



NIO WAVE

Accelerating the Fight Against Cancer

Pre-Decisional Enforcement Conference

NRC Region III

May 25, 2022

Public Session

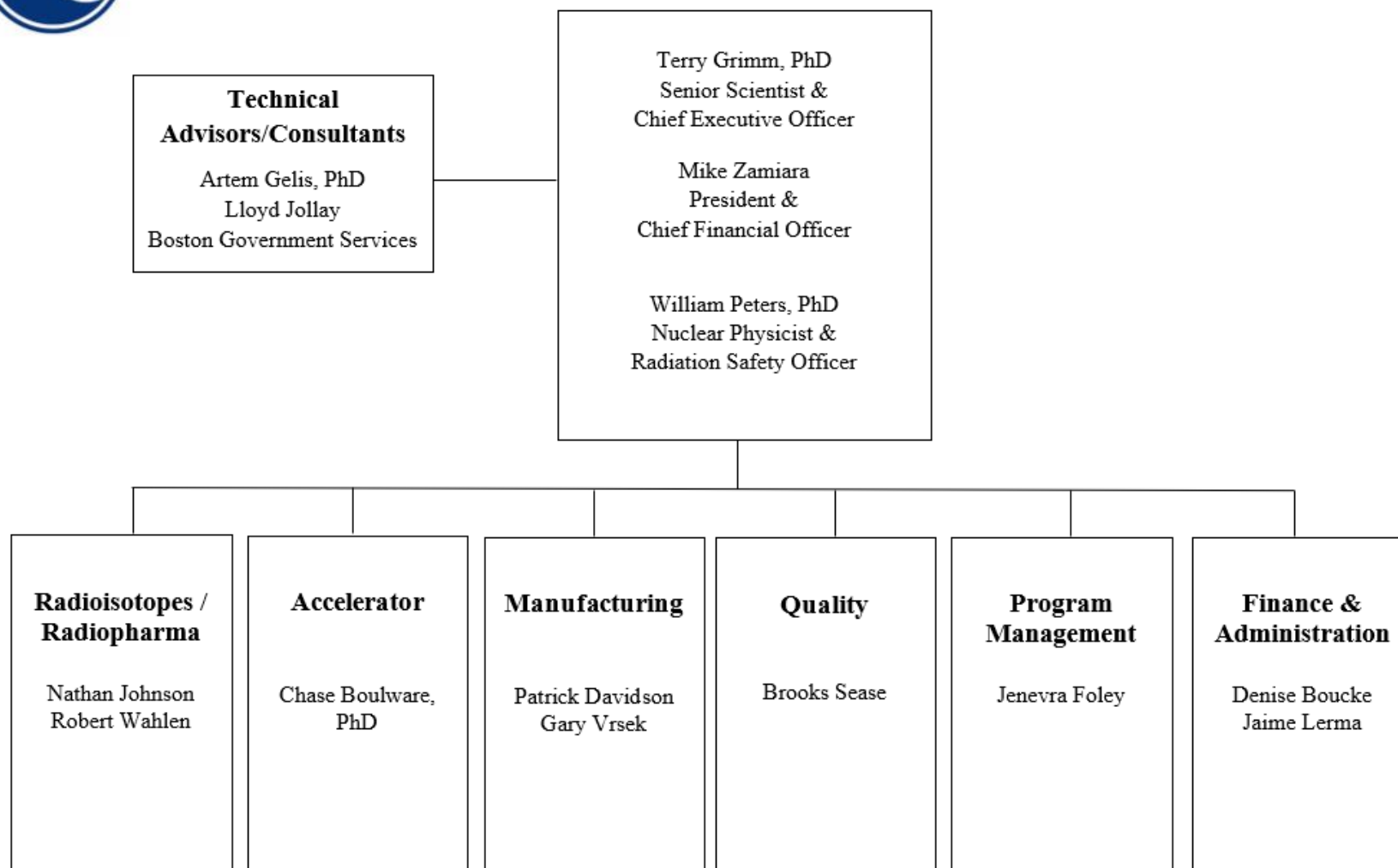
Outline

- Niowave Background
- Recap of Apparent Violations
 - Recall of Events
 - Immediate Response
 - Ad-hoc Rad Safety Committee
- Corrective Actions
 - Rad Safety Policies & Committee
 - Dosimetry
 - Training
 - Updated Hardware
- Current Operations
 - Y-90 Production
 - Dose Trends
 - Radiological Work Permits
 - HR
- CAPA Status
- Summary of Corrective Actions

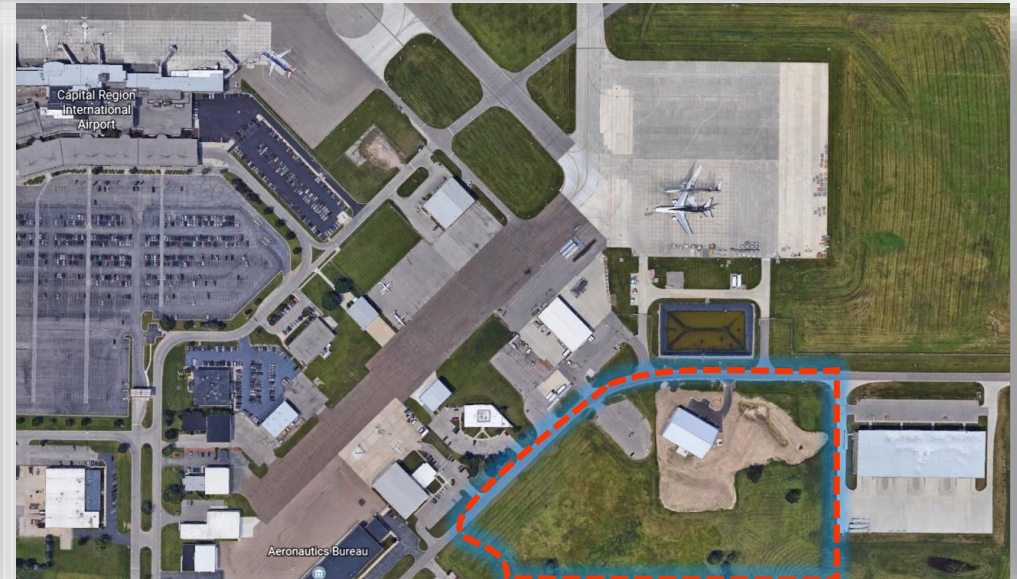




Niowave Organizational Chart

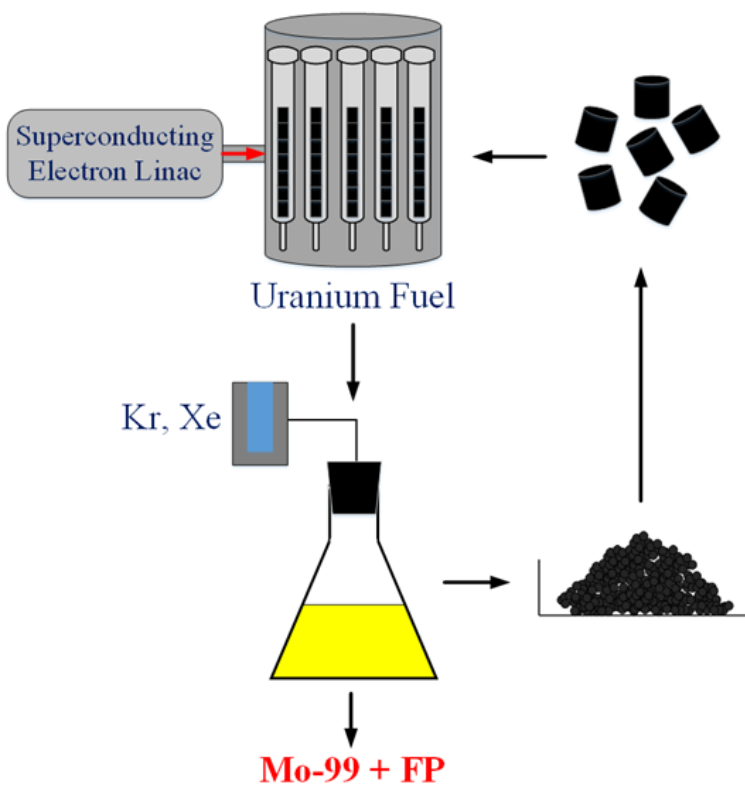


Facilities (Lansing, Michigan)

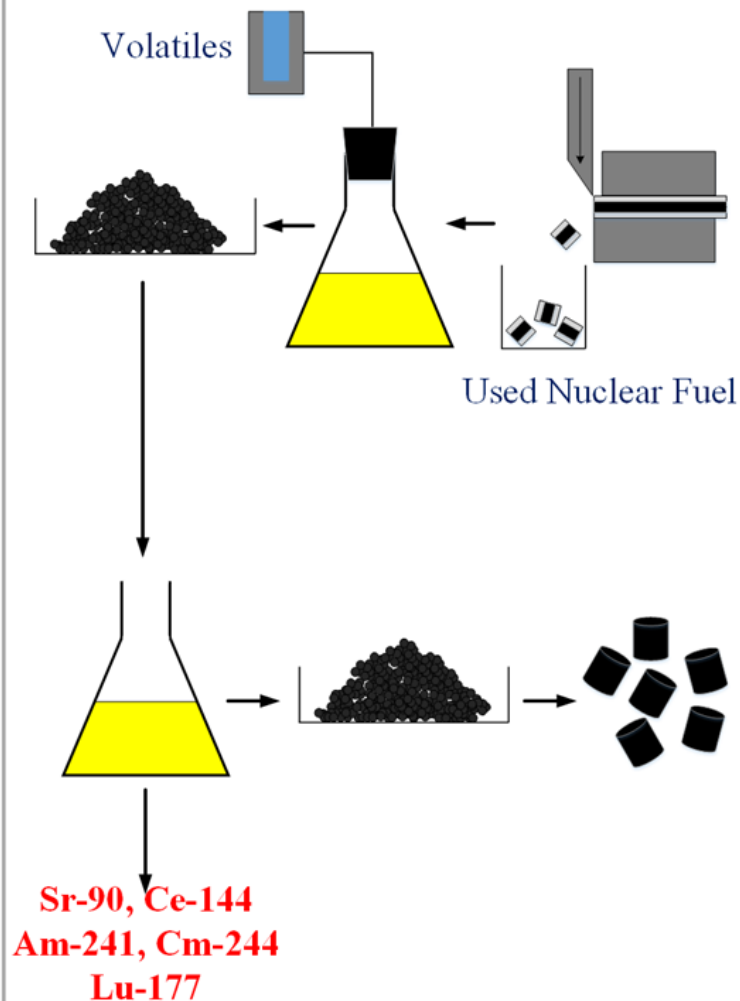


Isotope Program Overview

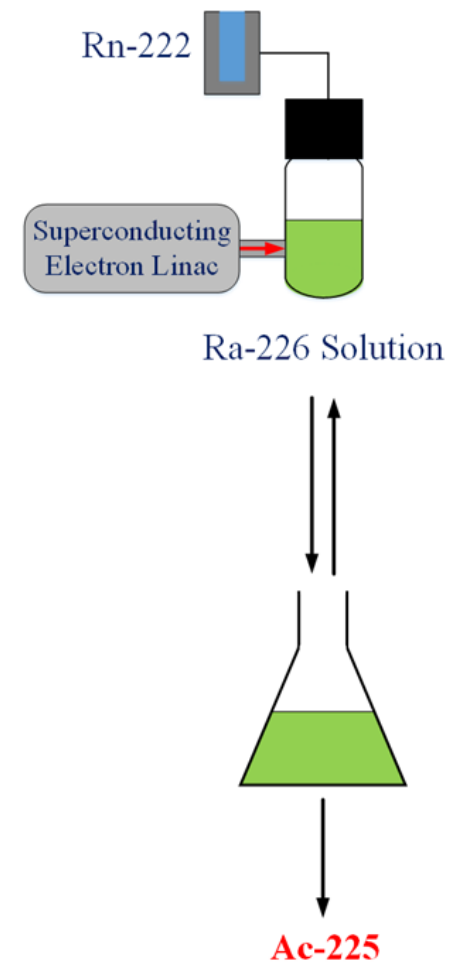
Mo-99 Program



Reactor Program

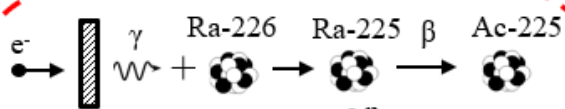
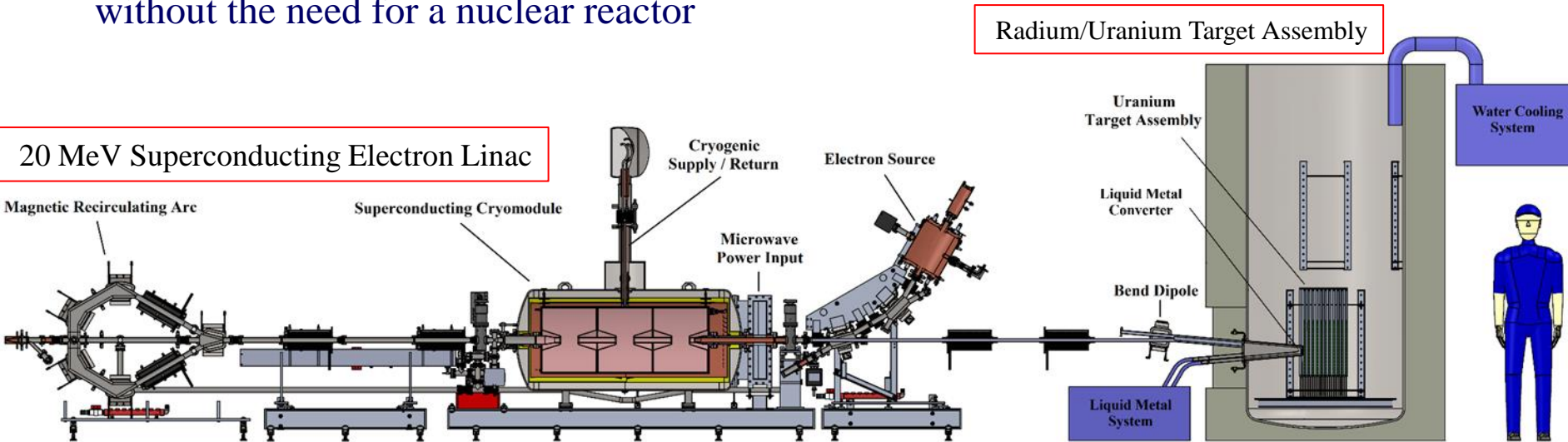


Ac-225 Program



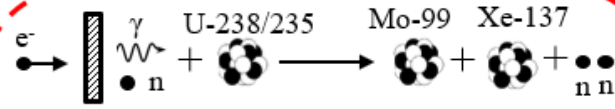
Therapeutic α and β Emitters

Niowave manufactures radioisotopes from radium and uranium
using a superconducting electron linear accelerator
without the need for a nuclear reactor



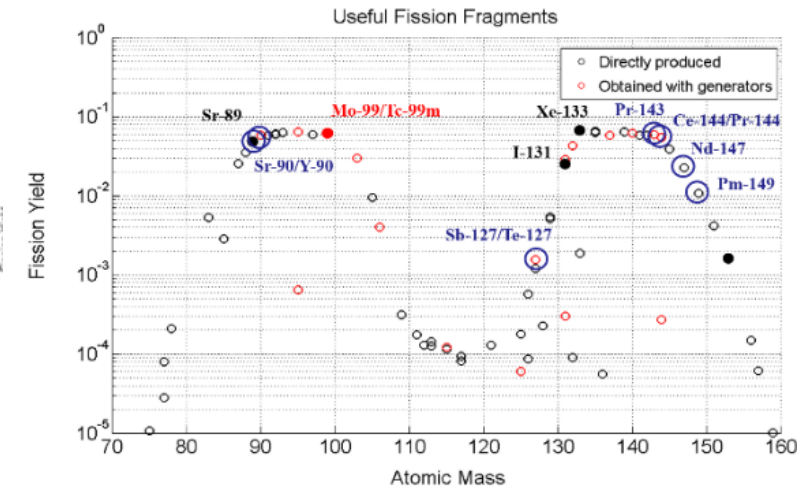
Radium
(Ra-226)
 α emitters

Ac-225	10 d
Rn-222	3.8 d
Po-210	138 d
Bi-210	5.0 d
Bi-213	46 m
Bi-214	20 m
Pb-214	27 m



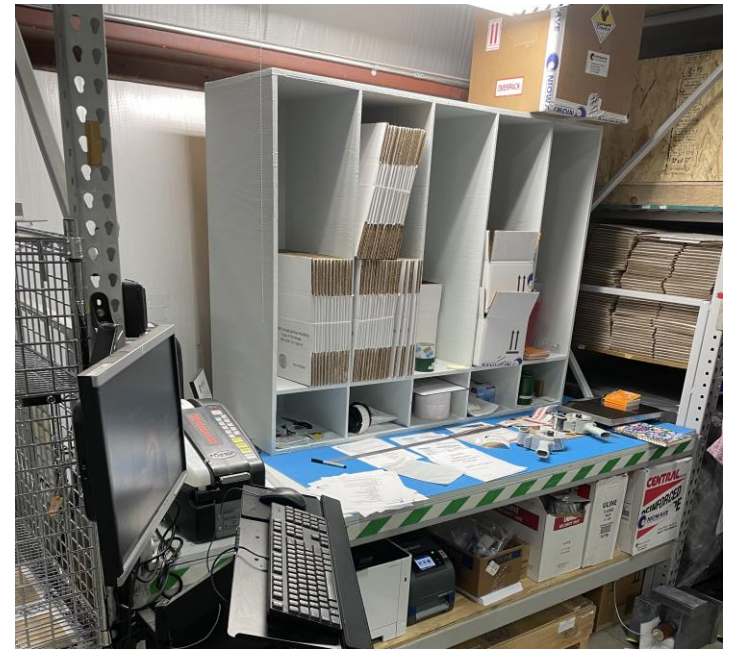
Uranium
(U-235/238)
 β emitters

Mo-99 \rightarrow Tc-99m	I-131
Sb-127 \rightarrow Te-127	Xe-133
Ba-140 \rightarrow La-140	Sr-89
Ce-143 \rightarrow Pr-143	Y-91
Sr-90 \rightarrow Y-90	Ce-141
Ce-144 \rightarrow Pr-144	Nd-147
	Pm-149



Sr-90/Y-90 Program

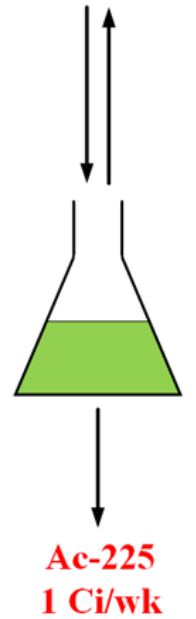
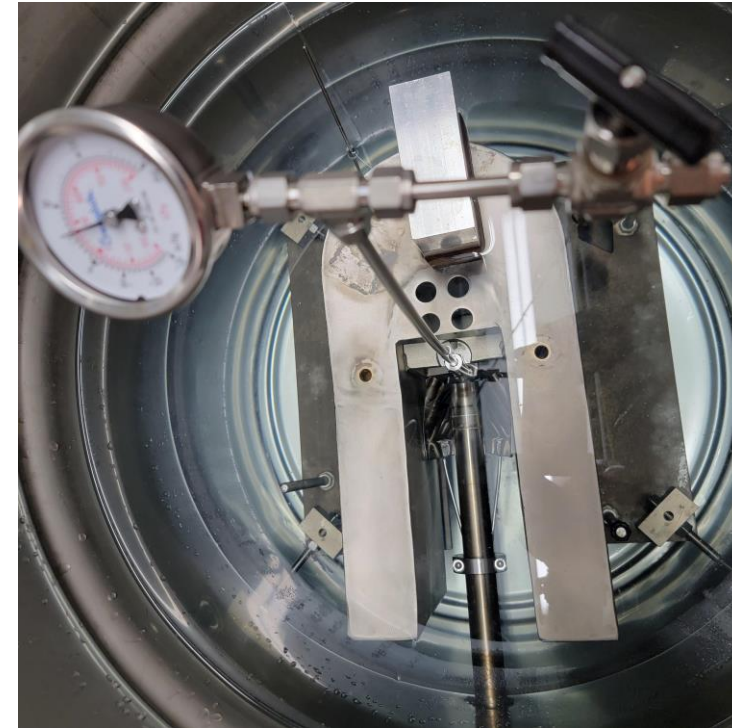
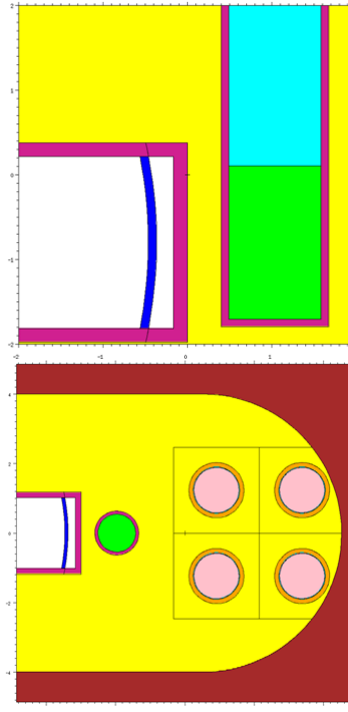
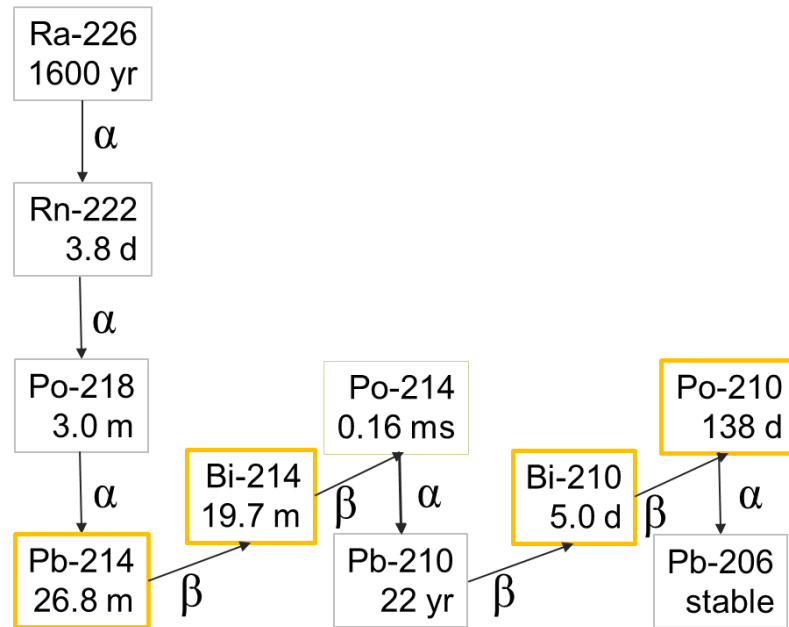
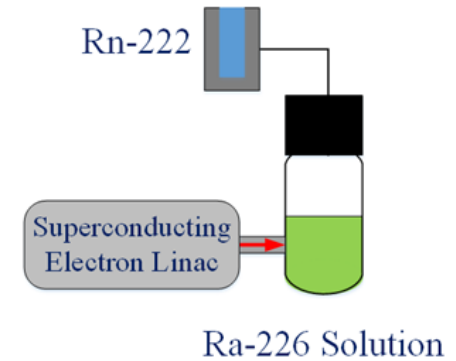
- Niowave's first commercial isotope
 - First shipment to treat cancer patients performed on 04/25
 - Commercially viable, Ci-scale
- Hot Cells & processing equipment for beta emitters
 - Niowave manufactured and compliant with ASTM standards & ANS hot cell design guide
- Quality system (ISO 13485 certified)
- Custom DOT Type A packages



Ac-225 Program [1]

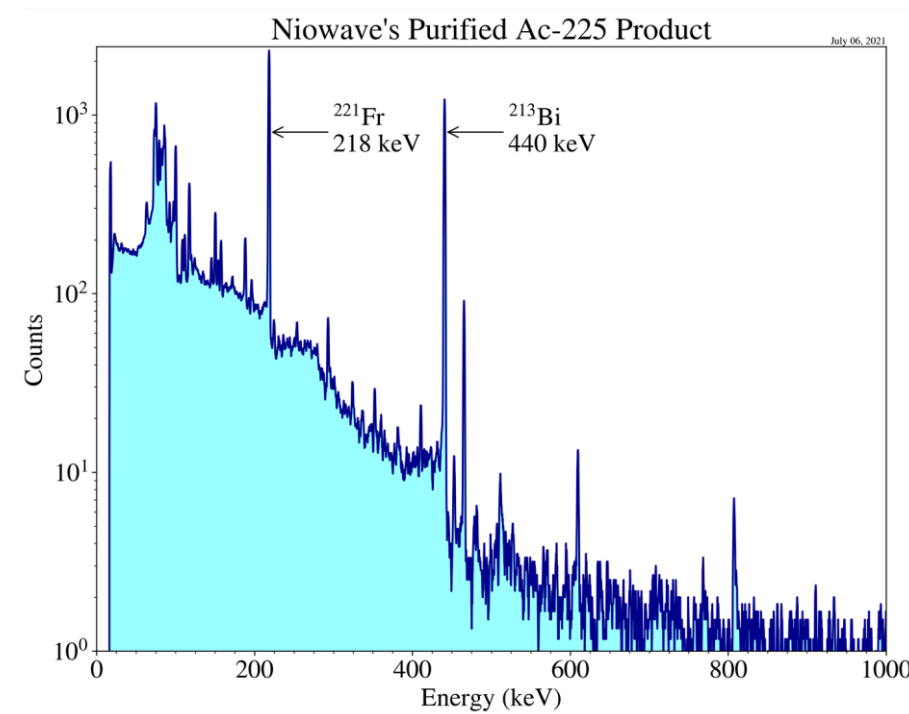
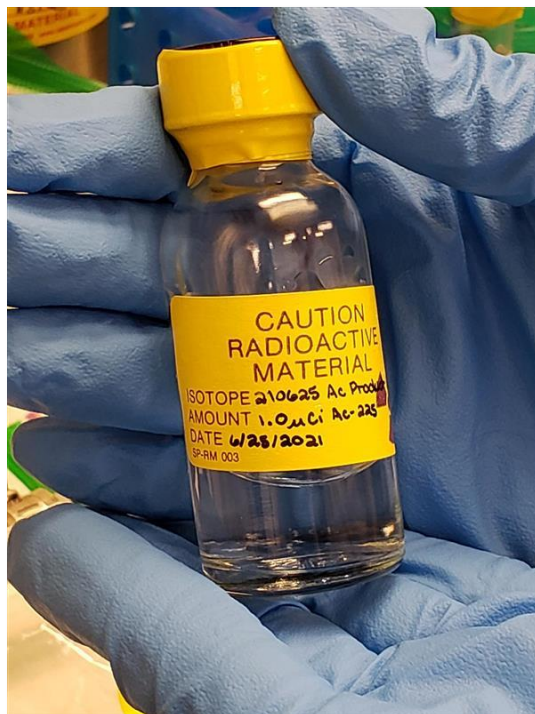
- Target alpha therapy using Ac-225 is demonstrating extreme potential for curing several types of cancer
- Niowave is ramping up from mg to g scale of Ra-226
- Isolating radon gas and purifying progeny for use in radiopharmaceutical development (α , β , and γ emitters)

Ac-225 Program



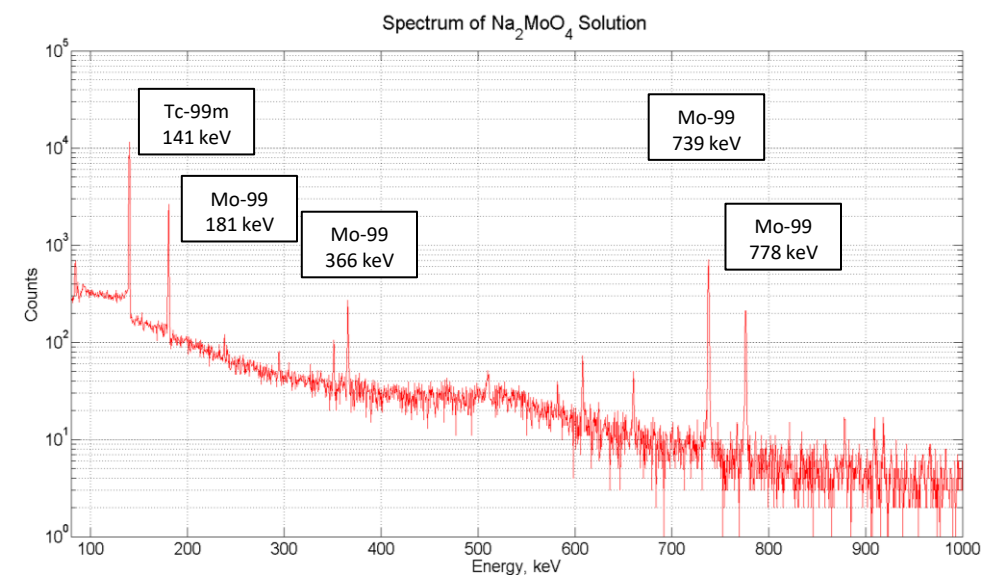
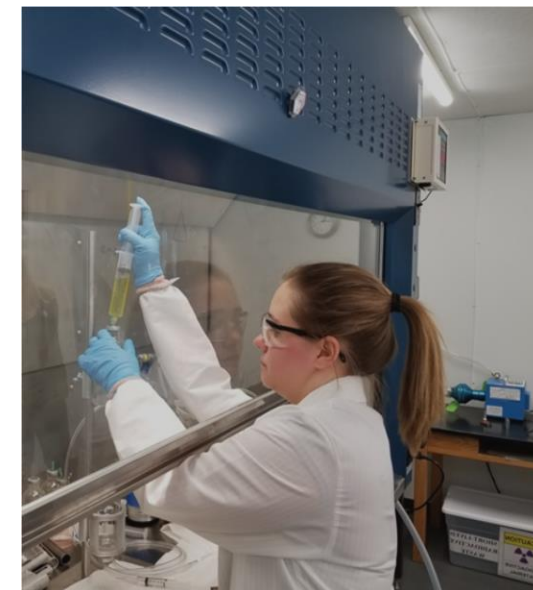
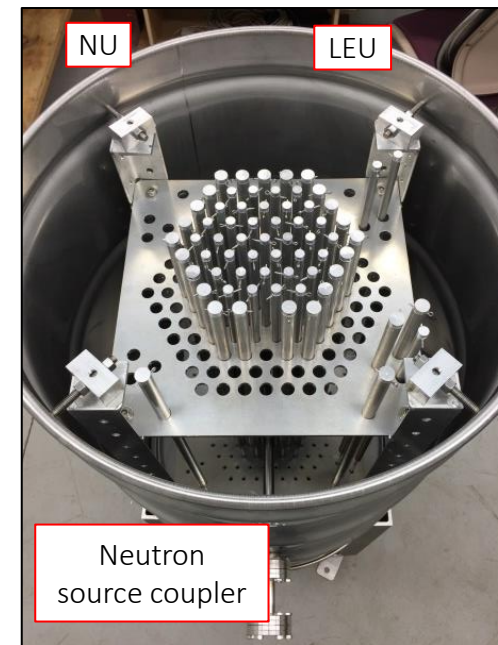
Ac-225 Program [2]

- Linac used to produce 1 mCi Ac-225 from Ra-226 target material
- Ac-225 product shipped to customers in 2021
- 1-2 mCi / week Ac-225 production in 2022



Mo-99 Program

- Congressional program to support domestic supply of Mo-99
- Mo-99 critical for nuclear medicine diagnostics
- Niowave is one of three private companies selected for program
- Niowave partners with National Labs supported by the NNSA through this program
- Involves separating fission products from irradiated uranium targets



National Lab & University Partners

Argonne – UREX, Mo-99 Chemistry

LANL – LBE Target

ORNL – Neutronics and Shielding Calculations

PNNL – Dissolution & Gas Extraction

SRNL – UREX

Y-12 – Uranium Recovery and LEU

UNLV – UREX, Mo-99 Chemistry, Other Isotopes

MSU – Other Isotopes, Radiopharmaceuticals



Quality System (QS)

- Implemented 21 CFR 820 / ISO 13485:2016 quality system
 - 200+ Documents released and trained
 - ISO 13485:2016 certified
- Passed multiple customer & certified body audits with zero findings within the last year
- Approved supplier of Y-90 for use in FDA approved cancer therapy (med device)



Regulatory Agencies

- State of Michigan
 - 40 MeV, 100 kW superconducting electron linac
- Department of Transportation (DOT)
 - HAZMAT & DOT compliant program
 - Shipped material as limited quantity, Type A, and Type B
 - Received material from IAC, MSC, NFS, Y-12, and universities
- Nuclear Regulatory Commission (NRC)
 - Current licenses through Region III (Chicago)
 - NSIR Office (DC) Emergency Plan reviewed
- Food and Drug Administration (FDA)
 - Implemented 21 CFR part 820 QMS in Q1 2021



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Recap of Apparent Violations

Recall of Events

- Niowave performed operations to optimize and validate Y90 production during September – December 2021
- Dosimetry results of October were received 12/03/21 – delayed 1 month
 - Two workers total dose was 30-40 rem (shallow, annual total), immediately paused work for these two workers
 - 2 – 3 x higher than dose estimates & real time monitoring indications
 - Dosimetry for November were sent in for rush processing the next day
- Partial dosimetry results for November received 12/13/21
 - One person received 97.4 rem shallow dose to hand, 87.1 rem in month of November.
- All radiological work at Niowave was paused on 12/14/21
- Full dosimetry results for November received 12/17/21
 - Two additional over exposures, 53.4 rem and 89.2 rem of shallow dose to hand (annual).
 - All personnel who received overexposure to hand received 1.0 to 1.1 rem of deep dose to body for whole calendar year
- Submitted report to NRC on 01/06/22

Areas of Improvement

In the subsequent investigation of the incident Niowave identified the following opportunities for improvements:

- **Training:** Personnel performing the operation needed more training on radiation safety with high activity material including hazards and accident scenarios in addition to the in-lab, on the job, mentoring and training.
- **Hardware and Procedures:** Equipment and methods to generate Y-90 was inadequate for increased activity needed for Y-90 production. Time, distance, and shielding could be improved.
- **Live monitoring, oversight, and radiation safety policies:** Connected to training, Niowave staff were not properly utilizing live monitoring equipment to evaluate dose in some situations, some live monitoring tools underreported dose. Oversight by experienced staff was not maintained during all hot operations.

Ad-hoc radiation safety committee

Ad-hoc radiation safety committee formed on 12/14/21:

- CEO/Senior Scientist
- President/CFO
- Radiation Safety Officer
- Director of Radioisotopes & Radiopharmaceuticals
- Director of Radioisotopes & Radiopharmaceuticals

Functions of the committee included:

- Oversee investigation of overexposure
- Approval of all radiological work (Dec – May)
- Monitor weekly radiation dose results
- Live oversight of dispersible rad work

Inspection

- Ryan Craffey performed inspection on January 18-19, 2022
- Detailed review of overexposure incident provided by Mike Zamiara (President/CFO), William Peters (RSO), and Brooks Sease (Director of Quality)
- Ryan Craffey interviewed Niowave personnel involved in Sr-90/Y-90 work and overexposure
- Audit of license 21-35144-04

Apparent Violations

- Exceed NRC limit for dose to extremity
 - 10 CFR 20.1201(a)(2)(ii)
- Adequate surveys to prevent overexposure
 - 10 CFR 20.1501(a)
- Adequate controls to achieve ALARA
 - 10 CFR 20.1101(b)



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Corrective Actions



Corrective Actions

- ✓ Revised Internal Policies
- ✓ Refined Dose Calculations
- ✓ Reinforced Dosimetry & Monitoring
- ✓ Formalized Training
- ✓ Improved Equipment

