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The Supply of Medical Radioisotopes

Final Report of the Third Mandate of the High-level Group on the Security of Supply of Medical Radioisotopes (2013-2015)

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Acknowledgements

This report would not have been possible without input from a significant number of supply chain participants and stakeholders including major reactor operators, major processors, generator manufacturers, representatives from nuclear pharmacies and nuclear medicine practitioners, as well as government and non-government organisations.

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This report was written by Kevin Charlton of the NEA Nuclear Development Division. Detailed review and comments were provided by the HLG-MR.

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Executive summary

At the request of its member countries, the Organisation for Economic Co-operation and Development (OECD) Nuclear Energy Agency (NEA) became involved in global efforts to ensure a secure supply of molybdenum-99 (^{99}Mo)/technetium-99m (^{99m}Tc). In April 2009, the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) was created and received an initial, two-year mandate from the NEA Steering Committee for Nuclear Energy to examine the causes of supply shortages of ^{99}Mo/^{99m}Tc and develop a policy approach to address them.

In its first mandate, the HLG-MR conducted a comprehensive economic study of the ^{99}Mo/^{99m}Tc supply chain, which identified the key areas of vulnerability and major issues to be addressed. It was clearly demonstrated that the fundamental issue in the market was an unsustainable economic model. The pricing structure at nuclear research reactors prior to the 2009-2010 supply shortage was based on some government subsidisation that led to market prices that were below full cost. This often led to an under-valuation of the costs of the product and of the associated medical procedure and to chronic underinvestment in infrastructure. It was identified that pricing must recover the full cost of production to promote the economic sustainability needed to ensure long-term security of supply of medical radioisotopes. The NEA also examined the global supply and demand for ^{99m}Tc and assessed potential alternative ^{99}Mo/^{99m}Tc production technologies.

The HLG-MR released a policy approach, including six principles (see Appendix 1) and supporting recommendations to help resolve the issues in the ^{99}Mo/^{99m}Tc market. The target was for full implementation within three years of adopting the policy approach (by June 2014; but this objective has not yet been achieved). To encourage the supply chain participants in the implementation of the policy approach and to continue to provide an international forum for discussion and collaboration, the HLG-MR mandate was renewed for a further two years.

In the second mandate (2011-2013), the HLG-MR worked to encourage the implementation of the six policy principles and promoted an industry transition away from the use of highly enriched uranium (HEU) targets for ^{99}Mo production. Projects were undertaken by the NEA that resulted in the publication of documents and reports to assist in implementing the HLG-MR policy approach. These focused efforts towards encouraging the implementation of full-cost recovery (FCR) pricing and the holding of paid outage reserve capacity (ORC). FCR is necessary to allow essential investments to be made in the supply chain and paid ORC helps ensure that adequate reserve production capacity is available at short notice in the event of an unplanned shutdown. ORC is an essential measure necessary to ensure supply reliability.

The NEA, with the participation of key stakeholders, devised a methodology for calculating the full costs of ^{99}Mo production and for valuing and paying for ORC. The NEA evaluated supply chain participants (through self-assessment) on their progress towards implementing the HLG-MR principles related to FCR and ORC, along with the role of governments in the ^{99}Mo/^{99m}Tc market. The review found that most reactor operators and processors were gradually implementing FCR for ^{99}Mo production, although this process was happening at differing speeds and not everywhere. It was revealed that paid ORC capacity was not yet widely accepted and used by the market.

The NEA also carried out a comprehensive study of the potential level of impact of converting from HEU to low-enriched uranium (LEU) targets for ^{99}Mo production, concluding that the impact would be mostly felt in the upstream segment of the industry. Another report presented a number of policy options for government decision-makers to consider that could encourage supply chain participants to convert to LEU targets. The NEA also published an update on likely ^{99}Mo supply and demand for the period to 2030, which identified some periods of potential supply shortage.

To increase awareness among governments of the importance of appropriate reimbursement for ^{99m}Tc and to assist in any potential actions taken, the NEA issued a discussion document on the separation of reimbursement for the radioisotope from the radiopharmaceutical and the diagnostic medical procedure. The objective was to help achieve greater transparency in determining the value of the radioisotope.

In summary, the second mandate showed that, while commendable progress had occurred in many areas, there were still major issues in the ^{99}Mo/^{99m}Tc market, with some continued government subsidisation, insufficient ORC and inadequate reimbursement for ^{99m}Tc. Potential future periods of supply shortage were identified, particularly concerning the likely loss of significant capacity around 2016. It was agreed that the HLG-MR mandate should be renewed for a further two years, until 2015.

In the third mandate, the HLG-MR continued its efforts to help ensure the global security of supply of ^{99}Mo/^{99m}Tc through implementation of the six policy principles. The NEA undertook a further self-assessment review of the ^{99}Mo/^{99m}Tc supply chain, focusing again on progress with implementing FCR and paid ORC and the role of governments in the market, this time on both an economic and also on a healthcare level. This again identified that overall progress was slow and concluded that it was unlikely that the supply chain itself would take the necessary actions for market reform without further direct action from governments.

In that context, the NEA was asked by the HLG-MR to develop a more formal statement of commitment to the HLG-MR principles. A consensus document, the Joint Declaration on the Security of Supply of Medical Radioisotopes, was developed and on 17 December 2014 the OECD Council formally noted that eleven countries had officially signed up to the Joint Declaration; subsequently three more countries confirmed their adherence. The Joint Declaration provides a co-ordinated political commitment to bring about necessary changes across the supply chain.

The NEA conducted two studies looking at the critical 2015 to 2020 supply period. The second of those studies identified that market demand for ^{99}Mo/^{99m}Tc was around 10% lower than had been previously estimated (around 9 000 6-day ^{99}Mo curie per week at end of processing) and that the demand level had been relatively flat for the period 2012 to 2014. The overall conclusion was that, in 2016, capacity should be sufficient to manage adverse events, but that mitigation capability would reduce in 2017, from when there was a clear need for additional processing capacity. If the planned additional capacity is successfully introduced in 2017, then the supply for the rest of the period to 2020 should also be secure. However, the supply would require careful planning and a high degree of supply chain co-operation for the foreseeable future.

During its normal bi-annual meetings, the HLG-MR reconsidered the six policy principle approach. This was supported as still being an appropriate approach; the Association of Isotope Producers and Equipment Suppliers (AIPES) on behalf of supply chain participants proposed a 7th policy principle. They proposed that "Sufficient medical reimbursement should be available to cover full-cost recovery throughout the supply chain in all markets." The proposal was debated in detail, but not adopted; the subject will be discussed further.

The NEA reviewed the status of the ^{99}Mo/^{99m}Tc market and reported the results during the HLG-MR meetings. Particular concern was identified regarding a reported decline in the market value at the generator step of the supply chain (>10% value decrease in 2013). Supply chain participants including nuclear pharmacies that were present at the HLG-MR reported on downward pressures that led to decreases in market pricing.

During its presentation to the HLG, the NEA expressed concern that a market that was financially contracting near the end-user seemed at odds with the process of accepting increased costs throughout the supply chain. Pressure on health care budgets has continued, with negative effects on nuclear medicine and only limited progress has been made in reviewing or adjusting reimbursement rates, which hampers change. The sustainability of the supply chain has not yet been achieved.

The NEA Committee for Technical and Economic Studies on Nuclear Energy Development and the Fuel Cycle (NDC) has approved a fourth mandate of the HLG-MR for the 2015-2017 period; the first meeting was held in February 2016.

1. Introduction to the third mandate

In April 2009, following the shortages of the key medical radioisotopes ^{99}Mo and its decay product ^{99m}Tc, the NEA Steering Committee for Nuclear Energy established the HLG-MR. During its first mandate (2009-2011), the HLG-MR, working with medical isotope stakeholders, examined the major issues that affected the short-, medium- and long-term reliability of ^{99}Mo/^{99m}Tc supply. They completed a comprehensive assessment of the key areas of vulnerability in the supply chain and identified the issues that needed to be addressed. The NEA also examined the supply and demand for ^{99m}Tc, undertook a full economic analysis of the supply chain, and reviewed potential alternative ^{99}Mo/^{99m}Tc production technologies. This work resulted in the release of several reports that have been issued under *The Supply of Medical Radioisotopes* series (see the References section). In conclusion of the first mandate, the HLG-MR released a policy approach to move the ^{99}Mo/^{99m}Tc supply chain to a sustainable economic basis. The policy approach included six principles (see Appendix 1), which were targeted to be implemented within three years of their release.

In April 2011, the NEA Steering Committee approved a second mandate (2011-2013) for the HLG-MR, in which the main objective was to implement the agreed policy approach in a timely manner. The NEA Steering Committee also agreed that the group would report to the Committee for Technical and Economic Studies on Nuclear Energy Development and the Fuel Cycle (NDC). Since then, the group's activities have been included in the NDC programme of work.

During the second HLG-MR mandate, the focus was on implementing the six principles and analysing the impact on the market of conversion from HEU to LEU targets. Priority was given to investigating the implementation by supply chain participants of the first two policy principles (on FCR and paid ORC) in a timely and globally consistent manner. The NEA, in co-operation with key stakeholders, created methodologies for calculating full costs and for valuing and paying for ORC. Reports on these methodologies and their implementation were issued, which were particularly useful to the upstream segment of the industry where the most change was needed. The NEA also worked with key stakeholders to ensure that the methodologies were applied in a consistent manner.

To better understand the transition from HEU to LEU targets for ^{99}Mo production, the NEA undertook a project to study the impacts on the ^{99}Mo/^{99m}Tc supply chain and to propose actions to support that transition, resulting in the release of two reports.

The NEA undertook a review of the ^{99}Mo/^{99m}Tc supply chain, by self-assessment. The review focused on progress with FCR and paid ORC, and government's role in the market. This identified those supply chain participants that were making good progress towards the implementation of the HLG-MR policy approach; it also highlighted those players that had not made significant progress (or had not yet started). The results were published as the first self-assessment report. The NEA also produced an update on ^{99}Mo/^{99m}Tc demand and supply for the period to 2030.

In October 2013, the third mandate of the HLG-MR was approved by the NDC at its 62nd meeting. The broad deliverables for the third mandate of the HLG-MR included:

- Carrying out studies related to the security of supply.
- Evaluating progress towards the implementation of the HLG-MR policy approach through a second self-assessment by the global supply chain.
- Taking closer engagement with downstream supply chain participants to explore issues related to implementation of full-cost recovery and isotope reimbursement.
- Re-examination of the six HLG-MR policy principles, in particular, those that had been reported as having significant implementation challenges.
- The sharing of information on the status of the ^{99}Mo/^{99m}Tc market, to increase transparency and encourage consistency in approach.
- Communication of the need to implement the HLG-MR policy approach to governments and other supply chain participants, including healthcare policy-makers and nuclear medicine professionals.
- Support in the implementation of all aspects of the HLG-MR policy approach, where appropriate and feasible. With possible measures identified including: encouraging the implementation of FCR for new/replacement ^{99}Mo production infrastructure; working with healthcare policy-makers to explore reimbursement approaches that would help achieve economic sustainability in the whole supply chain; pursuing options to encourage conversion to LEU targets for ^{99}Mo production; studying different isotope reimbursement models; discussing the advantages of separate reimbursement for the isotope from the radiopharmaceutical and the medical procedure; exploring the benefits of using ^{99m}Tc for diagnostic procedures compared to alternative isotopes/modalities.
- Providing regular reports to governments and other major stakeholders.

During the third HLG-MR mandate, the focus continued on implementing the six principles of the HLG-MR policy approach. Two studies were undertaken to review the global market demand and capacity looking forwards at the critical 2015 to 2020 time period. These reports reviewed and updated the capacity of the existing supply chain participants and investigated and reviewed the potential capacity of prospective projects. The second of the studies looked into demand in more detail, using a different approach to collect data and introducing a standardised approach to the collection of data for prospective new projects' timelines. The second study is discussed in more detail in section 4 of this report.

The NEA also undertook a second self-assessment review of the ^{99}Mo/^{99m}Tc supply chain, based on input from key supply chain participants (see section 2). The review focused on progress with implementing FCR and paid ORC and government's role in the market both on an economic and also a healthcare level. This again identified that overall progress was slow and it was concluded that it was unlikely that the supply chain itself would take the necessary actions without some further direct actions from governments.

In that context, at the 21-23 January 2014 HLG-MR meeting, the NEA was asked to look at developing a more formal statement of commitment to the HLG-MR principles (see section 3). Discussions were held with member countries and a consensus document, the Joint Declaration on the Security of Supply of Medical Radioisotopes, was developed. On 17 December 2014 the OECD Council formally noted that eleven countries had officially signed up to the Joint Declaration; subsequently three more countries confirmed their adherence.

During its normal bi-annual meetings, the HLG-MR reconsidered the six policy principle approach. This was largely supported as still being an appropriate approach, but the Association of Isotope Producers and Equipment Suppliers (AIPES) on behalf of supply chain participants proposed a 7th policy principle. The additional principle proposed was that "Sufficient medical reimbursement should be available to cover full-cost recovery throughout the supply chain in all markets." The potential wording of such a 7^{th} policy principle and its possible introduction was debated in detail during the fourth meeting of the third mandate, but a decision was taken not to adopt a 7^{th} policy principle during the third mandate. However, the subject will be discussed further.

The NEA reviewed the status of the $^{99}Mo/^{99m}Tc$ market and reported upon this in presentations made at two of the HLG-MR meetings. Particular concern was identified about the reported decline in the value of the market at the generator step of the supply chain. The market value decrease (e.g. >10% in 2013) was particularly notable in the US market, with the primary suppliers reporting market pressures that decreased both market pricing and, to an extent, market volume. During the same period, the US nuclear pharmacy sector also reported downward pressure on market pricing and wrote-off significant goodwill value in that business.

In its report to the HLG-MR, the NEA expressed concerns that a market that was financially contracting near the end of the supply chain was at odds with a market where increased costs were being pushed through the supply chain in the move towards FCR pricing. The final HLG-MR meeting of the third mandate also included representation from Cardinal Healthcare, the world's largest nuclear pharmacy group that represents between 20 and 25% of all ($^{99}Mo/^{99m}Tc$) generators purchased worldwide. The Cardinal Healthcare representative gave a useful presentation from the perspective of the nuclear pharmacy operator. Cardinal stated that the nuclear pharmacy point in the supply chain was under heavy stress from increasing upstream costs (implementation of FCR), but simultaneously was experiencing downward price pressures from the healthcare system on the services they were providing.

This report concludes the third mandate of the HLG-MR.

2. Second self-assessment of the global $^{99}Mo/^{99m}Tc$ supply chain

In June 2011, the HLG-MR released its policy approach to move the $^{99}Mo/^{99m}Tc$ supply chain to a sustainable economic basis and to ensure the security of supply of medical isotopes. The policy approach is based on six principles, which the HLG-MR agreed to implement by June 2014.

As a direct action to implement Principle 6, in February 2014, the NEA conducted a second self-assessment of the $^{99}Mo/^{99m}Tc$ supply chain. The main objective was to evaluate progress towards the implementation of the HLG-MR policy principles made by supply chain participants since the first self-assessment in 2012. A total of 62 questionnaires were sent to key supply chain participants – reactor operators, processors, generator manufacturers, nuclear medicine associations that represent end-users of $^{99}Mo/^{99m}Tc$, and governments. Fifty-two responses were received for an overall response rate of 84% (compared to 77% in the first self-assessment). By place and role in the global supply chain, the NEA surveyed: twenty-four government ministries and departments[1]; thirteen reactor operators (nine of which are currently part of the global supply chain); nine processors (six of which are currently part of the global supply chain); eight generator manufacturers; seven societies representing nuclear medicine professionals including three national societies; and one industry association representing companies active in the fields of nuclear medicine and/or medical imaging.

A large majority of governments and supply chain participants responded to the second self-assessment at each level of the supply chain. Particularly encouraging was the increased participation by generator manufacturers, which reflected their closer involvement in the work of the HLG-MR since the first self-assessment. It should be noted that the self-assessment process relies upon the self-reporting of the progress of individual organisations towards them achieving the goals of implementing the HLG-MR policy principles. Therefore the self-assessment reflects the perception of each individual organisation.

The second self-assessment also included the consideration of waste management costs in assessing progress towards full-cost recovery, as more information was provided by the supply chain. Hence those costs were considered in the development of progress indicators for individual supply chain participants. Countries and organisations were deemed to be covering waste management costs for the purpose of implementing full-cost recovery if they were paying for waste treatment and interim storage and were setting aside funds for final waste disposal and storage, according to their domestic legislative provisions.

Full-cost recovery

Progress towards implementing FCR by reactor operators and processors had continued to be slow since the first self-assessment. The most significant development in the intervening two years was the achievement of full recovery for operational costs related

1. In the first self-assessment, a single questionnaire was sent to governments. For the second self-assessment targeted questionnaires were sent separately to government ministries responsible for research reactors and health.

to ^{99}Mo production by more reactors through higher prices. However, the (relatively high) capital, decommissioning and waste management costs were still being subsidised to an extent by governments. Furthermore, it was unclear in the self-assessment results whether higher prices being achieved for ^{99}Mo irradiations and the consequently higher revenues for reactor operators had resulted in facility improvements that were aimed at increased supply reliability.

Although government subsidies had been reduced, they continued to act as a barrier to efforts to implement FCR everywhere. This was a negative signal to the rest of the market, with the effect of slowing down full implementation. Also, new reactor and processor infrastructure was being proposed to be built with public funds, which further risked undermining the process of moving towards economic sustainability.

Only two out of the nine reactors that were part of the global supply chain had fully implemented FCR (no change since the first self-assessment in 2012); the rest were at interim stages of implementation or had not yet started the process. The operators of the FRM-II reactor in Germany and the prospective new Korean reactor were surveyed as well, but these reactors were not yet in the supply chain. At the time of survey, the reactors at the Research Institute for Atomic Reactors (RIAR) and the Karpov Institute of Physical Chemistry (IPC) in the Russian Federation were irradiating primarily for the domestic market.

Table E1 shows the progress made at the time of the second self-assessment by the nine producing reactors in implementing FCR, expressed in terms of their normal available capacity, as reported in *Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the ^{99}Mo/^{99}Tc Market, 2015-2020* (NEA, 2014a). The values were compared to those from the first self-assessment in 2012.

Table E1. FCR implementation at producing reactors by normal available capacity

Progress indicator	Number of reactors, 2014 (2012)	Normal available capacity per week in 6-day Ci, 2014 (2012)[1]	Share of total normal available capacity in %, 2014 (2012)[2]
Fully implemented	2 (2)	4 000 (4 000)	14% (15%)
Significant progress made	3 (3)	14 880 (13 680)	53% (50%)
Some progress made	2 (0)	7 480 (0)	26% (-)
Not started	2 (4)	1 900 (9 800)	7% (36%)

1. The normal available capacity of OSIRIS has been revised up from 1 200 to 2 400 six-day curies/week at the end of processing (EOP). The normal available capacity of MARIA has been revised down from 1 920 to 1 500 six-day curies at the end of processing. The reactor operator of MARIA is working to increase this capacity to 2 200 six-day curies EOP from January 2015. The net result from these revisions is an increase of total normal available capacity by 780 six-day curies/week.

2. Total normal available capacity is the sum of all normal available capacities of producing reactors. Shares may not add to 100% due to rounding.

Table E2 presents the progress made at the time of the second self-assessment by processors that were part of the global supply chain in implementing FCR, expressed in terms of their stated operational capacity, as reported in *Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the ^{99}Mo/^{99}Tc Market, 2015-2020* (NEA, 2014a). The values again were compared to those from the first self-assessment in 2012. There had been very little progress at the processor level, reportedly due to resistance to price increases from the downstream supply chain and insufficient actions on isotope reimbursement.

Table E2. FCR implementation at processors by capacity

Progress indicator	Number of processors, 2014 (2012)	Capacity per week in 6-day Ci, 2014 (2012)[1]	Share of total capacity in %, 2014 (2012)[2]
Fully implemented	3 (3)	8 680 (11 200)	52% (62%)
Significant progress made	1 (1)	3 500 (2 500)	21% (14%)
Some progress made	0 (0)	-	-
Not started	1 (1)	900 (900)	5% (5%)
No response	1 (1)	3 500 (3 500)	21% (19%)

1. IRE's capacity has been revised up from 2 500 to 3 500 six-day curies/week, while Nordion's capacity has been revised down from 7 200 to 4 680 six-day curies/week. The net result is a reduction in processing capacity by 1 520 six-day curies/week.

2. Shares may not add to 100% due to rounding.

At the generator manufacturer level and further downstream, there was an increase in response rate to the self-assessment, showing their greater involvement in the work of the HLG-MR. A common theme in the responses received from generator manufacturers was the reported strong level of competition in the market; this made it challenging to increase the prices of generators to nuclear pharmacies or hospitals. As commercial entities, generator manufacturers are expected to fully recover their costs of producing ^{99m}Tc generators plus a profit. However, to the extent that below-full-cost-recovery prices may be passed down the supply chain from subsidised reactors, generator manufacturers may not be paying the "true" full cost of ^{99}Mo.

In the second self-assessment, medical end-users reported higher prices from their suppliers over the preceding two years without a corresponding increase in reimbursement, except for the limited Centers for Medicare and Medicaid Services (CMS) additional payment of USD 10 in the United States for non-HEU ^{99m}Tc. It was reported that the lack of increase in reimbursement had put pressure on hospital budgets and that there was concern that in the future this may lead to a noticeable substitution of ^{99m}Tc-based radiopharmaceuticals with other techniques. However, despite the higher prices, many end-users reported that they have been able to absorb the higher costs.

Outage reserve capacity

Despite some noticeable progress since the first self-assessment, paid ORC was still not universally accepted and used by the market at the time of the second self-assessment. ORC contributes significantly to the security of supply and should be appropriately valued and paid for. This was reported as occurring only in a few cases. In some other cases, reactors were in the process of renegotiating contracts with their processors for the provision and payment for ORC. In other cases, processors were reported as simply using unpaid spare (reserve) capacity at other reactors; only paying for that service when they actually used it.

Only four of the nine producing reactors stated that they had been able to fully implement ORC. Table E3 shows the progress by reactors at the time of the second self-assessment, expressed in terms of their normal available capacity, as reported in *Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the ^{99}Mo/^{99}Tc Market, 2015-2020* (NEA, 2014a).

Table E3. ORC implementation at producing reactors by normal available capacity

Progress indicator	Number of reactors, 2014 (2012)	Normal available capacity per week in 6-day Ci, 2014 (2012)	Share of total normal available capacity in %, 2014 (2012)[1]
Fully implemented	3 (3)	11 800 (11 800)	42% (43%)
Significant progress made	1 (0)	2 800 (-)	10% (-)
Some progress made	1 (2)	4 680 (7 480)	17% (27%)
Not started	4 (4)	8 980 (8 200)	32% (30%)

1. Shares may not add to 100% due to rounding.

Table E4 presents the progress made by processors at the time of the second self-assessment in implementing ORC, expressed in terms of their stated capacity, as reported in *Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the ^{99}Mo/^{99}Tc Market, 2015-2020* (NEA, 2014a).

Table E4. ORC implementation at processors by capacity

Progress indicator	Number of processors, 2014 (2012)	Capacity per week in 6-day Ci, 2014 (2012)	Share of total capacity in %, 2014 (2012)
Fully implemented	3 (2)	7 500 (4 000)	45% (22%)
Significant progress made	0 (1)	- (2 500)	- (14%)
Some progress made	0 (0)	- (-)	- (-)
Not started	2 (2)	5 580 (8 100)	34% (45%)
No response	1 (1)	3 500 (3 500)	21% (19%)

Governments' role in the ^{99}Mo/^{99m}Tc market

Governments are involved in the global ^{99}Mo/^{99m}Tc supply chain primarily at both ends – at the reactor and at the medical end-user levels. The vast majority of ^{99}Mo supply chain participants represented in-between are commercial, for-profit entities. Although governments had been reducing their support for ^{99}Mo irradiations at reactors, much still remained to be done to achieve universal implementation of FCR. It was reported that despite real progress since the adoption of the HLG-MR policy principles, some governments continued to subsidise ^{99}Mo production. While it is a government's prerogative to fund basic research at reactors, any commercial ^{99}Mo production as part of the global supply chain should comply with the principle of FCR to avoid distorting the global market.

Tables E5 and E6 show the level of government support for ^{99}Mo production at producing reactors at the time of the second self-assessment and the intended level of government support for future ^{99}Mo/^{99m}Tc production projects. This was based on information from the supply chain and the NEA's understanding of announcements made by countries. The level of government support is classified as "full subsidy", "partial subsidy" or "no subsidy", and is expressed in terms of normal available irradiation capacity per week, as reported in *Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the ^{99}Mo/^{99}Tc Market, 2015-2020* (NEA, 2014a). It should be noted that Table E5 hides the fact that governments had been steadily reducing support for ^{99}Mo production at existing reactors, which however, was counter balanced by the worrying sign of intentions to continue some government subsidisation, that were revealed in Table E6.

Table E5. Level of government support for ^{99}Mo production at producing reactors

Level of government support	Number of reactors, 2014 (2012)	Normal available irradiation capacity per week (in 6-day Ci), 2014 (2012)
Full subsidy	0 (0)	- (-)
Partial subsidy	7 (7)	24 260 (23 480)
No subsidy	2 (2)	4 000 (4 000)

Table E6. Level of intended government support for ^{99}Mo/^{99m}Tc production, projects under development, 2014

Level of intended government support	Number of new/replacement ^{99}Mo/^{99m}Tc projects	Potential new/replacement normal available production capacity per week (in 6-day Ci)
Full subsidy	4	6 500
Partial subsidy	2	1 300
No subsidy[1]	11	32 000

1. May include government loans or other support to be paid back by the ^{99}Mo/^{99m}Tc producer.

Further downstream, it was reported that very few governments intended to or had already reviewed their reimbursement rates for medical isotopes. At the time of the second self-assessment, the majority had not taken any action, with two exceptions. The Belgian government indicated it would be implementing separate reimbursement for ^{99m}Tc in early 2015, while the United States (US) government had added a supplementary USD 10 payment through CMS to reimburse qualifying hospitals for the use of non-HEU-produced ^{99m}Tc when produced under conditions of FCR.

The state of the ^{99}Mo/^{99m}Tc market

The results from the second self-assessment of the global ^{99}Mo/^{99m}Tc supply chain were similar to those from the first self-assessment, showing slower-than-desired progress towards implementing the six HLG-MR policy principles. This led to the deadline for full implementation that had been agreed by the governments represented on the HLG-MR of June 2014 being missed. With the exception of Principles 5 and 6, governments and supply chain participants had not taken sufficient action and the ^{99}Mo/^{99m}Tc market continued to be unsustainable.

Much of the experience since the 2009-2010 supply crisis had shown that short-term commercial considerations (e.g. increasing or retaining market share) continue to trump long-term sustainability considerations. Furthermore some governments were still subsidising ^{99}Mo production, despite their commitment to the HLG-MR principles; this continued to send negative signals to potential investors in future commercially based production and jeopardises the long-term security of supply by potentially perpetuating below-full-cost-recovery pricing.

Following the second self-assessment, the NEA commented that it was aware that the involvement of different types of organisations (governments, government-owned entities and private companies), with diverse and sometimes conflicting interests, at different levels of the same supply chain, creates unique challenges. It was concluded that voluntary commitments had not resulted in sufficiently effective actions towards implementing the HLG-MR policy approach and that there was a need for governments to take more direct action. The same conclusion had been made after the first self-assessment report, which underlined that work remained to be done to help the market become sustainable.

3. Development of a Joint Declaration

Following the publication of the second self-assessment report, the HLG-MR, working with the European Observatory on the supply of medical radioisotopes (European Observatory), examined the obstacles to reaching sustainability in the supply chain and sought to strengthen the interaction between producers of medical radioisotopes and the medical community. From those discussions, it was concluded that it was unlikely that those within the supply chain would take the necessary actions themselves without some further direct action from governments. In this context, the NEA Secretariat was asked by the HLG-MR to look at a more formal statement of commitment to the HLG-MR principles, while the six producing countries within the European Union, in co-ordination with the European Observatory, would seek a similar commitment within the European Union (see Appendix 2).

The concept of a joint declaration, which would not create binding obligations on its signatories, was proposed by the NEA Secretariat. Subsequently, the Joint Declaration on the Security of Supply of Medical Radioisotopes (Joint Declaration - provided in the Annex to this document), was developed by the HLG-MR. On 15 April 2014, the NEA Steering Committee noted the Joint Declaration, and requested the Secretariat to work with the countries participating in the HLG-MR to obtain governmental approval and adoption of the Joint Declaration in a timely and appropriate manner.

The purpose of the Joint Declaration was to provide a more formal and co-ordinated political commitment by governments of the countries participating in the HLG-MR that would foster the necessary changes needed across the supply chain, both in producing and user countries. While specifically targeted at all producers, potential producers and users of medical radioisotopes in the HLG-MR, it was intended that the Joint Declaration would be open for adherence by all NEA members and any other interested country.

The Joint Declaration that was developed contained a preamble to provide background information and actions that the countries participating in the HLG-MR agreed to take. It was intended to send a strong signal to the supply chain of the intention of governments to take co-ordinated action to ensure the long-term reliability of supply of these important medical radioisotopes. The intention was that the Joint Declaration would also provide the basis for ongoing discussions among countries participating in the HLG-MR and others, whether on a bilateral or multilateral basis, on their involvement or potential future involvement in the supply chain for ^{99}Mo and ^{99m}Tc.

As of November 2014, eleven out of the seventeen countries participating in the HLG-MR had adhered to the Joint Declaration: Australia; Canada; Germany; Japan; the Republic of Korea; the Netherlands; Poland; the Russian Federation; Spain; the United Kingdom and the United States. According to established practice, all Declarations adopted within the OECD framework are transmitted to the OECD Council, inviting the Council to "note" these instruments. This was done and the Joint Declaration was duly noted, added to the list of OECD legal instruments, and its text made available on both the OECD and NEA websites on 18 December 2014, with a list of adhering countries. Those website pages are routinely updated as appropriate.

The Joint Declaration remains open for adherence by the other countries participating in the HLG-MR and by any other country that wishes to do so. In the period since the Joint

Declaration was formally noted, Belgium, France and South Africa have added their adherence in 2015 to raise the number of adhering countries to 14.

4. Demand and Capacity Review 2015-2020

In August 2012, the NEA released an updated ^{99}Mo supply and demand projection from 2012 to 2030. According to that update, the period of greatest concern was 2016-2020, when ^{99}Mo/^{99m}Tc supply was projected to become strained from the scheduled permanent shutdown of the NRU reactor in Canada and of the OSIRIS reactor in France.

During the period of the third mandate, two demand and capacity updates for the period 2015 to 2020 were conducted to look in detail at this period of concern. Below is a summary abstracted from the most recent of those updates (see The Supply of Medical Radioisotopes: 2015 Medical Isotope Supply Review: ^{99}Mo/^{99m}Tc Market Demand and Production Capacity Projection 2015-2020 (NEA, 2015a)).

Demand update

During the collection of data for the latest demand and capacity projection, supply chain participants were requested to provide capacity utilisation data for their facilities. This data was to be provided in terms of a measure of the percentage of their production capacity utilised during each operating quarter during 2012, 2013 and 2014, along with the actual operating time periods per facility (e.g. operational days). This was a useful period for analysis as it contained periods of supply stress when a number of reactors and processing facilities suffered unplanned outage periods, with the result that other supply chain participants had to increase production levels to meet market demand and secure supply.

During this period, market supply was maintained successfully on an almost continuous basis, although some limited supply shortages were reported as occurring (for example in 2013 and 2014 in the Japanese market). The data was analysed to determine the level of recent market demand, with reported utilised capacity being taken as a surrogate for the demand in the market. The data was not 100% complete as one processor was not able to provide data; otherwise the exercise was successful and provided some new insight into recent global demand for ^{99}Mo. The overall supply levels reported were close to 9 000 6-day curies ^{99}Mo EOP per week, with some quarterly fluctuations. As the analysis period included some periods of minor shortages, the actual long-term demand trend was difficult to determine without full market data; for example, periods of limited supply shortage could appear as reduced market demand in this data set.

The fact that there were only relatively limited supply problems during 2013 and 2014 (when operational challenges to the supply chain were at times quite high), supports the notion that the market demand during that period was already around 9 000 6-day ^{99}Mo curies EOP per week. The reasons behind the market demand being lower than had previously been estimated are not fully clear. The continuation of measures to increase efficiency of use of ^{99m}Tc at the nuclear pharmacy and in the clinic, combined with some reduction in average injected dose due to some gamma camera and protocol improvements may have played some role. Also in a market where FCR pricing is being implemented in steps along the supply chain, with the result of increasing material prices, it would be understandable that efficiency of product use is a priority.

Capacity update

The NEA has recently updated the list of current and planned new ^{99}Mo/^{99m}Tc irradiation and processing projects, based on the most recent information available from the supply chain. The updates include: revisions to production start/end dates, additional "qualified" potential projects and anticipated impacts of some existing supply chain participants converting to using LEU targets.

The capacity analysis looked at three capacity scenarios for the 2015-2020 period and presented them in six-month intervals. These were:

- Scenario A: A "Reference" scenario – a baseline case that included only currently operational irradiation and processing capacity.
- Scenario B: The "Technological challenges" scenario – this added all of the anticipated projects, but did not include all of their planned new ^{99}Mo production capacity in some cases. For example, new reactor-based projects, given their proven technology and direct access of product to the existing supply chain, were assumed to start production on their announced commissioning dates and are only included from their first full year of production. On the other hand, new alternative technology projects (including reactor- and non-reactor-based), given the unproven nature of these technologies, were assumed to have a 50% probability of starting full scale production on their announced commissioning dates.
- Scenario C: A "Project delayed" scenario – built on the "technological challenges" scenario by further assuming that LEU conversion and all new projects would be delayed by one year beyond their anticipated first full year of production.

In all three scenarios, the six-month forecast intervals were based upon a 50/50 split of operating capacity between the two six-month periods in a year, unless a specific change had been identified for a specific six-month period. Also, scenarios B and C in the report did not include all of the announced new projects. Two projects were excluded as their likely commissioning dates had been delayed beyond 2020. It was not suggested that these projects would not become operational, but that they were not scheduled to operate in the forecast horizon (2015-2020).

For this report, the approach concerning the effects of LEU conversion was adjusted from the NEA 2014 report and a simple blanket effect of a 10% level of efficiency loss was applied in all cases. This seemed justified at this stage in the LEU conversion process, where dedicated targets are being developed by each of the processors, and where significant efforts have already been expended upon minimising efficiency losses in the processes.

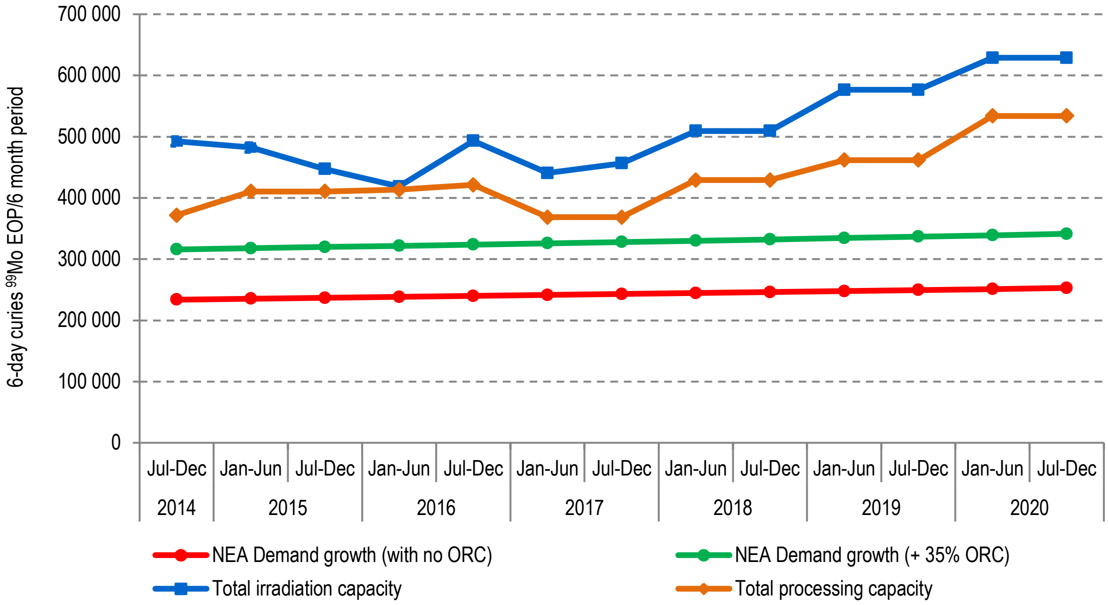
The "project delays scenario C" which was developed from the "technological challenges" scenario B by modelling a delay of all new projects and LEU conversion by one year, was seen as a likely scenario, given that previous experience had shown that large projects often take longer to complete than originally envisaged in this business. This effect had already been clearly demonstrated by reviewing the previous 2014 report, where anticipated delays in projects had in many cases already materialised.

"Project delays" scenario: C - Irradiation and processing capacity

Figure 4.1 (Figure 6.1 in the 2015 report) shows the projected global irradiation and processing capacity under the "project delays" scenario C. Under this scenario, delayed new capacity will have a negative effect on both irradiation and processing capacity compared to scenario B. However, delayed LEU conversion will have some opposite effect.

Over the six-year forecast period, the "delayed new capacity" effect will dominate over the "delayed LEU conversion" effect.

Figure 4.1. Current demand (9 000 6-day Ci ^{99}Mo/week EOP) and demand +35% ORC vs. total irradiation capacity and total processing capacity – projects delayed: Scenario C



Compared to scenario B, the irradiation and processing capacities under scenario C were almost identical in 2015 and 2016. Both capacities then decrease in the January-June 2017 period because this scenario modelled the effect of a one-year commissioning delay of additional conventional capacity being built in Australia. Total irradiation and processing capacity both then recover progressively, primarily due to the introduction of alternative technology that has been delayed.

The most important effect of scenario C was that the total processing capacity line drops and falls closer to the NEA demand +35% ORC line (which indicates a lower level of reserve capacity in 2017). The dip in 2017 underlines the importance of the on-time introduction of new irradiation and processing capacity in Australia; this project is currently reported to be running on time. The study also considered in some detail the potential additional contingency capacity that could be made available from the NRU reactor for an 18-month period between October 2016 and March 2018.

The overall conclusion of the latest NEA demand and capacity review was that, in the 2015-2016 period, the current irradiator and processor supply chain capacity should be sufficient and if well-maintained, planned and scheduled, be able to manage an unplanned outage of a reactor, or a processor.

From 2017, the capacity to manage adverse events would reduce; while being able to manage an unplanned reactor outage, the current processing capacity would have some limited scope to manage an unplanned event for the rest of the period. It was identified that the possible extension of the NRU operating period could be a useful stop-gap in the 2017 and early 2018 period. However, the need to add additional processing capacity by 2017 is clear and the on-time introduction of alternative processing technologies and the addition of planned substantial conventional processing capacity will be important. If these are achieved, then irradiation capacity and processing capacity should be secure for the rest of the period to 2020.

In conclusion, the supply situation will continue to require careful and well-considered planning to minimise security of supply risks, with a high degree of co-operation between the supply chain participants being essential for the foreseeable future. The market situation will continue to require regular monitoring, along with regular review of the progress of bringing the proposed new production capacity to market.

5. Future outlook and work plan

At the third meeting of the third mandate of the HLG-MR in February 2015, members and delegated participants proposed a renewal of the mandate of the HLG-MR for a further two years (2015-2017). The NEA Secretariat together with the HLG-MR developed a fourth mandate proposal, which was presented to and approved by the NEA NDC in June 2015. The primary focus of the fourth mandate will be to continue to work towards increasing the long-term security of supply of ^{99}Mo and ^{99m}Tc by focusing on specific issues that prevent the full implementation of the six principles.

This work will include actions to increase and maintain transparency of market demand and supply, report on global market developments, continue communication with the supply chain participants and end-users, further evaluate progress towards implementation of the policy principles and the provision of additional information and analysis where necessary. The main activities will continue to include

- Carrying out studies related to the security of supply.
- Evaluating progress towards the implementation of the HLG-MR policy approach through a third self-assessment by the global supply chain.
- Maintaining closer engagement with downstream supply chain participants to understand the impact of economic forces throughout the entire supply chain.
- Re-examining the six HLG-MR policy principles and considering if adjustment is required and additional policy principles appropriate.
- Sharing of information on the status of the ^{99}Mo/^{99m}Tc market and regular reporting on developments within the market.
- Communicating the need to implement the HLG-MR policy approach to governments and supply chain participants, including working with healthcare professionals and healthcare policy makers.
- Supporting the implementation of all aspects of the HLG-MR policy approach.
- Reporting regularly on HLG-MR actions to governments and other major stakeholders.

While the vast majority of irradiators and processors have shared a significant amount of information on their activities to support the work of the HLG-MR, there has been less useful information provided by downstream supply chain participants such as generator manufacturers, nuclear pharmacies and end-users. The NEA has already started to increase the engagement with these groups and intends to continue to increase engagement with the downstream supply chain participants in the future rounds of self-assessment.

The NEA has been encouraged by the helpful provision of additional levels of information from the supply chain participants in assessing demand and capacity and will work further with these groups to continue to improve the quality of that data. It is intended that data will be collected in a structured way every six months, in order to keep the information available on market demand and capacity as up-to-date as possible.

While most governments, where reactors operate, have been gradually withdrawing financial support for ^{99}Mo production, this move needs to reach a full conclusion in the near term in order to complete the transition to FCR in the upstream part of the supply chain. The support and construction of new ^{99}Mo production infrastructure with some public funding provides some challenges in this area and could, in the longer-term, lead to the creation of over-capacity in the market. The risk of over-capacity can be a drag on near-term commercial investment that could unintentionally have the reverse effect of leading to short-term supply issues.

To achieve near-term economic sustainability in the market and thus help ensure long-term reliable supply, the supply chain participants must fully implement the six HLG-MR policy principles; in particular, the principles relating to achieving FCR and paid ORC. The role of governments in supporting the implementation of the six principles within the marketplace remains essential, including recognition that FCR and ORC costs must be covered throughout the supply chain.

The conversion to LEU targets is expected to be completed during the fourth mandate period and progress will continue to be monitored through the demand and capacity studies.

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Available at: www.oecd-nea.org/med-radio/docs.

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Appendix 1. HLG-MR Policy Principles

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

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.

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.

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 (LEU) or to transition away from the use of highly enriched uranium (HEU), wherever technically and economically feasible.

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}Mo/^{99m}Tc and the value of international consensus in encouraging domestic action.

Principle 6: There is a need for periodic review of the supply chain to verify whether ^{99}Mo/^{99m}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.

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Appendix 2. Joint Declaration

JOINT DECLARATION ON THE SECURITY OF SUPPLY OF MEDICAL RADIOISOTOPES

WE, the Ministers and representatives of Australia, Canada, Germany, Japan, the Republic of Korea, the Netherlands, Poland, the Russian Federation, Spain, the United Kingdom and the United States of America, **SHARE** a common interest in ensuring the security of supply of the most widely used medical radioisotope, molybdenum-99 (^{99}Mo) and its decay product, technetium-99m (^{99m}Tc), which is used in approximately 40 million medical diagnostic imaging procedures per year worldwide enabling precise and accurate, early detection and management of diseases such as heart conditions and cancer, in a non-invasive manner.

WE ACKNOWLEDGE, on the one part, that the production of ^{99m}Tc depends largely on a small number of reactors that are ageing and facing unplanned outages, planned refurbishment outages or planned permanent shutdowns, which increases the risk of disruption of the supply chain, unless new infrastructure is developed to replace these facilities before they shut down.

WE RECOGNISE, on the other part, that an unsustainable economic structure is threatening the reliability of the ^{99}Mo/^{99m}Tc supply chain, and that global action to move to full-cost recovery is necessary to ensure economic sustainability and long-term secure supply of medical isotopes.

WE AFFIRM that any action to ensure the reliability of supply of ^{99}Mo/^{99m}Tc must be consistent with the political commitments to non-proliferation and nuclear security.

WE CONFIRM our acceptance of the principles set forth in the policy approach released in June 2011 by the High-Level Group on the Security of Supply of Medical Radioisotopes (the HLG-MR principles) to ensure the long-term secure supply of medical radioisotopes, which were formally endorsed by the Organisation for Economic Co-operation and Development's (OECD) Steering Committee for Nuclear Energy on 28 April 2011.

WE COMMIT, with the aim of jointly promoting an internationally consistent approach to ensuring the long-term secure supply of medical radioisotopes, to implement the HLG-MR principles in a timely and effective manner, and to:

- Take co-ordinated steps, within our countries' powers, to ensure that ^{99}Mo or ^{99m}Tc producers and, where applicable, generator manufacturers in our countries implement a verifiable process for introducing full-cost recovery at all facilities that are part of the global supply chain for ^{99m}Tc;
- Encourage the necessary actions undertaken by ^{99}Mo processing facilities or ^{99m}Tc producers in our countries to ensure availability of reserve capacity capable of replacing the largest supplier of irradiated targets in their respective supply chain;

- Take the necessary actions to facilitate the availability of ^{99m}Tc, produced on an economically sustainable basis, as outlined in the HLG-MR principles;
- Encourage all countries involved in any aspect of the ^{99m}Tc supply chain, and that are not party to the present Joint Declaration, to take the same approach in a co-ordinated manner;
- Take the necessary actions described above by the end of December 2014 or as soon as technically and contractually feasible thereafter, aware of the need for early action to avoid potential shortages of medical radioisotopes that could arise from 2016;
- Report on an annual basis to the OECD Nuclear Energy Agency (NEA) on the progress made at the national level and support an annual review of the progress made at the international level, both in light of this Joint Declaration.

WE INVITE the OECD Nuclear Energy Agency (NEA) to further the objectives set out in this Joint Declaration by, among other actions, undertaking periodic reviews of the progress of the supply chain with implementing the HLG-MR principles.