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CHALLENGES OF EXTRACTING AND PURIFYING FISSION-PRODUCED MOLYBDENUM-99

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Sandia National Laboratories (SNL) has produced limited quantities of fission-produced molybdenum-99 (^{99}Mo) within industry purity specifications using the Cintichem production process. The chemical extraction and purification of ^{99}Mo was performed using the Hot Cell Facility (HCF) located at Technical Area-V. To thoroughly understand the production process, two series of tests were designed, the first was a series of cold tests using 20 g samples of depleted or low irradiated uranium dioxide powder and the second series was conducted using irradiated targets. In addition, radiation effects tests were performed at the SNL Gamma Irradiation Facility (GIF) on chemicals and hardware used in the processing to evaluate the degradation due to the high radiation field expected during the chemical separation. Unique production hardware, fixtures and tools were developed for remote processing of irradiated targets at the HCF.

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Introduction

For more than forty years, the United States (U.S.) Department of Energy (DOE) and its predecessor agencies have produced and distributed isotopes through the national laboratories. In 1989, Congress established the Isotope Production and Distribution Program (IPDP) to bring together under one program all DOE isotope production activities. Among other activities, the IPDP has taken on the responsibility to establish a domestic capability to produce a reliable supply of ^{99}Mo for the US medical community. ^{99}Mo is the precursor to $^{99\text{m}}\text{Tc}$, which has become the most widely used radioisotope in nuclear medicine diagnostics.

Prior to 1989, a single supplier, Cintichem Inc. located in Tuxedo, NY, produced ^{99}Mo in the U.S. Because of problems associated with their reactor, in 1990 Cintichem elected to decommission the reactor rather than incur the costs for repair. The demise of the ^{99}Mo capability at Cintichem left the U.S. totally reliant upon a single foreign source, MDS Nordion International, located in Ontario Canada. At the present time they supply 90% of the ^{99}Mo used worldwide. ¹

In 1991 the DOE purchased the Cintichem technology and equipment which consisted of the Manufacturing Manual, the Drug Master File, Quality Control Manual, and processing hardware. ² DOE elected to establish production capability at Los Alamos National Laboratory (LANL), but in 1992 the LANL reactor was shut down after a high power scram incident and the subsequent discovery of an underground leak from the primary coolant. DOE decided not to restart the reactor and looked to SNL as a potential source for production. In 1996 the NEPA Environmental Impact Statement process was completed and the Record of Decision was signed to select Sandia National Laboratories (SNL) as the production site for ^{99}Mo . ³ Historically, the HCF and Annular Core Research Reactor (ACRR) had been used to support DOE Defense

Program's radiation effects testing on weapons systems and components and the Nuclear Regulatory Commission's fuels safety studies.

Process Description

^{99}Mo is produced by the fissioning of the uranium in a target in a reactor. The target, shown in Figure 1, consists of a 45.6 cm long, 3.2 cm diameter x 0.89 mm wall thickness stainless steel tube with a electrochemically coating of uranium oxide (UO_2) deposited on the inner surface of the tube. The target tube is sealed via welded end caps and then backfilled to 9 psi with helium.

Figure 1. Schematic of Mo-99 stainless steel target

After irradiation, the target is removed from the reactor and transported to a hot cell for processing where the end fixture is removed and a T-section containing a pressure gauge, injection port and quick disconnect is attached.

An acid mixture of 1.25 *M* sulfuric acid combined with concentrated nitric acid is injected through the T-section and the target is heated. The nitric acid oxidizes the UO_2 to aqueous UO_2^{+2} with the sulfuric acid providing the required acid media. The nitrous oxide which is formed, as well as noble gases and volatile iodine, are drawn off through the access valve following dissolution.

The acidic fission product solution is then drained from the target. Trace levels of iodine are precipitated as AgI and filtered out. The hold back carriers for ruthenium and rhodium are added. The Mo in the fission product solution is oxidized to Mo^{+4} with KMnO_4 and precipitated in the acid media using α -benzoin oxime in the following reaction.⁴

The precipitate is filtered and washed several times with 0.1 *M* sulfuric acid to remove contaminants trapped in the precipitate. The filtered precipitate is then dissolved using NaOH with 0.3% H_2O_2 , resulting in aqueous MoO_4^{-2} and various organic compounds in a 0.2 *M* NaOH solution.

The MoO_4^{-2} is purified by column chromatography. The first column contains Ag-coated charcoal; the second contains activated charcoal. These columns remove the organic compounds resulting from the breakdown of the α -benzoin oxime as well as impurity cations. Precipitation of trace iodine is repeated, and the solution is passed through a column with Ag-coated charcoal and hydrous ZrO. As a final step the product is filtered through a 0.3 μm / 0.2 μm filter assembly to remove any particulates. The final product is a solution of Na_2MoO_4 in 0.2 *M* NaOH.⁴

Cold and low irradiation tests, chemical separation

Although the Cintichem Drug Master File, Manufacturing Manual and Quality Control Manual were available, the process information was not complete and SNL had no production

knowledge from Cintichem's data. To thoroughly understand the process and identify critical steps in the chemical separation process, a series of tests was designed to reproduce the process and the results described in the manufacturing manual. These tests were designed to gain process knowledge, and to identify and resolve processing problems prior to processing an irradiated target. The first series of tests used 20 g samples of unirradiated or low irradiated depleted UO_2 powder samples. A 20 g sample was chosen because this was the typical loading on the Cintichem targets.

The chemical separation tests were performed in a fume hood using a pressure vessel to simulate the volume and conditions of the target dissolution vessel and an open beaker for the chemical separation. This provided an opportunity to simulate the target conditions during the heating/dissolution steps and observe the critical color changes that take place during the process. The use of a 0.19 MBq ($5\mu\text{Ci}$) ^{99}Mo spike added to the uranium powder provided a mechanism to evaluate the efficiency of the separation process. The last test in the cold series used a sample, which contained low levels of fission product impurities. This provided a mechanism to not only measure the efficiency of the separation process, but also to evaluate the performance of the purification columns. This was accomplished by irradiating a 20 g sample of UO_2 powder in the Sandia Pulsed Reactor for 6 hours at 14 kW steady-state power (302.4 MJ). The resultant yield of ^{99}Mo in the UO_2 was 18.5 MBq ($500\mu\text{Ci}$). At processing time the activity of ^{99}Mo was 260 μCi and the total radionuclide inventory was $\sim 1.1\text{ GBq}$ (30 mCi), calculated using ORIGEN2^{® 5}.

Hardware Development

The processing hardware and fixtures were developed in parallel with the cold tests and tested in a mock-up facility. The process uses double-ended serum bottles to contain solutions

and hypodermic needles, syringes and needle assemblies for the bottle-to-bottle transfer of solutions and reagent injection.. Hardware, fixtures and tools were designed for manipulator operations that involve solution transfer, reagent injection, processing equipment reconfiguration and general repairs (see Figure 2 and Figure 3). Guides were developed to facilitate the use of varying sized syringes used in the process and to minimize the potential of inadvertently using the wrong syringe in a process step.

Figure 2. Processing Hardware and Tools

Figure 3. Processing Fixture

Hot Tests, Chemical Separation

Following the cold tests and fabrication of processing hardware, a series of hot tests was designed using irradiated targets. These tests provided the opportunity to test the process remotely, identify problems prior to processing higher inventory targets and to optimize the process. The targets processed during these tests were below the fission product inventory expected for full production (see Table 1).

Table 1. Summary of Irradiation History and Inventory of Irradiated Target Tests

Test	Target Power (kW)/ Irradiation Time (hrs)	Post irradiation decay (hrs)	Total inventory (TBq*)/ decay inventory (TBq)	⁹⁹ Mo inventory (TBq)/ decay inventory(TBq)
1	5.0 / 24	24	700 / 29	2.1 / 1.6
2	3.8 / 8	16	520 / 15	0.56 / 0.48
3	3.7 / 10	16	520 / 16	0.67 / 0.56
4	3.5 / 24	24	520 / 20	1.4 / 1.1
5	4.1 / 149	6	670 / 111	5.9 / 5.6

*27 TBq = 1Ci

Dissolution problems were encountered during the first test when none of the uranium coating was removed during the dissolution process. As mentioned previously, the typical Cintichem target had a mass loading of 20 g of UO₂, the uranium loading on the target processed was 27 g. Consequently, the dissolution cocktail did not have sufficient concentration to dissolve the heavier target. Target dissolution tests were performed varying the quality and normality of each acid. Using the test data, the optimum mixture of H₂SO₄ and HNO₃ was determined. ⁶

Many of the initial problems were related to bottle-to-bottle transfer of liquid and the injection of reagents. These were resolved by several means including , pre-evacuation of the bottles and vacuum system assist. In addition vented charcoal columns were used to equalize the bottle pressure and trap any iodine gas that vented from the bottle. The color of the leaded glass

windows in the processing boxes interfered with the identification of critical color changes.

Initially, paint sample cards were used in the processing boxes as color comparisons.

Quality control testing of the product was conducted for all the tests, comparing the results to pharmaceutical purity specifications. The product from the final test was split between two pharmaceutical companies for cross-check evaluation and compatibility with their process. Both pharmaceutical companies verified that the purity specifications were met and the product was compatible with their production lines.

Radiation Effects Testing

At full production, SNL expects to process targets that could have twice the fission inventory of that Cintichem encountered. The hardware, glassware and processing chemicals could experience dose rates of 50-70 Gy/hr. A series of tests were designed to evaluate the radiation effects on the hardware, chemicals and the stability of the product from time of processing to use. The 30 kCi ⁶⁰Co source at the SNL GIF was used for these irradiation tests. The dose rate of the GIF, 11 Gy/hr, is comparable to the dose rate expected during the chemical separation, ~ 12 Gy/hr.

Processing Hardware. The processing hardware was divided into glassware, hard plastics, and soft plastics. Several sets were irradiated in the GIF for varying exposure times. They were removed from the irradiation chamber and examined periodically throughout the test at 0.5, 1.0, 3.85, 7.2, 24 and 71.43 hours. Typical processing time for separation is ~ 4 hours and purification time is ~ 3 hours. Although all hardware exhibited some radiation damage after the equivalent of one hour of processing time, none of the hardware experienced failure at a total dose of 100 Gy, twice that expected during processing. Precautions will be taken during processing to minimize the radiation effects by the use of time, distance and shielding. An

additional GIF test was performed on the septa used on the double-ended serum bottles containing target dissolution acids. During processing the septa would receive the highest continual dose and showed signs of radiation damage in the initial testing. Results of the tests confirmed the acid did not compromise the integrity of the septa.

Processing Reagents. Duplicate 80 ml sample sets of the dissolution cocktail were placed in the GIF irradiation chamber and removed at 0.5, 1.0, 4.0 and 8.0 hours. The samples were titrated to a phenolphthalein endpoint with standardized sodium hydroxide. The titration results show that there was no degradation of the acid cocktail at four hours. At eight hours the acid strength had decreased by an average of 4%, which is insignificant, since a stoichiometric excess of cocktail is used, and the typical processing time is four hours from dissolution of the target coating to precipitation of the molybdenum oxime complex.

Three sets of α -benzoin oxime samples were irradiated in the GIF and removed at 0.5, 1.0 and 4.0 hours. The samples were evaluated using FTIR spectral analysis and results showed there was evidence of degradation after 0.5 hours. Samples evaporated for FTIR analysis consisted primarily of unreacted oxime with a thin yellow layer of product on top. Based on microscopic examination, it is estimated that less than 10% of the oxime decomposed during 4 hours of irradiation. Since approximately 6 times more oxime is used than required to complex the maximum amount of ^{99}Mo that could be present, and the precipitation process typically takes about 15 minutes, this amount of decomposition is not significant for product isolation.

Other Component Testing

Additional testing was performed on critical components of the process to understand the processing variability and determine the parameters to be used during production:

Column characteristics. Information on the makeup of the purification columns was incomplete and resulted in several problems associated with the flow rate and performance of the columns. The filtration media must be kept basic or polymeric crystals of polymobdates ions can form⁷ and would be held up on the frit. The columns were prepared and equilibrated to pH=12, sealed and routinely checked over a period of three months. They retained a pH of 12, demonstrating that this would not be a problem during production operations.

Problems were experienced in obtaining gravity flow through the fritted purification columns. The optimum particulate size was evaluated by sieving the column media, constructing columns, and observing the effect on flow rate. Although the rate of the gravity flow in the filtration columns is influenced by the filtration media porosity, the problem of flow stoppage was a result of pressures in the system. The problem was resolved by the use of pressure equilibrium needles and tubes.⁸

Target Etching. During the dissolution process the stainless steel target undergoes some etching from the acid dissolution cocktail. This could result in an unwanted heavy metal impurity in the product and/or make the resultant acid waste solution a regulated waste. The dissolution process was reproduced using an uncoated target and the resultant solution analyzed by a contract laboratory for heavy metals. The analysis confirmed that heavy metal impurities would not be a problem in the product or in the resultant waste.

Reagents. The quantities of reagents currently used in the chemical separation were evaluated stoichiometrically to determine if the amounts were sufficient or needed to be increased for planned production levels. It was determined the reagents were sufficient for the expected production levels.

Waste Stabilization

The production process generates a high activity acidic liquid waste. Several waste stabilization agents were tested in the GIF for long-term effects of high dose rates. Based on these results Portland cement was selected as the stabilization agent. A waste-handling container of stainless steel was developed which would facilitate the stabilization and neutralization of waste in the processing box. The cement, in addition to stabilizing the waste, neutralized the waste resulting in a mixture with a pH of ~ 6. The fission product waste was drained into a container preloaded with cement and tumbled on a rock tumbler for 20 minutes to thoroughly mix the cement. The addition of excess sodium bisulfite to the acid waste solution prior to mixing with cement serves to keep any iodine that may be present in the waste as iodide and minimizing the amount of iodine produced.⁹

Summary

The successful reproduction of the Cintichem process and delivery of a product to pharmaceutical houses was a significant step toward the DOE goal of developing a reliable Supplier of ⁹⁹Mo within the U.S.

Although, the chemical process itself does not involve complex chemistry, when the process is combined with a high radiation field, it becomes more complex. Because of the range of movement is restricted by manipulator operations, efficiency in processing becomes critical and radiation effects are a major concern. Several challenges were experienced in identifying and understanding the variability in the process parameters. All the challenges were successfully met and resolved to produce an efficient production capability. The surrogate tests performed outside of the HCF have minimized the probability of having an unexpected component failure during the next phase of testing for FDA validation. Work is

currently in progress to modify the HCF and the Annular Core Research reactor (ACRR) to meet the goal of providing a reliable U.S. supply of ^{99}Mo .

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