

OECD-Nuclear Energy Agency's Policy Approach for a Reliable Supply of ⁹⁹Mo

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ABSTRACT

The OECD Nuclear Energy Agency (NEA) established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) to examine the reasons for the lack of security of supply of molybdenum-99 (⁹⁹Mo) and its decay product, technetium-99m (^{99m}Tc) and to develop a policy approach to address the challenges to reliable supply. This paper describes the key findings of the HLG-MR and its policy approach, which provides the steps necessary to ensure a long-term secure supply of ⁹⁹Mo and ^{99m}Tc. This policy approach is the result of two years of intensive examination of the supply chain. It includes ways to send strong price signals across the supply chain, ensuring international coordination of supply availability, improving communication and demand side management and establishing a mechanism for reviewing its implementation. The HLG-MR is continuing its work, focusing on the implementation of the policy approach by all producing and consuming nations.

1. Introduction

At the request of its member countries, the OECD Nuclear Energy Agency (NEA) established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in 2009. During its two-year mandate, the HLG-MR assessed the factors rendering the supply chain vulnerable and identified practical measures – near, medium and long term – to ensure the security of supply of this important medical isotope. Building on its findings and assessments, the HLG-MR developed a comprehensive policy approach to encourage long-term supply security of ⁹⁹Mo/^{99m}Tc, detailing the essential steps to be taken by governments, industry and the health community to address the vulnerabilities within the supply chain, including changing an economic structure that does not support or reinforce reliable supply.

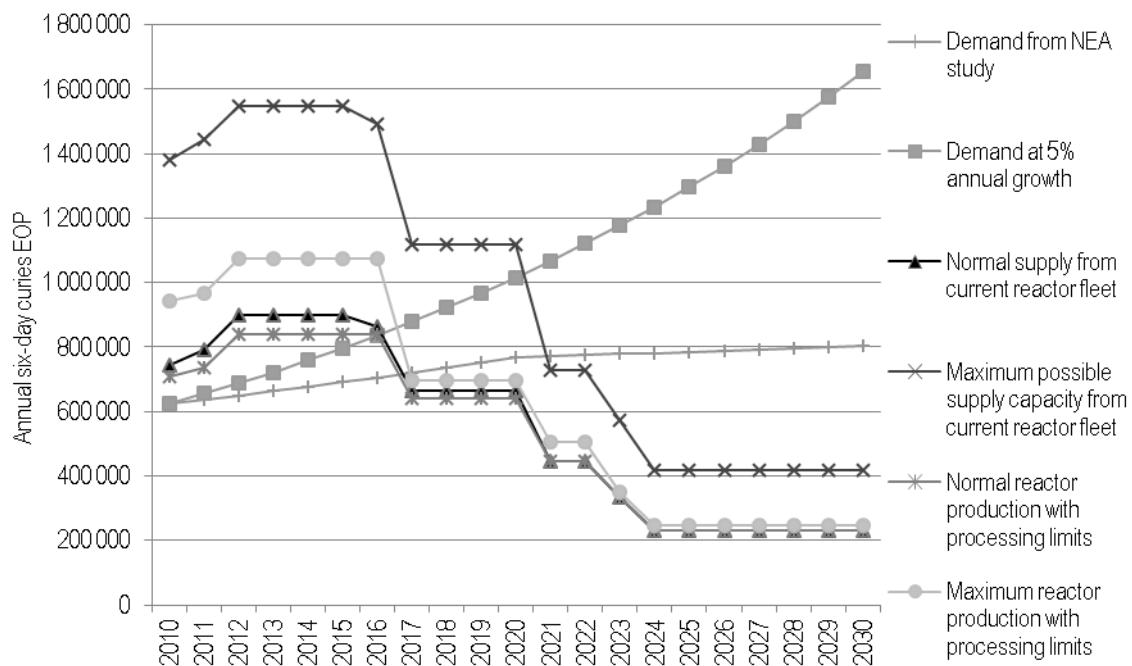
2. The current, ageing fleet will not be sufficient

Until recently, there were only five research reactors irradiating targets to produce 90 to 95% of global ⁹⁹Mo supply: three in Europe (BR-2 in Belgium, HFR in the Netherlands and OSIRIS in France), one in Canada (NRU), and one in South Africa (SAFARI-1). However, all these reactors are over 45 years old. Between 2009 and 2010, the Canadian and Dutch reactors were subject to extended shutdowns, causing global ⁹⁹Mo/^{99m}Tc shortages. These reactors have since come back on line and production of ⁹⁹Mo was able to return to levels seen before the supply shortage. In addition, a few research reactors joined the supply chain (MARIA in Poland, Řež in the Czech Republic and some of the Russian reactors at Dimitrovgrad) or expanded production beyond domestic needs during and following the shortages (OPAL in Australia and RA-3 in Argentina).

While this is positive news, the current capacity remains fragile and further supply shortages could be expected. A number of the producing reactors in the current ageing fleet are scheduled to be removed from the supply chain over the next decade, with the earliest

scheduled for 2015 (OSIRIS) and 2016 (NRU). Coupling these shutdowns with growing demand, supply could be insufficient within the next few years, even considering the reactors that have recently joined the supply chain.

Figure 1: Current supply versus demand with processing limitations



Taking all these factors into account, the future supply situation based on the current fleet of research reactor is estimated to be insufficient.

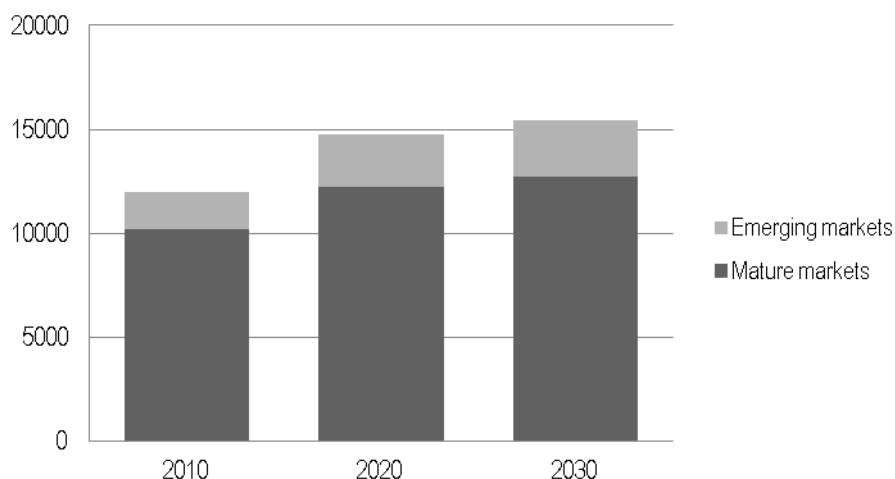
3. Long-term demand requires new investments

Understanding the future demand of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ is essential when discussing the need for new ^{99}Mo -producing reactors and related infrastructure, especially given the required level of investment.

Based on data from a global survey (713 responses from 52 countries) and an assessment by an expert advisory group, a demand forecast for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ in 2020 and 2030 was developed. Even though projecting out to 2030 seems long, and therefore reliability less certain, the forecast provides an indication of direction and degree of changes in demand in a time frame that would be meaningful for new ^{99}Mo -producing infrastructure.

Based on these results, it is reasonable to predict that ^{99}Mo demand will continue to grow at levels equal to approximately 2% annually until 2020, and then level off to a growth rate of less than 1% annually until 2030 (see Figure 2). Differences exist between mature and emerging markets.

Figure 2: Forecasted ^{99}Mo demand per week (six-day curies)



4. Proposed new projects may not be enough

Based on the 2009-2010 shortage, the ageing reactors and the impending longer-term shortage, a number of stakeholders are suggesting new projects to produce $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$. Many of these projects are reactor-based using existing research reactors that are currently not producing ^{99}Mo or new reactors that are at various stages of development. Projects are also being proposed based on alternative technologies, such as irradiation in power reactors or using accelerators or cyclotrons. If all these projected capacities were added, there would appear to be no concern over future supply.

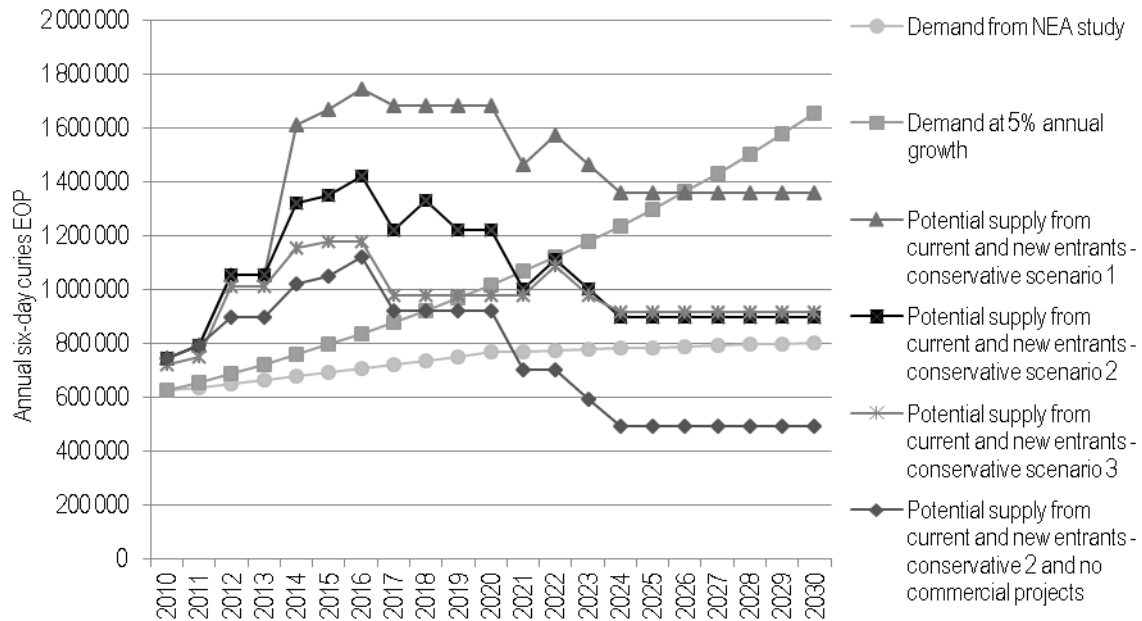
However, there are a number of reasons why this projection may not materialise:

- The values presented do not account for any regional processing constraints
- There are economic and technical hurdles to overcome related to the production of ^{99}Mo via these alternative projects.
- Another consideration that may affect security of supply is the ability to procure and transport enriched uranium and to transport radioactive material.

Recognising these challenges, Figure 3 presents four scenarios which apply conservatism to the likelihood of all projects succeeding or recognise the potential processing capacity limitations.

It is clear that major issues still remain when processing constraints are recognised or when considering the potential for some projects not to proceed. Even if some of the projects do move forward, there could be a shortage in the coming decades as the current fleet stops producing ^{99}Mo and demand continues to increase; in addition, the level of capacity that would be available as back-up would be greatly reduced.

Figure 3: Potential supply versus demand based on conservative scenarios



Another factor to keep in mind is the necessary conversion to using LEU targets for producing $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$; most of the current production uses highly enriched uranium (HEU) targets. All producing countries have agreed to LEU conversion for the production of medical radioisotopes, wherever technically and economically feasible. This conversion process may have an impact on the production capacity of the available reactors, depending on the pace to conversion and the results of efforts to increase density in LEU-based targets.

5. Why wasn't there more ^{99}Mo production capacity built? Quick answer: economics

In the current ^{99}Mo supply chain, all the major producers irradiate targets using multipurpose research reactors, which were originally constructed and operated with 100% government funding, mainly for research and materials-testing purposes. When ^{99}Mo production started, the reactors' original capital costs had been paid or fully justified for other purposes. As a result, ^{99}Mo was seen as a by-product that provided another mission for the reactor that could generate extra revenue to support research. This resulted in:

- Reactor operators originally only requiring payment of *direct*, short-run marginal costs.
- ^{99}Mo prices not covering any significant share of costs of overall reactor operations and maintenance, or capital costs or allowances for replacement or refurbishment.
- The by-product status remaining with no substantive pricing changes even as ^{99}Mo production became a more important part of reactor operating activities.

As a result, reactor prices were too low to sustainably support the ^{99}Mo -attributable portion of reactor operations, did not even cover short-run marginal costs in some cases, and did not provide enough financial incentive to support replacing or refurbishing ageing reactors. In addition, even if costs of conversion for a major ^{99}Mo producer are still uncertain, it is clear that the current pricing structure provides insufficient financial incentive for the development and operation of LEU-based infrastructure.

The processing component, originally funded by governments, was commercialised in the 1980s and 1990s. Commercialisation was originally thought to be beneficial to all parties;

however, contracts were based on historical perceptions of costs and pricing. This resulted in long-term contracts with favourable terms for commercial processing firms, with no substantial change to the prices for irradiation. Once these contracts were established, they set the standard for new processors and reactors that entered the market.

An unintended effect of commercialisation was establishing market power for processors. The contracts, in some cases, created a situation where the reactor had only one avenue for selling its ^{99}Mo irradiation services. Barriers to entry (both natural and created, such as aggressive pricing strategies) sustained the market power balance and contributed to maintaining low prices for irradiation services.

However, reactors continued to provide irradiation services even under these uneconomic conditions because of the social contract between governments and the medical imaging community. Governments subsidised the development and operation of research reactors and related infrastructure, including radio-active waste management. Using part of this funding, reactor operators irradiated targets to produce ^{99}Mo . In return, citizens received an important medical isotope for nuclear medicine diagnostic procedures.

Although reactor operators were aware that government financial support was increasingly used for ^{99}Mo production, this may not have been transparent to governments. In some cases, the magnitude of the change did not become clear until there were requests for specific funding to refurbish a reactor or to construct a new one. These subsidies were also supporting the production of ^{99}Mo that was being exported to other countries.

Recently, governments from almost all current, major producing countries have indicated that they are reconsidering or no longer interested in subsidising new or ongoing production of ^{99}Mo at the reactor level at historical levels (or at all) – some more formally than others – questioning whether it remains in the public interest. With a changed social contract, the economics have to become sustainable on a full-cost basis or the availability of a long-term reliable supply of ^{99}Mo will be threatened.

6. If irradiation prices increase, won't imaging tests become too expensive for patients?

Although a sustainable economic supply chain requires significant price increases upstream, the impact on the final cost of the procedure should be very small (<1%). Starting from a representative cost and pricing structure developed by the NEA and based on information from supply chain participants, levelised unit cost of ^{99}Mo (LUCM) calculations determined the magnitude of the price changes needed for economic sustainability. The scenarios range from using existing reactors to building a fully dedicated isotope reactor and processing facilities. Under the current economic situation it was found that, for existing reactors, the marginal revenue from production was lower than the marginal costs, with reactors facing a loss on every unit of ^{99}Mo produced.

The LUCM calculations indicated that significant price increases are necessary in the upstream supply chain in order to be economically sustainable (up to a maximum increase of 900%). However, the analysis finds that there is very little effect on the prices per patient dose; at pre-shortage prices, the irradiation price from the reactor is calculated to be only 0.11% of the final cost of the procedure. Even at the most extreme price increase from the reactor, the value of irradiation would increase to only represent 0.97% of the final procedure costs.

Table 1: Impact of price increases at hospital level

	Irradiation value within final radiopharmaceutical price (EUR)	Irradiation value as % of reimbursement rate
Pre-shortage situation	0.26	0.11
Required for economic sustainability	0.33-2.39	0.14-0.97

The analysis indicates that, while prices will increase for the downstream components, these should be able to be absorbed. For example, improving elution patterns from a generator can greatly increase the amount of ^{99m}Tc obtained and has the potential to more than offset any upstream price increases. However, this issue may require further study and possible assessment by hospitals and medical insurance plans, especially in the context of continued downward pressure on reimbursement rates or in cases where the health system provides fixed budgets to hospitals for radioisotope purchases.

It is clear that without ongoing financial support from governments, full-cost recovery from the market is required for the continued supply of reactor-based ^{99}Mo in the medium to longer term and the conversion to LEU-based production. Even as short-term supply has stabilised, it is important to stress that the symptom has been addressed but the underlying problem – the unsustainable economic structure – has not.

7. Alternative production technologies should also be considered

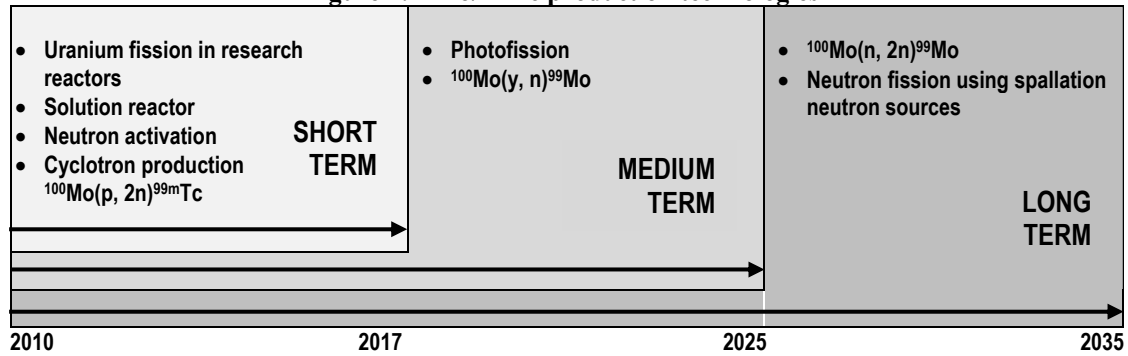
The importance of nuclear medicine and diagnostics throughout the world together with the recent shortage of ^{99}Mo supply has motivated investigations into alternative technologies. Alternative technologies could be reactor-based (such as neutron activation of ^{98}Mo) or accelerator-based (direct cyclotron production of ^{99m}Tc , photofission, etc.), and they are currently at very different development stages (see Figure 4).

The use of LEU targets for ^{99}Mo production has some advantages over HEU, including proliferation resistance, easier availability of the target material and easier compliance for target transport and processing. However, it currently has lower production yield than HEU and may require more targets to be irradiated with correspondingly increased volumes of waste. Increasing the uranium content of the targets (e.g. of the existing high density LEU targets, or using metallic foil targets), to counteract the lower production yield will be a key factor for LEU-based production, but there seems to be no technological or economic reasons not to deploy this technology.

Neutron activation in a research reactor has advantages in terms of safety, waste management and proliferation resistance, but has low specific activity and, with current technologies, would require the recycling of the highly enriched molybdenum in order to be cost-effective. This is currently not done. Also, more development and experience is needed in (gel) generator technology prior to eventual larger-scale deployment.

Direct ^{99m}Tc production using cyclotrons has potential advantages in terms of cost, waste management, proliferation resistance and ease of approval but can only provide local needs given the short half-life of ^{99m}Tc . The technology also requires significant amounts of highly enriched molybdenum (^{100}Mo). As a result, a large number of cyclotrons would be required to meet world demand and the product would not be able to be shipped far or exported to supply global needs.

Figure 4: $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production technologies¹



Based on the analysis, it is clear that there are other technologies that can be used to produce $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$; however, the uranium fission route is currently the most efficient technology and the most “market-ready”. The HLG-MR encourages the further development of these technologies, especially given their potential to minimise the use of HEU for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production.

8. How can a secure, reliable supply of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ be achieved?

The members of the HLG-MR and other key stakeholders have implemented changes to address some of the challenges affecting security of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ supply. For example, significant progress has already been achieved on improving the supply situation through increased communication, co-ordination of reactor schedules and a better understanding of demand-management opportunities. However, while these actions are important, much more is required since the underlying economic problem remains to be adequately addressed. Continued action is required on the part of all stakeholders.

The HLG-MR policy approach establishes a framework for addressing the problems and issues identified, provided that it is applied by all countries that have an impact on the global market, either as producers or consumers of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$. It provides a comprehensive, consistent and coherent policy approach covering all the key issues and challenges.

The HLG-MR established six principles (described below) to address the key issues affecting the ability to realise a long-term, secure $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ supply. For each principle, there are supporting recommendations, providing additional detail on the implementation of each of the principles. Further information on the policy approach can be found in the HLG-MR final report: *The Supply of Medical Radioisotopes: The Path to Reliability* (www.oecd-neo.org/med-radio).

9. Principles and supporting recommendations

Principle 1: All $^{99\text{m}}\text{Tc}$ supply chain participants should implement full-cost recovery, including costs related to capital replacement.

¹ These alternative technologies were classified as short-, medium-, and long-term technologies based on an assessment of their time frame for potential availability. Short-term technologies are those that have already been used for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production, or for which nuclear imaging tests have been performed.

Commercial arrangements in the supply chain, including contracts, must recognise and facilitate the implementation of full-cost recovery in order to move towards achieving economic sustainability.

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.

Supply chain participants, both public and private, should both continue and improve annual co-ordination efforts through the Association of Imaging Producers and Equipment Suppliers (AIPES) or another similar mechanism to ensure the appropriate use of available capacity, recognising a minimum necessary volume level at all $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ producing facilities. New entrants to the supply chain should join these co-ordination efforts.

Processors should voluntarily hold at every point in time outage reserve capacity equal to their largest supply (n-1 criterion), which can 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 trust in the supply chain. Reactor operators, processors and generator manufacturers should review the current contracts to ensure that payment for reserve capacity is included in the price of ^{99}Mo .

Principle 3: Recognising and encouraging the role of the market, governments should:

- establish the proper environment for infrastructure investment;
- set the rules and establish the regulatory environment for safe and efficient market operation;
- ensure that all market-ready technologies implement full-cost recovery methodology; and
- refrain from direct intervention in day-to-day market operations as such intervention may hinder long-term security of supply.

Governments should target a period of three years to fully implement this principle, allowing time for the market to adjust to the new pricing paradigm while not delaying the move to a secure and reliable supply chain.

Governments should:

- in co-operation with health care providers and private health insurance companies, monitor radiopharmaceutical price changes in order to support the transparency of costs;
- periodically review payment rates and payment policies with the objective of determining if they are sufficient to ensure an adequate supply of $^{99\text{m}}\text{Tc}$ to the medical community;
- consider moving towards separating reimbursement for isotopes from the radiopharmaceutical products as well as from the diagnostic imaging procedures.
- encourage continued supply chain participation in $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production schedule co-ordination efforts, including making such participation mandatory if voluntary participation wanes or commitments are not respected.
- monitor levels of outage reserve capacity maintained by the market and, if found to be below the set criterion, consider regulating minimum levels.

- where required, support financial arrangements to enable investment in $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ infrastructure using various forms of public-private partnerships with appropriate returns.
- consider $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production capacity requirements when planning multipurpose research reactors to ensure that the required capacity is available. However, the funding of the ^{99}Mo -related capacity development should be supported through the commercial market.

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.

Governments should consider encouraging as well as financing R&D related to LEU target conversion through participation in International Atomic Energy Agency (IAEA) efforts or by other means. They should address enriched uranium (LEU and HEU) availability and supply during and after conversion. They should also examine options to create a market justification to using LEU targets to ensure a level playing field between producers. In the meantime, they should consider financially addressing the price differential of ^{99}Mo produced with LEU targets in order to achieve agreed upon non-proliferation goals.

Governments should encourage the development of alternative (non-HEU) technologies to facilitate the diversity of the supply chain, wherever economically and technologically viable.

Principle 5: International collaboration should be continued through a policy and information sharing forum, recognising the importance of a globally consistent approach to addressing security of supply of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ and the value of international consensus in encouraging domestic action.

Domestic and/or regional action should be consistent with the proper functioning of the global market.

The IAEA and its partners are encouraged to carry on international dialogue and efforts to ensure that safety and security regulations, and their application, relating to $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production, transport and use are consistent across international borders. Regional (e.g. European Union) and domestic efforts towards facilitating transport and use of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ in a safe and secure manner should continue.

Industry participants could consider international collaboration to achieve other goals as well, such as harmonisation of targets.

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

This policy approach sets the foundation for consistent and comprehensive steps forward to ensure the long-term security of supply of the vital medical radioisotopes molybdenum-99 and its decay product, technetium-99m.