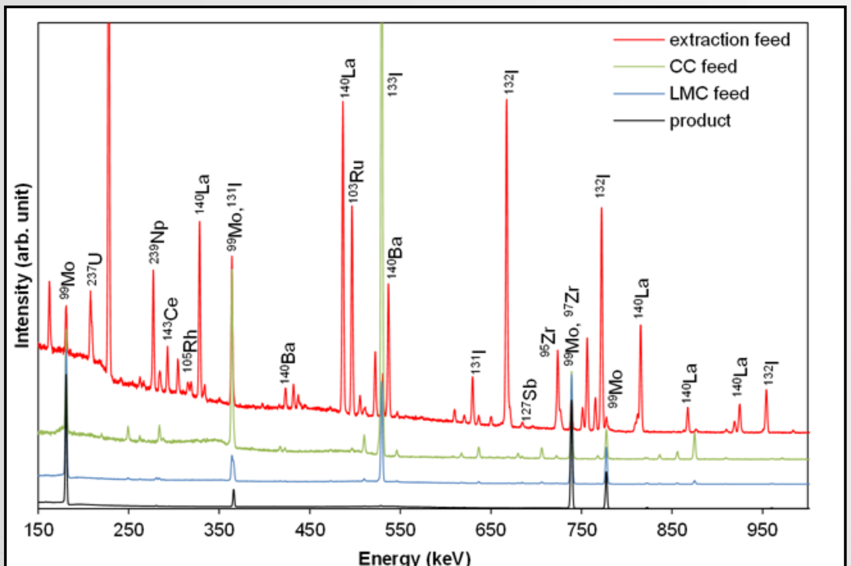
SHINE™ Medical Technologies

PRESS RELEASE

It Takes Two: GE Healthcare and SHINE team up to solve longstanding radiopharmaceutical supply concerns in medical imaging

Successful generation of Tc-99m is a supply chain advancement that can help ensure patient access to critical medical imaging scans.

CHALFONT ST. GILES, UK – 9 November 2015 – Technetium-99m (Tc-99m) is used in more than 40 million medical imaging procedures each year, primarily stress tests to assess heart disease, and bone scans to determine the stage of cancer progression. This essential medical isotope is generated in pharmacies and hospitals from another isotope—molybdenum-99 (Mo-99). Despite using half of the world’s supply of Mo-99, the United States does not produce any domestically and imports 100 percent of its supply from foreign nuclear reactors. Many of these reactors are beyond their originally intended lifespans and outages have caused major shortages of Mo-99.

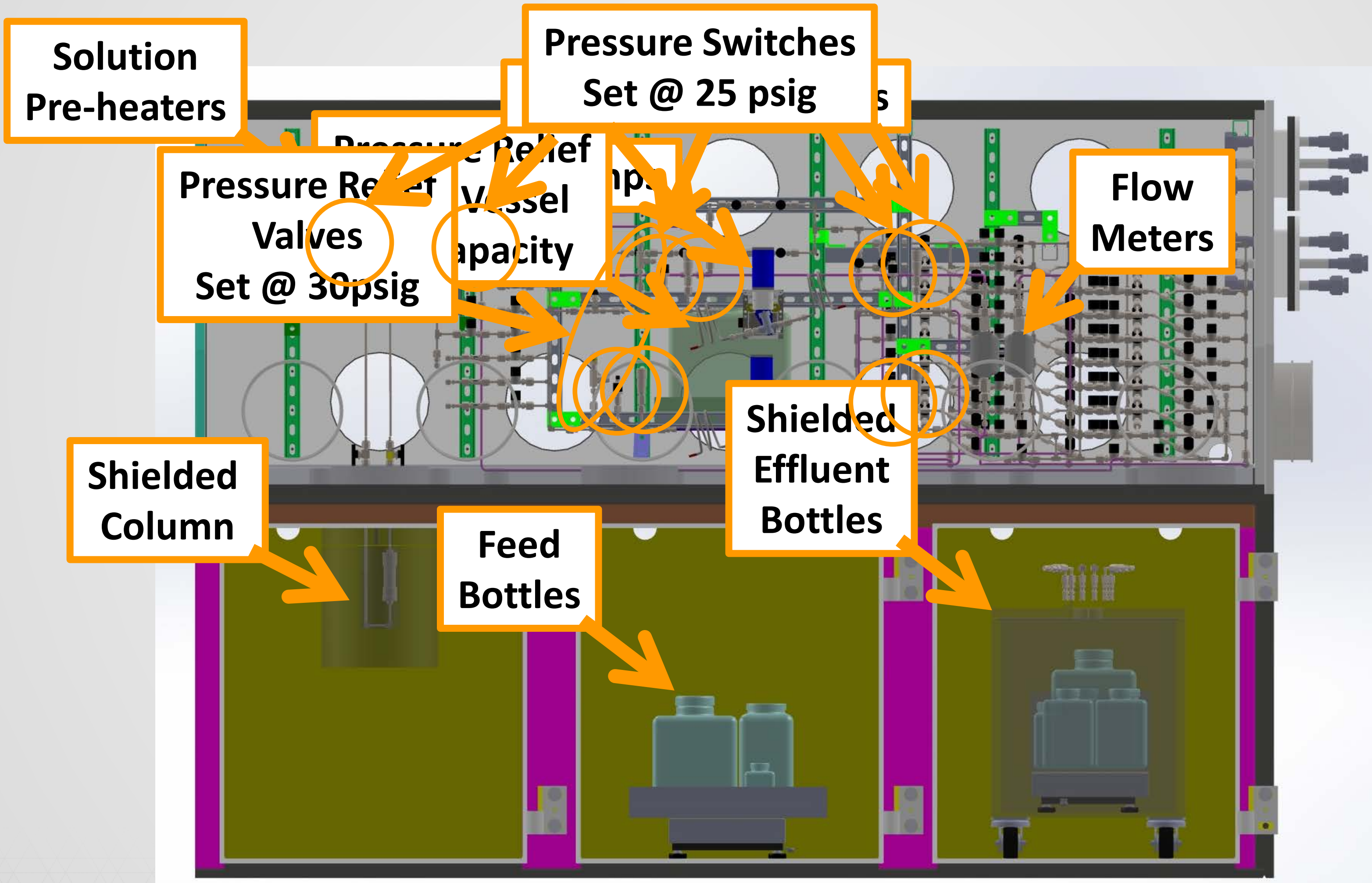


Ratio	Determined value 36 hrs after EOB	Product specification	Within specification
$^{131}I/^{99}Mo$	5.3E-06	$\leq 5\times10^{-5}$	YES
$^{103}Ru/^{99}Mo$	4.9E-06	$\leq 5\times10^{-5}$	YES
$\Sigma\alpha/^{99}Mo$	6.5E-12	$\leq 1\times10^{-9}$	YES

CHANGES FROM PHASE I TO PHASE II

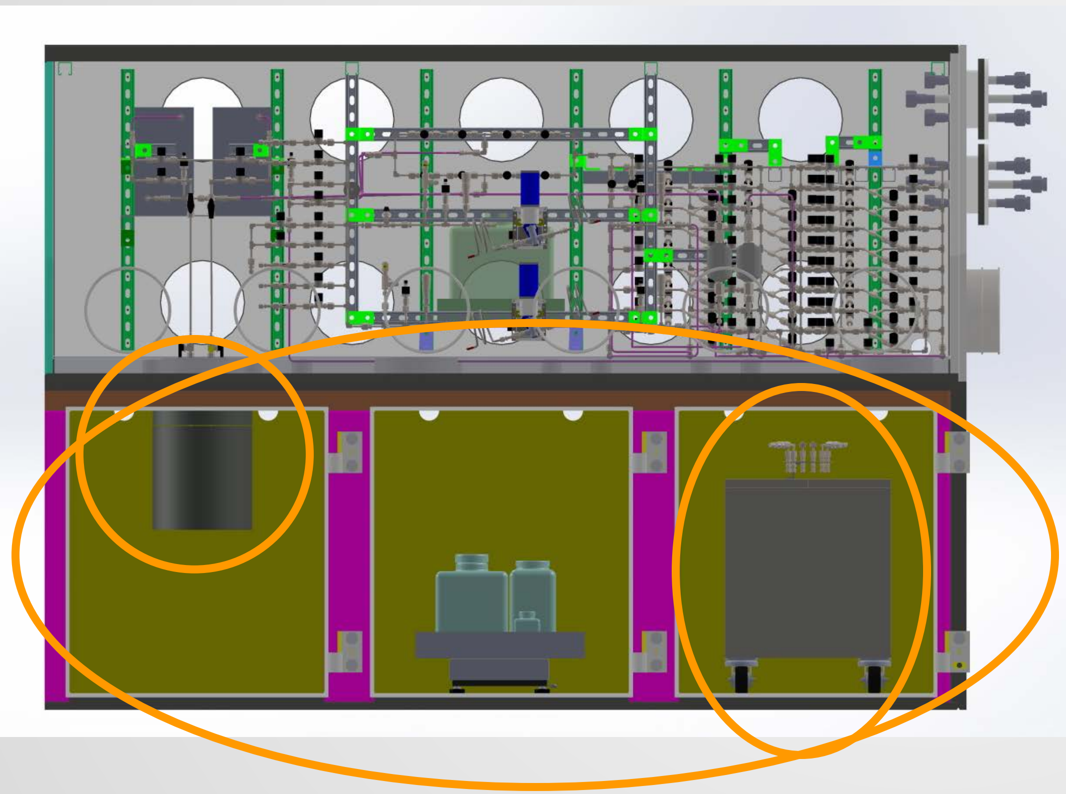
- Target solution volume increased: 5 L → 20 L
- Flow rates increased: 40 & 20 mL/min → 167 & 83.5 mL/min
- Tubing thickness increased: 1/8" OD→ 1/4" OD
- Second pump added for basic solutions
- One shielded glovebox replaced two unshielded gloveboxes
- Shielding added to column and effluent bottles
- Flow path no longer shared amongst sample loops
- Target solution verification measuring capability added
- Target solution monitoring components removed

PROCESS EQUIPMENT FOR PHASE II (FRONT VIEW)



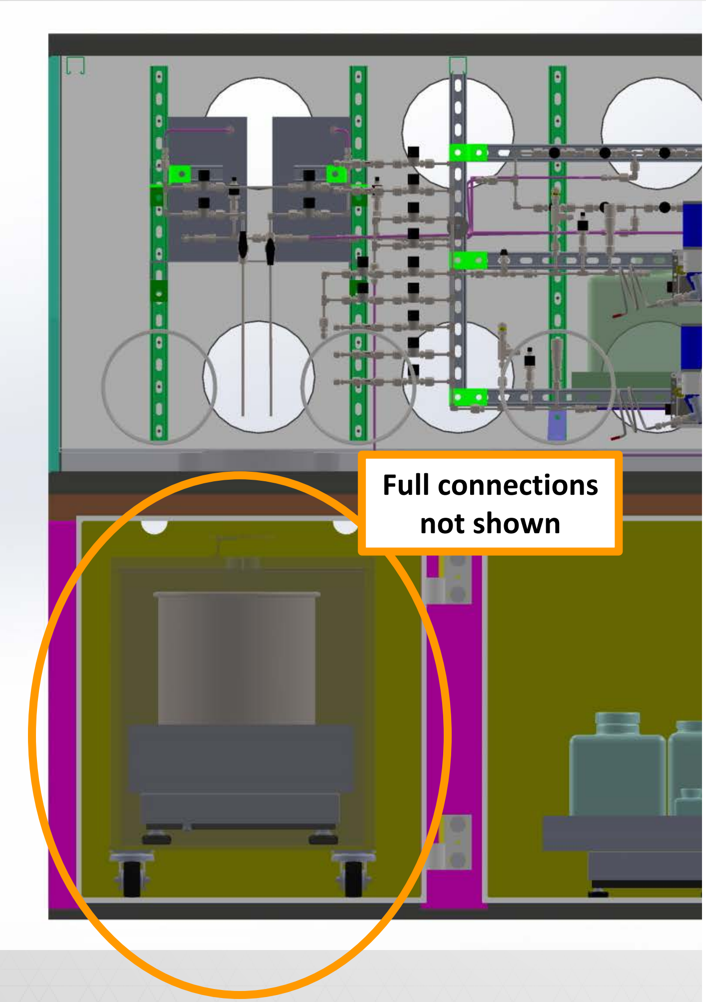
Poster by J. Krebs

PROCESS EQUIPMENT FOR PHASE II



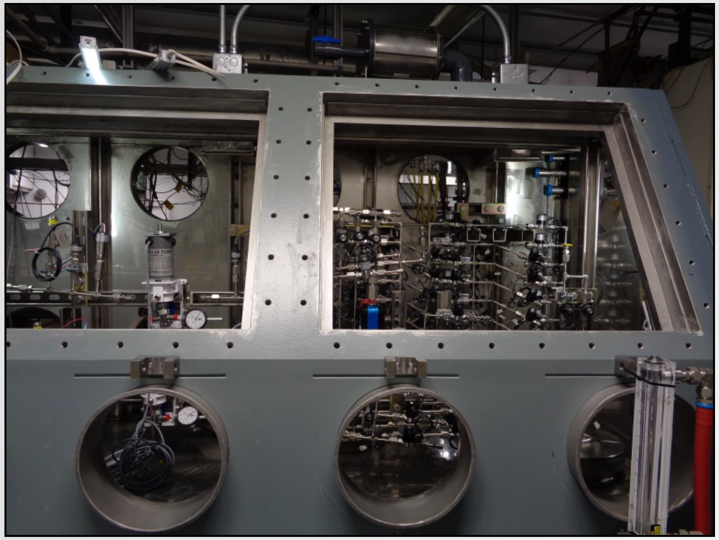
- Shielded Column Cart
  - Roll into position
  - Raise to interface with bottom of glovebox
  - Connections made in the glovebox
- Shielded Effluent Bottle Cart
  - Houses **ALL** effluent bottles
  - Post-load acid wash
  - Rinse bottle
  - Connections made in the cabinet
- Cabinet areas are part of ventilated volume of glovebox
- Recovered ^{99}Mo solution pumped to Purification mini-Hot Cell
- ^{99}Mo transport cask reserved for backup receipt vessel

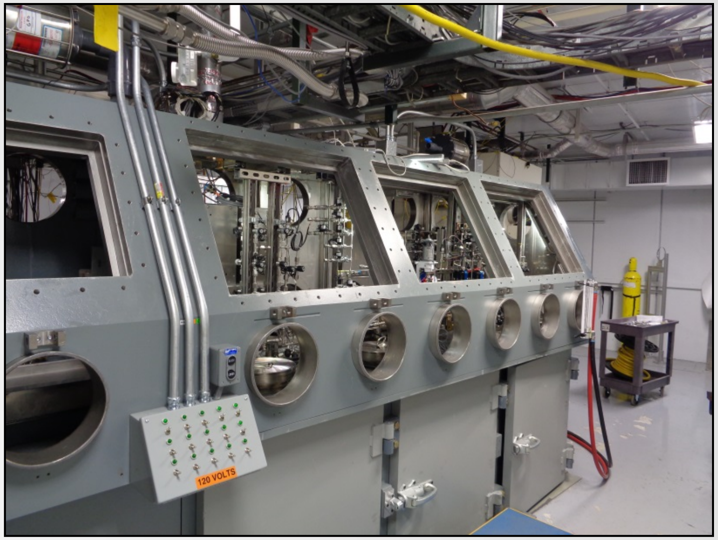
TARGET SOLUTION MASS VERIFICATION AND SAMPLE RETRIEVAL



- Shielded Target Solution Verification Cart
  - Roll into position
  - Connections made in the cabinet
- Verification vessel
  - 35 L slant bottom 316 SS tank
  - On 50 kg load cell
- Target solution pumped into verification vessel
- T-manifold in glovebox allows for:
  - Sampling
    - Concentration verification
    - Density verification
  - U makeup solution to be added as needed
- Target solution returned to target vessel
- Shielding required for residual target solution in vessel (< 50 mL)

PHASE II GLOVEBOX





PHASE II EXPERIMENTAL PLAN

- Leak test system, measure dead volumes, and ensure no cross-contamination during sample retrieval process – August-September 2016
- Sulfuric acid test with ^{99}Mo spike – no irradiation – September 2016
- Sulfuric acid test with ^{99}Mo spike – short irradiation (2 hours) – October
- Short uranium irradiations to get production rates – November-December 2016
- Full uranium irradiation – shipment to Lantheus Medical Imaging – January 2017
- Full uranium irradiation – shipment to GE Healthcare – February 2017

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