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INVAP/B&W Mini-Loop Production of Mo-99

T. A. Policke, D. E. Glenn, and S. B. Aase
Babcock & Wilcox – Technical Services Group (MIPS)
Lynchburg, VA 24504 – USA

and

D. Amaya and V. Wilkinson
INVAP SE
San Carlos de Bariloche, Rio Negro – Argentina

ABSTRACT

Through the partnership of B&W and INVAP, an approximate 1/400th scale, functional, small Medical Isotope Production System (MIPS) was designed, constructed, and operated to successfully demonstrate the Proof-of-Principle (P-o-P) for producing molybdenum-99 (Mo-99) from a low enriched uranium (LEU) uranyl nitrate solution. A 500mL volume of solution is irradiated in a reactor and the fission-produced Mo is extracted and purified. This scaled version was designed and constructed by INVAP and is being operated by the Comisión Nacional de Energía Atómica (CNEA) and INVAP personnel at the RA-6 facility in Bariloche, Argentina, producing Ci quantities of purified, high specific activity Mo-99 that meets specification to produce radiopharmaceutical grade technetium-99m (Tc-99m). The partnership has equipped the facility with a shielded cell that performs the extraction and purification processing, in addition to a laboratory area and the capability to perform the analytical work to support this research and development effort. An overview of the setup, performed tasks, and goals are covered in this presentation.

1. Introduction

The Babcock & Wilcox Company – Technical Services Group (B&W-TSG) is pursuing the development of a Medical Isotope Production System (MIPS) to produce 50% of the domestic need, within the United States of America, of Molybdenum-99 (Mo-99), the precursor to the radiopharmaceutical technetium-99m (Tc-99m). The US consumes around half of the total production of technetium (Tc).[1] The goal of the MIPS is to produce high specific activity Mo-99 through the fissioning of uranium-235 (U-235) using a solution of low enriched uranium (LEU) as uranyl nitrate (UN) in an aqueous homogeneous reactor (AHR).

As part of its nuclear non-proliferation mission, the National Nuclear Security Administration (NNSA) is working to develop a sustainable means of producing life-saving medical isotopes, such as Mo-99, without using highly enriched uranium (HEU). This program is part of the effort by NNSA's Global Threat Reduction Initiative (GTRI) to develop and implement technologies to minimize and, to the extent possible, eliminate the civilian use of HEU, including in research reactors that produce medical isotopes.[2]

The MIPS and its use of an AHR are ideal for this purpose: 1) LEU is utilized in support of the Department of Energy (DOE) initiative to reduce use of high enriched uranium (HEU), assisting in the GTRI and 2) the spent fuel is drastically reduced since the uranium is re-used. Although the AHR technology is not new, its dedicated and continual use as a production reactor for the production of Mo-99 is new and will, therefore, require thorough testing, or Proof-of-Principle (P-o-P), in order to achieve licensing from both the US Nuclear Regulatory Commission (US NRC) and the US Food and Drug Administration (US FDA).

Thus, B&W-TSG contracted with INVAP to develop, design, construct, and test a "Mini–Loop" concept to provide that P-o-P; which is, to produce Mo-99 by fission of U-235 in solution of low enriched uranyl nitrate, in a reactor environment with similar conditions as the intended industrial facility. Indirectly, the Mini-Loop will also provide a demonstration of the proposed irradiation technique.

The goals for the Mini-Loop irradiations include providing insight into the operation and pertinent parameters of reactor operations for the production of Mo-99 from the fissioning of U-235, assessing the effect of radiation on the separation of Mo using a selected inorganic sorbent, understanding the fate of radionuclide and stable species generated from the process in order to promote fuel reuse and develop composition profiles through extraction and into and through purification, providing supporting information related to the presence and/or absence of precipitates potentially formed during or after irradiation, working toward optimization of the extraction process, developing a tailored process for purification, and performing demonstrations that produce purified Mo that is acceptable as a precursor to the radiopharmaceutical Tc-99m.

The system has been operated six (6) times and each run has produced Curie quantities of Mo-99. The Mo-99 from the last run was actually loaded onto a Tc-99 generator. The initial tests from the generator show that the product meets the required pharmaceutical specification. This paper provides an overview of the Mini-Loop, its setup, goals, and performed tasks to date.

2. Experimental Set-Up

The starting material, LEU as uranium metal, 19.75% U-235, was obtained from Oak Ridge National Laboratory. The LEU material was converted to uranium oxide (U_3O_8) and characterized by CNEA and the following concentrations of pertinent elements were reported: 5.3ugMo/gU, < 1ugRu/gU, < 1ugTe/gU, and 3.2ugZr/gU. The U_3O_8 was dissolved to produce the uranyl nitrate (UN) solution in the RA-6 facility. A half-liter of the UN solution was contained in an irradiation capsule. The irradiation capsule with the uranyl nitrate was placed in the RA-6 reactor pool of the CNEA facility and irradiated per the conditions in Table 1.

Table 1: Irradiation Information

Neutron flux (n/cm^2-sec) in irradiation capsule (uranyl nitrate solution)	1E+12
Power density (kW/L)	1
Heat Flux (W/cm^2) referenced to the irradiation capsule wall	~ 1.3

The power density is the equivalent of that in the conceptual design for MIPS. The intent is to use the same UN solution for all irradiation runs in order to obtain fuel cycle information as well as behavior of the process as the fuel is aged. Figure 1 shows the capsule, Figure 2 shows the installation, and Figure 3 depicts the capsule in the reactor grid.

Figure 1: Capsule

Figure 2: Installation

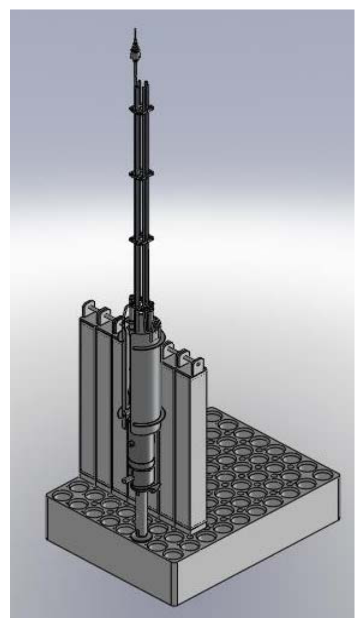

Figure 3: Capsule in grid

The irradiation facility is equipped with a system for the treatment of gases as iodine, noble gases, hydrogen, and oxygen. Thus, it has a functional off-gas handling system that at the same time constitutes the prototype for the MIPS. The Mini-Loop also has the following components:

an acid pump for the addition of nitric acid (HNO_3) in order to adjust the pH as desired during irradiation, a self-powered neutron detector (SPND) to measure the flux at the exterior surface of the UN solution irradiation capsule and a sensor to measure hydrogen. During the irradiations a number of items are monitored as a function of time, such as pressure and temperature in various tanks, hydrogen concentration, and temperature at different locations.

After irradiation, the UN solution is transferred by vacuum under the reactor pool water to a transport container, which is then transported to a shielded cell for pH adjustment if needed, sampling, extraction, and purification per the flow diagram in Figure 5.

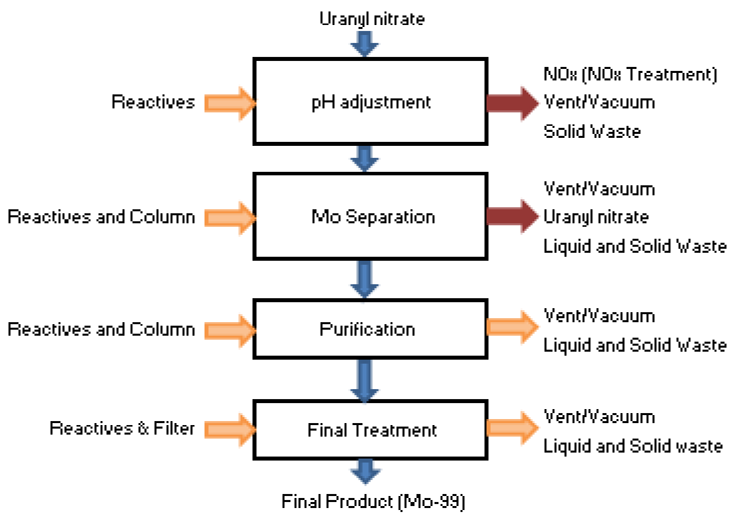

Figure 5: Block diagram of the processes in the shielded cell

The Mo extraction process starts with passing the irradiated solution through an inorganic sorbent column. The extraction process and INVAP's column design are proprietary to B&W. The sorbent retains the Mo and the passing solution is retained for another irradiation cycle. The column material is then rinsed with a combination of acid and water. Finally, the Mo is stripped from the sorbent with an alkaline solution. The column also contains, under the appropriate conditions, a portion of the produced iodine created in the fissioning process. This alkaline solution is then passed through the purification process. Upon final treatment, purified Mo is produced.

There are fourteen (14) sampling points throughout the extraction and purification stages to profile the entire process. The measurements, depending upon the sample and location, include pH, uranium concentration, and radiochemistry for alpha, beta, and gamma determinations.

All of these functions occur in the single shielded cell which contains all of the necessary equipment and utilities to perform the work, as can be seen in Figure 6.

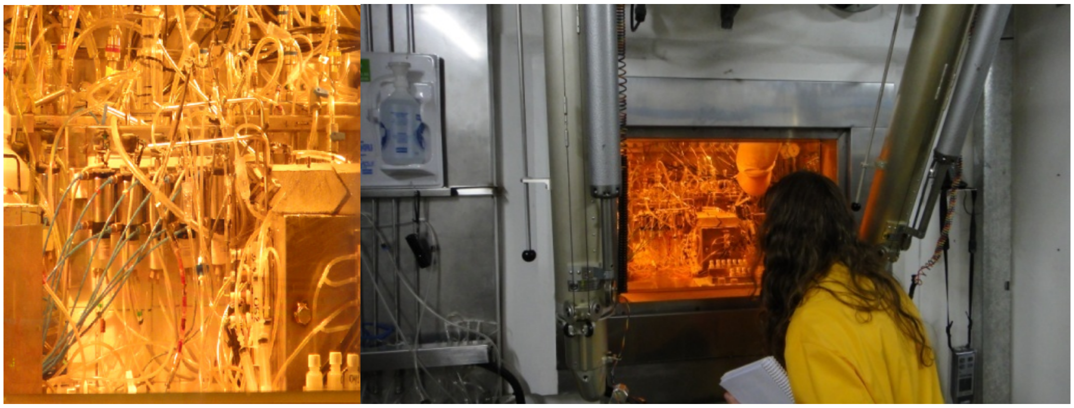

Figure 6: Shielded Cell

The partnership of B&W and INVAP helped equip the RA-6 facility with the necessary equipment to support this experiment and processing. The INVAP design for the processing system includes the setup for remote operation of valves, heaters, pumps, and other pieces of equipment through the use of a programmable logic controller (PLC). The facility is also equipped with a split glove box with shielding in one side, a gamma spectrometer, an ionization chamber, a liquid scintillation counter, a UV-Vis spectrophotometer, and other basic laboratory equipment.

The main purpose of the Mini-Loop is to provide the P-o-P for producing high specific activity Mo-99 using neutrons to fission U-235 in a solution of uranyl nitrate. Indirectly, the Mini-Loop will also provide a demonstration of the proposed off-gas handling for the MIPS. Finally, beyond the Mini-Loop, the goals for the rest of the setup include understanding and optimizing the extraction process, as well as determining the effect of radiation/dose on the extraction process for Mo and other radionuclides, identifying sorptive species that compete with Mo, and producing purified Mo.

3. Results

To date, six (6) irradiation runs have been performed. The first three runs were successful from irradiation through purification. Due to a cross contamination issue in the shielded cell, the product from Run #1 was above the specification level for zirconium-95 (Zr-95) and ruthenium-103 (Ru-103). The contamination was determined to occur midway through the purification process and was related to the work in a unique and small shielded cell. This issue was remedied with a thorough cleaning of the shielded cell equipment as well as a modification to the processing procedure. Future runs did not show this contamination issue. Run #4 was aborted after extraction of the Mo due to an unanticipated process difficulty at the onset of purification. Run #5 was aborted during the underwater transfer of the UN solution from the capsule to the transfer container, in which a leak occurred in the transfer line resulting in the dilution of the UN solution and slight contamination of the reactor pool water.

A small subset of the actual Run Details and Data (those that are non-proprietary) are presented in Table 2. This subset is presented to show that INVAP and B&W have knowledge of this particular process of creating Mo-99 by fission of U-235.

As can be seen by the results in Table 2, Ci amounts of Mo-99 were produced during each run. Runs #1 through #5 were approximately 20 hours with Run #6 being 50 hours.

Table 2: Run Details and Data

Attribute/Run	**1**	**2**	**3**	**4**	**5**	**6**
Initial pH	0.5	0.9 - 1.1	0.9 - 1.1	0.9 - 1.1	0.9 - 1.1	0.7-0.9
Irradiation Time (hour)	20	17:50	18	17:05	18	50
HNO_3 added (mL)	0	4	3.3	6.4	2.1	8
Mo-99 produced	Curies	Curies	Curies	Curies	NM	Curies
pH after irradiation	2.5 - 3	0.9 - 1.1	1.1 - 1.4	0.5 - 0.7	--	0.9-1.1
pH before extraction	0.9 - 1.1	0.9 - 1.1	0.7 - 0.9	0.5 - 0.7	--	0.9-1.1
I-131, Ru-103, Te-132, Zr-95, Mo-99	Determined by gamma spectroscopy to follow the process, including sorptive and release behavior					
Mo-99 after extraction (Ci)	Curies	Curies	Curies	Curies	--	Curies
Extraction Efficiency (Mo %)	42	87	87	99	--	97

NM = Not Measured

The calculated extraction efficiency for Runs #2 through #6 was greater than 85% with Run #4 and Run #6 above 95%, which exceeds the conceptual design goal 90%. The extractions for Runs #1 through #4 were also carried out at the ambient shielded cell temperature instead of the determined optimal temperature for extraction, which would have increased the efficiency. In Run #6, a heated alkaline solution was used for stripping to simulate the optimal temperature extraction process.

With the exception of the first run, due to a cross contamination issue, the Mo-99 produced has met the specification requirements for use in a technetium-99 (Tc-99) generator. The Mo-99 from the last run was actually loaded onto a Tc-99 generator showing the good quality of the product. The tests from the generator show that the product meets the required pharmaceutical specification.

Table 3 contains the results for the final product: Mo-99 in alkaline solution. Unfortunately, due to the work being done in one shielded cell and the operations being the first of a kind, the product material from Run #1 picked up Zr-95 and Ru-103 contamination at the end of the purification process. The other attributes were within the specification requirements. After a thorough clean up of the shielded cell and equipment, Runs #2, #3 and #6 produced Mo-99 that met the specification requirements.

Table 3: Results for Runs #1, #2, #3 and #6

Attribute			Spec[1] [3]	Run #1	Run #2	Run #3	Run #6[*]
Radiopurity	Gamma	I-131	< 0.05	ND In Spec	ND; In Spec	Detected; In Spec	Detected; In Spec
		Ru-103	< 0.05	Contam Out of Spec	Detected; In Spec	Detected; In Spec	Detected; In Spec
		Te-132	< 0.05	ND In Spec	ND; In Spec	ND; In Spec	ND; In Spec
		Other than Mo-99	< 0.05	NS	NS	Detected; In Spec	Detected; In Spec
		Zr-95	part of Other	Detected; Out of Spec	ND; In Spec	ND; In Spec	ND; In Spec
	Beta	Sr-89	< 6E-04	ND In Spec	ND; In Spec	Detected; In Spec	NM
		Sr-90	< 1.5E-5	NM –Sr-89 is In Spec	NM –Sr-89 is In Spec	NM –Sr-89 is In Spec	NM
	Alpha	Total	< 1E-6	NM	ND; In Spec	ND; In Spec	NM

ND = Not Detected
NS = Not Searched
NM = Not Measured
Contam = Cross contamination of final product.
[1] units are microCi/milliCi Mo-99
* The Mo-99 from this run was loaded onto a Tc-99 generator.
The initial tests show that the product meets the required pharmaceutical specification.

4. Conclusions

The Mini-Loop experiment is a success. It has provided the B&W program with the majority of the P-o-P in demonstrating that Mo-99 can be produced by the fissioning of U-235 in a solution and the Mo-99 can be suitably extracted with acceptable efficiency. Also, the entire process has demonstrated the feasible production of high specific activity, pharmaceutically acceptable Mo-99, as a precursor for Tc-99m, with the initial tests of the Tc-99m meeting the required pharmaceutical specification.

With its many data collection and measurement points, much is being learned about reactor operations, solution chemistry, radionuclide fates, precipitation phenomena, and information relevant to the extraction and purification processes. The experimental design is prototypic of MIPS and, thus, its data should directly support licensing by the US NRC as well as by the US FDA.

5. Acknowledgements

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6. References

[1] Global Nuclear Medicine Market (Medical isotopes / Radiopharmaceuticals) in PET/SPECT Imaging and Therapy – Competitive Landscape, Current trends and forecasts (2010 – 2015), Marketsandmarkets, 2011

[2] NNSA fact sheet, January 25, 2010

[3] Marion J. McDonald, Susan D. Carson, Gerald E. Naranjo, and Jeffrey A. Wemple, *Ind. Eng. Chem. Res.*, 2000, *39* (9), pp 3146–3150 (with the exception of Total alpha)