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Demonstration Plan of ^{99}Mo Manufacturing System Development for New Research Reactor

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1. Introduction

Molybdenum-99 (^{99}Mo) and its daughter isotope ^{99m}Tc has been the most commonly used medical radioisotope which covers 85% of overall nuclear diagnostics. Commercial-scale ^{99}Mo production is based on the fission of ^{235}U. The ^{99}Mo generated from the fission (fission ^{99} Mo) exhibits very high specific activity (~10^4Ci/g) compared with ^{99}Mo generated from the other routes: neutron activation or accelerator-driven. [1] These days, international ^{99} Mo supply is very unstable due to the aging of the main ^{99}Mo production reactors causing frequent and unscheduled shutdowns. Situation in Korea is even worse, because 100% ^{99}Mo is imported from abroad. Historically, the most ^{99}Mo producers have been used highly enriched uranium (HEU) targets so far. However, to reduce the use of HEU in private sector for non-proliferation, all producers are forced to convert their HEU-based process to use low enriched uranium (LEU) targets. Consequently, overall cost for the production of the fission ^{99}Mo increases significantly with the conversion of fission ^{99}Mo targets from HEU to LEU. It is not only because the yield of LEU is only 50% of HEU, but also because radioactive waste production increases 200%. Therefore, finding optimal treatment of radiowastes from fission ^{99}Mo production process become more important. [2, 3]

Under these circumstances, KAERI is developed LEU-based fission ^{99}Mo production process from 2012 to 2018 to be implemented to the new research reactor (MIRARO), which is being constructed in Gijang, Busan, Korea. However, for the commercial-scale production of the ^{99}Mo, capability to produce systems and product in production representative environment is required using pilot line. In this study, we presented production demonstration plan of the ^{99}Mo manufacturing system. The plan covers from MRL7(Manufacturing Readiness Level) to MRL9.

2. Methods

Today, all industrial-scale producers of ^{99}Mo use dedicated targets with a configuration similar to the reactor fuels. Since fuels of early times were generally uranium-aluminum alloy cladded with aluminum shell. KAERI developed plate-type LEU target composed of UAl_x meat dispersed in Al-6061 cladding. The targets are irradiated in the MIRARO reactor core for about 7 days. Then, irradiated targets transferred from the reactor to the fission ^{99} Mo production facility for processing. The targets are dissolved in alkaline solution to extract ^{99}Mo from the the solution. Other fission products including unreacted uranium and actinides are removed from the solution. Medical-grade ^{99}Mo can be extracted after series of separation and purification process. [4, 5, 6]

3. Result and Discussion

Quality of the process as well as the product should be verified and demonstrated through repeated cold and hot pre-production. Safety and efficacy data shall be the output of the demonstration, too. Those quality, safety and efficacy information should be formatted in common format (CTD: common technical document). In parallel, GMP validation plan for the radiopharmaceutical production facilities was presented.

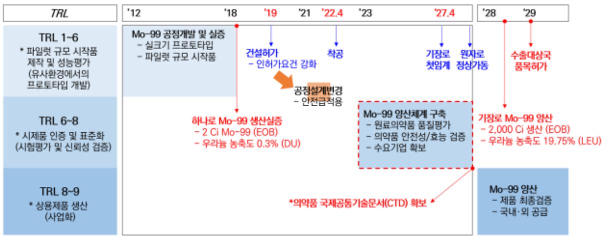

Fig. 1. Milestone for the fission Mo-99 manufacturing at MIRARO.

Technology readiness level (TRL) provides insight of technology development for various systems in nine-stages. However, in the view point of commercial-scale radioisotope production, implementation of manufacturing readiness level with ten-stage fits better, as shown in the Fig. 2. Here, from MRL1 to MRL6 fall into the research and development stage. MRL7 and 8 are pre-production stage, and MRL9 and 10 are mass production step.

Fig. 2. Manufacturing Readiness Level (MRL) for Mo-99 production.

^{99}Mo process development has been demonstrated once in pilot scale (1/8 scale in size, 1/1000 scale in radioactivity) at HANARO in 2018. Since the demonstration didn't continued until now, MRL of the current ^{99}Mo process development level is MRL6. To produce ^{99}Mo by the time of normal operation of MIRARO in 2028, pre-production and quality standardization for domestic and foreign market should be prepared on-time.

The operation readiness covers validation of the facilities, production and quality analysis equipment, human resources, organization, quality assurance, nuclear safety regulation and pharmaceutical regulation.

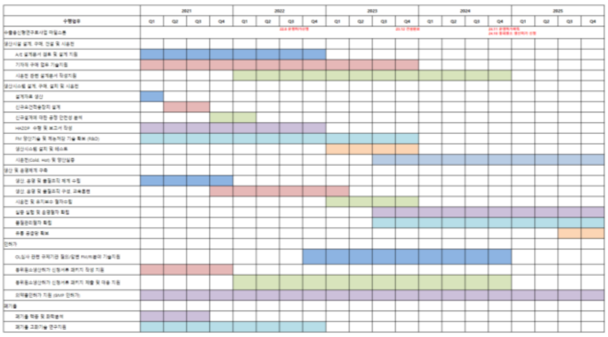

Fig. 3. Operational Readiness for Mo-99 production

As a result, documentations for operation license and cold/hot commissioning for the fission molybdenum-99 production facility (FMPF) will be produced. After establishment of the validation mater plan (VMP), qualification documents (DQ/IQ/OQ/PQ) will be produced for GMP validation of the radiopharmaceutical production facility. [7] Finally, set of pharmaceutical quality, safety and efficacy documents will be produced through repeated cold and hot demonstrations at HANARO and MIRARO in internationally common document format (CTD). [8]

4. Conclusions

For the weekly productivity of 2000 Ci/week fission ^{99}Mo from the MIRARO, KAERI developed the fission ^{99}Mo production process until 2018. The amount corresponds to the 20% of international ^{99}Mo market.
MIRARO, the new research reactor, and the FMPF will be constructed in 2027, and will start normal operation in 2028.

However, to produce ^{99}Mo on time, pre-production stage of MRL7 and 8 should be prepared before the full-scale mass production. In the pre-production period, qualification and validation of the facilities, process and product for targeting market should be made. These activities should be supported by proper human resources and organization structure.

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