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CORAR Position on the Security of Supply of Medical Isotopes
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During the past five years, the medical community in the United States has experienced regular and significant shortages of the medical isotope molybdenum-99 (Mo-99) and consequently its decay product, technetium-99m (Tc-99m). As Tc-99m is used in approximately 80% of all nuclear medicine procedures, these shortages have created significant hardships in the United States on physicians, health care workers, and their patients.

To better understand how to address these supply interruptions and the adverse impact experienced by patients, the Organization for Economic Cooperation and Development – Nuclear Energy Agency (OECD/NEA) established the High-Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in 2009. The purpose of the HLG-MR was to examine the underlying reasons for the shortages – including through an economic analysis of the Mo-99 supply chain - and to develop a policy approach to ensure the long-term security of the supply of medical radioisotopes. In 2011, the HLG-MR published its policy recommendations for governments, industry, and the health care community to utilize in developing a long-term solution to the fragile and insufficient supply of medical radioisotopes.

The Council on Radionuclides and Radiopharmaceuticals (CORAR) is committed to working with all U.S. and international stakeholders to ensure a reliable, sufficient and sustainable supply of medical radioisotopes from non-Highly enriched Uranium (HEU) production sources. For example, CORAR has expressed its support on a number of occasions for U.S. legislation and U.S. Government efforts to establish a domestic source of Mo-99 from non-HEU sources. CORAR offers the following comments in particular regarding the HLG-MR policy approach and its' recommendations.

CORAR Comments on the HLG-MR Principles and Recommendations:

Specifically, CORAR offers comments and recommendations on the six HLG-MR principles below:

HLG-MR Principle 1: All Tc-99m supply chain participants should implement full-cost recovery, including cost related to capital replacement.

The principle of full-cost recovery ensures that alternate suppliers of medical isotopes will be able to invest in the industry and enhance their ability to compete with government sponsored facilities operating at subsidized cost levels. The concept of full-cost recovery is necessary to support a sustainable manufacturing and distribution industry for medical isotopes. In addition, the substantial costs associated with the conversion from Highly Enriched Uranium (HEU) to Low Enriched Uranium (LEU), in support of the Global Threat Reduction Initiative (GTRI), as well as the planning and development of new Mo-99 manufacturing capacity must be accounted for.

CORAR supports this principle and urges all countries and market participants to implement this recommendation. CORAR believes that the development of new Mo-99 manufacturing capacity using non-HEU sources (including LEU) must be done in a way that allows industry to recover all additional costs while delivering an adequate return on investment to the developers of new medical isotope production facilities.

The first independent attempt to understand the required costs of new production capacity throughout the Mo-99 supply chain was conducted by the HLG-MR, beginning in 2009 – published in 2010 by the OECD; *The Supply of Medical Radioisotopes, An Economic Study of the Molybdenum-99 Supply Chain*. The results of this study demonstrate that supply chain costs are projected to increase substantially as the industry develops future Mo-99 manufacturing capacity to ensure a reliable and sufficient supply.

However, CORAR believes the HLG-MR economic study results underestimate the full cost impact on production because:

1. The HLG-MR cost data used in the economic study lacks U.S. market data. Mo-99 based product utilization and distribution models differ between the U.S. and most other countries and these differences were not captured by the HLG-MR analysis.
2. The HLG-MR cost data was collected prior to industry movement towards the implementation of full-cost recovery, outage reserve capacity, and conversion to LEU-based Mo-99 initiatives throughout the current Mo-99 supply chain beginning in 2010.

On a related note, CORAR believes that the HLG-MR economic study results would be more meaningful if the supply chain cost impact was separated from the reimbursement rate of the procedure. In the United States, nuclear medicine facilities segregate the cost of radiopharmaceuticals from the other costs associated with imaging. In relating the substantial supply chain cost impact as a percent of the procedure reimbursement in the economic study, the HLG-MR removes the transparency needed for proper evaluation by the medical community and diminishes the impact of costs related to establishing new manufacturing capacity on industry.

HLG-MR Principle 2: Reserve capacity should be sourced and paid for by the supply chain. A common approach should be used to determine the amount of reserve capacity required.

The HLG-MR has advanced the principle of reserve capacity to ensure adequate supply of Mo-99 during scheduled maintenance and unexpected down-time throughout the supply chain. In addition, the HLG-MR recommends that “Processors” voluntarily hold, at every point in time, outage reserve capacity equal to their single largest supply source (n-1 criterion). This may come from anywhere in the supply chain as long as it is credible, incremental, and available on short notice. Reserve capacity options should be transparent and verifiable to ensure reliability in the supply chain.

Mo-99 producers have implemented this principle over the last two years by adding outage reserve capacity to their routine production capabilities. This has been accomplished by paying for additional access to radiation positions in the reactors that irradiate HEU (or LEU) targets. Increased capacity has enhanced industry’s backup capability as seen in recent maintenance shutdowns of the NRU reactor in Canada. During these shutdowns, Mo-99 producers were able to meet market demand with no disruptions. However, implementation of outage reserve capacity has increased the cost of producing Mo-99 to these producers since the additional radiation positions in the reactors must be paid for whether they are used or not.

CORAR supports the principle of reserve capacity advanced by the HLG-MR. Expansion of reserve capacity will continue to help industry avoid another severe and disruptive shortage of Mo-99. In addition, the added costs associated with maintaining the back-up capacity described in the HLG-MR policy approach under outage reserve capacity should be considered part of the overall costs associated with the development of a reliable and adequate medical isotope supply and accounted for using full-cost recovery.

Additional capacity for Mo-99 production will also come from new technologies and new manufacturing practices that utilize non-HEU (including LEU) targets. For example, CORAR supports the investment of the US Government, the Canadian Government, and industry in the development of new commercial sources of Mo-99 which will allow for expanded manufacturing of Mo-99 abroad as well as in the United States.

HLG-MR Principle 3: Recognizing and encouraging the role of the market, government should; 1) establish the proper environment for infrastructure development, 2) set the rules and establish the regulatory environment for safe and efficient market operation, 3) ensure that all market-ready technologies implement full-cost recovery methodology, and 4) refrain from direct intervention in day-to-day market operations as such intervention may hinder long-term security of supply.

To assure a reliable and sufficient supply of medical isotopes in the future, the HLG-MR policy approach provides several principles which support market-driven changes in the implementation of full cost-recovery for the production and distribution of Mo-99.

CORAR supports the principle of separate and appropriate reimbursement for all diagnostic radiopharmaceuticals. This will allow for an appropriate return on the investments made in new technologies, plant conversions, and new reactor construction. In addition, separate reimbursement preserves competition and innovation as well as facilitating transparency in costs to Medicare, private payers and patients (in the U.S.).

In addition, CORAR believes that all government policies should be formulated and implemented to minimize impact to industry with regards to increased cost, decreased manufacturing and operational flexibility. This includes the ability of individual Mo-99 processors to contract with specific reactor operators for irradiation services. In particular, pricing, volumes, and other service requirements should remain unregulated and subject to applicable contract agreements, including confidentiality to the extent agreed.

HLG-MR Principle 4: Given their political commitments to non-proliferation and nuclear security, governments should provide support, as appropriate, to reactors and processors to facilitate the conversion of their facilities to low enriched uranium or to transition away from the use of highly enriched uranium, wherever technically and economically feasible.

CORAR supports this principle and international efforts to minimize and eliminate the use of HEU targets from civil nuclear applications in particular due to the nuclear security risks that arise from potential theft or diversion of the HEU targets. The transition to using non-HEU sources (including LEU target) in the production of Mo-99 is recognized as an important step in international nonproliferation and nuclear security efforts.

CORAR also supports the U.S. Government's efforts to transition the production of Mo-99 from HEU targets to non-HEU sources (including LEU targets). However, CORAR notes that currently, there are only a few global suppliers of LEU produced Mo-99.

The amount of LEU produced Mo-99 provided by these suppliers represents a small fraction of the quantity needed in the U.S. each week. LEU produced Mo-99 is more expensive to produce due to lower uranium density in the targets and increased waste. In addition, there is significant decay loss due to lengthy transportation requirements given that the only current LEU producers are located great distances from North America. Therefore, any U.S. LEU market adoption incentive must be based on the accessibility and availability of material if LEU produced Mo-99 is to be effectively "pulled" into the domestic market.

Efforts to promote the use of LEU-produced Mo-99 must be closely monitored to ensure that U.S. patients are not adversely impacted either by:

1. Supply shortages due to inadequate or unreliable supply sources, or
2. Insufficient reimbursement for higher cost non-HEU Mo-99 (including LEU).

However, it is important to note that industry may not be able to sustain the initial and ongoing conversion efforts due to the high costs related to this conversion unless there is an appropriate return on investment. Separate and sufficient reimbursement for all diagnostic

radiopharmaceuticals is necessary as it will provide for transparency and predictability in the conversion process and will support the concept of full-cost recovery.

HLG-MR Principle 5: International collaboration should be continued through a policy and information sharing forum, recognizing the importance of a globally consistent approach to addressing security of supply of Mo-99/Tc-99m and the value of international consensus in encouraging domestic action.

The HLG-MR recognizes in its policy recommendations the increased level of international collaboration in the recent past and the positive effect this has had on improving the security of supply, determining the root causes of Mo-99 shortages, and developing solutions to improve supply during a crisis. **CORAR strongly supports this principle, as well as the OECD recommendation that all countries must adhere to and implement the OECD policy recommendations.** CORAR supports the ongoing collaboration between CORAR, AIPES, IAEA, NEA HLG-MR, and the European Commission to increase coordination of worldwide Mo-99 production including manufacturing and processing capabilities. These activities help to improve the safety, supply, and access to medical radioisotopes and radiopharmaceuticals.

HLG-MR Principle 6: There is a need for periodic review of the supply chain to verify whether Mo-99/Tc-99m producers are implementing full-cost recovery and whether essential players are implementing the other approaches agreed to by the HLG-MR, and that the coordination of operating schedules or other operational activities have no negative effects on market operations.

The HLG-MR recommends periodic review of the principles provided in its 2011 policy recommendations in support of the transition to a market-driven manufacturing structure. **CORAR supports the periodic review of these principles** and the OECD's policy recommendations but would emphasize that this type of review must balance the need for sufficient information with the confidential nature of certain business information and data.

In closing, CORAR would like to reiterate its commitment to working constructively with the U.S. Government, the European Commission, the OECD, and the IAEA to achieve a reliable, sustainable, and secure supply of Mo-99 and other radioisotopes.