SAND97-0803 C

CONF-970424--1

Initial Generation and Separation of ^{99}Mo at Sandia National Laboratories*

Darren G. Talley, Susan C. Bourcier, Marion J. McDonald,

Susan W. Longley, and Edward J. Parma

Sandia National Laboratories

Albuquerque, NM

Methods and Applications of Radioanalytical Chemistry IV Conference

Kailua-Kona, HI, April 6-12, 1997

Medical Radioisotopes Production

April 11, 1997

* Sandia is a multiprogram laboratory operated by Sandia corporation, a Lockheed Martin Company, for the U. S. Department of Energy under contract DE-AC04-94AL85000.

DISCLAIMER

Introduction

Medical isotopes play an important role in the medical industry in both the United States and the world. Isotopes such as ^{99m}Tc, ^{201}Tl, ^{111}In, and ^{123}I are utilized in diagnostic imaging studies, while others such as ^{131}I and ^{89}Sr are used as therapeutic agents.[1] The particular medical isotope ^{99m}Tc is used in 80% of all nuclear medical procedures in the United States. This isotope is produced from the decay of ^{99}Mo, which has a 66 hour half-life. The importance of ^{99m}Tc and the fact of its 6 hour half-life indicate the necessity to maintain a constant supply of ^{99}Mo. The most prominent method for the production of significant quantities of ^{99}Mo is by fission in highly-enriched uranium loaded targets.

Prior to 1989, Cintichem, Inc., of Tuxedo, New York, was the major U. S. supplier of ^{99}Mo. With the shutdown of Cintichem in 1989, the DOE recognized a need to develop another U. S. supplier and acquired the rights to the Cintichem ^{99}Mo production process. The DOE has designated Sandia National Laboratories in Albuquerque, New Mexico (SNL) as the preferred site for the production of ^{99}Mo. In late 1994, SNL was authorized by the DOE to perform initial evaluations and studies to determine feasibility of production of ^{99}Mo in the U.S.[2] With the issue of a Record of Decision by the DOE on the Environmental Impact Statement SNL was authorized to begin full implementation of a ^{99}Mo production capability utilizing SNL's Annular Core Research Reactor (ACRR) and Hot Cell Facility (HCF). This implementation will proceed consistent with DOE project funding profiles.

The recent work done by SNL in an experimental campaign demonstrated that the Cintichem process could be utilized to produce limited quantities of ^{99}Mo within certain purity specifications. A secondary goal was to demonstrate that SNL ^{99}Mo product was compatible with pharmaceutical company ^{99m}Tc generators.

Experimental

The Cintichem process consists of four primary stages: 1) irradiation of a UO_2-coated isotope production target, 2) the irradiated UO_2 coating is dissolved from the inner surface of the target, 3) the Mo in the dissolved coating solution is precipitated, filtered out and redissolved, and 4) the Mo solution is purified of dissolution by-products and contaminants. This process is depicted in Figures 1 and 2.

The Cintichem process begins with the irradiation of an isotope production target produced by Los Alamos National Laboratory. A target consists of a 45.6 cm long, 3.2 cm diameter x 0.89 mm wall thickness stainless steel tube with a UO_2 coating which has been electrochemically deposited on the inner surface of the tube. The target tube is sealed via welded end caps. Each target is backfilled with 9 psia of helium. To generate fission isotopes, the target is placed in the flux of a nuclear reactor for a prescribed amount of time. Seven to fourteen days of irradiation is sufficient to optimize the inventory of ^{99}Mo within the target. After irradiation, the target is removed from the reactor and transported to a hot cell for processing and fitted with a fixture which includes a rubber septum port, an access valve, and a pressure gauge.

An acid mixture of 80 ml of dilute (1.25 *M*) sulfuric acid combined with 5 ml of concentrated nitric acid is injected through the rubber septum, 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 reaction is as follows.

$$3UO_2(s) + 3H_2SO_4(aq) + 2HNO_3(aq) \rightarrow 3UO_2^{2+}(aq) + 2NO(g) + 4H_2O(l) + 3SO_4^{2-}(aq)$$

The generation of NO gas pressurizes the target, providing an indication of the extent of completion of the reaction. The NO, as well as noble gases and volatile iodine are drawn off through the access valve following dissolution.

The acid fission liquor is then drained from the target. Trace levels of iodine are precipitated as AgI and filtered out. Ruthenium and rhodium holdback carriers are also added. The Mo in the fission liquor is oxidized to Mo(VI) using $KMnO_4$ and precipitated in the acid media using α-benzoin oxime in the following reaction.

$$MoO_4^{2-} + 2C_6H_5CH(OH)C(:NOH)C_6H_5 + 2H^+ \rightarrow MoO_2[C_6H_5CH(O)C(:NOH)C_6H_5]_2 + 2H_2O$$

The separation produces a tan flocculent precipitate which has a large surface area for contaminants to be carried to the next stage. Therefore, the precipitate is filtered and washed several times with very dilute (0.1 *M*) sulfuric acid. The filtered precipitate is then redissolved using NaOH with 1% H_2O_2, resulting in aqueous MoO_4^{2-} and various organic compounds in a NaOH solution.

The final stage involves the purification of the MoO_4^{2-} for delivery to a pharmaceutical company. The redissolved precipitate is passed through a series of resin columns. The first column contains Ag coated charcoal; the second contains activated charcoal. The 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. A 0.3 μm / 0.2 μm filter assembly is then used to remove any particulates. The final product is a solution of Na_2MoO_4 in dilute (0.2 *M*) NaOH.

From October through December of 1996, four ^{99}Mo generation and separation tests were conducted with fully-enriched UO_2 coated targets. Table 1 shows the target power level and irradiation times for the four tests, along with the estimated ^{99}Mo inventory at the end of irradiation. Each target was irradiated in vacated fuel element location in the ACRR. The ACRR is a pool-type reactor fueled by 236 stainless steel clad UO_2-BeO loaded fuel elements arranged in

a tightly-pitched hexagonal core arrangement about a stainless steel lined hexagonal dry central cavity which is normally used to locate relatively large (up to 22 cm in diameter) experiment packages for irradiation. The nominal steady-state power of the ACRR is currently 2 MW.

The final ^{99}Mo product solution from each of the tests was sampled for analysis. The ^{99}Mo concentration was determined via gamma-spectroscopy analysis of a diluted sample of the final product. The concentration analyses indicated process recovery efficiencies which initially appeared to exceed 100%. Some of the excess may be attributed to uncertainties in the calculated fission energy coupling between the target and the ACRR core. However, this also indicated the need to refine the quality assessment procedures which were still in a development stage. Based upon earlier studies of the Cintichem process with ^{99}Mo tracers, the expected efficiency of the process was in the range of 85 - 95 %.

The gamma-emitting impurities, excluding iodine, were determined by gamma-spectroscopy on a final product sample from which ^{99}Mo had been extracted using a thiocyanate technique. Iodine impurities were extracted from a diluted final product sample using chloroform as an organic solvent for the iodine. The ^{131}I in the chloroform solution was determined by gamma-spectroscopy. The values for ^{89}Sr and ^{90}Sr were determined by ratios based upon measured ^{140}Ba activity, since these isotopes are generated in known proportions during the fission process. The gross alpha contamination was determined via a gas-flow proportional counter analysis of a diluted sample of the final product.

In addition, from the final test in December 1996, two samples were prepared and packaged for shipment out of SNL. The first sample of 72 Ci of ^{99}Mo was shipped to Mallinckrodt Medical in St. Louis, Missouri. A second sample of 10 Ci was shipped to Nordion International in Canada. The analysis report from Mallinckrodt showed that the SNL product was compatible

with their ^{99m}Tc generators and met all purity specifications. The ^{99}Mo concentration in the product sample was less than the required 350 mCi/ml because the target was intentionally irradiated at powers less then an eventual production target. The response from Nordion was that the product would have been acceptable as "raw ^{99}Mo" input to their final purification process. Nordion did not provide data on product purity with respect to "purified ^{99}Mo" specifications. Table 2 shows the results of the radionuclidic purity assessments made by SNL and Mallinkrodt. Since purity assessment procedures at SNL were in the development stage, the SNL results in Table 2 should be taken only as giving a qualitative indication of potential product purity.

Discussion

The ^{99}Mo inventory in an eventual production target (20 kW - 7 days) would be approximately 800 Ci. Thus, as seen in Table 1, the tests performed to date are at about 1/5th the power level of such a target. The power level in these tests was limited since the only available irradiation locations were in the ACRR core itself, which is undermoderated. For production, the ACRR core will be modified by removing the dry central irradiation cavity and installing a water-filled region in which the pitch between the targets can be increased, providing more neutron moderation and thereby increasing the target-to-core power coupling. Analysis has shown that such arrangements in the ACRR can provide up to 130% of the current U. S. demand for ^{99}Mo.[3]

Assuming constant process decontamination factors, the effect of increased target power on impurity levels should be minimal, since both the ^{99}Mo and impurity inventories scale directly with power in an essentially constant ACRR neutron spectrum. In addition, the increase of irradiation time from 7 to 14 days would significantly increase only the impurities with long half-lives. For ^{89}Sr, ^{90}Sr, and ^{103}Ru, with half-lives of 50.52 days, 29.1 years, and 39.27 days respectively, each

would increase by about a factor of 2. However, the ^{99}Mo inventory would increase by about 20% resulting in a net individual^{89}Sr, ^{90}Sr, and ^{103}Ru increase of about 67% with respect to ^{99}Mo.

In most cases, the product from each test met most prescribed radionuclide purity requirements. Difficulty in meeting the gross α activity specification may be related to the analysis technique. The method described in the Cintichem ^{99}Mo Drug Master File, which was used by SNL, calls for gas-flow proportional counting of a diluted sample of the final product. Since the ^{99}Mo has not been removed from this sample, a significant β^- source exists which could result in detector "cross-talk" and an artificially high "detected" α activity. In addition, the alpha activity is dominated by the amount of ^{234}U originally present in the target coating and should remain essentially constant. Thus, an increase in target power will result in a decrease in the alpha impurity level because of the concomitant increase in^{99}Mo inventory.

Conclusions

SNL has made significant progress toward the DOE goal of using SNL nuclear facilities to provide ^{99}Mo to pharmaceutical companies. The Cintichem ^{99}Mo production process was demonstrated by processing UO_2 irradiated at power levels of approximately 1/5th scale to a production target. Initial product purity tests at SNL have shown that the final ^{99}Mo product can be purified to meet pharmaceutical radionuclide purity specifications. In-house quality assessment techniques need to be more fully developed, but purity and generator compatibility feedback from Mallinckrodt and Nordion was positive. Work is currently in progress to modify the ACRR and the HCF toward the goal providing a reliable domestic supply of ^{99}Mo within DOE ALARA guidelines. Following such modifications and development of a process infrastructure meeting pharmaceutical company and FDA good manufacturing practices requirements, SNL will be in a position to ensure a reliable supply of^{99}Mo to the U. S. health-care system.

Acknowledgments

The authors wish to acknowledge the diligence and commitment to excellence of Gerald Naranjo and Jeff Wemple and to the members of the ACRR staff, HCF staff, and Radiation Protection Operations staff whose hard work was vital to the success of this limited production campaign. The authors would also like to acknowledge the accomplishments of the isotope target fabrication team at Los Alamos National Laboratory.

References

[1] LANGTON, M. A., "Radioisotope Requirements and Usage in the Radiopharmaceutical Industry," *Transactions of the American Nuclear Society*, **72**, p. 134, (1995).

[2] COATS, R. L., "The ^{99}Mo Production Program at Sandia National Laboratories," *Transactions of the American Nuclear Society*, **72**, p. 141, (1995).

[3] PARMA, E. J., "Reactor Physics Calculations for ^{99}Mo Production at the Annular Core Research Reactor," *Transactions of the American Nuclear Society*, **73**, p. 401, (1995).

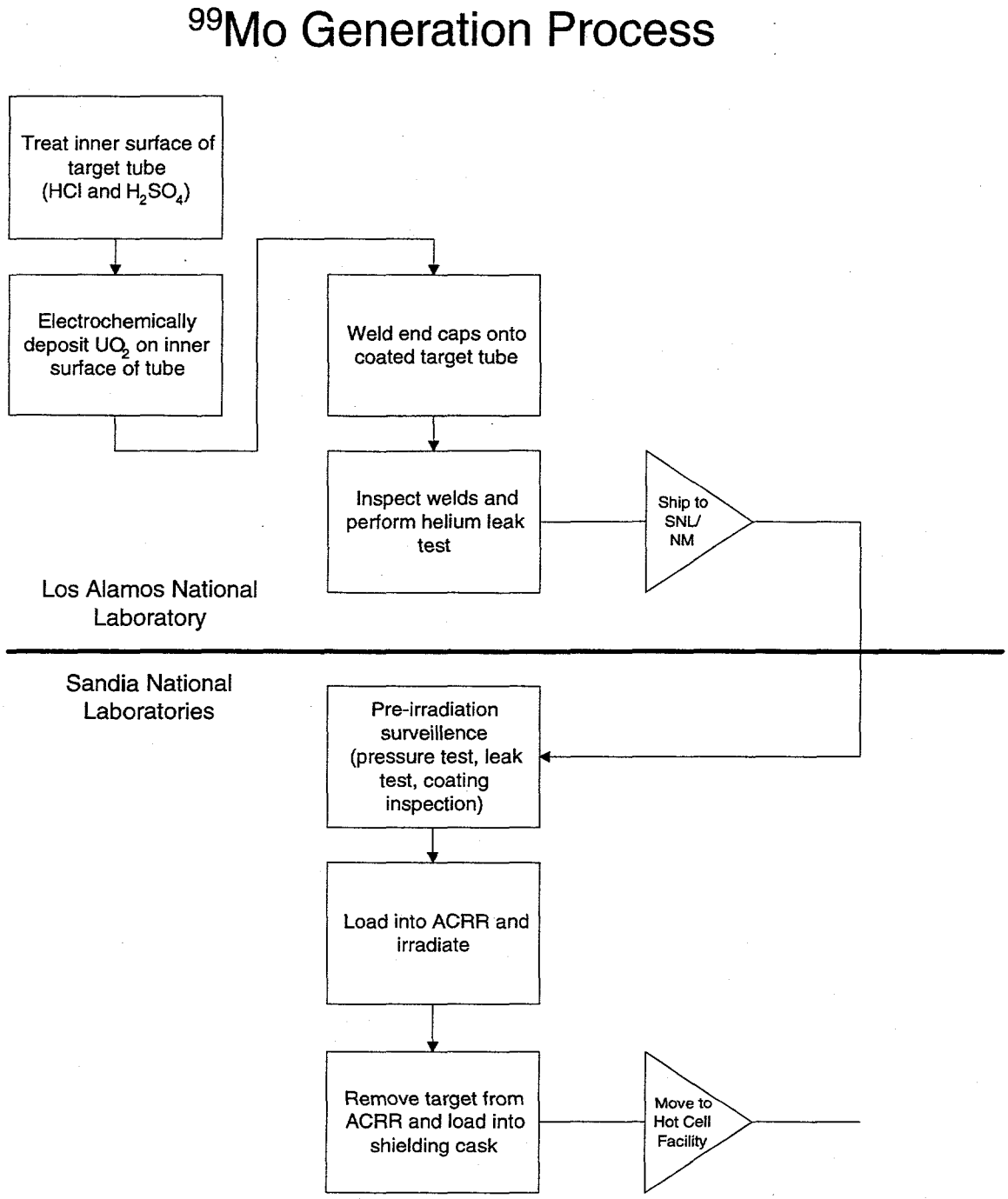

Figure 1. The ^{99}Mo Generation Process.

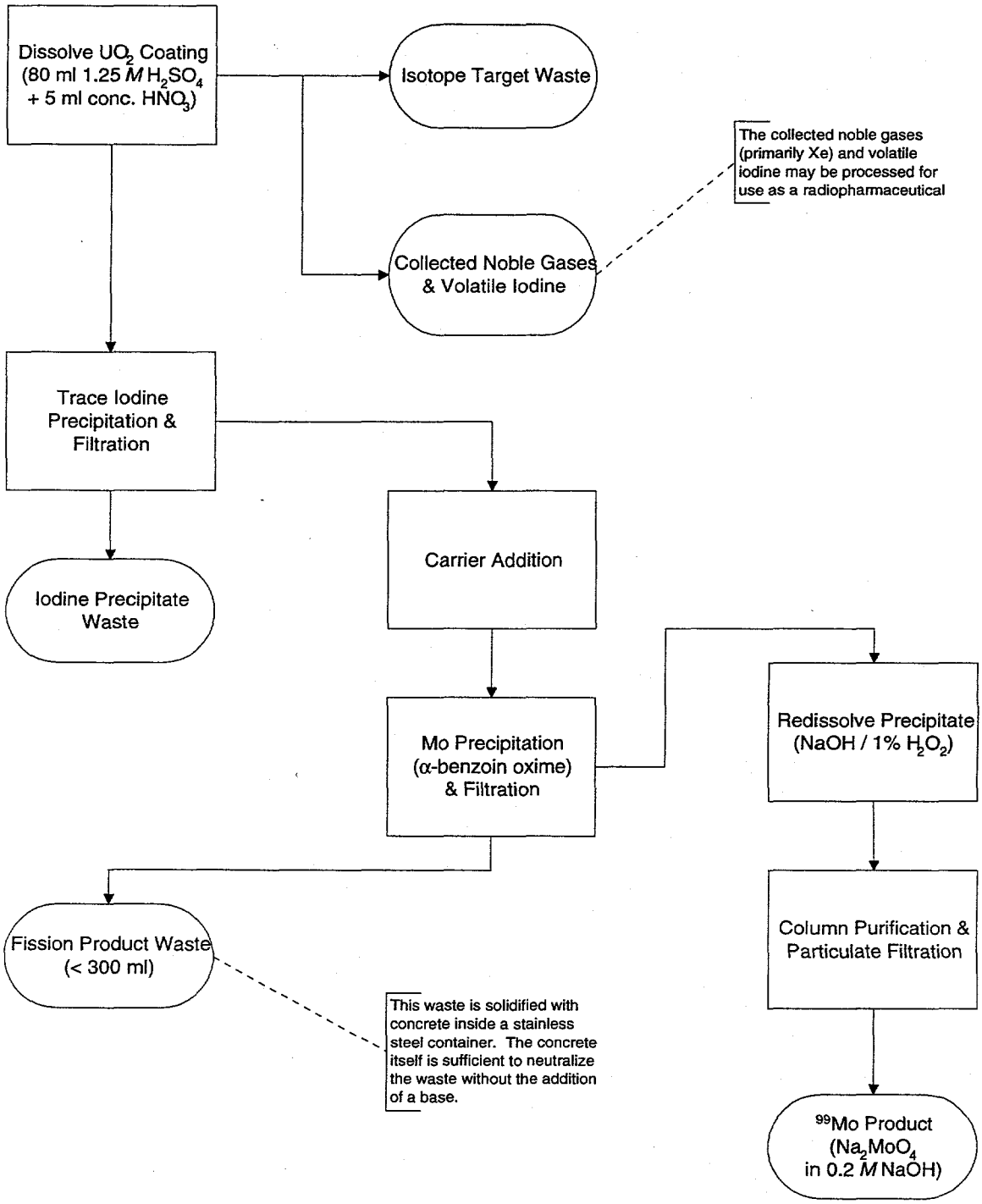

Figure 2. The ^{99}Mo Separation Process.

Table 1. Isotope target irradiation parameters.

Test	Estimated Target Power[a] (kW)	Irradiation Time (h)	UO_2 Mass (g)	Estimated ^{99}Mo Inventory[b] (Ci)
7.1	3.8	8	25.6	15
7.2	3.7	10	25.2	18
8.1	3.5	24	23.5	39
9.1	4.1	149	25.4	160

a. ACRR Power = 2 MW.

b. ORIGEN2 Calculations.

Table 2. Product purity evaluation based on SNL and Mallinckrodt analyses.

Nuclide	Specification (μCi/mCi-^{99}Mo)	Test 7.1[a]	Test 7.2[a]	Test 8.1[a]	Test 9.1[b]
^{131}I	$<5.0\times10^{-2}$	N	Y	Y	Y
^{103}Ru	$<5.0\times10^{-2}$	Y	Y	Y	Y
^{105}Rh	$<5.0\times10^{-2}$	Y	Y	Y	Y
^{132}Te	$<5.0\times10^{-2}$	Y	Y	Y	Y
^{112}Pd	$<3.0\times10^{-3}$	Y	Y	Y	Y
Total γ	$<5.0\times10^{-2}$	Y	Y	Y	Y
^{89}Sr	$<6.0\times10^{-4}$	N	N	Y	Y
^{90}Sr	$<1.5\times10^{-5}$	Y	Y	Y	Y
Gross α	$<1.0\times10^{-7}$	N	N	N	Y

a. SNL quality analysis techniques were still in the development stage. Results should be viewed as qualitative.

b. Data from Mallinckrodt analysis report.