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The Supply of Medical Radioisotopes

2015 Medical Isotope Supply Review: $^{99}Mo/^{99m}Tc$ Market Demand and Production Capacity Projection 2015-2020

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Acknowledgements

This report would not have been possible without the contributions of a large number of supply chain participants and stakeholders, including major reactor operators and processors, generator manufacturers, and nuclear medicine associations representing radiopharmacies, hospitals and nuclear medicine professionals.

The OECD Nuclear Energy Agency (NEA) greatly appreciates the information provided by supply chain participants on the current molybdenum-99 (^{99}Mo)/technetium-99m (^{99m}Tc) production capacity situation to facilitate the creation of an updated demand and capacity projection for the 2015-2020 period. This projection is intended to help policy makers, producers, and other stakeholders take appropriate actions to ensure the long-term security of supply of the key medical isotopes ^{99}Mo and its decay product, ^{99m}Tc.

This report was written by Mr Kevin Charlton of the NEA Nuclear Development Division. Detailed review, comments and suggestions were provided by the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR).

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Chapter 1. Introduction

Medical diagnostic imaging techniques using technetium-99m (^{99m}Tc) account for approximately 80% of all nuclear medicine procedures, representing 30-40 million examinations worldwide every year. Disruptions in the supply chain of these medical isotopes – which have half-lives of 66 hours for molybdenum-99 (^{99}Mo) and only 6 hours for ^{99m}Tc, and thus must be produced continuously – can lead to cancellations or delays in important medical testing services. Unfortunately, supply reliability has been challenged over the past decade due to unexpected shutdowns and extended refurbishment periods at some of the mostly ageing, ^{99}Mo-producing research reactors and processing facilities. These shutdowns have at times created conditions for extended global supply shortages (e.g. 2009-2010).

At the request of its member countries, the Nuclear Energy Agency (NEA) became involved in global efforts to ensure a secure supply of $^{99}Mo/^{99m}Tc$. Since June 2009, the NEA and its High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) have examined the causes of supply shortages and developed a policy approach, including principles and supporting recommendations to address those causes. The NEA has also reviewed the global ^{99}Mo supply situation periodically, using the most up-to-date data available from supply chain participants, to highlight periods of potential reduced supply and to underscore the case for implementing the HLG-MR policy approach in a timely and globally consistent manner.

In 2012, the NEA released a ^{99}Mo supply and demand forecast up to 2030, identifying periods of potential low supply relative to demand. That 2012 forecast was updated with a report "Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the $^{99}Mo/^{99m}Tc$ Market 2015-2020" (NEA, 2014) in 2014 that focused on the much shorter 2015-2020 period. This report[1] updates the 2014 report, and continues to focus on the potentially critical 2015-2020 period. In that period, the OSIRIS reactor in France will permanently shut down operations and one of the largest irradiators for medical isotopes, the National Research Universal (NRU) reactor in Canada, will cease routine ^{99}Mo production and the associated Canadian processing capacity will move offline. In the same period, new reactor- and non-reactor-based $^{99}Mo/^{99m}Tc$ projects are expected to be commissioned in various countries. It is important to analyse the overall impact and timing of these events to understand how global production capacity might be affected.

This report presents global irradiation and processing capacity under three main capacity scenarios. As in the previous 2014 report, the projected demand and production capacity are presented in six-month intervals (January-June and July-December) during the forecast period. The NEA recognises that, as forecast time intervals decrease (e.g. from one year to six months), the timing accuracy of the forecast events may also decrease. The results in this report, however, should be interpreted in terms of the projected future trends as opposed to actual forecast values and dates.

1. The scenarios presented by the NEA in this report should not be construed as a prediction, forecast or expectation of which projects will proceed and when. The scenarios are only meant to be illustrative of possible future situations, whether planned new projects materialise or not.

Chapter 2. Demand update

In 2011, the NEA released a study with the results of a global survey of future demand for $^{99}Mo/^{99m}Tc$ (NEA, 2011), developing a scenario based on a data assessment by an expert advisory group. The study showed $^{99}Mo/^{99m}Tc$ demand growth up to 2030 in both mature and emerging markets, with stronger growth forecast in emerging markets.

In a subsequent report, *A Supply and Demand Update of the Molybdenum-99 Market* (NEA, 2012a), the NEA estimated global ^{99}Mo demand at 10 000 6-day curies ^{99}Mo per week[1] at end of processing (EOP). This was a decrease from the previously estimated 12 000 6-day curies ^{99}Mo per week EOP, which had resulted from a number of changes that had occurred in the market as a consequence of the 2009-2010 global supply shortage. These changes included: better use of available $^{99}Mo/^{99m}Tc$, more efficient elution of ^{99m}Tc generators, adjustments to patient scheduling, and some increased use of substitute diagnostic tests/isotopes that continued to prevail after the ^{99m}Tc supply shortage period was over.

The April 2014 report used as a starting point, the NEA 2012 estimate of 10 000 6-day curies ^{99}Mo EOP per week from processors, but with modified expected annual demand growth rates of 0.5% for mature markets and 5% for developing markets during the forecast period, those growth rate adjustments were based on information provided at the time by supply chain participants.

During the collection of data for this report, supply chain participants were requested to provide capacity utilisation data for their facilities 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 in order to meet market demand.

During this period, market supply was maintained successfully on an almost continuous basis, but 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.

1. A six-day curie is the measurement of the remaining radioactivity of ^{99}Mo six days after it leaves the processing facility (i.e. at the end of processing – EOP). In International System (SI) Units, 1 Ci is equal to 37 Giga becquerels.

For the purposes of this report, the market demand has been adjusted to 9 000 6-day curies ^{99}Mo EOP per week at a base time point of end 2014, this level has been reviewed and confirmed by supply chain participants. This market demand level is lower than that used in the 2014 report on two counts. On one count, the base level demand in this report is lower by 1 000 6-day curies ^{99}Mo EOP per week. On the second count, the base time point used for the market demand is now 2014 instead of 2012. The previous report while using 10 000 6-day ^{99}Mo curies EOP per week, used 2012 as the base time point, so 2 additional years of market growth were included in the scenario projections. For this report, the market growth rates have been kept unchanged at 0.5% for mature markets and 5% for developing markets during the forecast period. Mature markets are estimated to account for 84% of the global demand for $^{99}Mo/^{99m}Tc$, while emerging markets for 16%. The latest NEA market demand analysis does not fully support this level of projected market growth, but for the purposes of this report and to maintain continuity where that is possible, the previous rates have been retained. The resulting demand curves in this report are lower than in the 2014 report, but are considered by the NEA to be representative of the present market situation and this view has also been confirmed by open session discussions with supply chain participants at HLG-MR meetings.

The fact that there were only relatively limited supply problems during the 2013 and 2014 supply periods (where the operational challenges to the supply chain were at times quite high), supports the notion that the market demand during that period was already below 10 000 6-day ^{99}Mo curie EOP per week. The reasons behind the market demand being now lower than previously estimated are not fully clear. The continuation of the previously mentioned 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 full cost recovery (FCR) pricing is being implemented in steps along the supply chain, with the result of increasing materials prices, it would be understandable that efficiency of use is a priority.

What capacity level is required to ensure that $^{99}Mo/^{99m}Tc$ demand is met?

As in previous reports, the NEA has no direct way to measure the amount of paid outage reserve capacity (ORC) that is held in the market, but all supply chain participants agree that the principle of having paid ORC is essential to sustaining reliability of supply. The need of the market for ORC was illustrated in 2013 and 2014, with unplanned outages at major ^{99}Mo producers (e.g. the HFR reactor and the Mallinckrodt processing facility in the Netherlands, and NTP's processing facility in South Africa, which also blocked irradiation capacity from the SAFARI reactor). These significant outages tested the supply chain's ability to ensure reliable supply. This challenge was largely met by the supply chain by using available ORC and resulted in only a small number of limited supply shortages.

The ageing production infrastructure and the continued risk of similar outages in the future require the constant availability of ORC. As a result, the capacity level required to ensure that $^{99}Mo/^{99m}Tc$ is met needs to be established and this capacity must include some level of paid ORC. In the HLG-MR principles, it was proposed that a processor should hold sufficient paid reserve capacity to replace the largest supplier of irradiated targets in their supply chain and likewise participants further down the supply chain should hold similar levels of ORC. This is the so-called (n-1) criterion. In fact, there have been occasions over the last few years when, for some suppliers, the (n-2) criterion (replacing the two largest suppliers) may have been more appropriate. The actual levels for (n-1) and (n-2) criterion vary depending upon the supply diversity of each supply chain participant and the actual levels also change as part of a dynamic process; for example as producers enter and exit the market. The 2014 report estimated the levels at the beginning of 2014 for the (n-1) criterion as "demand + 35% ORC" and for the (n-2) criterion as "demand +62% ORC".

In this report, the minimum capacity level required to meet demand is expressed at a level of market demand plus ORC of +35%. Analysis of historical data has shown that the security of supply comes under stress whenever the theoretical maximum available production capacity falls below the level of demand +35% ORC. In this report production capacity is compared to this level of "demand +35% ORC", with the level of demand without ORC also presented as a reference in the document in all scenarios. Supply chain participants have in the past indicated that an ORC of 50% would give an acceptable probability of reliable supply of irradiated targets to the processor. A recent analysis of a (n-2) criterion indicates that the supply chain is now more diversified and as a result the (n-2) criterion level is less than the previously used 62%. The level is also lower for irradiation capacity than it is for processor capacity.

Given that the actual ORC level required will change over time, the ORC level in this document should only be used with caution in providing advice or making decisions. For comparison the figures all show the demand curve with no ORC. However, the NEA does not believe that the demand curve without ORC is a good representation of a "safe" level of capacity to meet market demand with an adequate level of security. This position is supported by the periods of shortage experienced over the past few years, the HLG-MR principle that supports having paid ORC available and the advice received from the supply chain participants on the importance of holding paid ORC for maintaining reliability of supply.

Chapter 3. Scenarios and assumptions for ^{99}Mo/^{99m}Tc production capacity

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 low-enriched uranium (LEU) targets. Appendix 1 provides a list of current and potential ^{99}Mo/^{99m}Tc producers, along with the status of "qualified" projects as of March 2015. It should be noted that not all potential new production facilities may be operational by the indicated times or even at all. This is particularly the case for projects that rely on commercial funding, given the prevailing below-full-cost-recovery prices in the market and the resulting challenges to develop solid business cases.

Supply chain participants acknowledge that, given the inability to store these radioisotopes for later use, the weekly ^{99}Mo/^{99m}Tc supply will generally match demand. Therefore, the intent of this forecast is not to predict the actual level of ^{99}Mo/^{99m}Tc supply based on changes in production capacity. It is intended to identify periods of increased risks of supply shortages in order to inform government policy makers, industry, and nuclear medicine professionals. Such higher-risk periods are when the production capacity curve is close to or below the projected NEA demand curve +35% ORC.

In this report, the forecast horizon for ^{99}Mo/^{99m}Tc production capacity is the six-year period (2015-2020), a period that reflects important changes in global production capacity, including the planned exit from the supply chain of the OSIRIS reactor in France (December 2015) and the NRU reactor and Canadian Nuclear Laboratories (CNL) and Nordion processing capacity in Canada (October 2016). The period also anticipates the commissioning of new reactor- and non-reactor-based projects in Europe, North and South America, Australia and the Far East.

The capacity scenarios presented in this document are based on the data in Appendix 1, with some caveats[1] for current irradiators and processors. Appendix 1 provides the current normal available capacity for producing reactors and processors. The capacity and production values used in the different scenarios also incorporate the impacts from LEU conversion, which is anticipated to reduce overall production capacity (see *Market Impacts of Converting to Low-enriched Uranium Targets for Medical Isotope Production* – NEA, 2012b).

This document explains the results obtained from three capacity scenarios for the 2015-2020 period, presented in six-month intervals (January-June and July-December):

- Scenario A: "Reference" scenario – a baseline case that includes only currently operational irradiation and processing capacity.
- Scenario B: "Technological challenges" scenario – this adds all of the anticipated projects, but not all of their planned new ^{99}Mo production capacity in some cases. New reactor-based projects, given their proven technology and direct access of

1. See the notes appended to each table in Appendix 1.

product to the existing supply chain, are assumed to start production on their announced commissioning dates and are included from their first full year of production. New alternative technology (including reactor- and non-reactor-based) projects are assumed to have a 50% probability of starting full scale production on their announced commissioning dates; so given the unproven nature of these technologies and in some cases, more difficult access routes to the market, only 50% of this new capacity is included in the projection.

- Scenario C: "Project delayed" scenario – this builds on the "technological challenges" scenario by further assuming that LEU conversion and all new projects are delayed by one year beyond their anticipated first full year of production.

A so-called "all-in" scenario (where all the planned new/replacement projects are included at full projected capacity) is not reported in this updated projection. If all new potential projects proceed at the capacities as announced, there will be significant overcapacity of supply in the ^{99}Mo/^{99m}Tc market by 2020, which is unsustainable by the market in the long term.

In all three scenarios, the six-month forecast intervals are based upon a 50/50 split of operating capacity between the two six-month periods in a year, unless a specific change has been identified for a specific six-month period.

It should be noted that the scenarios B and C in this report do not include all of the announced new projects included in Appendix 1. Two projects have been excluded as their likely commissioning dates have now been delayed beyond 2020. This is not to suggest that these projects will not become operational, but that they are now not scheduled in the forecast horizon (2015-2020).

In the 2014 Report, the NEA took a slightly different approach with regards to the impacts from LEU conversion on ^{99}Mo/^{99m}Tc production capacity compared to previous reports. In *Market Impacts of Converting to Low-enriched Uranium Targets for Medical Isotope Production* (NEA, 2012b), the presented capacity scenarios include three different impact levels on ^{99}Mo production capacity – "very low", "low", and "high". However, since the publication of that document, it has become clear that there are significant challenges to conversion, which have led to an extension of the timelines for full conversion at all major producers that are converting. In the 2014 Report, it was assumed that the impact from LEU conversion on ^{99}Mo production capacity would be "high" and only that level was incorporated in the capacity scenarios.

The approach for this report concerning the effects of LEU conversion is further adjusted from the 2014 report and a simple blanket effect of a 10% level of efficiency loss has been applied in all cases. This adjustment has been made because the term "high" used in the previous reports included a number of different levels of efficiency loss that was perceived at the time of the first report and in addition some lower "exceptions" had been assumed. The range of these variants and exceptions does not seem justified at this stage in the LEU conversion process, where dedicated targets are being developed by each of the processors and where significant effort has been expended upon minimising efficiency losses in the processes.

Chapter 4. Reference scenario: A

The reference scenario includes only current ^{99}Mo production capacity – major irradiators and processors that are part of the global supply chain plus Argentina. Although currently not a major producer, Argentina is working towards increasing its production capacity to 2 500 6-day Ci Mo-99 per week EOP (both irradiation and processing capacity) by the end of the decade, which would move it to a leading global supplier position. The supply capacity from the Russian reactors and processing facilities are also included in the base reference scenario as international contracts are now being fulfilled from that supply source.

Reference scenario: A – Irradiation and processing capacity

As discussed in previous NEA studies, the current fleet of irradiators is ageing and some are expected to stop irradiating targets for ^{99}Mo production within the next few years. The planned exit from the global supply chain of the OSIRIS and the NRU reactors will significantly decrease the available irradiation capacity, but other reactors in the current fleet are adding some capacity through additional and improved irradiation facilities. The planned exit of the NRU reactor will also take out of operation the processing capacity presently provided by CNL/Nordion, although other new projects are being proposed that may bring some of that processing capacity back into operation. Processors in the current fleet are also adding some substantial capacity through facility adjustments.

Figure 4.1. Demand (9 000 6-day Ci ^{99}Mo/week EOP) and demand +35% ORC vs. current irradiation and current processing capacity, 2015-2020: Scenario A

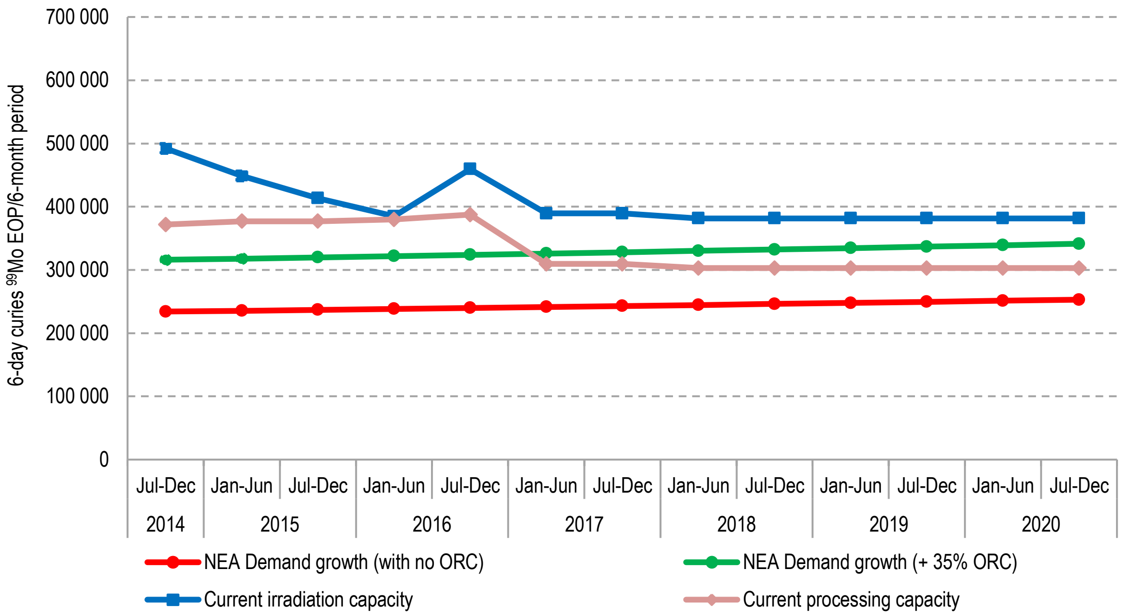


Figure 4.1 shows the projected 2015-2020 global NEA demand estimate for ^{99}Mo, the NEA demand estimate +35% ORC and the projected current irradiation capacity and processing capacity based on the presently operating fleet of irradiators and processors, inclusive of planned capacity adjustments to those facilities. The NEA has added the 6-month period (July-December 2014) to the graph, a period that precedes the forecast horizon, to highlight the impact on current irradiation capacity of the 16-month refurbishment period of the BR-2 reactor in Belgium. This refurbishment started in early 2015.

The global available irradiation capacity decreases substantially through to the January-June 2016 period due to the effects of the BR-2 refurbishment outage and the end of OSIRIS operation (December 2015). It then recovers in the July-December 2016 period with the return to service of the BR-2. Capacity then falls again in the January-July 2017 period due to the end of routine ^{99}Mo production from the NRU, before stabilising for the rest of the period to 2020 above the NEA demand + 35% ORC line. Irradiation capacity appears to be sufficient to assure supply throughout the period, however, with the progressive slow increase in demand modelled, there is less reserve capacity available by the end of the period.

It should also be noted that the timelines for some current irradiators include an assumption that operating licence extensions will be granted by the relevant authorities. However, licence extensions may require refurbishments to the reactors and the decision to proceed with those investments may be subject to the economic conditions that prevail in the market at that time. If the decision is not to proceed with the necessary refurbishments, then the capacity level in later years could be lower than presented in Figure 4.1.

Although global irradiation capacity underpins the supply chain, it represents only a partial picture and does not account for some of the geographical limitations relating to the production of bulk ^{99}Mo.

In this scenario, the global processing capacity increases slightly through the period to July-December 2016 as current processors add capacity and prepare for LEU conversion; it then drops in the January-June 2017 period as the end of operation of the CNL/Nordion processing capacity feeds in. It then drops slightly in the January-July 2018 period due to LEU conversion efficiency losses and then remains stable at a level between the NEA demand +35% ORC and the NEA demand line for the rest of the period to 2020.

In the 2015-2016 period, global processing capacity should be sufficient, but in 2017 the processing capacity reduces and the capacity does not fully provide sufficient reserve capacity for the rest of the forecast period. The planned full conversion to LEU targets is projected to slightly reduce global processing capacity, although the processors involved continue to work on mitigation strategies to minimise or neutralise that effect.

The non-European ^{99}Mo-irradiating reactors each have associated processing facilities, while in Europe, a network of five reactors supply two processing facilities. The total European irradiating capacity under normal operating conditions is greater than the total European processing capacity. The additional irradiation capacity that exists in the European network can be seen by comparing the irradiation and processing capacity curves in Figure 4.1. The gap between irradiation and processing capacity reduces in 2015 and approaches zero in the first half of 2016, but following the return to service of the BR-2 the situation recovers from the July-December 2016 period onwards. This shows that the European network will have little or no excess irradiation capacity in the early 2016 period, but that position will be redressed when the BR-2 returns to operation.

Overall, the current irradiator and processor supply chain, if well maintained, planned and scheduled, will be able to manage limited unplanned outages of a reactor, or a processor in the 2015-2016 period. This capacity to manage adverse events will reduce to only being able to manage an unplanned reactor outage from 2017 and the processing capacity will have some limited scope to manage an unplanned event from 2017 onwards.

Figure 4.1 does not intend to provide justification for building or not building new irradiation and/or processing facilities, but it does identify the greater relative risk associated with current processing capacity from 2017 onwards in this reference scenario.

Figures 5.1, 5.2, 6.1 and 6.2 in later sections of this report present the projected changes in potential irradiation and processing capacity under the scenarios B and C.

Of note, the Government of Canada's recent announcement to support the extension of the NRU operations until 31 March 2018, can help support global medical isotope demand only in the unexpected circumstance of shortages and only if alternative technologies or other sources of supply are not available, a kind of contingency capacity. Therefore, Figures 4.1, 5.1, 5.2, 6.1 and 6.2 do not forecast any production from the NRU reactor past 2016.

Chapter 5. "Technological challenges" scenario: B

The "technological challenges" scenario in this report has carried over the principles from the 2014 report. The scenario is a direct extension of the reference scenario A presented in the previous section, and includes qualified new reactor- and non-reactor-based projects around the world in addition to the existing global irradiation and processing capacity. In the preparation of this report; the tables A1.1 to A1.4 shown in Appendix 1 were thoroughly reviewed and revised in consultation with the supply chain participants. In addition, a standard format project plan was developed and agreed upon for each potential project with the associated reactor and/or processor. It should be mentioned that not all new projects announced around the world have been included in this "technological challenges" scenario. Only those projects that have been "qualified", where adequate levels of data have been provided to the NEA and where the operational timeline is within the 2015-2020 forecast horizon are included. More specifically, the NEA has decided to consider only new projects that are likely to be commissioned and operational at least one year before the end of the forecast horizon. Excluded projects include those that have unspecified construction start and commissioning dates, or for which there is inconclusive information about likely start dates and/or the scale of production capacity.

By making such a determination, the NEA is not suggesting that excluded projects will never materialise, but rather that they may not be commissioned within the forecast period. In the longer term, after 2020, the ^{99}Mo demand-supply schedule may look different with these projects operating, with potentially greater levels of supply available in the market.

Furthermore, all new alternative technology projects are assumed to have a 50% probability of being commissioned within their announced timelines. This assumption is to account for the fact that alternative technologies have yet to be proven on a large scale in the ^{99}Mo/^{99m}Tc market. This has been translated as applying only 50% of the expected maximum capacity to the forward forecasts for each of those projects.

Appendix 1 (Tables A1.3 and A1.4) presents all planned new "qualified" projects to be commissioned by 2020. The scenarios B and C (see also Chapter 6) include all but two of these projects. The two exclusions from the scenarios are:

- the new Jules Horowitz Reactor, which is now scheduled to have its first full year of operation irradiating targets for ^{99}Mo in 2021;
- the China Advanced Research Reactor and associated ^{99}Mo processing facility where no firm project planning to achieve operation by 2020 could be ascertained (this is shown as 2019+ in the relevant tables).

Compared to the 2014 report, the Korean reactor and processing capacity are now included, but at very modest production levels and the Polish ^{99}Mo processing facility is also included.

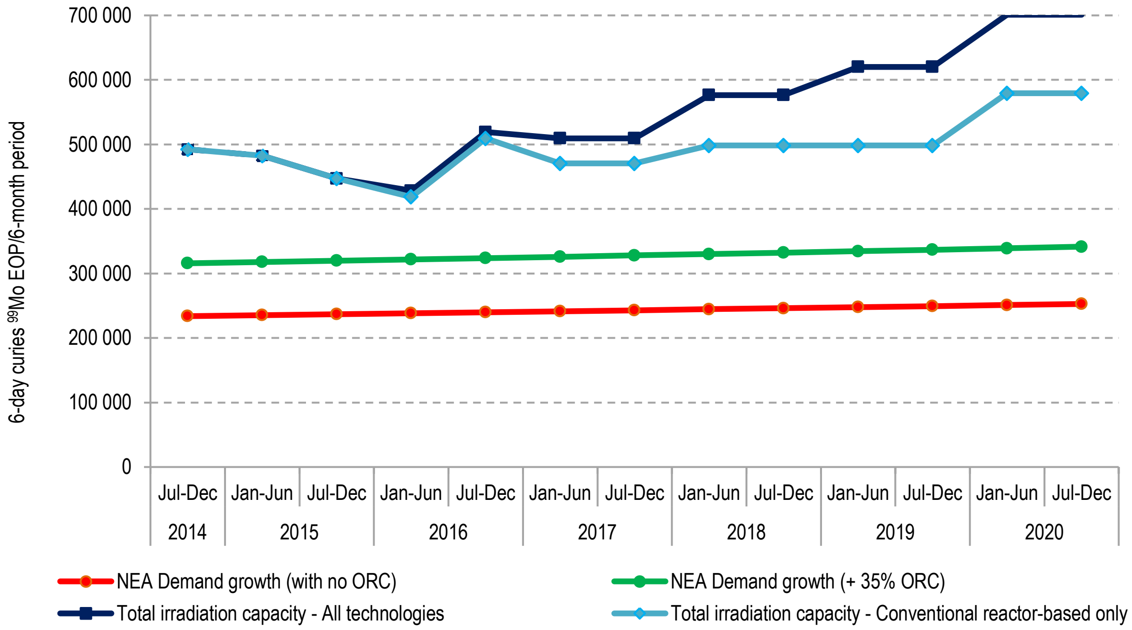
The review of potential projects has indicated project timeline slippage since the 2014 report of at least one year in many cases; further similar levels of timeline slippage can be assumed for projects that have not yet finalised a detailed project build timetable, secured full funding and acquired relevant licence approvals. However, there are some recently announced projects that are not yet in this analysis which may have the potential for becoming operational earlier than 2020.

In the timeframe beyond 2020, the currently proposed projects for ^{99}Mo/^{99m}Tc irradiation and associated processing capacity, if all completed, would significantly exceed projected market demand. However, this apparent future excess capacity should not imply that long-term security of supply is assured as it does not take into account any current capacity being retired early, or in the future beyond 2020, or consider the likely sustainability of potential "over-capacity" in the market.

"Technological challenges" scenario: B – Irradiation capacity

Figure 5.1 presents the NEA projected demand, demand +35% ORC and the irradiation capacity under the "technological challenges" scenario B. This shows both total capacity "all technologies" and capacity "conventional reactor-based only". It can be seen that even without all planned new irradiation projects being included, the global capacity of both lines looks to be sufficient to meet projected demand +35% ORC throughout the six-year forecast period. Notwithstanding the expected exit from the market of the OSIRIS and the NRU reactors, planned new capacity in Asia, Australia, Europe and North and South America, should more than compensate for the capacity losses seen in the reference scenario A.

Figure 5.1. Current demand (9 000 6-day Ci ^{99}Mo/week EOP) and demand +35% ORC vs. irradiation capacity – total and conventional reactor-based only, 2015-2020: Scenario B



To compare the effect that alternative ^{99}Mo/^{99m}Tc production technologies may have upon irradiation capacity, Figure 5.1 separates out conventional (reactor-based) irradiation capacity from total irradiation capacity. These lines start to diverge as early as the January-June 2016 period as initial quantities of product from alternative technologies are expected to enter the market.

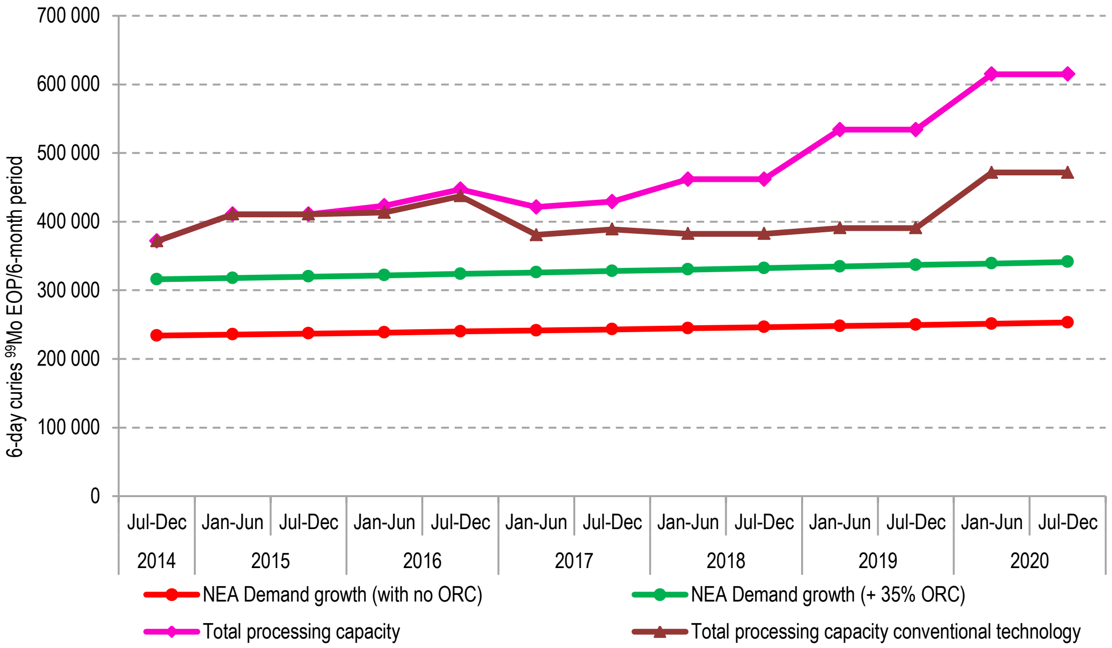
After the capacity peak following the return to service of the BR-2 in 2016 and drop due to the exit of the NRU reactor in 2017; through the course of the period 2017 until 2019 the conventional reactor-based capacity is projected to remain relatively flat, with some increased irradiation capacity added in Germany (2018) following LEU target conversion by processors. Additional new-build reactor-based capacity does not show any influence until 2020; this confirms the long lead-time associated with adding reactor-based new-build facilities. The additional capacity in 2020 is due to the commissioning of new reactor capacity and associated processing capacity in South America and Asia.

From 2017, the additive irradiation capacity from "alternative technology" projects primarily in the United States is progressive and quite substantial throughout the period, indicating that the additive capacity of "alternative technology" will support overall security of supply during the 2017 to 2020 period.

"Technological challenges" scenario: B – Processing capacity

Figure 5.2 presents the NEA projected demand, demand +35% ORC and the processing capacity under the "technological challenges" scenario B. This shows both total processing capacity "all technologies" and processing capacity "conventional technology only". It can be seen that even without all planned new processing projects being included, the total "all technologies" processing capacity looks to be sufficient to meet the projected demand +35% ORC requirement, throughout the six-year forecast period.

Figure 5.2. Current demand (9 000 6-day Ci ^{99}Mo/week EOP) and demand +35% ORC vs. processing capacity – total and processing capacity – conventional only, 2015-2020: Scenario B



The "conventional technology" processing capacity is projected to decline over the period from January-June 2016 until January-June 2017 as the end of operation of the CNL/Nordion processing capacity feeds in, the capacity then flattens to remain above the projected demand +35% ORC line for a 3-year period. This then increases in 2020 with the planned commissioning of processing capacity associated with reactor new-build programmes. The cessation of processing in Canada in 2016 is partially offset by increased processing capacity in the existing fleet and additional processing capacity in Australia (2017).

In contrast, from 2017, the additive processing capacity from "alternative technology" projects primarily in the United States is progressive and quite substantial through the period, indicating that the additive capacity of "alternative technology" will increase the overall security of supply during the 2017 to 2020 period. In principle, the majority of the additional "alternative technology" processing capacity is linked one-to-one with "alternative technology" irradiation capacity, indicating that both the irradiation and the processing components of these projects must be successful for those technologies to provide additional capacity to the supply chain.

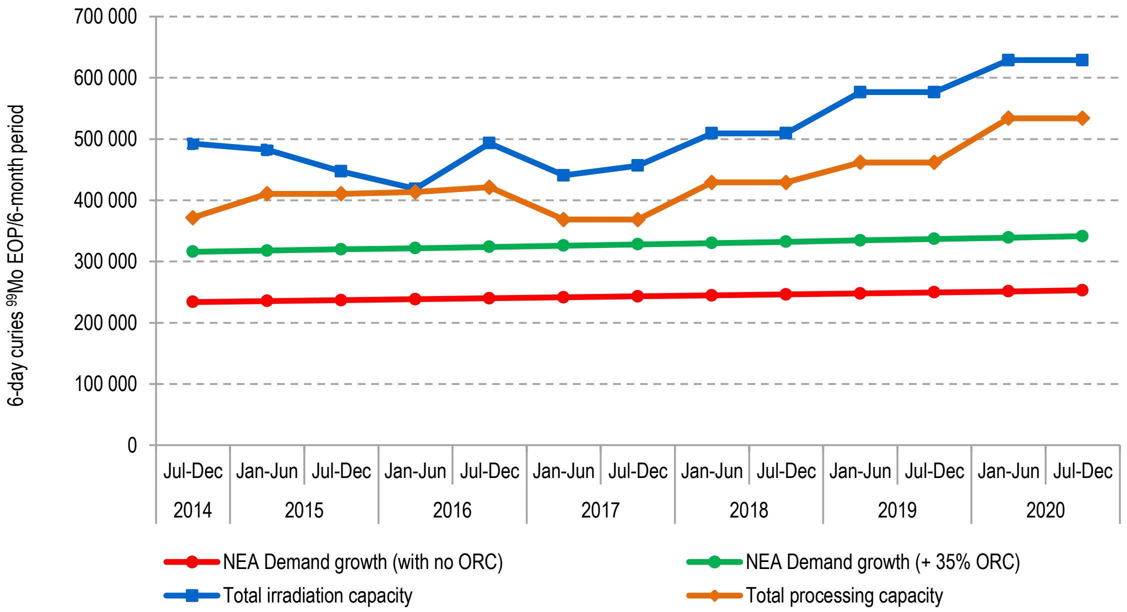
Chapter 6. "Project delays" scenario: C

The project delays scenario C has been developed from the technological challenges scenario B by modelling a delay of all new projects and LEU conversion by one year. This scenario considers the theoretical impact to future irradiation and processing capacity when considering the technical complexity of new reactor-based projects and the ground-breaking efforts in reaching large-scale, commercial production by alternative technologies. Furthermore, the majority of the new projects included in this scenario intend to apply full-cost recovery for their future ^{99}Mo production and need to develop distribution networks for their product, which may provide an additional challenge to implementation. Most importantly, however, experience has shown that large projects often take longer to complete than originally envisaged. This has already been clearly demonstrated by reviewing the 2014 report, where anticipated delays in projects identified in that report have in many cases already materialised.

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

Figure 6.1 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, but at the same time, delayed LEU conversion will have some opposite effect, provided that sufficient inventories of HEU are available for the period of any delay. Over the six-year forecast period, the "delayed new capacity" effect will dominate over the "delayed LEU conversion" effect.

Figure 6.1. 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

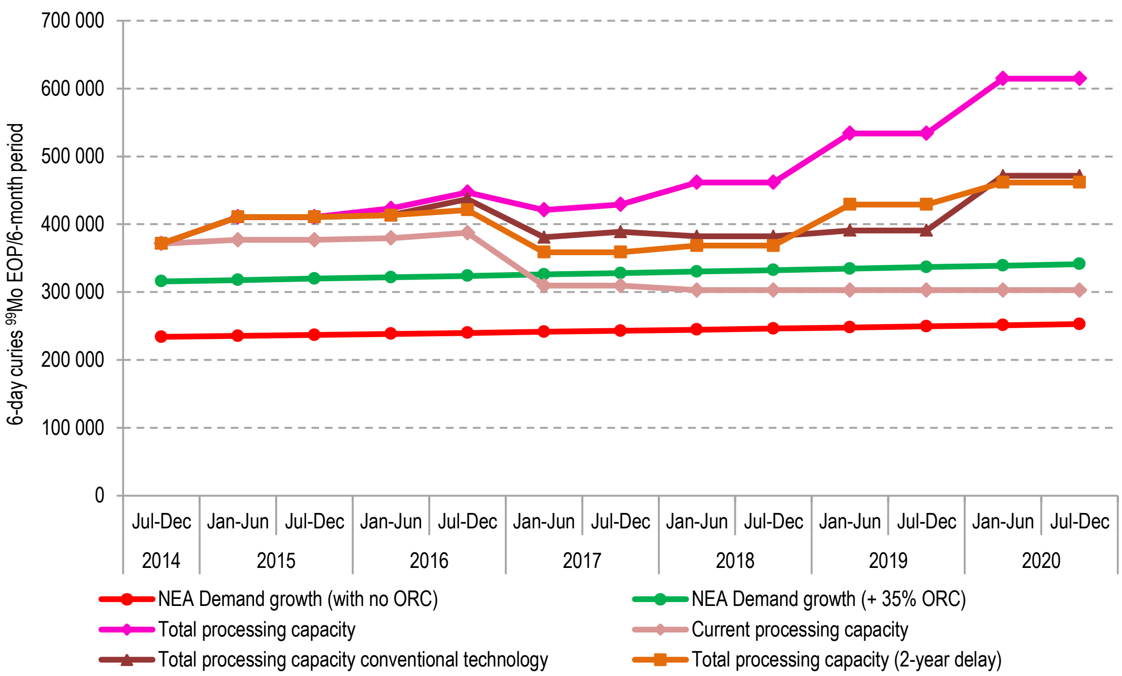


Compared to scenario B, irradiation and processing capacity under scenario C are almost identical in 2015 and 2016. Both then decrease significantly in the January-June 2017 period because this scenario models the effect of a one-year commissioning delay of the additional Australian capacity. Total irradiation 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 is 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 potential impact of project delays is relevant as experience confirms that most projects experience some delays, so further delays in various potential projects are modelled in this report. Figure 6.2 looks at the potential impact of further delays and concentrates on processing capacity, which has lower levels of reserve capacity. Figure 6.2 shows the demand and demand +35% ORC lines compared to the current processing capacity, the total processing capacity and, the conventional technologies only capacity (all with no project delay) with a total processing capacity line with a two-year project delay. The graph lines therefore represent the minimum, the maximum and two potential intermediary lines for processing capacity that represent different types of challenge.

Figure 6.2. Current demand (9 000 6-day Ci ^{99}Mo/week EOP) and demand +35% ORC vs. processing capacity – current, total, total conventional only and total two-year delay: Scenarios A + B + C (two-year delay)



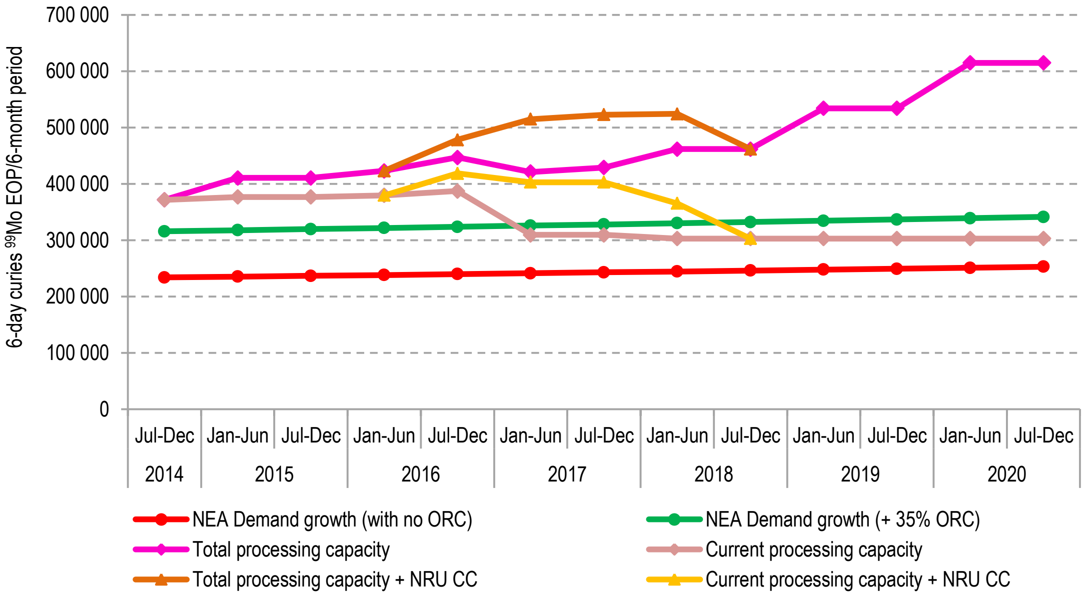
It is interesting that the impact of assuming only new processing capacity from conventional technologies has a similar pattern to assuming two years total delay in all processing projects. Both these intermediate projections show reductions in the January-July 2017 period, then remain relatively flat above the NEA demand +35% ORC line for periods of two to three years, before increasing again. Notably, the effect of a “two-year total delay” is slightly deeper, but recovers earlier than the “conventional technologies only” projection. Both of these intermediate projections confirm a reduction in overall processing capacity occurs when projects are delayed and identify the value of additional capacity from alternative technologies.

Chapter 7. Potential NRU contingency capacity

On 6 February 2015, Natural Resources Canada announced adjusted plans for the NRU reactor that affected the potential supply of ^{99}Mo, proposing a "supply of last resort" from the NRU reactor, supported by the CNL and Nordion processing capacity. Subject to licencing approvals it was proposed to operate the NRU reactor for the period from 31 October 2016 to 31 March 2018 for non-^{99}Mo purposes, with the effect of keeping the NRU reactor in "hot operation" for that time period. In addition the associated facilities required for ^{99}Mo production and processing would be kept in a "hot standby" mode for the same period.

The NRU reactor and the associated processing facilities would be made available under special conditions of market supply shortage, this contingency capacity would be used only in the unexpected circumstance of significant shortages and only if alternative technologies or other sources of supply were not available to meet demand. In this way a form of additional contingency capacity could be available on top of the ORC held within the rest of the supply chain. The NEA considered that it would be useful to model the effect upon potential irradiation and processing capacity of this contingency capacity. Figure 7.1 concentrates upon the effect that the potential NRU contingency capacity (NRU CC) could have upon total available processing capacity, as this has been identified in the earlier scenarios as having lower levels of reserve capacity in all scenarios. Figure 7.1 shows the demand and demand +35% ORC lines compared to current processing capacity only – Scenario A (both with and without NRU CC) and the total processing capacity – Scenario B (with and without NRU CC).

Figure 7.1. Current demand (9 000 6-day Ci ^{99}Mo/week EOP) and demand +35% ORC vs. processing capacity – current and total, with and without NRU CC, 2015-2020: Scenarios A + B + A with NRU CC + B with NRU CC



These forecast lines represent the maximum and minimum processing capacity lines from the earlier scenarios and show that the effect of the potential NRU CC available is significant. In the case of the total processing capacity line (from Scenario B), the total capacity is boosted to a very safe level of processing capacity for a two-year period before falling back to the total processing capacity line in the July-December 2018 period. In the case of current processing capacity only (from Scenario A), the processing capacity line is kept safely above the NEA demand +35% ORC for an additional 18-month period, before stablising at a level between the NEA demand +35% ORC and the NEA demand line for the rest of the period to 2020.

To consider the two extreme cases presented; in the maximum case, it is unlikely that the contingency capacity would be required, but an extra security buffer for 18-months would apply, while if the minimum processing capacity forecast is followed, the contingency capacity may be needed and would provide an important 18-month buffer period. It can be seen from the structure of the two sets of forecast lines, that in any of the alternative or intermediate scenarios, the scale of the potential contingency capacity would provide an additional 18-month buffer period, but in each case the processing capacity line will return back to the original processing capacity line in the July-December 2018 period.

It will be important to ensure that in the event of the availability of NRU contingency capacity for such an 18-month period, that it does not delay the introduction of other irradiation and processing capacity.

Chapter 8. Conclusions

Global demand has been re-evaluated at a level of around 9 000 6-day Ci ^{99}Mo per week EOP. This lower demand level has been a factor in allowing the existing supply chain to continue to provide a near to full service level in the last 3 years, despite some significant operational problems experienced by some supply chain participants. Reasons for demand reduction are not fully clear, but most likely include a reflection of some supply chain reaction to higher price levels (FCR), creating increased operating efficiencies within the supply chain and possibly some reductions in the average injected dose per patient following technology improvements and some changes to clinical procedures.

Overall, 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, this capacity to manage adverse events reduces; while being able to manage an unplanned reactor outage, the current processing capacity will have some limited scope to manage an unplanned event for the rest of the period.

The need to add additional processing capacity by 2017 remains clear; the on-time introduction of alternative processing technologies and the addition of substantial conventional processing capacity in Australia will be important. If these are achieved, then irradiation capacity and processing capacity should be secure for the rest of the period to 2020.

The possible extension of the NRU operating period could also be a useful stop-gap in the 2017 and early 2018 period, with the potential provision of substantial contingency capacity, but in the event that slow progress is made with alternative technologies, or when all processing projects are substantially delayed, then the projected processing capacity would fall back to reference levels in 2018.

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 require regular monitoring, along with regular review of the progress of bringing the proposed new production capacity to market.

References/further reading

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

NEA (2011), "The Supply of Medical Radioisotopes: An Assessment of Long-term Global Demand for Technetium-99m", OECD, Paris.

NEA (2012a), "A Supply and Demand Update of the Molybdenum-99 Market", OECD, Paris.

NEA (2012b), *Market Impacts of Converting to Low-enriched Uranium Targets for Medical Isotope Production*, OECD, Paris.

NEA (2014), "Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the $^{99}Mo/^{99m}Tc$ market 2015-2020", OECD, Paris.

Appendix 1.

Table 1. Current irradiators including those in transition by 2020

Reactor (Fuel)	Current targets[8]	Normal operating days/year	Anticipated ^{99}Mo production weeks/year	Expected available capacity per week (6-day Ci ^{99}Mo)	Expected first full year of ^{99}Mo production[9]	Expected available capacity per year (6-day Ci ^{99}Mo) by 2020	Estimated end of operation
BR-2[1] (HEU)	HEU	190	27	7 800	NA	210 600	2026
HFR[2] (LEU)	HEU	266	38	5 400	NA	228 000	2024
LVR-15[2] (LEU)	HEU	210	30	2 400	NA	72 000	2028
MARIA (LEU)	HEU	200	36	2 700	NA	95 000	2030
OPAL (LEU)	LEU	300	43	1 000	NA	42 900	2055
RA-3 (LEU)	LEU	230	46	400	NA	18 400	2027
SAFARI-1[3] (LEU)	HEU/LEU	305	44	3 000	NA	130 700	2030
OSIRIS[4] (LEU)	HEU	182	26	2 400	NA	~~62 400~~	~~End 2015~~
NRU[5] (HEU)	HEU	280	40	4 680	NA	~~187 200~~	~~Late 2016~~
RIAR[6] (HEU)	HEU	350	50	1 000	2015	50 000	Not Known
KARPOV[6] (HEU)	HEU	350	50	350	2015	17 500	Not Known
OPAL[7] (LEU)	LEU	300	43	+2 500	2017	107 500	2055
FRM-II[8] (HEU)	LEU	240	32	2 100	2018	67 200	2054

Notes: 1). BR-2 Out of operation for parts of 2015 and 2016, 2). HFR capacity increases from 4 680 to 5 400 per week and LVR-15 capacity increases from 1 920 to 2 400 per week during 2015, 3). SAFARI capacity limited by temporary processing limits in 2015, 4). OSIRIS ends operation before 2020, at the end of 2015, 5). NRU will cease routine ^{99}Mo production after 31 October 2016, but the reactor will follow a regular operating schedule and all ^{99}Mo capabilities will remain in "hot standby" until 31 March 2018, 6). RIAR and KARPOV material requires licensing in some markets, 7). OPAL extra irradiation capacity is additional and ready but market entry dependant on new ANSTO processing capacity, 8). FRM II market entry dependent upon conversion of processors to LEU targets, 8). HEU >20% enriched Uranium, LEU <20% enriched Uranium, 9). NA = Not Applicable.

Table 2. Current processors including those in transition by 2020

Processor	Targets[7]	Anticipated ^{99}Mo production weeks/year	Available capacity per week (6-d Ci ^{99}Mo)	Expected available capacity per year (6-d Ci ^{99}Mo) by 2020	Expected first full year of ^{99}Mo production[8]	Expected year of conversion to LEU targets	Estimated end of production
ANSTO Health	LEU	43	1 000	42 900	NA	LEU	2055
CNEA	LEU	46	400	18 400	NA	LEU	2027
IRE[1]	HEU	52	3 500	182 000	NA	2016	At least until 2028
Mallinckrodt[2]	HEU	52	5 000	260 000	NA	2017	Not Known
NTP[3]	HEU/LEU	44	3 000	130 700	NA	2015	At least until 2030
CNL/Nordion[4]	HEU	48	4 680	~~187 200~~	NA	No conversion	~~2016~~
RIAR[5]	HEU	50	1 000	50 000	2015	No date	Not Known
KARPOV Institute[5]	HEU	50	350	17 500	2015	No date	Not Known
ANSTO Health[6]	LEU	43	+2 500	107 500	2017	LEU	2055

Notes: 1). IRE maximum capacity remains dependent upon regulator agreement, 2). Mallinckrodt capacity increase from current facilities introduced by 3Q 2016, 3). NTP capacity limited by temporary processing limits in 2015, 4). CNL/Nordion will cease routine ^{99}Mo processing of NRU material after 31 October 2016, but all ^{99}Mo processing capabilities will remain in "hot standby" for NRU material until 31 March 2018, 5). RIAR and KARPOV material requires licensing in some markets, 6). ANSTO extra processing capacity is additional and is required to use OPAL additional irradiation capacity, 7). HEU >20% enriched Uranium, LEU <20% enriched Uranium, 8). NA = Not Applicable.

Table 3. Potential irradiators entering in period 2015 to 2020

Irradiation source (Fuel)	Targets/technology[5]	Expected operating days/year	Anticipated Mo-99 production weeks/year	Expected available capacity per week (6-d Ci ^{99}Mo) by 2020	Potential annual production (6-day Ci ^{99}Mo) by 2020	Expected first full year of production	Project status (Dec 2014)
MURR/NorthStar (HEU)	Natural Mo in CRR	339	52	750	39 000	2015	Reactor capacity and irradiation facilities in place
MURR/NorthStar[1] (HEU)	Enriched Mo in CRR	339	52	+2 250	+117 000	2017	Transition to enriched Mo targets starts in 2016
NorthStar	Non-fissile from LINACs	352	52	3 000	156 000	2018	Final design 2016
SHINE (LEU)	LEU solution with DTAs and SAAs	350	50	3 500	175 000	2019	Construction not yet started
Korea (LEU)[2]	LEU in CRR	300	43	400	17 200	2019	Detail design
Brazil MR (LEU)	LEU in CRR	290	41	1 000	41 400	2020	Preliminary design completed, construction starts 2017
RA-10 (LEU)	LEU in CRR	315	48	2 500	120 000	2020	Preliminary design completed, construction starts 2015
Jules Horowitz RR[3] (LEU)	LEU in CRR	220	32	4 800	153 600	2021	Under construction
China Advanced RR[4] (LEU)	LEU in CRR	240	34	1 000	34 000	2019+	Existing reactor under modification

Notes: 1). MURR/NorthStar Enriched Mo capacity is additional to the Natural Mo capacity when introduced, 2). Korea capacity is planned to increase further in stages after 2020, 3). JHR reactor begins active commissioning in 2019, but ^{99}Mo capacity not expected to be available until 2021, 4). CARR is already operational, but date of ^{99}Mo availability is unknown and is not before 2019, 5). Mo = inactive Molybdenum, either natural or enriched, CRR = Conventional Research Reactor, LINACs = multiple linear accelerators, LEU <20% enriched Uranium, DTAs = multiple deuterium-tritium accelerators, SAAs = multiple subcritical aqueous assemblies.

Table 4. Potential processors entering in period 2015 to 2020

Processor	Targets[5]	Anticipated Mo-99 production weeks/year	Expected available capacity per week (6-day Ci) by 2020	Expected available capacity per year (6-day Ci ^{99}Mo) by 2020	Estimated first full year of production	Project status (Dec 2014)
MURR/NorthStar	Natural Mo target	52	750	39 000	2016	Processing capacity in place (natural Mo targets)
MURR/NorthStar[1]	Enriched Mo target	52	+2 250	+117 000	2017	Transition to enriched Mo targets starts in 2016
NorthStar	Non-fissile	52	3 000	156 000	2018	Final design 2016
SHINE	LEU solution	50	3 500	175 000	2019	Construction not yet started
MARIA: Mo-99 2010[2]	LEU	40	1 000	40 000	2019	Financing – preliminary agreement
Korea[3]	LEU	43	400	17 200	2019	Detail design
Brazil MR	LEU	41	1 000	41 400	2020	Preliminary design concluded
CNEA	LEU	48	2 500	120 000	2020	Preliminary design 2015
China Advanced RR[4]	LEU	34	1 000	34 000	2019+	No financing available

Notes: 1). MURR/NorthStar Enriched Mo capacity is additional to the Natural Mo capacity when introduced, 2). MARIA uses existing capacity at the MARIA Reactor, 3). Korea capacity is planned to increase further in stages after 2020, 4). CARR is already operational, but date of ^{99}Mo processing capacity availability is unknown and is not before 2019, 5). Mo = inactive Molybdenum, either natural or enriched, LEU <20% enriched Uranium.