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The Security of Supply of Medical Radioisotopes

Demand and Capacity Projections for $^{99}Mo/^{99m}Tc$ for the 2023-2027 Period

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The Security of Supply of Medical Radioisotopes

Demand and Capacity Projections for 99Mo/99mTc for the 2023-2027 Period

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ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

The OECD is a unique forum where the governments of 38 democracies work together to address the economic, social and environmental challenges of globalisation. The OECD is also at the forefront of efforts to understand and to help governments respond to new developments and concerns, such as corporate governance, the information economy and the challenges of an ageing population. The Organisation provides a setting where governments can compare policy experiences, seek answers to common problems, identify good practice and work to co-ordinate domestic and international policies.

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NUCLEAR ENERGY AGENCY

The OECD Nuclear Energy Agency (NEA) was established on 1 February 1958. Current NEA membership consists of 34 countries: Argentina, Australia, Austria, Belgium, Bulgaria, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Korea, Luxembourg, Mexico, the Netherlands, Norway, Poland, Portugal, Romania, Russia (suspended), the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Türkiye, the United Kingdom and the United States. The European Commission and the International Atomic Energy Agency also take part in the work of the Agency.

The mission of the NEA is:

– to assist its member countries in maintaining and further developing, through international co-operation, the scientific, technological and legal bases required for a safe, environmentally sound and economical use of nuclear energy for peaceful purposes;

– to provide authoritative assessments and to forge common understandings on key issues as input to government decisions on nuclear energy policy and to broader OECD analyses in areas such as energy and the sustainable development of low-carbon economies.

Specific areas of competence of the NEA include the safety and regulation of nuclear activities, radioactive waste management and decommissioning, radiological protection, nuclear science, economic and technical analyses of the nuclear fuel cycle, nuclear law and liability, and public information. The NEA Data Bank provides nuclear data and computer program services for participating countries.

Foreword and acknowledgements

This report was prepared by Kevin Charlton for the Nuclear Energy Agency (NEA), with a project team from the NEA's Division of Nuclear Technology Development and Economics (NTE) closely following the work. It was approved by the NEA Nuclear Development Committee (NDC) on 25 September 2023.

The report would not have been possible without the contributions from NEA member countries and intergovernmental organisations, including supply chain participants, research reactor operators, radiopharmaceutical processors, generator manufacturers, nuclear pharmacies, nuclear medicine professionals and hospitals.

It includes information provided confidentially by supply chain participants to support this new work of the NEA, which follows previous work undertaken by the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR), whose fourth and final mandate ended in December 2018. This report honours the NEA's commitment made at the conclusion of the HLG-MR to continue monitoring the supply situation.

Comparing NEA demand estimates with projections of production capacity and facility utilisation for molybdenum-99 (^{99}Mo)/technetium-99m (^{99m}Tc), this report provides scenarios for the security of supply up to 2027, for the first time since 2019. These projections are intended to help policymakers, producers of medical radioisotopes and other stakeholders make the appropriate decisions to ensure an economically sustainable, long-term and secure supply of the key medical isotope ^{99}Mo and its decay product, ^{99m}Tc, until 2027 and beyond.

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List of abbreviations and acronyms

ANM	ANSTO Nuclear Medicine
ANSTO	Australian Nuclear Science and Technology Organisation
CT	Computed tomography
EOP	End of processing
ERT	Emergency Response Team (Nuclear Medicine Europe)
ESA	European Supply Agency
FCR	Full cost recovery
FDA	Food and Drug Administration (United States)
HEU	High-enriched uranium
HLG-MR	High-level Group on the Security of Supply of Medical Radioisotopes
IRE	Institute for Radioelements (Belgium)
JCT	Joint Communication Team
LEU	Low-enriched uranium
MRI	Magnetic resonance imaging
NEA	Nuclear Energy Agency
NMEU	Nuclear Medicine Europe
NRR	Nuclear research reactor
NRU	National Research Universal reactor (Canada)
NTE	Division of Nuclear Technology Development and Economics (NEA)
OECD	Organisation for Economic Co-operation and Development
ORC	Outage reserve capacity

Chapter 1. Introduction

Nuclear medicine diagnostic scans can image and demonstrate the physiology and function of many body parts, including the heart, skeleton, thyroid and salivary glands, and brain, supporting a broad range of medical specialities. Many medical scans involve the administration of trace amounts of radioactive pharmaceuticals, referred to as radiopharmaceuticals, into a patient's body. Preparation of a patient dose involves the "labelling" of a non-radioactive biomolecule, which is specific to the organ system or anatomical area scanned, with a radioactive medical isotope. Once internalised by a patient, radiopharmaceuticals are physiologically distributed within the body. As they undergo radioactive decay, they emit gamma photons, which are captured by gamma cameras. Each detected photon is registered as a point. Hundreds of thousands of points are collected during a scan to form an image.

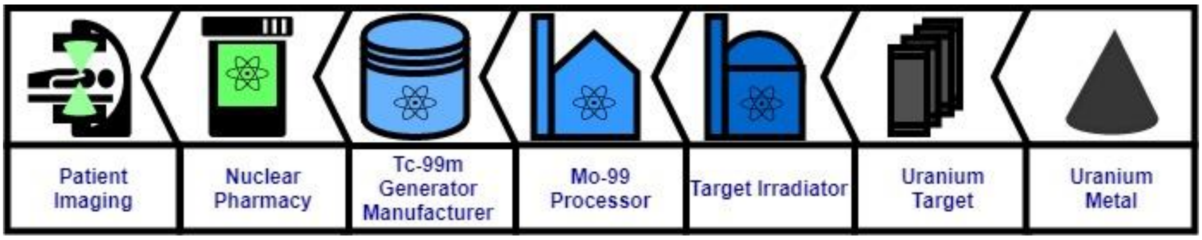
Nuclear medicine diagnostic scans are called a functional imaging modality as they visualise normal and abnormal organ and tissue physiology, based on the bio-distribution of the radiopharmaceutical used. It thus allows assessing the function or physiology of various tissues, organs or organ systems. This is in contrast to other common imaging modalities, such as x-ray, computed tomography (CT) and magnetic resonance imaging (MRI), which characterise the body anatomy and structure but not necessarily its functions, and are therefore referred to as anatomical imaging.

Medical diagnostic imaging techniques using technetium-99m (^{99m}Tc) account for approximately 80% of all nuclear medicine procedures, representing around 40 million examinations worldwide every year. ^{99m}Tc is obtained from radioactive decay of its parent isotope, molybdenum-99 (^{99}Mo). While ^{99}Mo has a half-life of 66 hours, the half-life of ^{99m}Tc is only six hours. Therefore, these products cannot be stored and supply is a just-in-time activity that requires sufficient capacity for ongoing production plus a reserve in case of unplanned outages. Disruptions in the supply chain of these medical isotopes, which thus must be produced continuously, can lead to the delay or cancellation of important medical procedures, with consequent effects on patients, their treatment and ultimately their health.

To prepare doses for patient scans, specialised pharmacies, called nuclear pharmacies, elute ^{99m}Tc daily from ^{99}Mo generators or source vessels and their manufacturers require marketing authorisation by the pharmaceutical regulatory authority responsible for each jurisdiction to sell them. Pharmaceutical companies, which include firms specialised in nuclear medicine as well as large and diversified firms, manufacture and sell ^{99m}Tc generators commercially. They buy ^{99}Mo in bulk from processing entities that transform irradiated uranium, or molybdenum into a ^{99}Mo liquid used to fill ^{99m}Tc generators or source vessels. Target materials are procured as raw materials that are either independently irradiated, or irradiated under contract with nuclear research reactors (NRRs) that perform irradiation services.

Figure 1.1 shows the main steps in the supply chain. NRRs, also referred to as irradiators, have a range of purposes aside from medical isotope production and were not originally designed for the commercial supply of medical isotopes. Their activities include nuclear technology testing, fundamental scientific research and industrial isotope production. Some of these activities are undertaken on a commercial basis; however, most commonly they are funded by governments, in part or in full.

Figure 1.1: Simplified structure of the conventional ^{99}Mo/^{99m}Tc supply chain



Source: NEA (2019)

Supply reliability has often been challenged over the past years due to unexpected shutdowns and extended refurbishment periods at some of the ^{99}Mo-producing research reactors, processing facilities and generator manufacturing facilities, many of which are relatively old. During this period, several significant facilities ended operation and a few new facilities, including two new technologies, have been brought into operation. These new technologies have some differences in the early steps of the conventional ^{99}Mo/^{99m}Tc supply chain.

Disruptions have at times created conditions for extended global supply shortages (e.g. the 2009-2010 global ^{99}Mo supply crisis) and indeed periods of shortage were again experienced in late 2017, in 2018 and most recently in 2022. As this is a just-in-time product, supply reliability can also be challenged by disruption to international distribution networks, in particular air transportation.

As a consequence of the 2009-2010 global ^{99}Mo supply crisis and at the request of its member countries, the Nuclear Energy Agency (NEA) became involved in global efforts to foster economically sustainable, long-term secure supply of ^{99}Mo/^{99m}Tc. Over the course of four mandates, from June 2009 until December 2018, the NEA and its High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR), examined the causes of supply disruptions and developed a policy approach, including principles and supporting recommendations, to address those causes. One of the original concerns was the relative age of many of the facilities used in the production of ^{99}Mo. Some facilities available in 2009 have since ended operation, but many still remain in operation. The extended time needed to replace facilities and to introduce new technologies has been recognised as a major challenge.

Since the HLG-MR formally ended in December 2018, the NEA has continued some follow-on work, including this report. It was agreed at the final meeting of the HLG-MR that the NEA would continue to periodically review the global ^{99}Mo demand and supply situation to highlight any future periods of potential supply weakness. This report underscores the case for continuing to implement the policy principles established by the HLG-MR 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 potentially low supply relative to anticipated demand. That 2012 forecast was updated with a report in 2014 that focused on the shorter time period of 2015-2020; that report was then updated annually until 2019 when the NEA published "The Supply of Medical Radioisotopes: 2019 Medical Isotope Demand and Capacity Projection for the 2019-2024 Period" (NEA, 2019).

Every report on ^{99}Mo demand and capacity has identified that unplanned events and disruptions can take place in the existing supply chain and that substantial delays do occur during the implementation of new projects, even when only looking at a relatively short time window.

This report[1] makes projections over the 2023-2027 period and builds upon both recent data and past experience. It is unique in reporting after a four-year time period that has elapsed since the preceding report. This has been an exceptional period during which, due to the COVID-19 pandemic, both general healthcare systems and the supply chain for medical radioisotopes in particular have faced extraordinary challenges. These challenges affected both the demand and supply sides of the industry and had an impact on international air transport distribution services.

It was also a period that followed the planned removal from service of a number of important production facilities, including the irradiation facilities at the OSIRIS reactor in France in late 2015, the irradiation facilities at the National Research Universal (NRU) reactor in Canada and the associated processing facilities operated by Nordion. Following an 18-month standby period, both Canadian facilities permanently ended operation in March 2018. They had been securely held offline with the potential to restart services in the event of a supply emergency, but were not recalled to service.

^{99}Mo supply performance around the time of the 2019 report

At the time of the last demand and capacity report in 2019, the supply chain had been experiencing an extended period of supply stress, primarily due to the unplanned outage of the NTP processing facility (South Africa), in a series of events that had begun in late 2017. These were important because the outage of the NTP processing facility blocks supply of irradiation capacity from the co-located SAFARI reactor. In early 2018, the NTP processing facility had returned to limited service with plans to move stepwise towards full capacity during 2018, but further problems led to a further outage period in the second half of 2018.

From late 2018 the NTP facility again returned to operation at a reduced operating capacity. The 2019 report anticipated that the NTP facility would progressively return to full operating capacity during the course of 2019. This was achieved from the third quarter of 2019, after which the facility remained at full operating capacity.

The extent and duration of the NTP outages drew the global processing capacity below a key level, the "NEA demand + 35% outage reserve capacity (ORC)" line, resulting in a persistent supply shortage of ^{99}Mo in some markets at various periods during 2018. Despite these problems, the Canadian facilities mentioned above that were held securely offline did not returned to service in an emergency backup role.

During a period of time in late 2018 and early 2019, a problem was also experienced with generator production in Australia, leading to the need to airfreight bulk ^{99}Mo from Australia to the United States for generator production and then airfreight back completed generators to Australia. This "outsourcing" of generator production and the associated extensive air transportation of bulk material and finished generators involves additional ^{99}Mo decay losses. This additional decay loss put more stress on ^{99}Mo capacity during a period when total capacity was already restricted.

Separately, in late 2019, problems were experienced in Australia with the newly commissioned ANSTO Nuclear Medicine (ANM) processing facility, restricting the total processing capacity. Processing capacity at ANM was gradually increased between 2020 and 2022, but total processing capacity at the ANM facility has not yet reached the levels originally envisaged in the 2019 report.

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

Major progress has been made on conversion to LEU targets

A major achievement for the industry has been the successful conversion away from production based on highly enriched uranium (HEU). This had been a long-standing regulatory objective. Conversion was desired for nuclear non-proliferation reasons, but involved major challenges, including the use of more expensive and less efficient processes. Conversion was also challenging as it was performed during a period when total global production capacity was scheduled to drop and supply reliability was in question.

The Curium (Netherlands) processing facility confirmed successful conversion to 100% use of low-enriched uranium (LEU) targets in mid-January 2018 and has produced bulk ^{99}Mo using only LEU targets since. Conversion to LEU targets by the Institute for Radioelements (IRE, Belgium) processing facility started in the second quarter of 2020, with complete conversion achieved in March 2023. It is estimated that following complete conversion by the IRE, more than 90% of all global bulk ^{99}Mo production capacity is now produced from sources that do not use HEU targets. Only limited production capacity in the Russian Federation remains based on HEU targets.

During conversion, some reduction in irradiation capacity associated with the use of LEU targets was confirmed by some reactor operators; but in all cases irradiators took successful mitigation actions to preserve, or even increase, total irradiation capacity. Both Curium and the IRE overcame the difficult technical challenges of conversion to processing LEU targets. They were also able to increase their total processing capacity during the conversion process.

The successful preservation and, in some cases, increase in total production capacity during the process of conversion to LEU targets by supply chain members is a testament to the thorough research, planning, co-operation and project execution of all the parties involved in these technically challenging processes.

Earlier NEA reports expressed some valid concerns about the potential scale of the losses in efficiency and production capacity from conversion to LEU. Efficiency loss factors were included in the capacity projections in those reports. As successful conversion has now been proven and largely implemented, it is no longer necessary to consider efficiency loss within this or any future demand and capacity reports.

The successful introduction of alternative technologies

February 2023 saw the 5th Anniversary of the introduction of the first non-conventional ^{99}Mo/^{99m}Tc production process. Marketing approval was first granted for the NorthStar[2] (United States) RadioGenix© System by the US Food and Drug Administration (FDA) in early 2018. That allowed supply of ^{99}Mo/^{99m}Tc from neutron-activated natural molybdenum targets, rather than uranium-based targets. The molybdenum targets were still irradiated in a conventional research reactor and were supplied to the US market as the RadioGenix System. Further developments and licence approvals have since allowed the introduction of neutron activation of enriched molybdenum targets to produce ^{99}Mo used in the RadioGenix System source vessels. This achievement substantially increased the production capacity available from this new technology.

The establishment of the RadioGenix System, with both natural and enriched molybdenum targets, represent an important milestone in the diversification of ^{99}Mo/^{99m}Tc supply. This new source of production capacity has been continuous since 2018 and capacity continues to increase.

In this report, the supply capacity from these non-conventional NorthStar processes

2. This report was finalised before the announcement by NorthStar Medical Radioisotopes of plans to cease production of Molybdenum-99 (99Mo) by 31 December 2023. While NEA does not anticipate outages to result in the broader market, the closure highlights the presence of continued uncertainty when projecting the security of supply for medical radioisotope production internationally.

is included within the “Reference” scenario of existing suppliers. Further potential increases in supply capacity at NorthStar utilising accelerator systems as a non-conventional production technology remain in the “Technical Challenges” scenario (see Chapters 4 and 5).

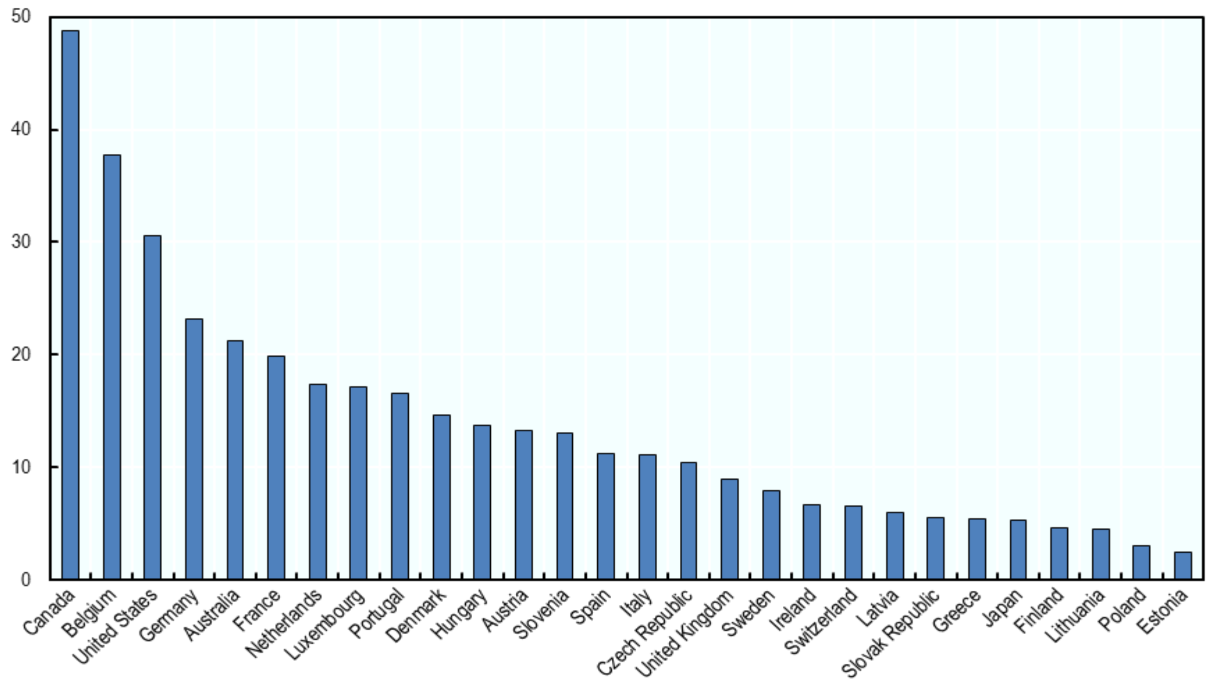
This report presents global irradiation and processing capacity projections under the same three main capacity scenarios as set out in reports since 2015. The information in this report should be interpreted as projected future trends and not as actual forecast production values and implementation dates.

Chapter 2. Demand update and ORC review

Diagnostic imaging modalities using ^{99m}Tc account for around 40 million examinations worldwide every year and approximately 80% of all nuclear medicine diagnostic scans. Following a decrease with the 2009-2010 supply crisis, demand for ^{99m}Tc has stabilised and tended to grow slowly in the following years.

There are large differences between countries in the utilisation rates of nuclear medicine diagnostic imaging relative to the population. For example, estimates collated by the OECD indicate that only about 2-3 ^{99m}Tc -based scans are performed per 1 000 of population per year in Estonia and Poland, while 31 and 38 scans are performed per 1 000 of population per year in the United States and Belgium, respectively, and this number may be close to 50 in Canada. Figure 2.1 shows estimates of the rate of ^{99m}Tc-based nuclear medicine diagnostic scan per 1 000 of population.

Figure 2.1: Number of ^{99m}Tc-based nuclear medicine diagnostic scans per 1 000 of population per year



Source: OECD/NEA (2019).

A large proportion of total nuclear medicine diagnostic activity is found in countries that have large populations and/or relatively high nuclear medicine diagnostic imaging rates.

There are also significant differences between countries in the utilisation patterns by organ system and anatomical areas scanned. The potential impacts of future shortages and the scope for substitution are therefore not the same across countries.

NEA demand projections go back some time. In 2011, the NEA released a study with the results of a global survey of future demand for $^{99}Mo/^{99m}Tc$ (NEA, 2011), based on an assessment by an expert advisory group. That study anticipated $^{99}Mo/^{99m}Tc$ demand would grow up to 2030 in both mature and emerging markets, with stronger growth seen in emerging markets.

In a subsequent report, “A Supply and Demand Update of the Molybdenum-99 Market” (NEA, 2012), the NEA estimated global ^{99}Mo demand at 10 000 6-day curies ^{99}Mo per week[3] at the end of processing (EOP). This demand was lower than the previous estimate of 12 000 6-day curies ^{99}Mo per week EOP and the difference primarily resulted from market changes that occurred as a consequence of the 2009-2010 global ^{99}Mo supply crisis. Those changes included more efficient use of the available ^{99}Mo/^{99m}Tc, including adjustments to patient scheduling and some increased use of substitute diagnostic tests/isotopes. When supply improved after 2009-2010, some of those market changes had become embedded.

The April 2014 report, “The Supply of Medical Radioisotopes: Medical Isotope Supply in the Future Production Capacity and Demand Forecast for the ^{99}Mo/^{99m}Tc Market, 2015-2020” (NEA, 2014), 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 annual demand growth rates of 0.5% for mature markets and 5% for developing markets. This change was based on information provided at that time by supply chain participants.

The August 2015 report, “The Supply of Medical Radioisotopes: 2015 Medical Isotope Supply Review: ^{99}Mo/^{99m}Tc Market Demand and Production Capacity Projection 2015-2020” (NEA, 2015), introduced an adjusted world demand estimate of 9 000 6-day curies ^{99}Mo EOP per week from processors. This was based on a new set of data collected by the NEA from supply chain participants on actual capacity utilisation during the period 2012 to 2014. That, along with data concerning the operational periods for each facility (e.g. the actual number of operational days) provided useful information, as it included periods of identified supply stress that had occurred due to unplanned facility outages.

The reasons why the August 2015 market demand estimate was lower than in earlier reports were not clear. The continuation of measures mentioned previously to increase the efficiency of isotope use at the nuclear pharmacy and in the clinic played a role and a contributing factor was the reduction in average injected patient dose for some tests. This was possible due to some technical improvements in gamma camera technology and to some changes to imaging protocols.

Furthermore, in a market where progress was being made towards implementing full cost recovery (FCR) pricing by producers, with the result of some substantial price increases, it was understandable that efficiency of use of materials was a priority for all supply chain participants.

This report builds upon the same approach as the subsequent 2019 report; it is based upon analysis of supply chain data for the period from 2012 to 2022. Following careful consideration, the estimated market demand growth rates in this report have been kept unchanged at 0.5% for mature markets and 5% for developing markets during the whole projection period until 2027. On this basis, at the end of 2022, mature markets were estimated to account for 78.6% of the global demand for ^{99}Mo/^{99m}Tc, while emerging markets accounted for 21.4%.

The latest data has been analysed to determine the level of recent market demand as described above, with reported global capacity utilisation being taken as a surrogate for market demand. The data set is not 100% complete. In this report, one irradiator, one processor and one consolidated irradiator/processor did not fully provide the requested data.

For the purposes of the scenarios presented in this report, the market demand for ^{99}Mo is based on the 2014 demand of 9 000 6-day curies ^{99}Mo EOP per week. With the growth rates used in this report, the total market demand at the end of 2022 had increased to be approximately 10 000 6-day curies ^{99}Mo per week, an increase of approximately 11% since the end of 2014. Demand is assumed to increase a further 5% by 2027 in the baseline scenario.

3. A 6-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, or EOP). In International System (SI) Units, 1 Ci is equal to 37 Giga Becquerels.

Total ^{99}Mo demand increased following the end of NRU operations

There are indications that the level of production required to supply the ^{99}Mo market increased following the end of routine production at the NRU in late 2016. This is due to the fact that the end of NRU production extended the supply lines to service the large US market, with an increased volume of bulk ^{99}Mo material being delivered from outside North America. This in turn lead to greater decay losses due to longer transport times. The short half-life of ^{99}Mo (66 hours) – the product form that is transported internationally to generator manufacturers – results in approximately 1% of the entire quantity of product being lost through decay for every additional hour of distribution time. This is equivalent to a total 22.3% decay loss during an additional day of distribution.

Increased distribution time has the direct effect of adding to the weekly demand for product at the time point EOP. The decay loss effect due to extending distribution time was again evident in 2018 when generator production problems were experience in Australia, as discussed earlier. As an example, the actual level of ^{99}Mo production required at time point EOP must increase by 28.7% to offset the decay loss sustained when distributing that product for an extra day. This demonstrates how production capacity may need to increase or decrease from time to time without an equivalent change in the end-user demand for patient doses.

The effects of the COVID-19 pandemic on ^{99}Mo demand and supply

The period since the NEA 2019 demand and capacity report was influenced by the COVID-19 pandemic, particularly during 2020 and 2021, when waves of the pandemic swept through countries and regions at different times, with varying speeds and intensities. The response to COVID-19 varied country to country with a wide range of measures, from only limited restrictions to total societal lockdown. The duration of each response was also individual, but wherever a national COVID-19 societal response was significant, the national healthcare system faced serious challenges.

Many nuclear medicine procedures utilising ^{99m}Tc are elective and many healthcare systems chose to limit and reduce elective procedures during periods of heightened COVID-19 risk. At the same time, nuclear medicine imaging is useful for investigating patients with cardiac and pulmonary problems, and both were typically found in patients suffering severe COVID-19 complications. There were reports of a reduction in the use of nuclear medicine in some countries (Graham, 2022), but there were other reports of a change in the mix of nuclear medicine studies being performed.

The data collected for this report does not indicate a reduction in the overall global demand of ^{99}Mo/^{99m}Tc during the pandemic period. This perhaps reflects the need for healthcare systems to retain the availability of sensitive diagnostic tools even during very unusual periods of stress on healthcare systems.

A further point that should be noted is that a significant percentage of bulk ^{99}Mo supplies and many finished ^{99}Mo generators are transported on commercial airlines. The COVID-19 pandemic period saw a sudden and substantial reduction in air travel, with the frequency of flights on many routes being reduced and in some cases, routes being terminated altogether. As ^{99}Mo/^{99m}Tc supply is a “just-in-time” process that relies upon excellent logistics, the substantial reduction in commercial air traffic was an important additional challenge for the whole supply chain.

That the supply chain members were able to manage and adjust their production programmes and logistics to maintain global supply throughout the pandemic period is a testament to their resourcefulness and resilience. It is notable that the global supply of some other medical imaging agents and some drugs was badly disrupted during the pandemic – see, for example, a report on iodinated contrast material shortage (RSNA, 2022).

What capacity level is required to ensure that patient demand is met?

The total level of production capacity required to ensure that patients always receive their scans on time must include a sufficient level of redundant production capacity. In this report, that additional capacity is referred to as paid outage reserve capacity (ORC).

In the HLG-MR policy principles, it was proposed that a processor should hold a level of paid ORC sufficient to be able to replace the largest supplier of irradiated targets in their supply chain. Likewise, participants further down the supply chain should hold similar levels of ORC. This is the so-called (n-1) criterion, that is, the level of ORC required by a customer to ensure that no supply disruption to the clinic occurs when their largest individual supplier has an unplanned supply problem.

There have been occasions over the past 15 years when, for some participants, an (n-2) criterion (e.g. the ability to replace their two largest suppliers) may have been a more appropriate measure for ensuring security of supply. The actual levels of ORC needed to maintain the (n-1) and (n-2) criteria vary for each supply chain participant and are dependent upon the diversity of each individual supply chain. The actual levels of ORC required by each supply chain participant can also change as part of a dynamic process, for example when suppliers in different geographic locations enter and exit the market and when distribution conditions change.

In the early and mid-period covered by this series of reports, the number of separate supply chain participants initially decreased, with the result that the market shares of the remaining participants mostly increased. However, since 2018, with the introduction of alternative technologies, that trend has started to reverse. Likewise, the general level of risk associated with an (n-1) and (n-2) type supply problems increased until 2018, but has reduced since.

When considering the potential risk of supply disruption, the level of maximum theoretical reserve capacity available to the market during that period is a good indicator. Long-term analysis has shown that from 2012 to 2021, the periods of highest risk were in 2014 and in 2018, when supply was under stress and some supply shortages were reported.

In this report, the projected potential production capacity is compared to “demand +35% ORC”, with the level of demand without any ORC also being shown as a reference line. The “demand +35% ORC” level is based on a calculation of required ORC to maintain supply. This was first calculated by the NEA in the period after the 2009-2010 global ^{99}Mo supply crisis period and reflects the (n-1) criterion for outage reserve capacity.

Changes to the market share of the various supply chain members has been reviewed. While the highest individual market share recorded in 2022 is now lower than in 2019, it remains above the levels originally recorded in 2012, meaning that production is more concentrated in 2022 than it was in 2012. A higher concentration of production does not increase the risk of the occurrence of an unplanned supply event, but it does increase the risk of an unplanned event being disruptive. When all is considered, the criterion of “demand +35% ORC” continues to provide appropriate guidance for (n-1) supply situations, at least for the degree of change in market share that underlies this report.

This statement is made on the clear provision that all of the members of the supply chain do hold paid ORC in a full and appropriate way.

Paid Outage Reserve Capacity is important to supply stability

It is important to indicate that the level of theoretical reserve capacity is not the same thing as contracted paid ORC. As mentioned in previous reports, the NEA has no direct way to measure the actual amount of paid ORC that is held within the supply chain. The actual level and form of paid ORC is the subject of commercial agreements held between two or more supply chain participants.

Contracted paid ORC itself can be provided in several ways; these include the holding of additional supply contracts with supply chain members higher up the chain, and/or additional supply contracts held horizontally between supply chain members at the same level within the chain. Demand-side ORC can also be provided by supply agreements held with individual customers. For example, a customer could accept for their supplier to activate demand-side ORC measures during supply stress periods and thereby the customer accepts to receive less material, perhaps for a financial compensation.

Whichever ORC mechanism is used, the key principles must include that the agreed ORC level must be constantly available and must be immediately dispatchable to the full extent that is covered. The provider of the ORC service must also be fully reimbursed for all the costs involved in providing services, even if those services are not actually used. Any reserve capacity available in the market that is not contracted, or that cannot be immediately and fully dispatched, or that is not fully paid for, is not "true" ORC. Reserve capacity that is not "true" ORC is economically damaging to the security of the supply in the long term as it can deter investment in new capacity.

Given that the actual ORC level required for each supply chain participant may change over time, the ORC level in this document should be used with caution in providing advice or making decisions. The NEA believes that a level "NEA demand +35% ORC" remains a good representation of a "safe" level of paid ORC capacity required to meet market demand under an (n-1) supply stress situation. However, this is fully dependent on the reserve capacity of market players being "true" ORC that fully meets the key principles discussed in the section above.

What have been the challenges and changes to overall levels of reserve capacity?

All supply chain participants agree that the principle of holding paid ORC is essential to ensure reliable supply. The need for ORC was clearly illustrated in 2013, 2014, 2015, in late 2017 and 2018, and most recently in 2022. Unplanned outages occurred at one or more major ^{99}Mo producers during each of these periods. Any significant unplanned outage of a producer tests the ability of the whole supply chain to ensure reliable supply.

In general, there was sufficient reserve capacity in the system in the early years covered by the NEA reports, and supply challenges were largely met by using available ORC or perhaps by temporarily sourcing non-contracted reserve capacity available at that time. This resulted in only a small number of limited supply shortages in some countries.

Analysis of the global reserve capacity theoretically available to the market (total available capacity minus actual utilised capacity) for the period 2012 to 2022 shows quite significant peaks and troughs. From 2012 until 2016 there was an overall positive trend in the level of global reserve capacity for all services. This was achieved by positive actions by the market players of the time in anticipation of the planned withdrawal of services in Canada and France (mentioned earlier), and the loss of some irradiation capacity in Germany. There was then a sustained trough period that started from the fourth quarter of 2016. This was anticipated and was the result of the planned withdrawal from active service of the NRU Reactor and the associated processing capacity.

The supply stress events that started in late 2017 were challenging because the level of global reserve capacity had become more limited. Unplanned outages in South Africa, which affected both irradiation capacity and processing capacity, had a duration of many months and as a result there was an extended shortage of ^{99}Mo throughout much of 2018. There were some short periods of greater shortage and some supply problems of short duration for other associated isotopes such as iodine-131 (^{131}I).

In the 2019 report, it was identified that the levels of global reserve capacity were still in that trough period, but that reserve capacity was projected to improve during 2019. The future reserve capacity levels for both irradiation and processing capacity from existing market players, based on their planned operating regimes, were projected to increase progressively to be above the long-term trend lines by 2020. In that 2019 report, the projected increases were noted as being dependent upon the level of capacity from South Africa returning to historic levels and additional capacity from the new ANM (Australia) processing facility entering the market to schedule.

In retrospective analysis for this report, the low point for global reserve capacity was during the third and fourth quarters of 2018. The chronic supply shortages experienced in 2017 and 2018 were driven by extended periods of unplanned outage These were periods when there was essentially no reserve capacity available to the market.

Additional supply challenges in recent years

Following the problems experienced in 2017 and 2018, supply stabilised and global reserve capacity improved through 2019 and then remained stable in 2020 and 2021. This was achieved despite periods of local operational stress experienced by individual supply chain members due to the COVID-19 pandemic and the slower-than-anticipated addition of capacity from the ANM facility.

Further supply problems were experienced from early 2022, when the High Flux Reactor (HFR) (Netherlands) reactor had an extended unplanned outage and was out of operation for around two months. Other reactors in the European network were able to add some additional irradiation capacity at short notice to help compensate, but despite those actions, some supply shortages were reported for ^{99}Mo and some reactor-based therapy isotopes. Overall, with the co-ordination of the Nuclear Medicine Europe (NMEU) "Emergency Response Team" (ERT), the supply chain was able to mitigate most of the problems encountered during that period. Stable supply was re-established from mid-March 2022.

The ERT work is strongly supported by the Joint Communication Team (JCT) led by the European Supply Agency (ESA) under the umbrella of the ESA/NMEU European Observatory on the Supply of Medical Radioisotopes. The overall structure and objectives of this group are well described in the EURATOM Supply Agency Annual Report 2020 (ESA, 2020).

In August 2022, the ERT identified a potential supply risk for the reactor-based therapy isotope ^{131}I (Communication from NMEU of 24 August 2022, see Appendix 2). This was anticipated due to a planned extended outage at the MARIA (Poland) reactor for essential maintenance and refurbishment work from September 2022 through February 2023. The MARIA reactor supplies one of the three primary global producers of iodine-131 (^{131}I), while also playing an important role in the ^{99}Mo supply chain.

In October 2022, during the period of the scheduled MARIA outage period, both the SAFARI (South Africa) and the BR-2 (Belgium) reactors experienced unplanned outages. The SAFARI outage was relatively short and the reactor returned to normal service levels after a few days, but the BR-2 outage was extensive and the reactor was only able to return to service in late December 2022. Unfortunately, these two unplanned outages coincided with a period when the LVR-15 (Czech Republic) reactor was also unavailable due to a planned maintenance period of approximately 10 weeks and the HFR reactor was unavailable due to a planned maintenance period of approximately 4.5 weeks.

This combination of unplanned outages and extended planned maintenance periods led to significant global shortages of ^{99}Mo and reactor-based therapy isotopes. The BR-2 reactor has the highest irradiation capacity in the global supply chain and had been scheduled to operate alone in Europe from late October through much of November 2022. The unplanned BR-2 outage resulted in there being no irradiation capacity from the network of European reactors from late October 2022.

No irradiation capacity in Europe directly stops the operation of the extensive ^{99}Mo processing capacity in Europe, leading directly to global supply shortages. The LVR-15 reactor was able to respond and returned to service earlier than had been scheduled in mid-November 2022, but this was insufficient to overcome all of the shortages, which resulted in difficulties for generator manufacturers, nuclear pharmacies and clinical services. Security of supply for ^{99}Mo only recovered when the HFR reactor also returned to service from planned maintenance in late November 2022.

A review of reactor scheduling, co-ordinated by NMEU, identified that from mid-2022 until mid-2023 was a particularly weak period for reserve irradiation capacity. There were extended periods when individual reactors were scheduled to operate alone in Europe. Periods when individual reactors operate alone and without direct backup capacity are of high risk for the security of supply of ^{99}Mo, as a single point failure will lead directly to supply shortages. These are periods when there is essentially no functional ORC being held by important parts of the supply chain.

Further investigation identified that the weak period for reserve irradiation capacity described above had in part developed because of the COVID-19 pandemic period. During that period, all organisations with hands-on production operations had to introduce new and novel operating regimes to reduce risks to staff, especially the risk of COVID-19 transmission within and between key worker groups.

As discussed earlier, the pandemic period also added complications to supply flexibility and distribution. Many supply chain members worked different schedules and adjusted programmes to ensure security of supply. One particular consequence of the period was a growing backlog of non-essential maintenance as a condition that leads to essential maintenance over time. The mid-2022 to mid-2023 period required the scheduling of some extensive maintenance periods, in part to address that backlog.

At the time of this report, there has been an announcement that the planned maintenance period for the MARIA reactor has been extended until at least July 2023. This report anticipates that the MARIA reactor will effectively remain unavailable to the supply chain throughout the third quarter of 2023. The irradiation capacity from the European network of reactors is anticipated to remain weak while the MARIA reactor remains unavailable, with some identifiable periods of increased risk of single point failure in the European reactor network until the end of 2023.

Chapter 3. Scenarios and assumptions for 99Mo/99mTc production capacity

The list of current and planned new ^{99}Mo/^{99m}Tc irradiation and processing projects has been updated for this report. The updates include revisions to production start/end dates and a review of the status of likely projects. The estimated capacity for irradiation and processing presented in the figures of Chapters 4, 5, 6 and 7 are based on the data in Appendix 1. Appendix 1 provides four tables that list current and potential new ^{99}Mo/^{99m}Tc producers, along with the status of likely projects as of the end of March 2023.

The data in Appendix 1 provide a snapshot of the progress made on projects in the four-year period since early 2019, when data for the preceding report was collected. Comparing the data in Appendix 1 with the equivalent data in earlier reports, it is clear that many potential supply projects continue to experience long delays in their implementation, or indeed fail to materialise at all. This is true irrespective of whether the technology that is planned is conventional or novel.

It should be noted that these tables are not exhaustive and do not include every potential project for ^{99}Mo/^{99m}Tc production that exists around the world. Inclusion in any of the tables in this report does not indicate the NEA's expectation that a facility may be operational by the indicated times shown, or even at all.

Given the fact that ^{99}Mo/^{99m}Tc is a non-storable product, actual weekly production levels will need to match demand. This ability to match demand will depend on the available capacity, which is the crucial determinant of the security of supply of ^{99}Mo/^{99m}Tc. The intent of this report is thus not primarily to predict the actual level of ^{99}Mo/^{99m}Tc produced in a specific period, which is assumed to follow demand. It is instead to inform government policymakers, the industry and nuclear medicine professionals by identifying any periods of increased risk to the security of supply due to actual or emerging capacity shortages. Such periods of increased risk arise when the projected production capacity is close to or below the projected NEA demand +35% ORC (outage reserve capacity), which is shown as the green line in all figures of this report.

The time horizon in this report for estimates of ^{99}Mo/^{99m}Tc production capacity is the period 2023-2027. The period anticipates the commissioning of new projects around the world, most of which are based on novel technologies. The capacity scenarios presented in this document are based on the data in Appendix 1, with some caveats[4]. Tables 1 and 2 provide the current available maximum weekly capacity for irradiators and processors under normal operating conditions. It should be noted that this maximum capacity level may not always be available for every week of operation within a specific time period and does vary, for example when there is planned maintenance of a specific facility.

This report explains the results obtained from three capacity scenarios, each presented in six-month intervals (January-June and July-December). In all scenarios, the six-month projection intervals are based upon a weighted split of planned operating capacity for that year, adjusted for anticipated operational programmes where details are known:

- Scenario A, "Reference" scenario: a baseline case that includes only currently operational irradiation and processing capacity. In addition to conventional irradiation and processing capacity from the irradiation of uranium targets in research reactors, this scenario now includes the capacity available from neutron-activated molybdenum and enriched molybdenum supplied by NorthStar.

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

- Scenario B, “Projected capacity additions” scenario (called the “Technological challenges” scenario in previous reports): this scenario adds capacity from anticipated projects shown in Tables 3 and 4 to scenario A. Not all of the ^{99}Mo production capacity from planned new projects is included. Conventional research reactor-based projects, given their proven technology and the direct access of their product to the existing supply chain, are assumed to start production on their anticipated commissioning dates and are included in the analysis from their first full year of operation. Alternative, non-conventional technology projects (including reactor- and non-reactor-based projects) are assumed to have a 50% probability of starting full-scale production on their announced commissioning dates. Given the unproven nature of these alternative technologies and, in some cases, their more difficult access routes to market, only 50% of their anticipated new capacity is included in projections from their anticipated first full year of operation.

- Scenario C, “Delays to projected capacity additions” scenario: this builds on scenario B by assuming that all new projects, whether conventional or non-conventional technology, will be delayed by one or two years beyond their presently anticipated first full year of operation. A delay to all new projects of two years is also considered. Past reports have identified that project delays of one year or more occur quite frequently.

It should also be noted that scenarios B and C in this report do not include every potential project for $^{99}Mo/^{99m}Tc$ production that exists around the world. This is not to suggest that other projects will not become operational, but this report does not anticipate them to be operational in the period until 2027.

In the 2019 report, it was noted that the likely effects of LEU conversion had changed compared to earlier reports. Successful implementation of LEU conversion has been achieved and no further effects on projected production capacities are anticipated in this report.

Chapter 4. Scenario A: "Reference"

Scenario A, or the "Reference" scenario, includes only currently existing ^{99}Mo production capacity, the irradiation and processing capabilities which are part of the current global supply chain. These include supply from Argentina, Russia and neutron activation ^{99}Mo from NorthStar in the United States.

The 2019 report identified that existing supply chain members had successfully implemented additional capacity in small steps in 2016 to raise the level of capacity in the reference scenario, but that in 2018 some irradiation capacity reductions linked to the conversion to LEU targets had been reported. Those changes are reflected in the historic data in this report.

In this report, all capacity added in Australia since the introduction of the ANM facility is now included within the reference scenario. It should be noted that the level of capacity from the ANM facility is presently lower than had been anticipated in the 2019 report, but further capacity increases are anticipated throughout the period of this report. Additional capacity from the use of enriched molybdenum targets at NorthStar is also included within the reference scenario and that capacity is anticipated to continue to increase through 2024.

As previously discussed, the supply chain was disrupted in late 2017 and during 2018 due to unplanned outages of the NTP facilities. The effects of those unplanned outages and the resulting reduced capacity of both irradiation and processing capacity during 2018 are visible in the scenario: A "Reference".

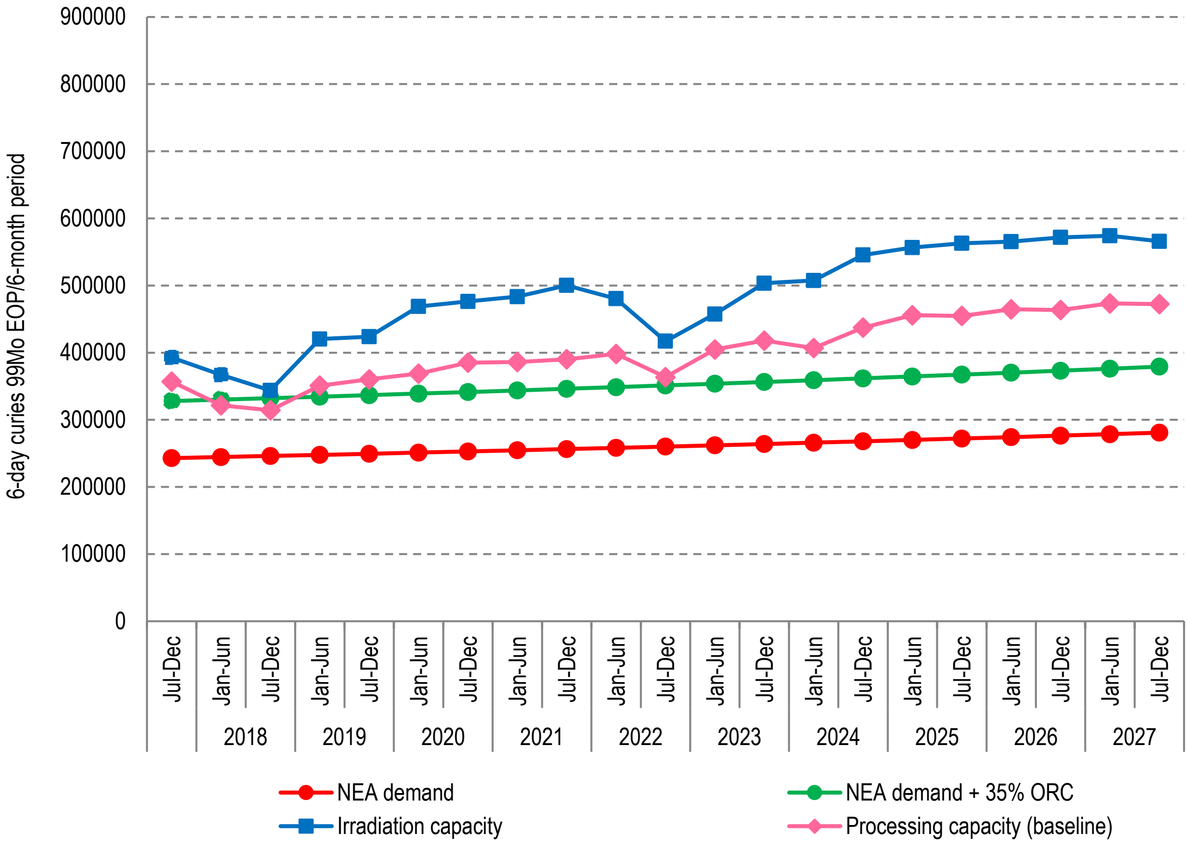
The period between the last report in 2019 and 2021 although challenging at times, was a period of stable ^{99}Mo supply. The unplanned outage periods at the HFR reactor and the BR2 reactor reduced irradiation capacity in 2022. This is shown clearly in scenario: A "Reference", in the second half of 2022 when unplanned outages coincided with a period of reduced reserve irradiation capacity in Europe due to maintenance scheduling.

It should be noted that data shown in these scenario graphs indicate the total actual irradiation and processing capacity available in the years up to and including 2022, this reconfirms that the global market is likely to experience some supply shortages when the reference scenario A capacity is near or below the green NEA demand estimate +35% ORC line. Data from the July-December 2017 period have been retained in all the scenario graphs in this report to indicate the capacity that existed prior to the supply problems that were experienced in 2018. Data from 2023 onwards show projections of anticipated total capacity.

Irradiation and processing capacity

Figure 4.1 shows the projected 2023-2027 global NEA demand estimate for ^{99}Mo with no ORC (red line), the NEA demand estimate +35% ORC (green line), and the projected current irradiation capacity (blue line) and projected current processing capacity (pink line) based on Scenario A ("Reference"). This is the historically available capacity of the present fleet of irradiators and processors and a projection of future capacity, inclusive of any planned capacity adjustments to those existing facilities.

Figure 4.1: NEA demand and NEA demand +35% ORC vs. irradiation and processing capacity (2017-2027)



Irradiation capacity

Figure 4.1 of Scenario A ("Reference") also shows the reduction in irradiation capacity (blue line) experienced in 2018 and the recovery in 2019. The further increase in irradiation capacity from 2020 is mainly due to increases in irradiation capacity per week and the number of operating days available at the BR-2 reactor. The January-June 2022 period shows a mild decline due to the unplanned outage of the HFR reactor and the July-December 2022 period shows the significant impact of the unplanned outage of the BR-2 reactor. The sharp reduction in irradiation capacity in the July-December 2022 period was partially because the BR-2 has a very high individual irradiation capacity. This substantial unplanned loss in capacity was compounded by planned maintenance in the July-December 2022 period at both the LVR-15 (Czech Republic) and the MARIA (Poland) reactors. This significantly reduced the level of reserve irradiation capacity in Europe.

In Europe, a network of four reactors supplies two processing facilities, while irradiation facilities outside Europe each have individual associated processing facilities. In normal operating years, the total European irradiation capacity has been greater than the total European processing capacity. An indication of the level of that reserve irradiation capacity can be seen by comparing the irradiation and processing capacity curves in Figure 4.1. A reduction in reserve irradiation capacity in Europe can be clearly seen in the 2018, 2022 and January-June 2023 periods.

Overall irradiation capacity is projected to partially recover in the first half of 2023, with the successful return to service of the BR-2 reactor, but levels are projected to remain lower than in 2020 and 2021 as the MARIA reactor remains on extended maintenance shutdown. This report anticipates that the MARIA reactor will return to service in the fourth quarter of 2023, but the irradiation capacity available will remain lower than projected in this graph if the MARIA reactor does not return to service during that period.

The extended unavailability of the MARIA reactor does not reduce the total irradiation capacity to a level of concern. However, it does decrease the flexibility of the integrated European supply chain, increasing the duration of periods when the operational schedule in Europe relies upon a single reactor. Those periods are higher risk because a single point failure during those periods may lead directly to global supply problems.

Total irradiation capacity from existing supply chain members is projected to then stabilise before increasing further in the July-December 2024 period, with minor capacity fluctuation in 2026 and 2027 anticipated due to reactor scheduling. The increase in irradiation capacity associated with the anticipated return to service of the MARIA reactor masks the planned extended outage of the OPAL (Australia) reactor in the January-June 2024 period.

Total irradiation capacity is projected to recover to be above the NEA demand +35% ORC line in 2023 and remain well above throughout the rest of the projection period. Overall, the irradiation capacity appears to be sufficient to assure supply throughout the projection period, although some structural scheduling weakness is noted during periods in 2023 and 2024.

Processing capacity

Figure 4.1 of Scenario A ("Reference") also shows the level of processing capacity (pink line) during 2018, reflecting the unplanned, extended loss of NTP capacity, with total processing capacity in 2018 being structurally below the important NEA demand +35% ORC line (green line). During much of 2018, a chronic level of supply shortage was experienced at the generator level of the supply chain, with some supply shortages in some markets experienced throughout the period.

The year 2019 began with the NTP facilities returning to service, but at reduced processing capacity. As a result, total processing capacity remained close to the NEA demand +35% ORC line in the January-June 2019 period before recovering slowly through 2020, 2021 and the first half of 2022. Total processing capacity reduced again in the July-December 2022 period as the substantial processing capacity in Europe was completely blocked for three and a half weeks due to a combination of planned and unplanned outages at European reactors that occurred at the same time. Global processing capacity was significantly affected during this period, with direct effects on generator manufacturers, nuclear pharmacies and clinical services.

Processing capacity from existing supply chain members is projected to recover in 2023 and is then projected to remain relatively stable, with minor variations due to scheduling, and to remain well above the key NEA demand +35% ORC line until 2027. A minor dip in processing capacity is noted in the January-June 2024 period when the ANM processing capacity is scheduled to be unavailable due to planned maintenance at the OPAL reactor.

The level of projected processing capacity in the reference scenario A has substantially improved since the 2019 report where the level of projected global processing capacity remained uncomfortably close to the NEA demand +35% ORC line throughout that projection period (until 2024). This important increase in the level of projected total processing capacity has been achieved because the additional processing capacity from the ANM facility and the neutron activation projects at NorthStar (United States) are all fully operational and included in Scenario A ("Reference"). It is quite clear that the supply problems experienced in 2022 would have been more severe if the added processing capacity from the ANM and NorthStar projects had not been available.

Overall conclusions

The current irradiators and processors, if well maintained and well scheduled, should be able to manage limited periods of unplanned outage during the projection period to the end of 2027. The capability to manage large-scale or longer-term adverse events, such as the 2022 loss of irradiation and processing capacity in Europe, is restricted in 2023 and in 2024 and will remain restricted until the MARIA reactor fully returns to service. Resilience will also be lower during the scheduled OPAL maintenance period in the first half of 2024.

Projected capacity from 2025 through 2027 from the existing supply chain in Scenario A ("Reference") looks adequate to meet the projected demand.

Chapter 5. Scenario B: "Projected capacity additions"

Scenario B, or "Projected capacity additions", in this report is based on the same principles as previous reports. The scenario is thus a direct extension of Scenario A ("Reference") presented in the previous section, and includes the addition of new irradiators and processors and also alternative technology projects.

In the preparation of this report, the tables in Appendix 1 were thoroughly reviewed and revised in consultation with existing and potential supply chain participants using a standard format of project timeline reporting. Unsurprisingly, many previously anticipated projects suffered delays during the COVID-19 pandemic and some were abandoned. The 2019 report included a Table 5 that listed projects considered out of scope for the Scenario B projection. Some projects from Table 5 in the 2019 report have progressed and are now reported in Tables 3 and 4. It should be noted that not all projects announced around the world have been included in this report.

More specifically, this report only includes new projects that are likely to be commissioned and operational for at least one year before the end of 2027. It excludes projects with unspecified construction start, licencing and/or commissioning dates, or inconclusive information about likely operational or licencing dates, or that have not secured funding. By making such a determination, the NEA is not suggesting that any projects that do not appear in Tables 3 and 4 will never materialise, but rather that facilities may not be commissioned within the forecast period and their products licenced. Projects are not included or excluded on the basis of their proposed technology.

Furthermore, all new technology projects, whether reactor-based or non-conventional reactor-based, are assumed to have a 50% probability of being commissioned within their announced timelines as noted in Tables 3 and 4. This assumption takes into account the fact that most alternative and non-conventional technologies have yet to be proven at a large scale in the ^{99}Mo/^{99m}Tc market.

Appendix 1 (Tables 3 and 4) contains only some of the planned projects included in the previous NEA reports. It should be noted that these tables do not contain any new projects announced since the 2019 report, as no such projects will be completed by 2027. Scenario B ("Projected capacity additions") and Scenario C ("Delays to projected capacity additions") (see also Chapter 6) include only projects that appear in Tables 3 and 4.

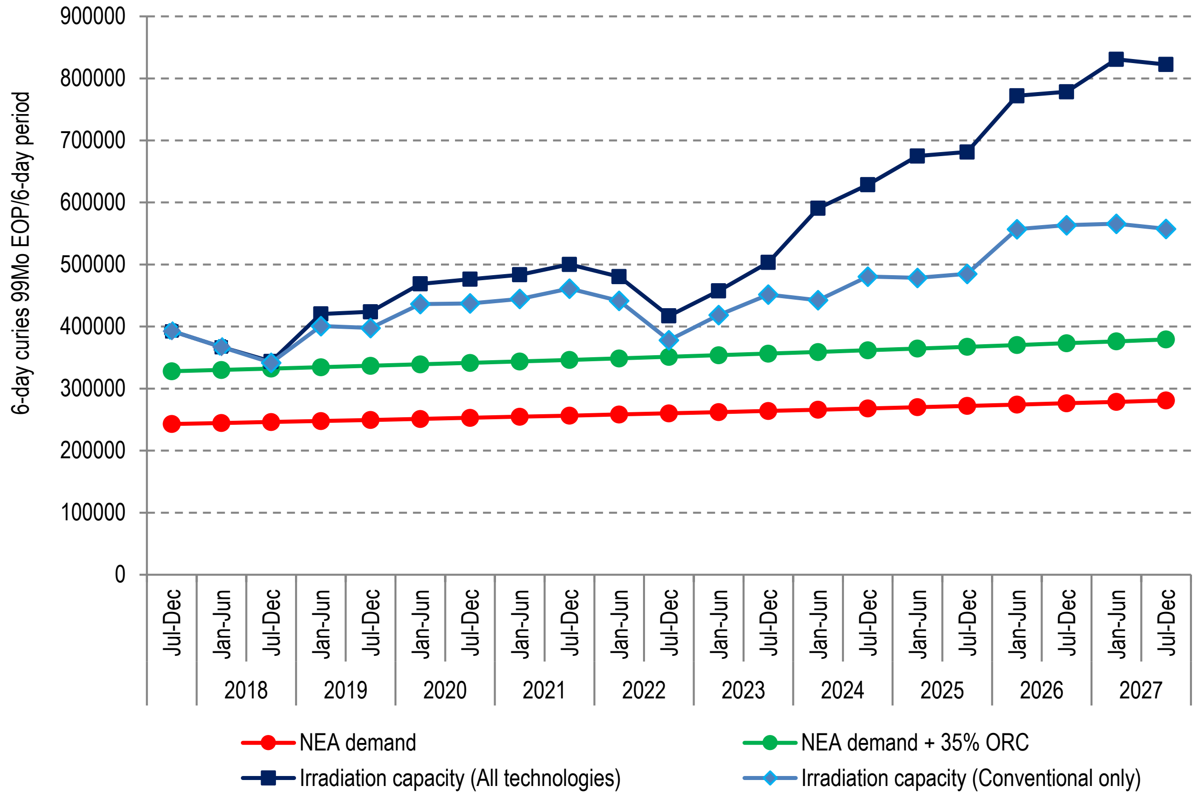
All of these projects have already seen multi-year delays. A review of all projects over sequential NEA reports (see Chapter 7) identifies many multi-year delays involving both conventional and alternative technologies. Multi-year delays are often linked to budget problems, although some delays are also due to technical and licencing delays. It should be assumed that timeline slippage will continue to be a feature affecting many projects.

In Scenario B ("Projected capacity additions"), there are no projects scheduled to enter service in 2023. In the period beyond 2024, the proposed projects for ^{99}Mo/^{99m}Tc irradiation and associated processing capacity, if all completed, would significantly exceed the projected market demand. However, this apparent future excess capacity should not imply that long-term security of supply is assured. It does not take into account any current capacity being retired early, or the potential for continued multi-year delays of projects, or consider any commercial sustainability effects that future potential "overcapacity" may have on the market.

Irradiation capacity

Figure 5.1 presents the NEA projected demand, projected demand +35% ORC and the irradiation capacity under Scenario B ("Projected capacity additions"). This shows both total capacity, "all technologies" (dark blue line), and the irradiation capacity for "conventional reactor-based only" (light blue line). It can be seen that following the recovery of irradiation capacity in the January-June 2023 period, even without all planned new projects being fully included, the global capacity of both lines looks to be sufficient to meet projected global demand throughout the projection period to 2027.

Figure 5.1: NEA demand and NEA demand +35% ORC vs. total and conventional-only irradiation capacity (2017-2027)



This figure visualises the contribution that alternative 99Mo/99mTc production technologies have made to irradiation capacity. Figure 5.1 separates out conventional (reactor-based) irradiation capacity from total irradiation capacity. These lines started to diverge from 2018 when the first alternative technology capacity from the NorthStar RadioGenix project became available. So the gap between the lines represents the past and future anticipated contribution from alternative technologies.

Conventional reactor-based irradiation capacity is projected to recover in 2023, but dip in the January-June 2024 period due to the scheduling of extended maintenance at the OPAL reactor and then recover through late 2024 and 2025. It is then projected to increase in 2026 with additional conventional irradiation capacity being added from the new RA-10 reactor (Argentina) and the existing FRMII reactor (Germany), then stabilise in 2027.

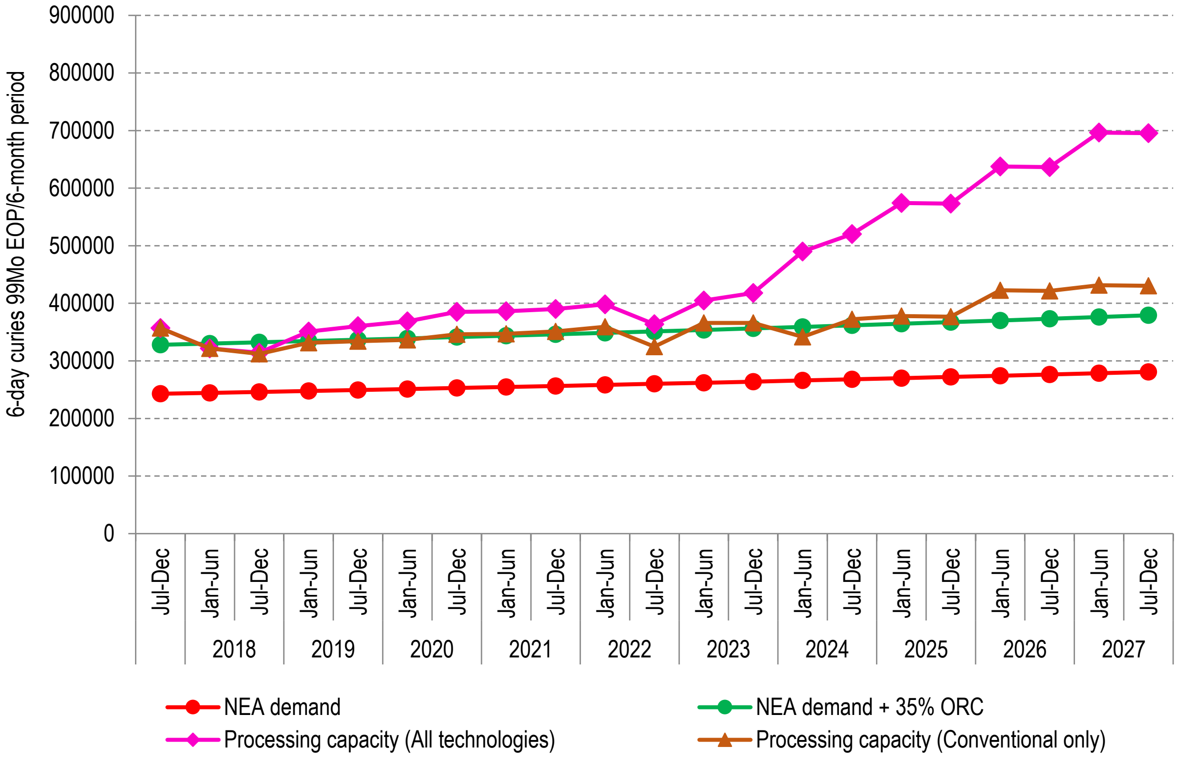
The additional irradiation capacity from alternative technologies has increased slowly since 2018 and will continue to do so through 2023, but only from existing projects. Substantial capacity is projected to be added from "alternative technologies" in 2024, 2025, 2026 and 2027. While increased total irradiation capacity is projected from alternative technologies, in the short term this additional capacity will most likely be only available in North America, but this should still add to overall global security of supply.

Processing capacity

Figure 5.2 presents the NEA projected demand, the NEA projected demand +35% ORC and processing capacity under Scenario B ("Projected capacity additions"). This shows both total processing capacity "all technologies" (magenta line) and processing capacity from "conventional technology only" (dark brown line). It can be seen that following the recovery of processing capacity in the January-June 2023 period, even without all planned new projects being fully included, the projected total processing capacity including the contribution from alternative technologies looks to be sufficient to meet projected global demand throughout the projection period to 2027, while total processing capacity from conventional technologies remains uncomfortably close to the NEA demand +35% ORC line until at least 2025.

The contribution that alternative 99Mo/99mTc production technologies have made to total processing capacity is illustrated in Figure 5.2. It is the gap between the two processing capacity lines. The lines started to diverge in 2018, when the first alternative technology processing capacity from the NorthStar RadioGenix project became available.

Figure 5.2: NEA demand and NEA demand +35% ORC vs. total and conventional-only processing capacity (2017-2027)



It should be noted that the processing capacity from "conventional technology only" (the processing of enriched uranium targets irradiated in research reactors) dipped below the important NEA projected demand +35% ORC line in 2018, before recovering to closely follow that line from 2019 to 2021. Further problems were experienced in late 2022 when conventional European processing capacity was blocked due to a combination of planned and unplanned outage events at European reactors. It is projected that conventional processing capacity will recover in 2023, before falling below the NEA projected demand +35% ORC line again in the January-June 2024 period, when the ANM processing facility will be unavailable due to extended planned maintenance at the co-located OPAL reactor.

Additional conventional processing capacity is projected to be added from the Argentinian project in 2026, which, if achieved, will represent a delay of around five years compared with the projections for that project made in the 2019 report.

In contrast, the total processing capacity "all technologies" remains above the NEA projected demand +35% ORC line and the contribution from alternative technologies is projected to increase substantially from 2024 onwards (see Table 4). It should be noted that when new processing capacity is linked one-to-one with new irradiation capacity, both the processing and irradiation components of those projects must be successfully deployed for those technologies to provide additional ^{99}Mo capacity to the supply chain.

While increased total processing capacity is projected from alternative technologies, in the short term this additional capacity will most likely be only available in North America, but this should still add to overall global security of supply.

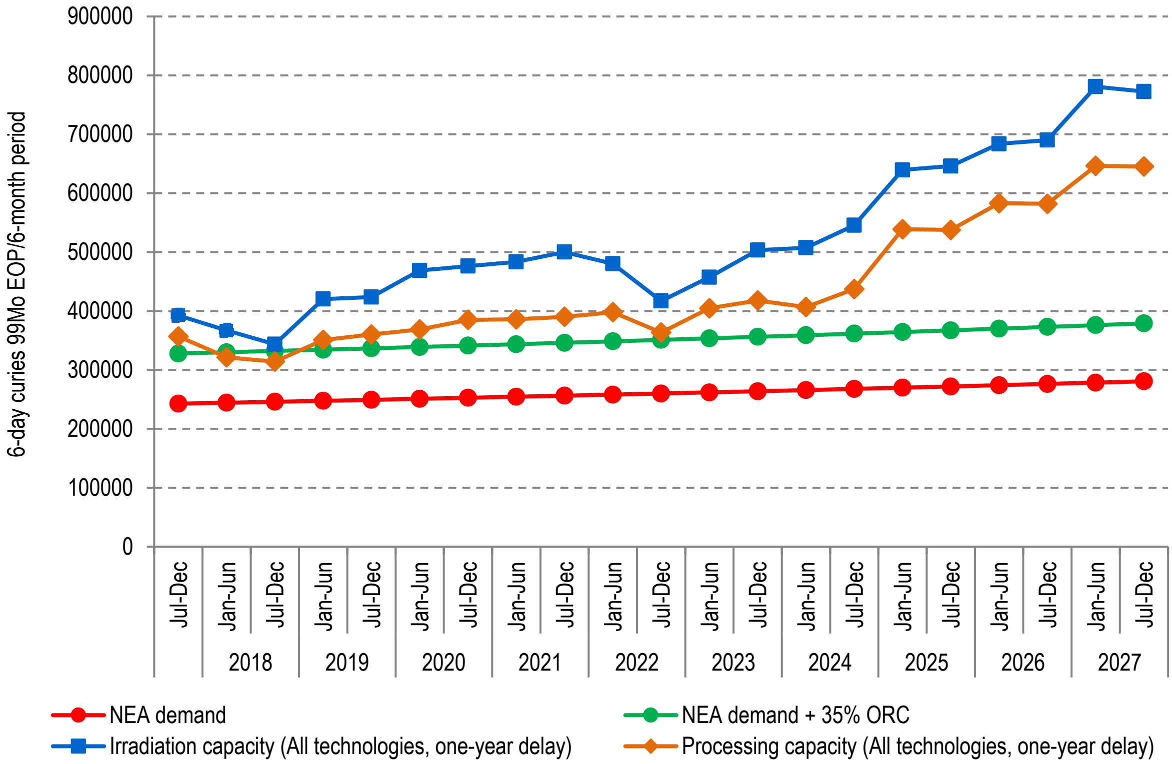
Chapter 6. Scenario C: "Delays to projected capacity additions"

Scenario C, which is the "Delays in projected capacity additions" scenario, is developed from Scenario B ("Projected capacity additions") by modelling a delay of either one or two years to all new projects. This scenario considers the impact on future capacity when considering the technical complexity of new reactor-based projects and the often ground-breaking efforts needed to reach large-scale, commercial production using alternative technologies. A review of past performance shows that large projects often take much longer to complete and licence than originally envisaged, with multi-year delays being common. As demonstrated in previous NEA reports, the time taken to fully scale up production can also be significant. Assuming only a one-year delay, Scenario C ("Delays in projected capacity additions") may thus still be considered to be optimistic.

Irradiation and processing capacity

Figure 6.1 shows the projected global irradiation and processing capacity under Scenario C ("Delays in projected capacity additions"). In this scenario, delays in project completion will lower both the projected irradiation (blue line) and processing (mid brown line) capacity compared to Figures 5.1 and 5.2. In Scenario C, with no new projects scheduled in 2023 and with a one-year delay anticipated for projects scheduled to come on-stream in 2024, projected irradiation and processing capacities will remain unchanged from the levels of Scenario A ("Reference") until 2025.

Figure 6.1: NEA demand and NEA demand +35% ORC vs. irradiation and processing capacity including a one-year delay in capacity additions (2017-2027)



This report is unusual as no additional capacity from either irradiation projects, or from processing projects is anticipated in 2023, the first year of projections. The consequence for Scenario C ("Delays in projected capacity additions"), is that with a one-year delay no additional capacity can be anticipated the Scenario A ("Reference") during the first two years of projections.

A conclusion from Scenario A is that the ability of the existing supply chain to manage large-scale or longer-term adverse events is restricted in 2023 and 2024. In particular, this ability will remain constrained until the MARIA reactor returns to service (scheduled for 2023) and during the scheduled maintenance of the OPAL reactor in 2024. Those concerns are therefore repeated in the early years of Scenario C ("Delays in projected capacity additions") as no additional capacity can be anticipated to mitigate the concerns expressed in the Scenario A ("Reference"). From 2025 onwards, substantial additional irradiation and processing capacity is projected even under Scenario C.

The potential impact of project delays that are more extended is relevant. History shows that many projects experience delays that can span several years. Figure 6.2 looks at the potential impact of even longer delays and concentrates only on processing capacity because it has a lower level of reserve capacity in all scenarios.

Figure 6.2: NEA demand and NEA demand +35% ORC vs. processing capacity with and without a two-year delay in capacity additions (2017-2027)

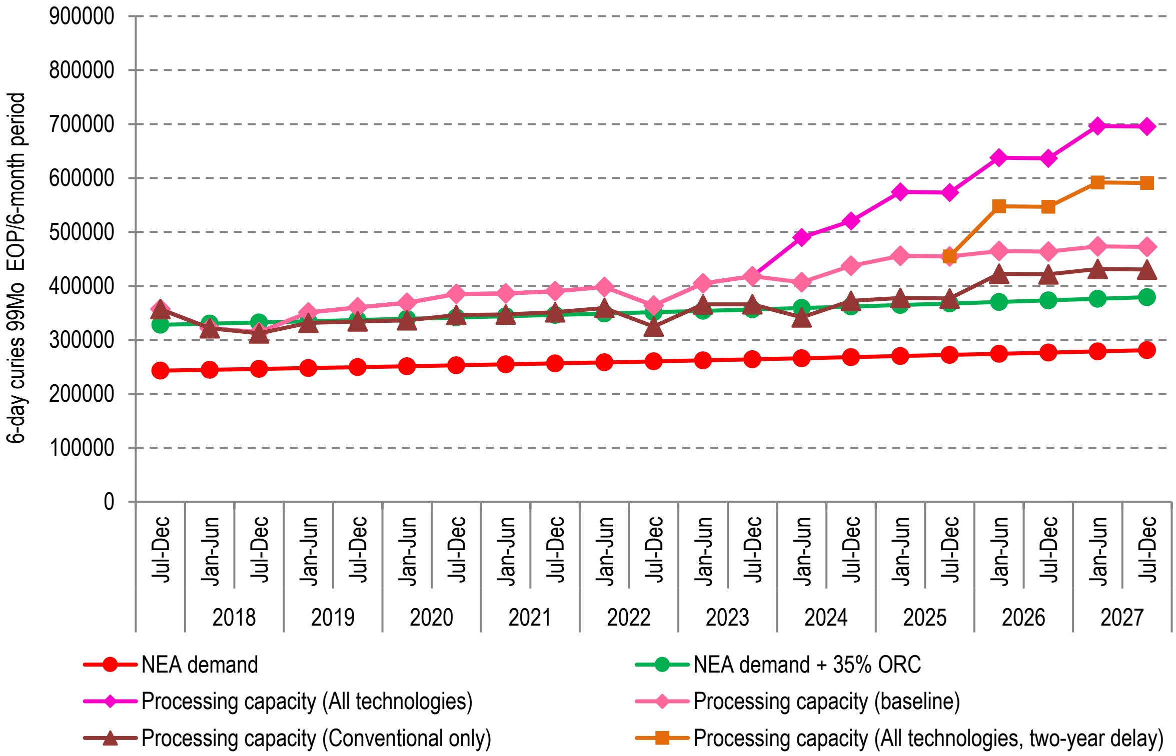


Figure 6.2 shows NEA projected demand and NEA projected demand +35% ORC compared to the baseline processing capacity (pink line from Scenario A, the "Reference" scenario), the projected total processing capacity "All technologies" (magenta line from Scenario B, the "Projected capacity additions" scenario) and the projected total capacity for conventional technologies only (dark brown line from Scenario B "Projected capacity additions"). These lines assume that all projects come on line as planned. Figure 6.2, however, also includes a total processing capacity line that assumes a two-year delay in new projects (sand brown line). These lines therefore represent the projected contribution from conventional technology only, compared to the maximum of all technologies together and two intermediate projections representing different challenges for processing capacity through the period to 2027.

Figure 6.2 also shows that if all the projected processing capacity from all technologies is available as scheduled (magenta line), a substantial level of reserve capacity will have developed by 2025. That increases further to nearly double the 2022 processing capacity by 2027. The anticipated level of contribution from alternative technologies is projected to be significant during the projection period.

However, the processing capacity from conventional technology alone (dark brown line) is projected to remain at or below NEA demand +35% ORC line for the period until at least 2026. This line only increases in a meaningful way when additional conventional technology is added in Argentina.

The total processing capacity from current producers (pink line) is projected to improve from 2023, with a mild dip in 2024 due to schedule maintenance, before rising a little in 2025 and then stabilising until 2027. This projection for capacity from current producers comes with all the previous caveats concerning the potential effects of unplanned outages mentioned in discussion of Scenario A ("Reference").

The effects of further project delays could be important. This is illustrated when the maximum line of all projected processing capacity is delayed by two years (sand brown line). This projection shows that total processing capacity only improves above the Scenario A ("Reference") line from 2026 onwards.

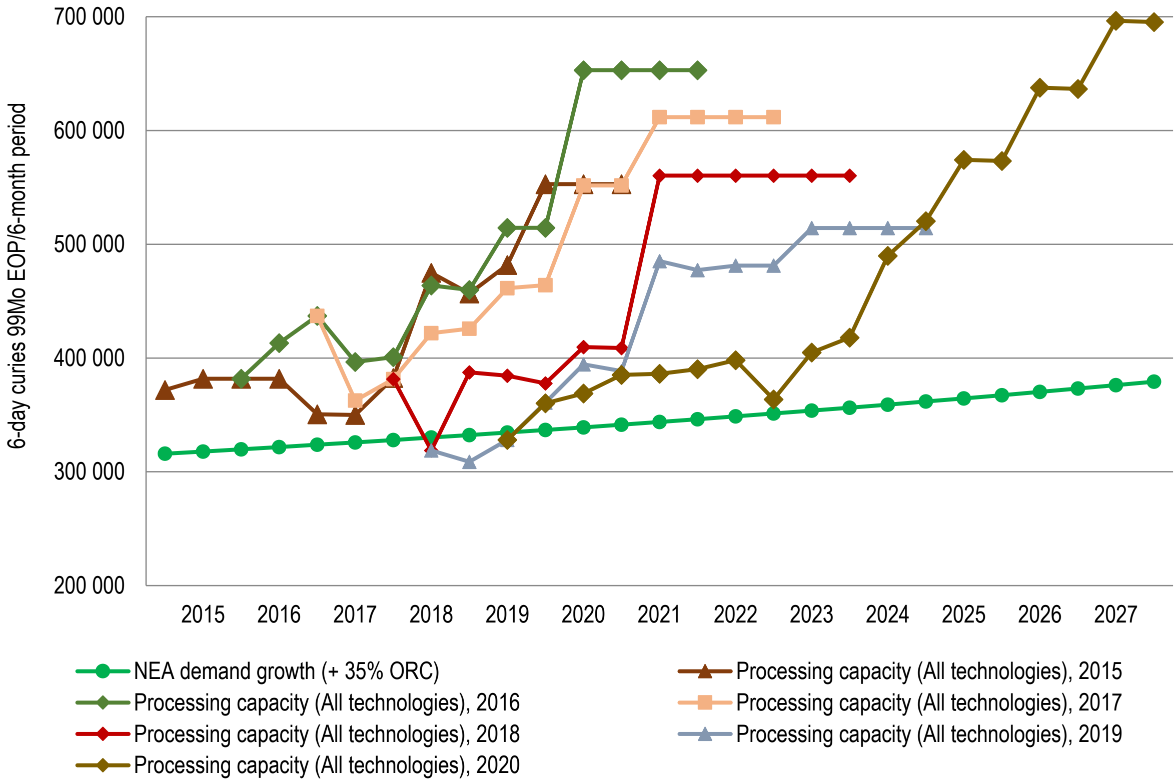
This analysis reconfirms the importance of additional processing capacity from alternative technologies and identifies that further extended delays in those projects will leave processing capacity vulnerable as it will remain at the level of Scenario A ("Reference") until further alternative technology projects become operational.

Chapter 7. The impact of historic project delays on capacity estimations

Since the NEA began reporting on the irradiation and processing capacity for ^{99}Mo production in 2014, multi-year delays have been observed to potential new projects. The NEA thus added an analysis of the effects of such extended project delays in both the 2018 and 2019 reports. That analysis has been continued in this report, albeit with a four-year time gap between the 2019 and 2023 projections. Figure 7.1 shows the cumulative effect of project delays by comparing the projections for processing capacity under Scenario B ("Projected capacity additions", previously called "Technological challenges") for each year reported, starting in 2015.

An important difference in this analysis compared to previous reports is that the four-year time gap between this and the 2019 report has the effect of making the years 2019, 2020, 2021 and 2022 of the new 2027 projection line a series of actual data points that represent the processing capacity available during each of those years. In Figure 7.1, the sequential projections for Scenario B ("Projected capacity additions") starting from 2015 are shown against the key NEA demand + 35% ORC line (green line).

Figure 7.1. Current and historic projections of processing capacity under scenario B "Projected capacity additions"



The projection under Scenario B ("Projected capacity additions") in 2015 (dark brown line) anticipated a reduction of processing capacity by 2017 in the period after the end of routine production in Canada. Capacity was projected to recover by 2018 and then increase in steps until 2020.

The following projection under Scenario B ("Projected capacity additions") for 2016 (orange line) anticipated that substantial actions taken by the existing supply chain members would increase capacity from existing facilities, or by adding capacity and making transition plans. Those actions anticipated adding capacity ahead of the end of routine production in Canada, but still anticipated some reduction in capacity in 2017, when the production in Canada stopped. The capacity projection then stabilised before increasing from 2018 onwards. The 2016 projection under Scenario B ("Projected capacity additions") anticipated that the total processing capacity available by 2020 would be higher than had been anticipated in the 2015 report as other new projects had been added.

The 2017 projection under Scenario B ("Projected capacity additions"), marked as the pink line, shows that not all of the additional capacity anticipated in the 2016 report had been achieved by 2017. The 2017 projection also anticipated some minor delays in some projects from 2018 onwards (the pink line moves a little to the right of the orange line). It also projected a decrease in the total anticipated capacity by 2021 as some capacity estimates for new projects were scaled back.

The 2018 projection under Scenario B ("Projected capacity additions"), marked as the red line, started from an even lower capacity base due to the initial negative effects of the extended unplanned outage in South Africa. The 2018 projection also identified more extended delays to planned projects (the red line substantially shifted lower and to the right of the pink line) and some projects were withdrawn.

The 2019 projection under Scenario B ("Projected capacity additions"), marked as the blue line, shows the even stronger negative impacts on global processing capacity experienced following the unplanned outages in South Africa in 2018 and 2019 and some problems in capacity scaling in Australia. The 2019 projection again identified further project delays (the blue line projection shifted lower and to the right of the red line). Thus total capacity anticipated by 2021 in the 2019 projection was further reduced compared to all the earlier projections and the total capacity anticipated by 2024, the end of the projection period, was also substantially lower.

When compared with the 2016 projection (orange line), the 2019 projection (blue line) showed that the bulk of potential projects that had been anticipated to be introduced by 2018 had been progressively delayed by at least three years or had even been cancelled. The cumulative effect of delays can be seen in the sequential scenarios under Scenario B ("Projected capacity additions") as indicated capacity moves progressively to lower levels and to later time points.

Consequently, the updated projection for 2023 (black line) for Scenario B ("Projected capacity additions") changed considerably, as the actual availability of total processing capacity from 2019 through 2022 evolved in combination with the projected capacity developments from 2023 through 2027. It can be seen that actual processing capacity tracks the 2019 projection in 2019, diverges a little lower in 2020, and then diverges significantly lower from 2021 onwards. The divergence in 2021 was in part because the conventional processing project in Argentina was substantially delayed during the COVID-19 pandemic, projects in Australia and the United States did not add capacity as quickly as had been anticipated, and some projects did not reach maturity.

The projection for 2023 under Scenario B ("Projected capacity additions") shows the temporary loss of existing processing capacity in Europe in 2022 and the anticipated recovery in 2023. Significant additional capacity from previously delayed projects in the United States are anticipated in 2024 and further additional capacity is projected in each subsequent year.

Interestingly, total capacity by 2027 is now projected to be substantially higher than in any previous projections. The past experience of project delays, some of multi-year duration, suggest that it is unlikely that this extremely high level of processing capacity will be achieved by 2027, especially for projects that are presently in their earlier stages and are only envisaged to enter service late in the projection period.

The 2019 report identified that the cumulative effect of unplanned outages, multi-year project delays and some project cancellations suggested that total processing capacity would remain under pressure until at least 2021. Reviewing this after the event, it can be seen in this report that total processing capacity, while well managed during the COVID-19 pandemic period, remained close to the NEA demand +35% ORC line throughout the 2019-2022 period, when there were disruptions. Therefore, the concerns identified in the 2019 report were well founded and it seems that total processing capacity is likely to remain vulnerable until at least 2024.

A word of caution applies. It should be noted that the projections shown in Figure 7.1 result from Scenario B ("Projected capacity additions") and are therefore relatively optimistic. The projections shown in Figure 6.2, resulting from Scenario C ("Delays to projected capacity additions"), may be more realistic concerning the total processing capacity that will become available during the 2023 to 2027 period, with the result that total processing capacity could remain under pressure until 2026.

Chapter 8. Conclusions

This report shows that the global estimate of demand growth has been maintained, with the projected demand level increasing to approximately 10 000 6-day Ci ^{99}Mo per week at EOP at the reference time point "end of 2022".

Good progress has been made in the conversion from production using HEU targets to production using LEU. This report anticipates that during 2023, more than 90% of all bulk ^{99}Mo production will have been from non-HEU sources. Capacity reductions from conversion to less efficient LEU targets have been mitigated, and in many cases overall production capacity was increased.

Delays have continued to be experienced in many alternative technology projects. Conventional technology project delays have also continued, with some now pushed beyond 2027. Multi-year delays and project withdrawals remain a concern and their effects are discussed in Chapter 7.

Despite the many significant challenges posed by the COVID-19 pandemic, the ^{99}Mo supply chain members all maintained continuous service in 2020 and 2021, showing a commitment to manage critical "just-in-time" services.

Before that period, unplanned outages at the NTP (South Africa) facility had pushed global processing capacity below the NEA guideline of demand +35% outage reserve capacity (ORC) in 2018 and 2019, resulting in ^{99}Mo supply shortages. NTP returned to service in 2019 and total processing capacity has since recovered.

In late 2022, a combination of extended planned maintenance and unplanned outages led to significant global shortages of ^{99}Mo and reactor-based therapy isotopes. A single reactor had been scheduled to operate in the European network, but unplanned outages led to an extended period with no irradiation capacity available from the network. No irradiation capacity in Europe directly blocks significant ^{99}Mo processing capacity, leading to global supply shortages.

Reactor scheduling is co-ordinated. A detailed review identified that, due to essential maintenance demands, scheduling for reserve irradiation capacity was weak from mid-2022 until at least mid-2023, with extended periods in which a sole reactor was operating in Europe. These are periods of increased risk, where a single point of failure can lead directly to ^{99}Mo supply shortages. These periods, albeit relatively short, reflect a vulnerability in the absence of a functional ORC guarantee by critical parts of the supply chain.

The projected total processing capacity in Scenario A ("Reference") in this report improved compared to the 2019 report. In 2019, capacity was projected to remain uncomfortably close to the key NEA demand +35% ORC line. The improvement in this report has been achieved through the addition of conventional processing capacity at ANM (Australia) and at the NorthStar facilities (United States), which successfully introduced two alternative technology projects. Both suppliers plan increased capacity from their facilities.

This report concludes that, overall, the current irradiators and processors, if well maintained and well scheduled, should be able to manage limited periods of unplanned outage during the projection period. The capability to manage large-scale or longer-term adverse events, such as an event equivalent to the 2022 loss of capacity in Europe, is restricted in 2023 and 2024. Projected capacity from 2025 through 2027 from the existing supply chain looks adequate to meet demand. No additional capacity from new projects is anticipated in 2023 and any further delays in anticipated projects could leave 2024 and 2025 looking vulnerable.

Maintaining adequate levels of capacity for the irradiation and processing of sufficient amounts of ^{99}Mo to cover demand from the medical community requires that sufficient levels of ORC be maintained at all times. The $^{99}Mo/^{99m}Tc$ that the medical profession works with are non-storable goods. Future demand and supply mismatches thus need to be avoided as much as possible through careful forward planning. The current criterion of "demand +35%" has served well in the past; however, switching to an n-2 criterion might provide a more useful indicator for assessing potential supply risk and greater transparency for decision making.

Independent of the specific quantitative indicator employed, the supply situation will continue to require careful monitoring and well-considered planning to minimise the risks to security of supply. A fully resilient supply chain will require that production and processing capacity become more diversified and that all ORC be truly operational and fully financed. A high degree of co-operation between all stakeholders in the industry and policymakers will continue to be essential for the foreseeable future. Future NEA reports may provide proposals as to the appropriate format and reporting requirements for the monitoring of the ^{99}Mo supply chain.

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5. All NEA and OECD reports are available at: www.oecd-nea.org/med-radio

Appendix 1

Table 1. Current irradiators

Reactor (Fuel)	Current targets[6]	Normal operating days/year	Anticipated ^{99}Mo production weeks/year	Expected available capacity per week (6-day Ci ^{99}Mo)	Expected available capacity per year (6-day Ci ^{99}Mo) by 2027	Estimated end of operation
BR-2 (HEU)[1]	LEU	203	29	8 600	249 400	2036
HFR (LEU)	LEU	265	38	6 200	235 600	2030
LVR-15 (LEU)	LEU	210	30	3 000	90 000	2028
MARIA (LEU)	LEU	200	36	2 200	79 200	2040
MURR (HEU)[2]	EnMo in CRR	339	52	3 000	156 000	2037
OPAL (LEU)[3]	LEU	308	44	3 200	140 800	2057
RA-3/RA-10 (LEU)[4]	LEU	230	46	500	23 000	2027 or earlier based on RA-10 introduction
SAFARI-1 (LEU)	LEU	305	44	3 000	130 700	2030
RIAR[5] (HEU)	HEU	350	50	540	27 000	At least until 2025
KARPOV[5] (HEU)	HEU	336	48	350	16 800	At least until 2025

Notes: 1). BR-2 total capacity substantially increased since 2019 report with increased weekly capacity and additional operating days; 2). MURR capacity is limited by NorthStar processing capacity, capacity is planned to increase progressively until 2024 reaching the level shown in this table; 3). OPAL capacity is restricted by ANM processing capacity, capacity is planned to increase progressively from 2022 until reaching the 2027 level shown in this table; 4). RA-10 will be providing the irradiation for the 23 000 6-day Ci ^{99}Mo per year by 2027; 5). RIAR and KARPOV capacity remains reported at the 2019 report level, 6). EnMo = Enriched Mo^{98} target, HEU >20% enriched Uranium, LEU <20% enriched Uranium.

Table 2. Current processors

Processor	Targets[6]	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 2027	Expected year of full conversion to LEU targets[7]	Estimated end of production[7]
ANSTO Nuclear Medicine (ANM)[1]	LEU	44	3 200	140 800	LEU	2057
CNEA[2]	LEU	46	500	23 000	LEU	2027 or earlier based on RA-10 introduction
Curium	LEU	52	5 000	260 000	LEU	NK
IRE[3]	LEU	52	3 500	182 000	LEU	At least until 2032
MURR/NorthStar[4]	EnMo	52	3 000	156 000	NA	At least until 2037
NTP	LEU	44	3 000	130 700	LEU	At least until 2030
RIAR[5]	HEU	50	540	27 000	NK	At least until 2025
KARPOV Institute[5]	HEU	48	350	16 800	NK	At least until 2025

Notes: 1). ANM processing capacity is planned to increase progressively from 2022 until reaching the 2027 level shown in this table; 2). CNEA will be processing 23 000 6-day Ci 99Mo per year by 2027 from RA10; 3). The IRE started LEU target conversion in 2020 with full conversion achieved in March 2023; 4). MURR/NorthStar processing capacity is in a scale-up phase with maximum capacity planned by 2025; 5). RIAR and KARPOV capacity remains reported at the 2019 report level; 6). EnMo = Enriched Mo98 target, HEU >20% enriched Uranium, LEU <20% enriched Uranium, NA = Not Applicable, NK = Not Known.

Table 3. Potential irradiators entering in period 2023 to 2027

Irradiation source (Fuel)[2]	Targets/technology[2]	Expected operating days/year	Anticipated Mo-99 production weeks/year	Expected available capacity per week (6-d Ci ^{99}Mo) by 2027	Potential maximum capacity per year (6-day Ci ^{99}Mo) by 2027	Expected first full year of production	Project status (end March 2023)
NorthStar (non-U)	Non-fissile/Electron accelerators	339	52	2 541	132 132	2024	Operating/Preparing FDA submission
SHINE USA (non-U)	LEU in solution	350	50	4 000	200 000	2024	Under construction
Ontario Power Generation (NU)	NMo in PR	365	52	2 722	141 544	2025	Equipment Factory Acceptance Test complete
FRM II (HEU)	LEU in CRR	240	32	2 100	67 200	2026	Irradiation facility under construction
RA-10 (LEU)[1]	LEU in CRR	315	48	+2 000	+96 000	2026	Finish building mid-2023
Niowave (non-U)	NU and LEU/Electron Linac	336	48	1 550	74 400	2026	Pre-licencing phase
SHINE Europe (non-U)	LEU in solution	350	50	4 000	200 000	2027	Pre-licensing phase

Notes: 1). MU Notes: 1). The RA-10 +96 000 6-day Ci ^{99}Mo irradiation capacity by 2027 is additive to the activity shown in Table 1; 2). CRR = Conventional Research Reactor, HEU >20% enriched Uranium, LEU <20% enriched Uranium, NMo = Natural Molybdenum, NU = Natural Uranium, non-U = a non-Uranium fuel, PR = Power Reactor.

Table 4. Potential processors entering in period 2023 to 2027

Processor	Targets[2]	Anticipated Mo-99 production weeks/year	Expected available capacity per week (6-day C ^{99}Moi) by 2027	Potential maximum capacity per year (6-day Ci ^{99}Mo) by 2027	Estimated first full year of production	Project status (end March 2023)
NorthStar	Non-fissile	52	2 541	132 132	2024	In production scale up
SHINE USA	LEU in solution	50	4 000	200 000	2024	Under construction
BWXT Medical	NMo	52	2 722	141 544	2025	Cold-run commissioning complete
CNEA[1]	LEU	48	+2 000	+96 000	2026	Building start by beginning 2024
Niowave	NU and LEU	48	1 550	74 400	2026	Pre-licencing phase
SHINE Europe	LEU in solution	50	4 000	200 000	2027	Pre-licensing phase

Notes: 1). MURR Notes: 1). The CNEA +96 000 6-day Ci ^{99}Mo irradiation capacity by 2027 is additive to the activity shown in Table 2; 2). LEU <20% enriched Uranium, NMo = Natural Molybdenum, NU =Natural Uranium