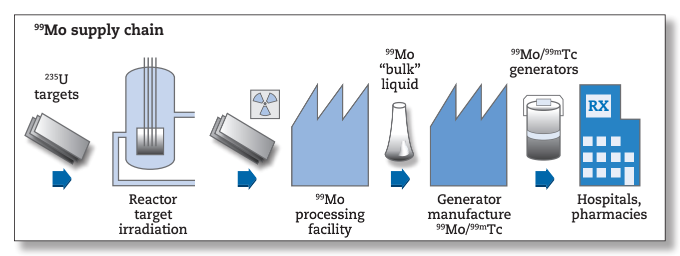
Nuclear Development
2011

OECD

The Supply of Medical Radioisotopes

The Path to Reliability



AEN NEA

NUCLEAR ENERGY AGENCY

Nuclear Development ISBN-978-92-64-99164-4

The Supply of Medical Radioisotopes: The Path to Reliability

NEA No. 6985

NUCLEAR ENERGY AGENCY
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

The OECD is a unique forum where the governments of 34 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.

The OECD member countries are: Australia, Austria, Belgium, Canada, Chile, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Mexico, the Netherlands, New Zealand, Norway, Poland, Portugal, the Republic of Korea, the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, the United Kingdom and the United States. The European Commission takes part in the work of the OECD.

OECD Publishing disseminates widely the results of the Organisation's statistics gathering and research on economic, social and environmental issues, as well as the conventions, guidelines and standards agreed by its members.

NUCLEAR ENERGY AGENCY

The OECD Nuclear Energy Agency (NEA) was established on 1 February 1958. Current NEA membership consists of 30 OECD member countries: Australia, Austria, Belgium, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Luxembourg, Mexico, the Netherlands, Norway, Poland, Portugal, the Republic of Korea, the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, the United Kingdom and the United States. The European Commission also takes 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 friendly and economical use of nuclear energy for peaceful purposes, as well as

– 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 policy analyses in areas such as energy and sustainable development.

Specific areas of competence of the NEA include the safety and regulation of nuclear activities, radioactive waste management, 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. In these and related tasks, the NEA works in close collaboration with the International Atomic Energy Agency in Vienna, with which it has a Co-operation Agreement, as well as with other international organisations in the nuclear field.

Corrigenda to OECD publications may be found online at: *www.oecd.org/publishing/corrigenda*.

Preface

The interruptions to global supply of technetium-99m over the past few years made the international community aware of the need for collective action to improve the security of supply of this critical and widely used medical radioisotope. The global nature of the supply chain, as well as a lack of transparency regarding its capacities, responsiveness and economic structure meant that focused, high-level international dialogue and action were required to develop a common understanding of the challenges, to help address short-term supply disruptions, and to find solutions necessary to promote secure and reliable supply over the longer term.

Under the OECD Nuclear Energy Agency (NEA), the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) was established in 2009. The HLG-MR was given a two-year mandate to assess factors rendering the supply chain vulnerable and identify practical measures – near, medium and long term – which could be taken to ensure security of supply of this important medical isotope.

The members of the HLG-MR, representing public authorities from Argentina, Australia, Belgium, Canada, France, Germany, Italy, Japan, the Netherlands, the Republic of Korea, the Russian Federation, South Africa and the United States, as well as the European Commission and the International Atomic Energy Agency (IAEA), brought together a range of expertise connected to the field of medical radioisotopes. The HLG-MR also convened at its meetings representatives of the entire supply chain – including private distributors and representatives of the health care community – who provided, on a voluntary and collaborative basis, valuable support and advice through the course of its work.

The HLG-MR succeeded in achieving its goal: identifying and assessing the key issues that result in supply chain vulnerability, and identifying practical mechanisms to address them. It also succeeded in developing good lines of communications between producers and users, better co-ordination of efforts among supply chain participants and better understanding of both supply side issues and demand-management opportunities. The HLG-MR did so in conjunction with other global and regional collaborative efforts that provided that as solutions were identified, they could immediately be brought into effect for collective benefit and, ultimately, improved results for health care systems.

The information contained in the report represents the findings and recommendations of the HLG-MR after two years of intensive examination. In particular, it sets out a set of policy principles and formulates recommendations on how these principles can be carried forward. The actions need to be at all levels, from governments to producers to users. Although the HLG-MR has completed its two-year mission, work must continue to sustain collaboration and to implement fully the changes needed in the supply chain for security of supply, in a manner also consistent with shared commitments respecting nuclear non proliferation. I am pleased that the NEA has agreed to continue its efforts in the field of medical radioisotope security of supply and to work with all supply chain participants to assist in the implementation of the recommendations.

It has been an honour to serve as the Chair of the HLG-MR and I commend strongly the work, principles and recommendations that reflect our collective deliberations and our dialogue with invited participants. With the dedicated, professional support of the NEA Secretariat and the guidance of the NEA Steering Committee, the HLG-MR has provided an excellent example of how the global community can work together on practical solutions to issues of shared concern. I believe that the work of the HLG-MR has established solid groundwork for ensuring the long-term security of supply of technetium-99m and continued health benefits from nuclear medicine.

I thank sincerely all of the participants in the HLG-MR initiative and recommend highly this report to those involved in making decisions related to medical radioisotopes: governments, supply chain participants and members of the health community.

Serge Dupont, Chair of the HLG-MR

Foreword

At the request of its member countries, the OECD Nuclear Energy Agency (NEA) became involved in global efforts to ensure a reliable supply of molybdenum-99 (^{99}Mo) and its decay product, technetium-99m (^{99m}Tc), the most widely used medical radioisotope. The NEA established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in 2009 to examine the underlying reasons for the shortage and to develop a policy approach to ensure their long-term security of supply. The main objective of the HLG-MR is to strengthen the reliability of ^{99}Mo and ^{99m}Tc supply in the short, medium and long term.

During the two years of its mandate, the HLG-MR was able to examine the major issues that affect the short-, medium- and long-term reliability of ^{99}Mo/^{99m}Tc supply. The HLG-MR, working with medical isotope stakeholders, completed a comprehensive assessment of the key areas of vulnerability in the supply chain and identified the issues that need to be addressed. It examined the supply and demand for ^{99m}Tc, undertook a full economic analysis of the supply chain, and also reviewed potential ^{99}Mo/^{99m}Tc production technologies. This work resulted in the release of a number of reports detailing the findings from these studies, which have been issued under *The Supply of Medical Radioisotopes* series.

Through the work of the HLG-MR and its stakeholders, significant progress has been achieved on improving the supply situation through increased communication, co-ordination of research reactor schedules and a better understanding of demand-management opportunities. Although the current supply situation of ^{99m}Tc has stabilised with the return to service of two of the world's five main supplying research reactors, the underlying problem – that of an unsustainable economic structure – remains to be adequately addressed. The market has not restructured sustainably and thus, the long-term supply situation is no more stable or secure than it was during the shortage periods.

This report provides the findings and analysis of the HLG-MR concerning the supply chain issues and describes the policy approach developed by the HLG-MR that would help ensure long-term supply security of ^{99}Mo/^{99m}Tc. The recommendations of the policy approach detail the essential steps to be taken by governments, industry and the health community to address the vulnerabilities within the supply chain, including changing its economic structure which does not support or reinforce reliable supply.

In this report, the current capacity available from reactors and processors and their associated constraints are considered. It discusses work that has been done related to communicating the supply situation to downstream stakeholders, a study examining the long-term future demand of ^{99m}Tc and transport issues. The report provides a summary of the studies done for the HLG-MR on the economic situation of the supply chain and potential ^{99}Mo/^{99m}Tc production technologies. It also discusses findings concerning a related supply shortage of iodine-131.

The release of this report in June 2011 concludes the mandate of the HLG-MR.

Acknowledgements

This report would not have been possible without input from a significant number of supply chain participants and stakeholders including all major reactor operators, all major processors, generator manufacturers, representatives from radiopharmacies and nuclear medicine practitioners. Every HLG-MR meeting had an “open session” that provided a useful opportunity to share information and ideas with key nuclear medicine stakeholders. The participation of these stakeholders was an important element of the overall success of the meetings and the efforts of the HLG-MR.

The NEA acknowledges the input and participation of the HLG-MR members and other supply chain participants which was essential for successfully completing the mandate of the HLG-MR. The NEA greatly appreciates the participation of these stakeholders.

The ^{99m}Tc demand study (Chapter 5) was supported by an Expert Advisory Group (see Appendix 9 for the list of members) and by the Technopolis Group. The survey that provided the basis for the study was distributed globally by many medical, radiological and nuclear medicine associations. In addition, over 700 individuals in the field responded to the survey. The NEA appreciates the participation and efforts of all these individuals and organisations.

This report was written by Chad Westmacott, Alexey Lokhov and Ron Cameron of the NEA Nuclear Development Division. Detailed review and comments were provided by the HLG-MR.

Table of Contents

Figures

Tables

Executive Summary

Introduction

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

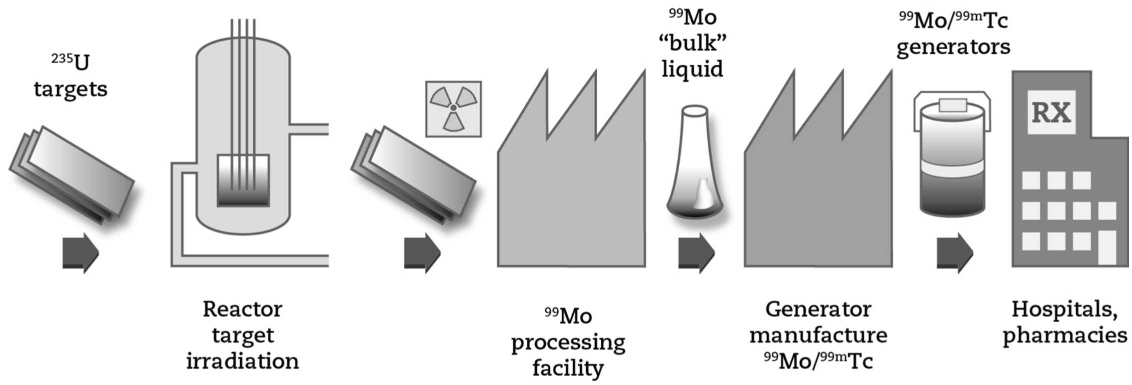
At the request of its member countries, the OECD Nuclear Energy Agency (NEA) established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in 2009. During its two-year mandate, the HLG-MR assessed the factors rendering the supply chain vulnerable and identified practical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

The current, ageing fleet will not be sufficient

The supply chain consists of uranium target manufacturers, reactor operators who irradiate the targets to create ^{99}Mo as part of the fission reaction, processors who extract the ^{99}Mo from the irradiated targets and purify it to produce bulk ^{99}Mo, generator manufacturers who produce generators with the bulk ^{99}Mo, and radiopharmacies and hospital radio-pharmacy departments who elute ^{99m}Tc from the generator and couple it with “cold kits” to prepare radiopharmaceutical doses for nuclear medical imaging of patients.

Until recently, there were only five research reactors irradiating targets to produce 90 to 95% of global ^{99}Mo supply: three in Europe (BR-2 in Belgium, HFR in the Netherlands and OSIRIS in France), one in Canada (NRU), and one in South Africa (SAFARI-1). However, all these reactors are over 45 years old. As the reactors age, longer downtime periods are needed between production cycles to repair or replace ageing parts or to undertake additional inspections to determine the effects of ageing on the reactor.

Figure E1: ^{99}Mo supply chain



Between 2009 and 2010, the Canadian and Dutch reactors were subject to extended shutdowns, causing global ^{99}Mo/^{99m}Tc shortages. These reactors have since come back on line and production of ^{99}Mo was able to return to levels seen before the supply shortage. In addition, a few research reactors joined the supply chain (MARIA in Poland, Řež in the Czech Republic and some of the Russian reactors at Dimitrovgrad) or expanded production beyond domestic needs during and following the shortages (OPAL in Australia and RA-3 in Argentina).

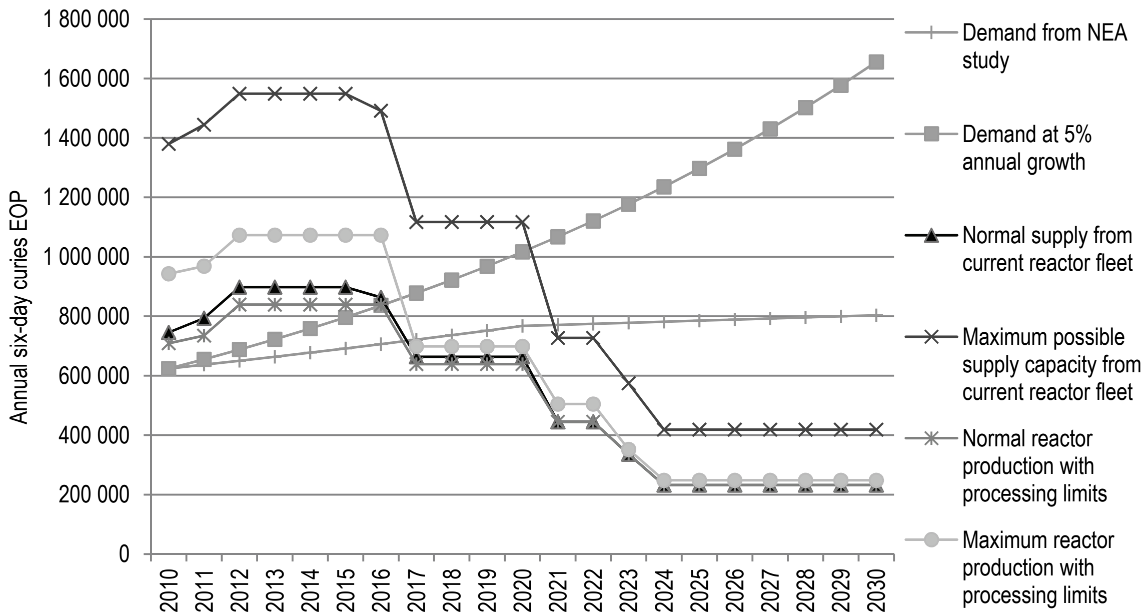
While this is positive news, the current capacity remains fragile and further supply shortages could be expected. A number of the producing reactors in the current ageing fleet are scheduled to be removed from the supply chain over the next decade, with the earliest scheduled for 2015 (OSIRIS) and 2016 (NRU). Coupling these shutdowns with growing demand, supply could be insufficient within the next few years, even considering the reactors that have recently joined the supply chain.

This looming supply shortage could be partially alleviated if reactors were to produce at their maximum capacity during all their production periods and there were no constraints on processing capacity. However, this production scenario is not realistic as it requires the forgoing of other activities in the reactor, such as important research projects, and assumes reactor and processor operating schedules that allow for full use of all the available capacity.

There are a number of factors that reduce the effective processing capacity, including regional limitations, differences between target designs in use, potential processing failures and the potential impacts of the conversion to low enriched uranium (LEU) targets. For example, irradiated targets are very difficult to transport long distances, requiring processing capacity to be located reasonably close to ^{99}Mo-producing reactors. In some regions processing capacity is not currently sufficient to support increased production of ^{99}Mo, to meet increasing demand, to deal with possible reactor outages globally or to address a changing supply structure as older reactors shut down.

Taking all these factors into account, the future supply situation based on the current fleet of research reactor is estimated to be insufficient. Figure E2 shows two demand scenarios.

Figure E2: Current supply versus demand with processing limitations



Long-term demand requires new investments

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

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

The study examined the impact of the key issues facing future demand, including:

- substitution of ^{99m}Tc-based imaging modalities with other modalities;
- development of new radiopharmaceuticals (whether ^{99m}Tc-based or for other isotopes);
- perceptions on stability of future ^{99m}Tc supply;
- whether strategies to cope with the recent shortages would remain;

- growing population, urbanisation and increases in wealth;
- ageing populations and changing prevalence of medical conditions.

The survey results indicate that:

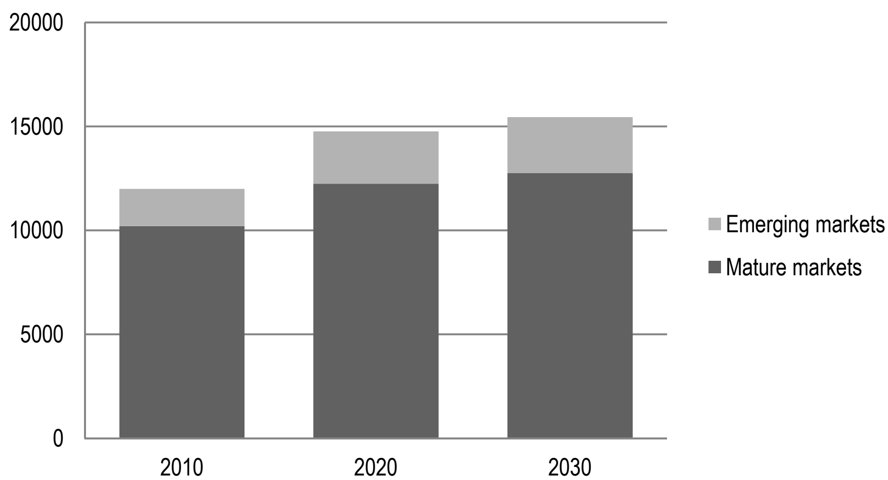
- Most of the changes undertaken during the recent supply shortages are not permanent.
- Substitution of ^{99m}Tc-based procedures by alternative modalities or isotopes will likely have an impact on the overall share of ^{99m}Tc in diagnostic procedures, but will not reduce the absolute amount of ^{99m}Tc being demanded.
- There will be growing demand for ^{99m}Tc at least until 2030, albeit at a slow pace (see Table E1). The share of ^{99m}Tc-based procedures within the overall imaging diagnostic market is expected to fall, but the absolute demand for ^{99m}Tc will not decrease between now and 2030.

Table E1: Expected ^{99m}Tc demand growth

	Mid-term average	Long-term average	Annual growth 2010-2020	Annual growth 2020-2030
Mature markets	~ +20%	~ +25%	~ +1.8%	~ +0.4%
Emerging markets	~ +40%	~ +50%	~ +3.4%	~ +0.6%
Global market	~ +23%	~ +28%	~ +2.1%	~ +0.5%

Note: Mature markets consist of Europe, North America, Japan, Korea and Oceania. Emerging ^{99m}Tc markets consist of South America, Africa and Asia (without Japan and Korea). Emerging markets currently represent about 15% of the global market.

Figure E3: Forecasted ^{99}Mo demand per week (six-day curies)



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

Proposed new projects may not be enough

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

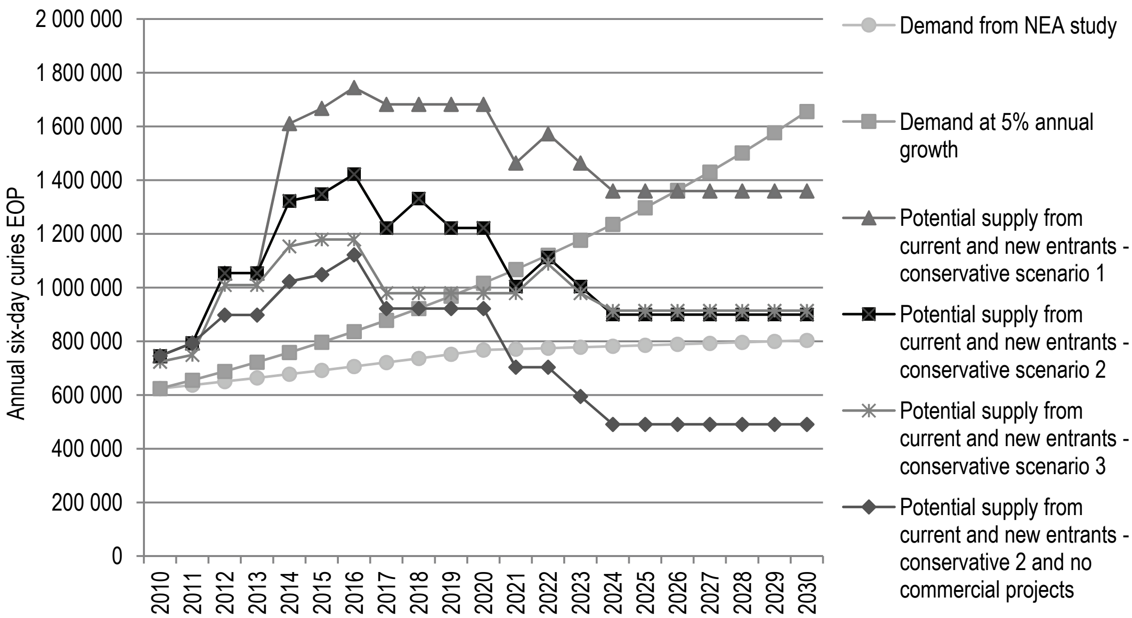
However, there are a number of reasons why this projection may not materialise:

- The values presented do not account for any regional processing constraints which can be a significant barrier to developing new irradiation capacity.
- There are economic and technical hurdles to overcome related to the production of ^{99}Mo via these alternative projects. If these projects proceed without any changes to the fundamental economic structure of the supply chain (explained later in this document), these projects could have a negative effect on other reactor operators, potentially being detrimental to the long-term economic sustainability of ^{99}Mo provision and therefore affecting long-term security of supply.
- Another consideration that may affect security of supply is the ability to procure and transport enriched uranium and to transport radioactive material. At each stage of the supply chain, radioactive material is transported, sometimes across a number of borders or even half-way around the world, requiring multiple approvals in multiple jurisdictions. There is also the concern that shipments of these vital medical radioisotopes are sometimes denied or delayed by carriers. Work is underway in various fora to address these issues, recognising the need to streamline and gain greater harmonisation in approval processes, and to tackle denials of shipment.

Recognising these challenges, Figure E4 presents four scenarios which apply conservatism to the likelihood of all projects succeeding or recognise the potential processing capacity limitations.

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

Figure E4: Potential supply versus demand based on conservative scenarios



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

Even in situations where the research reactor is currently under construction or already in existence, decision-makers should not be lulled into complacency regarding the infrastructure needs for medium- to long-term supply reliability. In all these cases, ongoing concentrated efforts on the part of governments and industry players are required to ensure that the projects do, in fact, come into existence and have the infrastructure to irradiate and process targets for the production of ^{99}Mo.

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

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

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

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

The processing component, originally funded by governments, was commercialised in the 1980s and 1990s. Commercialisation was originally thought to be beneficial to all parties; however, contracts were based on historical perceptions of costs and pricing. This resulted in long-term contracts with favourable terms for commercial processing firms, with no substantial change to the prices for irradiation. Once these contracts were established, they set the standard for new processors and reactors that entered the market.

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

A complicating factor was the historical existence of excess capacity of irradiation services. Some excess capacity is necessary to provide back-up at times when certain reactors are not operating, but operators were not compensated for maintaining this reserve capacity. This created an incentive for reactor operators to use the capacity to gain revenue rather than leaving it idle, driving down the prices of irradiation services further, reducing reliability and perpetuating processor market power.

Further downstream, pricing strategies of generator manufacturers were focused on encouraging sales of their cold kits. These strategies had an effect upstream, with profits not flowing back up the ^{99}Mo supply chain and limiting the flexibility to absorb proposed upstream price increases.

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

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

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

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

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

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

Table E2: Impact of price increases at hospital level

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

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

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

Alternative production technologies should also be considered

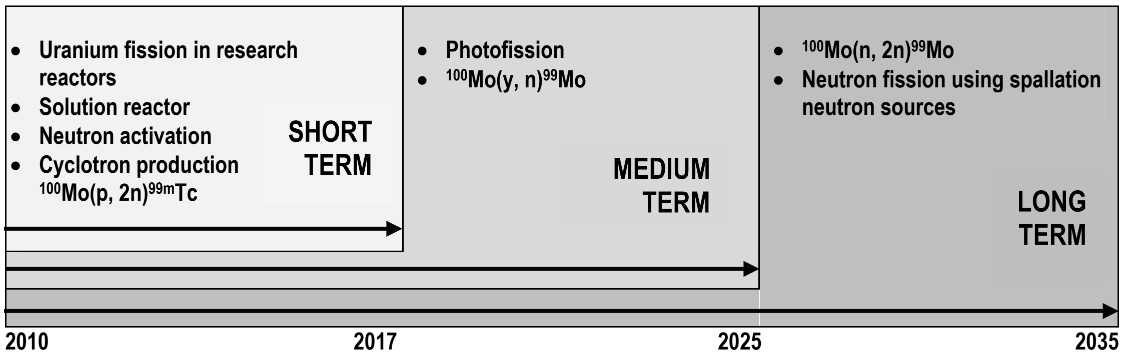
The importance of nuclear medicine and diagnostics throughout the world together with the recent shortage of ^{99}Mo supply has motivated investigations into alternative technologies. Alternative technologies could be reactor-based (such as neutron activation of ^{98}Mo) or accelerator-based (direct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

In order to get a sense of the potential of alternative technologies for producing ^{99}Mo/^{99m}Tc, the NEA, with the help of its HLG-MR and other experts, developed a common set of physical and economic criteria that could be used to compare all the technologies:

- Technology maturity
- Production yield
- Available irradiation capacity
- Distribution range and logistics
- Simplicity of processing
- Waste management
- Proliferation resistance
- Other isotope co-production potential
- Normalised capital costs
- Commercial compatibility
- Estimated levelised unit cost
- Ease of nuclear regulatory approval
- Ease of health regulatory approval
- Units required to supply world market

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

Figure E5: ^{99}Mo/^{99m}Tc production technologies[1]



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

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

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

How can a secure, reliable supply of ^{99}Mo/^{99m}Tc be achieved?

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

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

since the underlying economic problem remains to be adequately addressed. Continued action is required on the part of all stakeholders.

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

The HLG-MR developed the final policy approach around its "central pillars of reform". These pillars recognise the problems being faced by the industry and are the key high-level reforms that the policy approach seeks to address. The central pillars are:

- Market economics need to be improved.
- Structural changes are necessary.
- The government role has to be clearly defined.
- An effective, co-ordinated international approach is necessary.

In developing the policy approach to address the central pillars, the HLG-MR started from the premise that market-based approaches, where possible, should be the basis for policy action to address the market and policy failures that exist in the current economic structure and supply chain. Recognising, however, that the failures are complex, it is clear that there is an essential role for governments to ensure the proper setting in which the problems can be addressed.

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

Principles and supporting recommendations

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

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

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

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

To support effective co-ordination, contracts between reactors and processors should allow for open access to ^{99}Mo irradiation services.

Demand-management options should be encouraged as they could participate to support effective co-ordination efforts.

Processors should voluntarily hold at every point in time outage reserve capacity equal to their largest supply (n-1 criterion), which can come from anywhere in the supply chain as long as it is credible, incremental and available on short notice.

Reserve capacity options should be transparent and verifiable to ensure trust in the supply chain.

Reactor operators, processors and generator manufacturers should review the current contracts to ensure that payment for reserve capacity is included in the price of ^{99}Mo.

Communication efforts, providing three months advance notice to downstream stakeholders on generator supply should continue. In addition, industry communication protocols regarding unplanned outages should be implemented by all industry participants and remain active.

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

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

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

Governments should:

- in co-operation with health care providers and private health insurance companies, monitor radiopharmaceutical price changes in order to support the transparency of costs;
- periodically review payment rates and payment policies with the objective of determining if they are sufficient to ensure an adequate supply of ^{99m}Tc to the medical community;
- consider moving towards separating reimbursement for isotopes from the radiopharmaceutical products as well as from the diagnostic imaging procedures.

Governments should encourage continued supply chain participation in ^{99}Mo/^{99m}Tc production schedule co-ordination efforts, including making such participation mandatory if voluntary participation wanes or commitments are not respected.

Governments should monitor levels of outage reserve capacity maintained by the market and, if found to be below the set criterion, consider regulating minimum levels.

Governments should, where required, support financial arrangements to enable investment in ^{99}Mo/^{99m}Tc infrastructure using various forms of public-private partnerships with appropriate returns.

Governments should consider ^{99}Mo/^{99m}Tc production capacity requirements when planning multipurpose research reactors to ensure that the required capacity is available. However, the funding of the ^{99}Mo-related capacity development should be supported through the commercial market.

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

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

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

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

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

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

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

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

An international expert panel should be established to evaluate the $^{99}Mo/^{99m}Tc$ supply chain every two years.

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

Chapter 1

Introduction

1.1 The issue

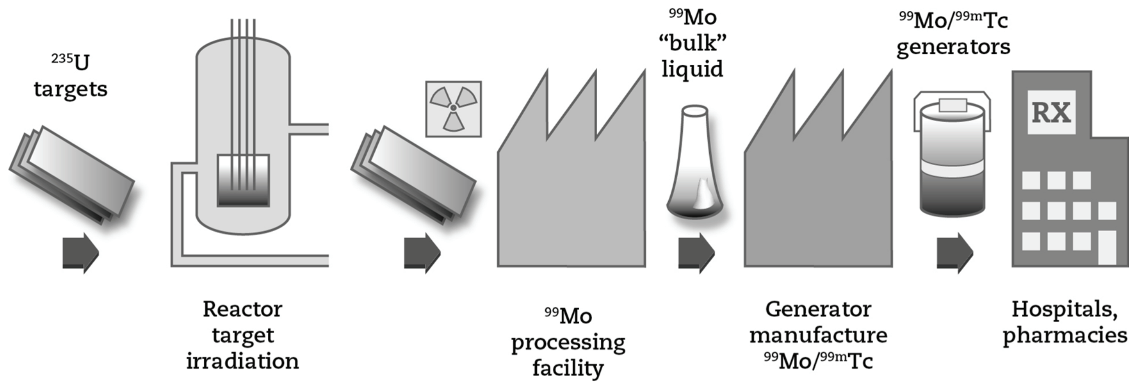
Molybdenum-99 (^{99}Mo) and its decay product, technetium-99m (^{99m}Tc), the most widely used medical radioisotope, are used in medical diagnostic imaging techniques which enable precise and accurate, early detection and management of diseases such as heart conditions and cancer, all in a non-invasive manner. The imaging can significantly impact medical decisions, for example, by providing predictive information about the likely success of alternative therapy options or whether or not there is a need for surgical intervention.

Technetium-99m medical imaging techniques account for over 80% of all nuclear medicine procedures, representing over 30 million examinations worldwide every year. Disruptions in the supply chain of these medical isotopes – which have half lives of 66 hours (^{99}Mo) and 6 hours (^{99m}Tc) respectively and thus must be produced continually – can prevent or delay important medical testing services.

The supply chain consists of uranium target manufacturers, reactor operators irradiating the targets to create ^{99}Mo as part of the fission reaction, processors extracting the ^{99}Mo from the irradiated targets and purifying it to produce bulk ^{99}Mo, generator manufacturers producing generators with the bulk ^{99}Mo, and radiopharmacies and hospital radiopharmacy departments eluting ^{99m}Tc from the generator and coupling it with "cold kits" to prepare radiopharmaceutical doses for nuclear medical imaging of patients (see Figure 1.1). Given the short half-lives of ^{99}Mo (66 hours) and ^{99m}Tc (6 hours), the logistical arrangements have to be quick and predictable, since the economics and medical utility of $^{99}Mo/^{99m}Tc$ depend on minimising decay losses.

Historically, five research reactors commissioned between 45 and 55 years ago produce 90 to 95% of the total global supply of ^{99}Mo. Given the age of these reactors, there are issues related to their reliability with unexpected shutdowns occurring more often. In fact, these isotopes have been in short supply a number of times over the last few years due to unexpected and/or extended shutdowns. Most recently the Canadian National Research Universal Reactor (NRU) was unexpectedly shut down in May 2009 as a result of a leak in the reactor vessel and only returned to service in mid-August 2010.

Figure 1.1: ^{99}Mo supply chain



The ages of the major producing reactors also raise issues related to reactor availability given the need for extended shutdowns for planned maintenance work and possibly for unplanned maintenance. For example, in 2010 both the High Flux Reactor in the Netherlands and the OSIRIS reactor in France were shut down for extended maintenance periods.

Additionally, some of these reactors are expected to reach their end of life in the next six years. The OSIRIS reactor is planned to be retired from service in 2015 and Canada has indicated that it will stop production of ^{99}Mo from the NRU reactor by 2016.

In addition to issues related to the reactors, there are also potential limits to processing capacity. The limitation is especially evident in regards to the geographical location of these facilities; there would be difficult transport problems and loss of product from decay if irradiated targets were to be transported long distances. This capacity is needed to extract and purify the ^{99}Mo from the irradiated targets, making bulk ^{99}Mo for use in ^{99m}Tc generators for medical procedures.

These issues have resulted in ^{99}Mo/^{99m}Tc supply that is currently vulnerable. Actions have to be taken by all stakeholders to improve the long-term security of supply of these important medical radioisotopes.

1.2 Formation of the High-level Group on Medical Radioisotopes

The NEA Steering Committee established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in April 2009 to examine the underlying reasons for the shortage and to develop a policy approach to ensure their long-term security of supply. This group was comprised of 21 experts from 13 countries, the European Commission and the International Atomic Energy Agency, and was funded by its members through voluntary contributions. The group oversaw and assisted, where necessary, efforts of the international community to address the

 THE SUPPLY OF MEDICAL RADIOISOTOPES: THE PATH TO RELIABILITY, ISBN-978-92-64-99164-4, © OECD 2011

challenges of medical isotope supply reliability. The NEA Secretariat supported the group and brought its expertise to the issue. Appendix 1 provides the members of the HLG-MR; Appendix 2 provides the delegated participants who actively supported the work of the HLG-MR members; Appendix 3 provides the NEA Secretariat members.

The main objective of the HLG-MR was to strengthen the reliability of ^{99}Mo/^{99m}Tc supply in the short, medium and long term. In order to reach this objective the group reviewed the ^{99}Mo supply chain, identified the key areas of vulnerability, the issues that need to be addressed and the mechanisms that could be used to address those issues. The HLG-MR recognised that governments have the ultimate responsibility for establishing an environment conducive to investment and also for regulations related to the ^{99}Mo supply chain.

The HLG-MR was aware that there are a number of other on-going fora related to medical isotope security of supply and ensured that efforts were not duplicated. The NEA's goal in getting involved in this issue was to add value to the ongoing work and to support member countries. Bringing the international community together to discuss, share and learn, and applying NEA expertise on nuclear issues and economic studies, represent important contributions to the current global effort.

1.3 The final report

This report provides the findings and analysis of the OECD Nuclear Energy Agency (NEA) High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR). In addition, the report provides the policy approach developed by the HLG-MR that would encourage long-term supply security of ^{99}Mo/^{99m}Tc. The recommendations of the policy approach detail the essential steps to be taken by governments, industry and the health community to address the vulnerabilities within the supply chain, including changing an economic structure that does not support or reinforce security of supply.

The report is organised to follow the supply chain through its various stages. Chapters 2 to 5 deal with the various parts of the supply chain. Chapters 6 to 9 deal with issues that are broader than only one section of the supply chain. Chapter 10 then provides the policy approach developed by the HLG-MR to address the issues and move towards security of ^{99}Mo/^{99m}Tc supply. The appendices to the report provide extra information about the HLG-MR, its mandate, meetings and action plans, the members of the Expert Advisory Group and consultants for the demand study, and further reading.

Chapter 2 is focused on the research reactors: a description of the current fleet; the challenges faced by the fleet; a projection of supply from the current fleet compared to future demand; efforts to co-ordinate reactors schedules; and a discussion of potential new projects and the impact they will have on supply and demand. Chapter 3 provides a discussion of the current situation of processors and generators, and then discusses the constraints related to the processing sector. Chapter 4 discusses the improvements that have occurred related to the communication of unexpected events. Chapter 5 provides the results of a demand study undertaken by the NEA to get an understanding of the long-term demand for ^{99m}Tc and ^{99}Mo.

Chapter 6 provides information about the major processes related to transportation and procurement within the supply chain and the issues around those processes, and provides recommendations to increase reliability and consistency. Chapter 7 highlights that the recent shortages are symptomatic of an uneconomical supply chain. Chapter 8 provides a review of $^{99}Mo/^{99m}Tc$ production technologies. Chapter 9 briefly describes the iodine-131 supply chain and demonstrates that vulnerability in research reactors affects other key isotopes. Chapter 10, as noted above, provides the culmination of the past two years of work by the HLG-MR and nuclear medicine stakeholders – the policy approach to address the issues and move towards security of $^{99}Mo/^{99m}Tc$ supply.

The release of this report in June 2011 concludes the mandate of the HLG-MR.

Chapter 2

Reactor Irradiation Capacities

2.1 Current situation

Historically, there were only five reactors that produced 90 to 95% of global ^{99}Mo supply: three in Europe (BR-2 in Belgium, HFR in the Netherlands and OSIRIS in France), one in Canada (NRU), and one in South Africa (SAFARI-1). All these reactors are over 45 years old. In the past, the Cintichem reactor in the United States, the FRJ-2 reactor in Germany, the NRX in Canada and the SILOE reactor in France also produced ^{99}Mo for the global supply chain. However, all of these reactors have been shut down: Cintichem in 1989, NRX in 1992, SILOE in 1997 and the FRJ-2 in 2006.

There are also the OPAL reactor in Australia and the RA-3 reactor in Argentina, which predominately produce for their local markets but have recently been exporting small quantities of ^{99}Mo (IAEA, 2010). The OPAL reactor has the potential to increase production substantially but is currently limited by the local processing capacity.

The newest additions to the ^{99}Mo global supply chain are the MARIA reactor in Poland, which started producing ^{99}Mo for global distribution in February 2010, the LVR-15 reactor in the Czech Republic, which started producing ^{99}Mo for global distribution in May 2010, and the ROSATOM reactors, which will produce ^{99}Mo for global distribution in 2011. There are also various reactors around the world that produce small quantities of ^{99}Mo for domestic use. Table 2.1 provides further information on the major ^{99}Mo producing reactors.

As mentioned above, the five main reactors were commissioned between 45 and 55 years ago. As the reactors age there is the requirement for longer downtime periods between production cycles to repair or replace ageing parts or to undertake additional inspections to determine the effects of ageing on the reactor. This requirement follows the increased likelihood of failures, as many components are not observable or serviceable without extended maintenance shutdowns (AECL, 2009). During these extended downtimes, the reactor is not irradiating materials to produce any ^{99}Mo.

In the past, the supply impacts of the regular downtime periods would normally be smoothed out by other reactors. The duration of the required extended maintenance periods has, however, created the need for longer-term expanded production at other reactors, leading to planning issues (including difficulty in balancing reactor operations with other research projects). In addition, these extended periods have become more frequent, leading to situations where more than one reactor is shut down at the same time. For example, in summer 2010 the HFR, the NRU and the OSIRIS reactor were all down for extended periods. As a result, the impacts of these extended periods of insufficient capacity are often no longer able to be smoothed out, greatly affecting the downstream component of the supply chain, especially the final user – the patient.

Table 2.1: Major current ^{99}Mo producing reactors

Reactor name	Location	Annual operating days	Normal production per week when operating[a]	Typical weekly % of world demand supplied when operating	Fuel/targets[b]	Date of first commissioning
BR-2	Belgium	120	5 200[c]	25-65	HEU/HEU	1961
HFR	Netherlands	300	4 680	35-70	LEU/HEU	1961
LVR-15[d]	Czech Republic	–	>600	–	HEU[e]/HEU	1957
MARIA[d]	Poland	–	700-1 500	–	HEU/HEU	1974
NRU	Canada	300	4 680	35-70	LEU/HEU	1957
OPAL	Australia	290	1 000	–[f]	LEU/LEU	2006
OSIRIS	France	180	1 200	10-20	LEU/HEU	1966
RA-3	Argentina	336	300	<2	LEU/LEU	1967
ROSATOM[g]	Russian Federation	365	900[g]	–[g]	HEU/HEU	1961-1970
SAFARI-1	South Africa	305	2 500	10-30	LEU/LEU[h]	1965

a. Six-day curies end of processing (EOP) during weeks when reactor is operating.

b. Fuel elements and targets are classified as either low enriched uranium (LEU), containing less than 20% of ^{235}U, or highly enriched uranium (HEU),which contains greater than 20% ^{235}U (in some cases greater than 93%).

c. Does not account for increase in capacity since April 2010 with the installation of additional irradiation capacity. This increases BR-2 available capacity to approximately 7 800 6-day curies EOP; however it is not yet clear what "normal" production will be at the facility with this new capacity.

d. These reactors started production in 2010 so some data are not yet available.

e. The LVR-15 reactor uses fuel elements that are enriched to 36% ^{235}U.

f. The OPAL reactor started ^{99}Mo production in 2009 for domestic use but has not yet exported significant amounts.

g. The project includes three reactors, two of which would be used to produce ^{99}Mo in a continuous fashion, with the third being a back up. ROSATOM indicated that they would start irradiating ^{99}Mo targets on a regular basis in 2011 in Dimitrovgrad-based Research Institute of Atomic Reactors (RIAR) at approximately 900 6-day curies EOP/week, with an expectation that the reactors would produce approximately 2 500 6-day curies EOP/week in 2012. Data are not yet available on typical weekly percentage of world demand as, at the time of publication, the production was not yet regular. ROSATOM has indicated that they are expected to produce up to 20% of world demand when operating by 2012.

h. SAFARI-1 is in the process of converting to using LEU targets (from targets with 45% ^{235}U) and expects to have completed conversion by the end of 2011, pending their customers receiving health approval to use their LEU-based ^{99}Mo.

A consequence of ageing reactors that is even more important for the reliable supply of ^{99}Mo is the increased occurrences of unexpected shutdowns at producing reactors. Between 2000 and 2010, there have been six unexpected shutdowns related to reactor safety concerns (Ponsard, 2010). Most recently the NRU was shut down in May 2009 as a result of a leak in the reactor vessel and it was returned to service in mid-August 2010, after an extended outage that lasted more than a year. During part of that out-of-service period, the HFR reactor was shut down for extended maintenance. These unexpected shutdowns disrupt the supply chain, especially when they occur at one of the two major production reactors (HFR and NRU); it is impossible for the other reactors to respond to these situations at very short notice by adding an additional production cycle or increasing production capacity.

Not all these reactors have aged at the same pace given specific operating schedules and maintenance programmes. Both the SAFARI-1 and BR-2 reactors expect to continue operations to 2022 and possibly beyond; the former partly as a result of its low usage between 1977 and 1993, and the latter as a result of a major refurbishment that occurred between 1995 and 1997. However, the OSIRIS reactor is planning to be retired from service in 2015, the Government of Canada has indicated that it will only seek to extend the NRU reactor licence to produce ^{99}Mo to 2016, and the HFR reactor is expected to be shut down around 2020.

The implications of these ageing reactors for reliable ^{99}Mo supply create economic factors that need to be addressed. As is discussed in Chapter 7 of this report and in the NEA publication, *The Supply of Medical Radioisotopes: An Economic Study of the Molybdenum-99 Supply Chain* (NEA, 2010a), the current economic return on producing irradiated targets containing ^{99}Mo at the reactor is not sufficient to support the development of new infrastructure for the production of ^{99}Mo; a new multi-purpose research reactor has been estimated to cost more than EUR 400 million.

An additional challenge that will affect the reactor component of the supply chain is the move to replace targets using highly enriched uranium (HEU) with targets using low enriched uranium (LEU) for security and non-proliferation reasons. As shown in Table 2.1, most of the major research reactors are currently using HEU targets to produce ^{99}Mo. However, all ^{99}Mo producing nations have agreed to encourage the conversion to LEU targets, where technically and economically feasible, most notably at the Washington Nuclear Security Summit in April 2010. In fact, one major producer (NTP) converted their reactor and processing facilities to be able to use LEU targets in 2010 (from targets of approximately 45% ^{235}U). NTP is already producing LEU-based ^{99}Mo for Lantheus Medical Imaging and it is expected that once health regulatory approvals have been received for their remaining customers, NTP will move to 100% production using LEU targets. There are also two reactors (the OPAL reactor in Australia and the RA-3 reactor in Argentina) that already use LEU targets, currently producing principally for their local markets.

The main technical issue is the obvious fact that LEU targets contain less ^{235}U compared to the HEU targets currently being used. Since ^{99}Mo is a product of the fission of ^{235}U in the targets irradiated in the reactor, there is an impact on the yield of product from a target with less ^{235}U. Two ways to compensate for this are to increase the density of total uranium in the targets or to increase the number of targets irradiated. While LEU targets have higher specific density that HEU ones, this is still a source of much current research, as is the development of new technologies and targets to increase yields. An increase in the number of targets irradiated may affect other missions within a research reactor or may require more irradiation positions, which may not be available.

Without further density augmentations, an increase in costs per curie produced will occur, as there will be a need for some degree of additional irradiation and processing capacity to continue to produce the same quantity of ^{99}Mo globally, depending on the uranium density that can be achieved in the target. There may also be an increase in waste management costs (capital and operational) since, in general, more total uranium waste and liquid wastes will need to be managed. However, until final disposal strategies are implemented, it is difficult to quantify the cost increases. Reduced physical protection costs as a result of dealing with LEU instead of HEU may help to partially offset any potential cost increases of using LEU targets.

At this time there is not yet an established body of knowledge as to the comparative yield, waste management costs, development costs, capital requirements and the related economic impacts that would be experienced by a major ^{99}Mo producer wishing to undertake conversion. Preliminary experience and estimates have indicated that the impact of conversion on the cost of the final health procedure is expected to be quite small. However, even with the uncertainty on the costs of conversion, it is clear that while the conversion to LEU targets is necessary, it is not currently supported financially by the market (NEA, 2010a).

An additional challenge facing the reactor component of the supply chain is related to the need for reserve capacity. There are two main reasons why this capacity is needed: i) to account for operational realities of research reactors and the technical characteristics of ^{99}Mo (explained below); and ii) to serve as a back-up in the event of unscheduled outages. However, the need for, and existence of, reserve capacity raises some economic challenges that will be discussed in Chapter 7 of this report.

With respect to the first reason, the key issues are the operational nature of research reactors, which also perform missions other than isotope production, and the extreme inefficiencies in stockpiling ^{99}Mo with its 66-hour half-life. Research reactors do not operate 100% of the time; they operate on the basis of cycles, with a number of days operating and then a period where the reactor is shut down for refueling, changing research project set-ups, regular maintenance, etc. In addition, some reactors do not operate for the full year, depending on their research demands and available funding (Table 2.1 provides the approximate operating days of the main ^{99}Mo producing reactors). Other reactors need to be able to irradiate targets during these shutdown periods, especially for those of longer duration, to ensure a smooth supply of ^{99}Mo to the market.

With respect to the second reason, the key issue is the reliability of producing reactors. When a reactor is unexpectedly shut down as a result of a technical problem or a safety concern that requires an extended repair period, the remaining reactors need to respond quickly to increase production of ^{99}Mo if the market supply is to be sustained at normal levels. Sustaining these levels is desired by the medical community so that patients can continue to have access to this medical nuclear imaging technique. As reactor availability and operational reliability decrease, the need for reserve capacity increases. The combination of reactor availability and the reliability issue becomes the main reason or rationale for reserve capacity, particularly as the reactors age and the occurrence of unexpected or extended repair shutdowns increases. In parallel, the market demand for ^{99m}Tc has continued to increase.

As a result of the two issues above, if one were to merely add up the irradiation capacity at the producing reactors it should significantly exceed 100% of demand. However, at any one moment in time the producing capacity should, in a preferred scenario, be just sufficient to meet global distribution and demand.

Currently, the available producing capacity of reactors exceeds the demand for ^{99}Mo. However, the recent supply shortage has drawn attention to the capacity of the ^{99}Mo/^{99m}Tc supply chain and the fact that there is a long-term supply issue looming. Figure 2.1 shows the supply situation out to 2030 based on the annual production of the current fleet of reactors and their expected final shutdown dates, compared to two demand scenarios (discussed further in Chapter 5).[1] The figure shows that if the current suite of reactors were producing at normal levels, demand would exceed the normal supply of ^{99}Mo by 2016 in a situation of 5% annual growth and by 2017 in a situation of approximately 2% annual growth to 2020 followed by slower growth between 2020 and 2030. In addition, reactors can produce above their normal levels for limited time periods, when required. Assuming that reactors were able to produce at their maximum capacity[2] during all of their production periods and processing facilities were unconstrained, this supply shortage would be postponed until around 2020 for the 5% scenario and 2021 for the NEA projected growth scenario. However, this latter production scenario is not realistic as the maximum production at most reactors would require the forgoing of other activities in the reactor, such as important research projects, and assumes perfect synchronisation of reactor and processor operating schedules that allows for full use of all the available capacity – a situation that is often not the case.

Another consideration when looking at future supply and demand is whether there are limitations to processing irradiated targets from the reactors. Figure 2.2 builds on the last figure by adding in data related to limitations in regional processing capacity. This regional limitation can impact the ability of reactors to utilise their full ^{99}Mo production capacity, under normal and maximum operating conditions (this issue will be discussed in more depth in Chapter 3). With these regional processing limitations the dates when demand exceeds supply will occur sooner under the maximum production scenario, occurring as early as 2017.

---

[1] One demand scenario was developed based on an NEA project to assess long-term demand and represents a growth rate of approximately 2% per year out to 2020 and then a levelling off to less than 1% per year between 2020 and 2030; the other scenario assumes 5% annual growth, which is likely to be too high, but presented for comparative purposes. Additional information on the NEA demand project is provided in Chapter 5.

[2] Based on information from reactors on past maximum production levels or potential maximum production.

Figure 2.1: Current supply versus demand

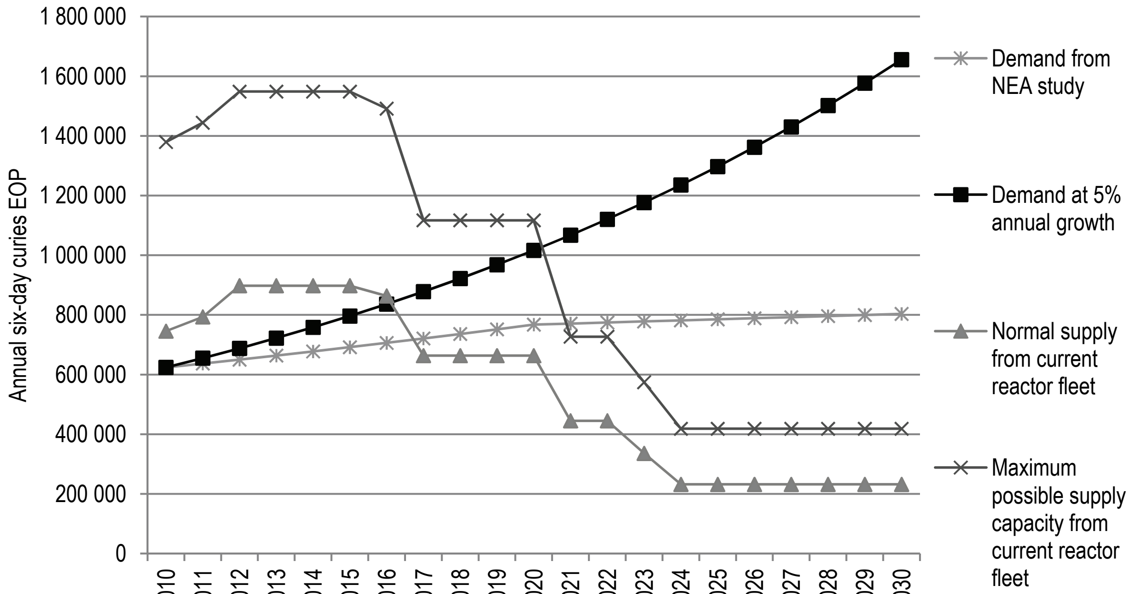
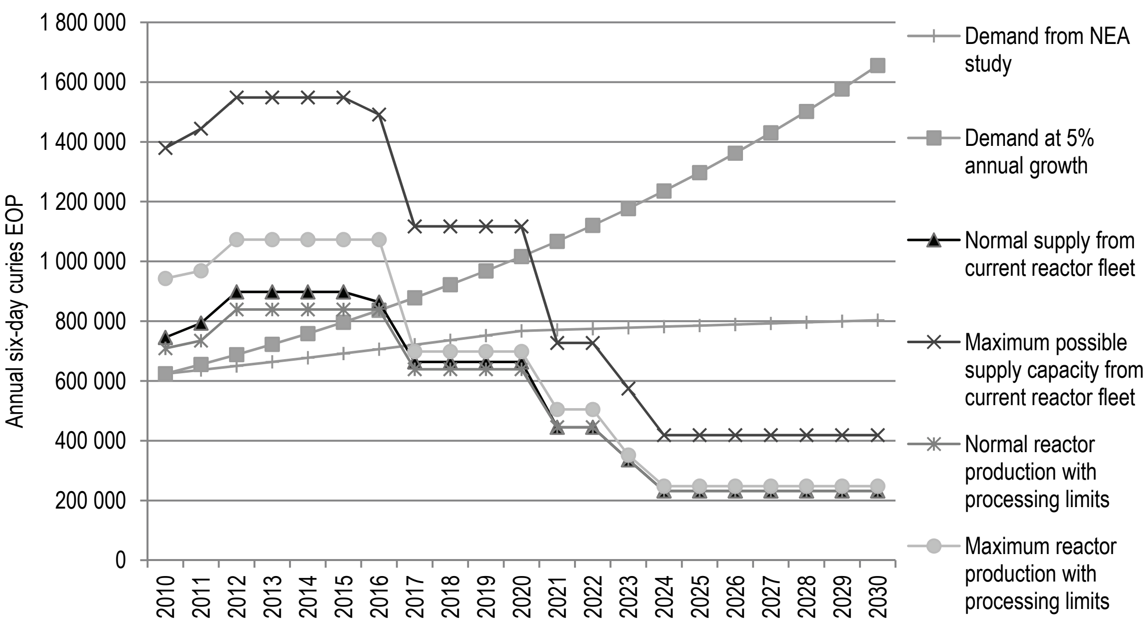


Figure 2.2: Current supply versus demand with processing limitations



The 2009 to 2010 supply shortages highlighted reliability concerns of the current reactor fleet, but the looming reactor and processing capacity limitations create significant challenges for continued supply in the short, medium and long term. The ^{99}Mo supply chain requires new production infrastructure but there are some significant barriers to its development, as will be discussed in Chapter 7.

2.2 Reactor scheduling co-ordination

In order to ensure the best use of the suite of available reactors during the 2009-2010 shortage period, the HLG-MR sought to better understand the available capacity and the production schedules, with a goal to encourage co-ordination among reactor operators. Without co-ordination, each reactor operator would determine their production schedule without the knowledge of the other capacity expected to be used. It was recognised that co-ordination would help to eliminate this uncertainty and ensure that the most beneficial production decisions are taken.

Following its first meeting, the HLG-MR asked the Association of Imaging Producers and Equipment Suppliers (AIPES) to work with its members to better co-ordinate reactor schedules in order to minimise the effects of the on-going and expected reactor outages. The goal was to be able to provide a schedule for the following 12-month period that would attempt to smooth out supply shortages and, where not possible, would provide advance notice to stakeholders to allow for better planning on their use of ^{99}Mo and ^{99m}Tc.

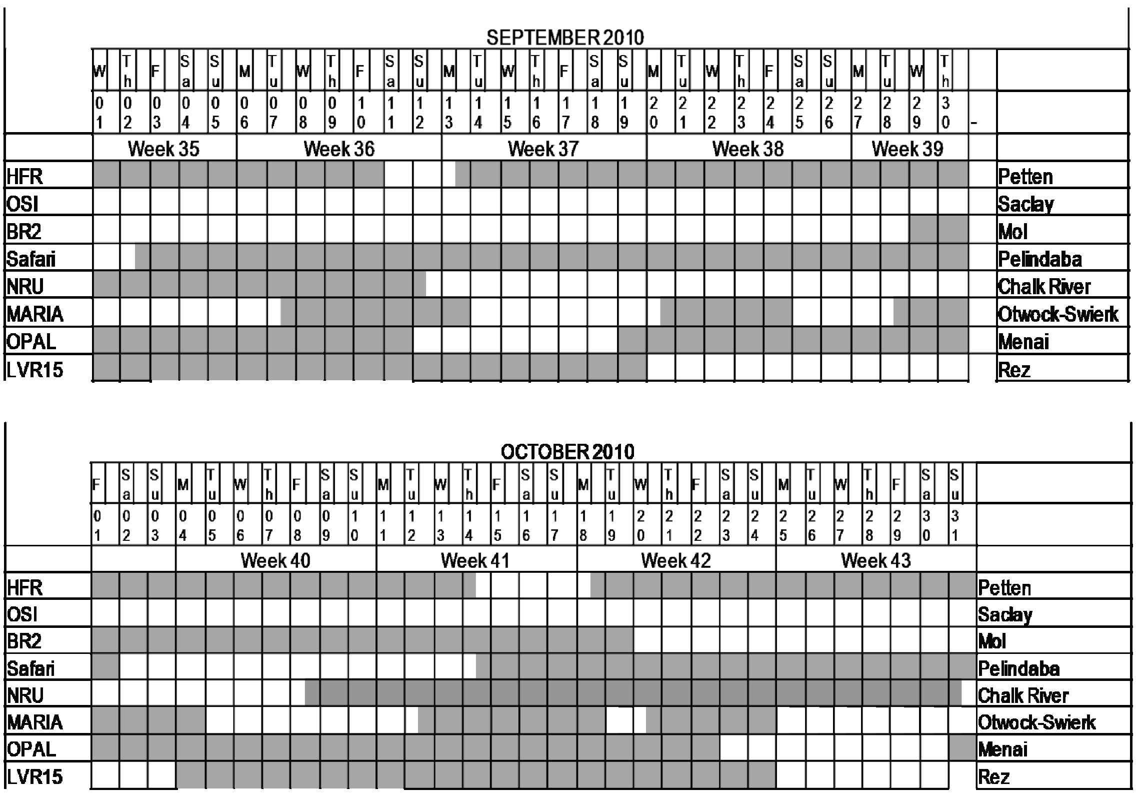
AIPES had already been managing reactor schedule co-ordination on a European scale. They moved to co-ordinate operating periods of reactors on a global scale and therefore undertook intensive communication between all its members and relevant non-members on capacity, timing, output, maintenance schedules and incidents. AIPES members, who now include all of the major reactor operators and processors, participated in these co-ordination discussions on a voluntary basis.

The co-ordination efforts were not straightforward, given the difficulties in defining the exact periods and timing of certain repairs. During the co-ordination process, it was necessary for AIPES and its members to consider the number of production days of each reactor, the planned or contracted research activities at the reactors, other priority contractual industrial activities, commercial agreements, the financing capacity and the number of trained and certified staff at the reactors and processing facilities. In addition, co-ordination efforts recognised the priority of safety and the role of national safety authorities. Of course, reactors and processors required approval for any significant changes to operations and schedules by national nuclear regulatory authorities and at times related ministers.

Under these constraints, reactors, processors and AIPES were able to arrive at a schedule that recognised the necessary repair work and maintenance periods, but that was able to minimise the periods of time when very little supply coverage was available. Through these efforts, schedules were altered and changed to increase supply availability in 2010; BR-2 added an additional cycle and the OSIRIS altered the timing of their extended shutdown period. In addition, all operating reactors and processors increased their level of production, where possible. Even with these efforts there were periods of significant shortages given that the NRU, one of the major reactor suppliers, was out of service from May 2009 until August 2010, and that the HFR, the other major reactor, was out of service from February to September 2010. However, the shortages would have been significantly worse if it was not for these co-ordination efforts. Figure 2.3 presents the results of these co-ordination efforts (as presented in June 2010). These co-ordination efforts are continuing and reactor schedules are derived on an annual basis, recognising that they may have to be updated where possible to respond to unforeseen events.

Moving forward, these co-ordination efforts will continue to be required to minimise shortages during unexpected events. In addition, as more capacity is added in the future, co-ordination efforts will be important for the proper management of reserve capacity to avoid the potential for price depression. This depression would negatively affect the ability of reactors to support ^{99}Mo production. Co-ordination efforts will need to ensure that this reserve capacity is not used to service the market when it is not required (NEA, 2010a).

Figure 2.3: Reactor schedule



Source: Cabocel and Turquet de Beauregard, 2010.

2.3 Potential new reactor-based ^{99}Mo production capacity

With the backdrop of the 2009-2010 shortage, ageing reactors and the impending longer-term shortage, a number of stakeholders are suggesting new projects to produce ^{99}Mo/^{99m}Tc. Many of these projects are reactor-based using existing research reactors that are currently not producing ^{99}Mo or new reactors that are at various stages of development. There are also proposed projects that are based on alternative technologies, such as irradiation in power reactors or using accelerators or cyclotrons. Chapter 8 discusses some of the key alternative production technologies based on the NEA publication "Review of Potential Molybdenum-99/Technetium-99m Production Technologies" (NEA, 2010b).

Some of the potential projects discussed in late 2009 have already become a reality. For example, in February 2010 Covidien and POLATOM announced that they were irradiating HEU targets at the MARIA reactor (Poland) for processing at Covidien's processing facility. In May 2010, IRE and Nuclear Research Institute of Rez announced that they were irradiating HEU targets at the LVR-15 reactor (Czech Republic) for processing at IRE's processing facility. ROSATOM has started producing ^{99}Mo and in 2011 will start regular production at approximately 900 6-day curies EOP/week. ROSATOM has indicated that by 2012 they will be producing 2 500 6-day curies EOP/week at their facilities.

With these announced potential reactor projects, it appears that there are many opportunities for production that are under consideration or development. Table 2.2 presents the various projects with their potential annual production and estimated production starting dates. Plotting these projects both independently and with current reactor capacity gives Figure 2.4 (including the shutdown of the various reactors of current fleet over the next decade, as presented in Figure 2.1). If all the capacities in Figure 2.4 were achieved, it would appear that there will be few concerns on supply as the potential projects should apparently be able to produce enough ^{99}Mo to meet growing demand.

However, this possible outlook assumes that all the projects go forward and that there are no other limiting factors that could affect the ability to get the product to market. For example, the values presented do not account for any regional processing constraints. These processing constraints are not included in the figure, as some of the projects include processing capacity and there is less information available on possible new processing capacity. However, as will be made clear in the next chapter, if there is no processing capacity in place, the new reactor capacity is not useful for increasing available ^{99}Mo supply. In addition, a number of the existing and proposed projects rely on HEU targets; the planned conversion to LEU targets will have an impact on multiple aspects of the production and supply chain.

Another possible limitation in terms of the timing of these projects supplying ^{99}Mo/^{99m}Tc to the market is related to transportation and health regulatory approval. The transportation of the isotopes has to be approved by all relevant jurisdictions (discussed more in Chapter 6) and all new sources of ^{99}Mo for pharmaceutical use have to be separately approved by health authorities in various markets. These regulatory approvals take a certain period of time and could result in supply reaching the market at a later time period than presented in Figures 2.4 and 2.5. However, it is clear that these regulatory review processes are important and necessary.

Table 2.2: Potential reactor-based projects for large-scale ^{99}Mo production

Reactor	Six-day ci EOP/yr	Six-day ci EOP/wk	Weeks/yr	Potential first year
Projects with processing facilities as part of project				
Northstar*	156 000	3 000	52.0	2012
Babcock and Wilcox	144 000	3 000	48.0	2014
China Advanced RR**	25 700	1 000	25.7	2015
SAFARI-2	108 930	2 500	43.5	2022
Projects requiring additional processing facilities****				
FRM-II***	124 800	3 640	34.3	2014
GE-Hitachi	144 000	3 000	48.0	2014
INR, Pitesti***	31 200	875	35.7	2014
Morgridge Institute for Research	144 000	3 000	48.0	2014
Jules Horowitz**	108 000	3 000	36.0	2015
BMR – Brazil	24 000	1 000	24.0	2017
PALLAS	312 000	7 280	42.85	2018
MYRRHA	156 000	4 550	34.3	2023
RA-10				

* The Northstar project is sourcing ^{99}Mo from the MURR reactor starting in 2012 from a neutron activation process; it is expected that they will use an accelerator for the neutron activation once it is available.

** Under active construction.

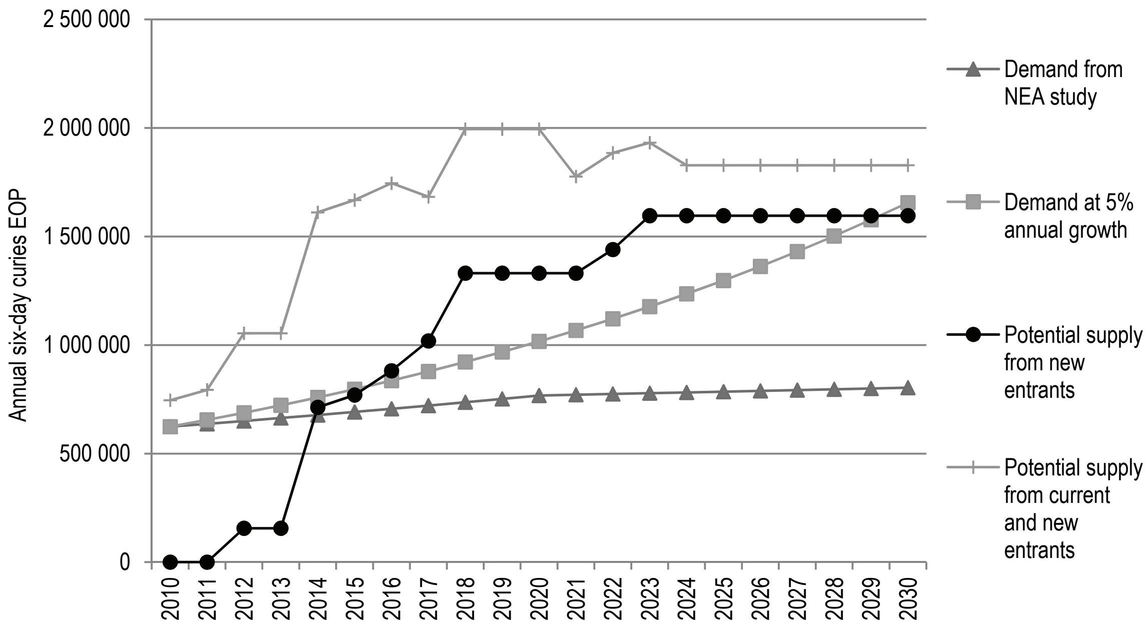
*** Research reactor already exists, but is not yet irradiating targets for ^{99}Mo production.

**** Projects in Europe would face a processing capacity limitation, explained in more detail in Chapter 3.

There are still economic and technical hurdles related to the production of ^{99}Mo via these alternative projects to overcome. If these projects materialise without any changes to the fundamental economic structure of the supply chain, these projects could have a negative effect on the current supply chain economics being faced by reactor operators. Depending on the remuneration provided to reactor operators and the related agreement with the host government, new projects could potentially be detrimental to the long-term economic sustainability of LEU-based ^{99}Mo provision. If any new project follows the historical remuneration model, paying only for the direct costs of irradiation with no or partial payment for the reactor investment costs directly related to ^{99}Mo production, it will be the responsibility of the host government to cover those costs not included. As a result, the continued production of ^{99}Mo under this situation will depend on the agreement with the host government (NEA, 2010a).

Overall, while these projects could help the supply situation if they proceed (and the processing capacity is available), the economic impacts on the market of the mix of commercial-based and government-supported projects could be detrimental to longer-term supply availability. If the pricing structure perpetuates the current economic situation whereby there are not sufficient financial incentives for new ^{99}Mo production infrastructure without government assistance, the commercial-based projects may not be able to come to fruition.

Figure 2.4: Potential supply versus demand

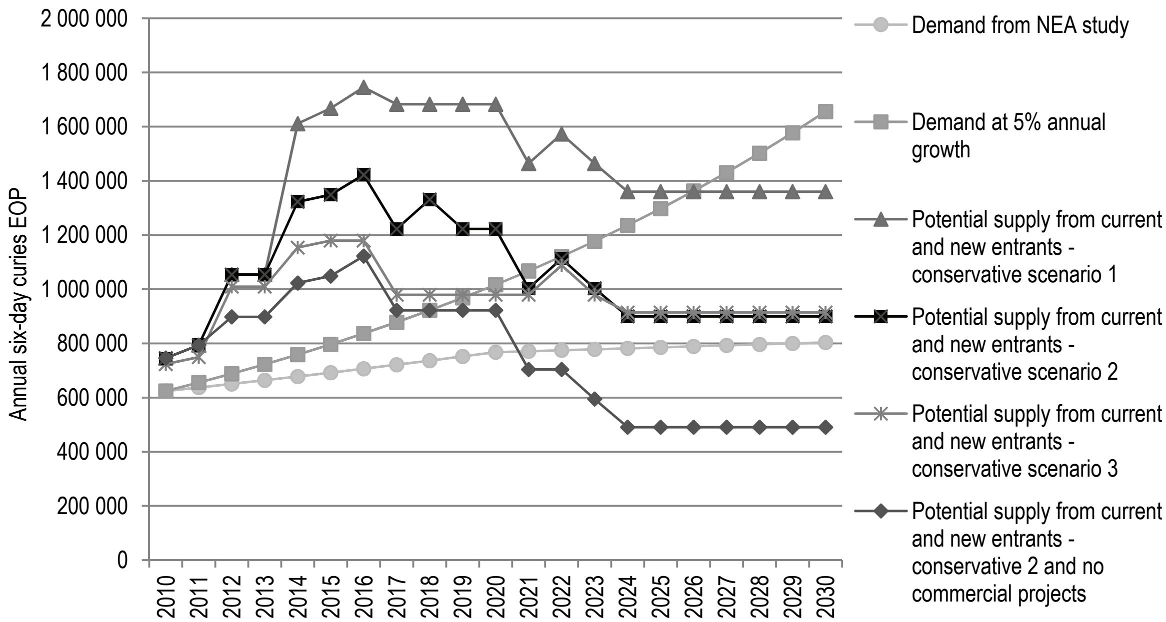


Recognising the challenges in ensuring a project moves forward, Figure 2.5 presents four scenarios where some of the projects identified in Table 2.2 and included in Figure 2.4 do not proceed and therefore do not produce ^{99}Mo for the global market. These four scenarios should not be construed as a prediction, forecast or expectation of which projects will proceed; they are entirely meant as illustrative of situations where some of projects do not proceed. The "conservative scenario 1" includes all the current producers and the potential projects listed in Table 2.2 with the exception of the PALLAS and MYRRHA projects. This scenario was created to show the impact if the two largest potential projects do not proceed as planned. The "conservative scenario 2" is more restrictive, only including the current producers and the following potential projects: Northstar, Babcock and Wilcox, FRM-II, China Advanced RR, Jules Horowitz and the SAFARI-2.

The "conservative scenario 3" eliminates any projects that do not have processing facilities available and accounts for processing limitations where they currently exist. For the scenario all the current producers are included; however, there is an annual processing capacity limitation in Europe (explained further in Chapter 3) meaning that for the European projects, the amount that can be processed in any given year is included as the capacity, if a limit exists. In terms of the potential projects identified in Table 2.2, the projects that currently are included in this scenario are: Northstar, Babcock and Wilcox, China Advanced RR and SAFARI-2, as well as any production from the current European reactors, and the FRM-II and Jules Horowitz for which there is processing capacity available.

The "conservative scenario 2 and no commercially-based projects" eliminates those projects from conservative scenario 2 that have indicated that they are fully commercial. This scenario is to reflect what may happen if the economic conditions of the current supply chain (see Chapter 7) remain and as a result, commercial-based production would not be economically viable.

Figure 2.5: Potential supply versus demand based on conservative scenarios



It is clear that the very positive medium-term outlook that was presented in Figure 2.4 becomes less optimistic when the potential that some projects do not proceed or do not produce ^{99}Mo is taken into consideration. Even if some of the projects proceed, there could be a shortage in the coming decades as the current fleet stops producing ^{99}Mo and demand continues to increase; in addition, the level of capacity that would be available as back-up would be greatly reduced. When the limitations on processing capacity are included in these possible future scenarios, the outlook becomes even less secure, with possible supply shortages starting as early as 2019 under the 5% growth scenario. Of even more concern is the future provided by the scenario where the economic situation does not change and therefore those projects which are clearly commercial based do not proceed. Under this scenario, possible supply shortage start as early as 2018 under the 5% growth scenario and in 2021 under the more realistic demand growth derived from the NEA demand study. It should be noted that this scenario still includes projects in "government-funded" reactors; however project proponents of these projects have also indicated that they will be looking for full-cost recovery. As a result, if the economic situation does not change, this scenario could become even more of a concern.

Another factor to keep in mind is the necessary conversion to using LEU targets for producing $^{99}Mo/^{99m}Tc$. As noted earlier, all producing nations have agreed to LEU conversion for the production of medical radioisotopes, where technically and economically feasible. This conversion process may have an impact on the production capacity of the available reactors. Taking this into account may result in supply shortages, based on the available and predicted capacity, within the next five years, depending on the pace to conversion and the results of efforts to increase density in LEU-based targets.

These potential projects provide the future source of reactor-based ^{99}Mo production and are currently seen to be necessary to ensure the reliable supply of $^{99}Mo/^{99m}Tc$ in the medium to long term. The fact that the projects are being discussed should not be a reason for decision makers to assume that they will proceed. Even with projects where the research reactor is currently under construction or already in existence, decision makers should not be lulled into a situation of complacency to the infrastructure needs for medium- to long-term supply reliability. In all these cases, on-going concentrated efforts on the part of governments and industry players are required to ensure that the projects do, in fact, come into existence and have the infrastructure to irradiate targets for the production of ^{99}Mo and have access to sufficient processing capacity.

Chapter 3

Processing Capacities and Constraints

3.1 Introduction

During the 2009-2010 shortage of medical radioisotopes, there has been much attention focused on the current and future capacity of reactors to produce these isotopes. What is often missed in the examination of the situation is whether there are limitations to processing facilities that either create or perpetuate unreliability in the supply chain.

The processing component of the supply chain generally involves the transportation of the irradiated targets from the reactor to the processing facility, the extraction of ^{99}Mo from the target and the purification of the ^{99}Mo. At these facilities the irradiated targets are dissolved through chemical processes and the ^{99}Mo is separated and then purified through additional chemical processes to produce raw ^{99}Mo. This very complex and demanding process is required to obtain the bulk ^{99}Mo and to ensure that it meets or exceeds the minimum levels of impurities that are required for its medical application. Once purified, the bulk ^{99}Mo is transported around the world from the processing facility to generator manufacturing facilities, predominately on roads and commercial airlines, to be prepared for application in medical procedures.

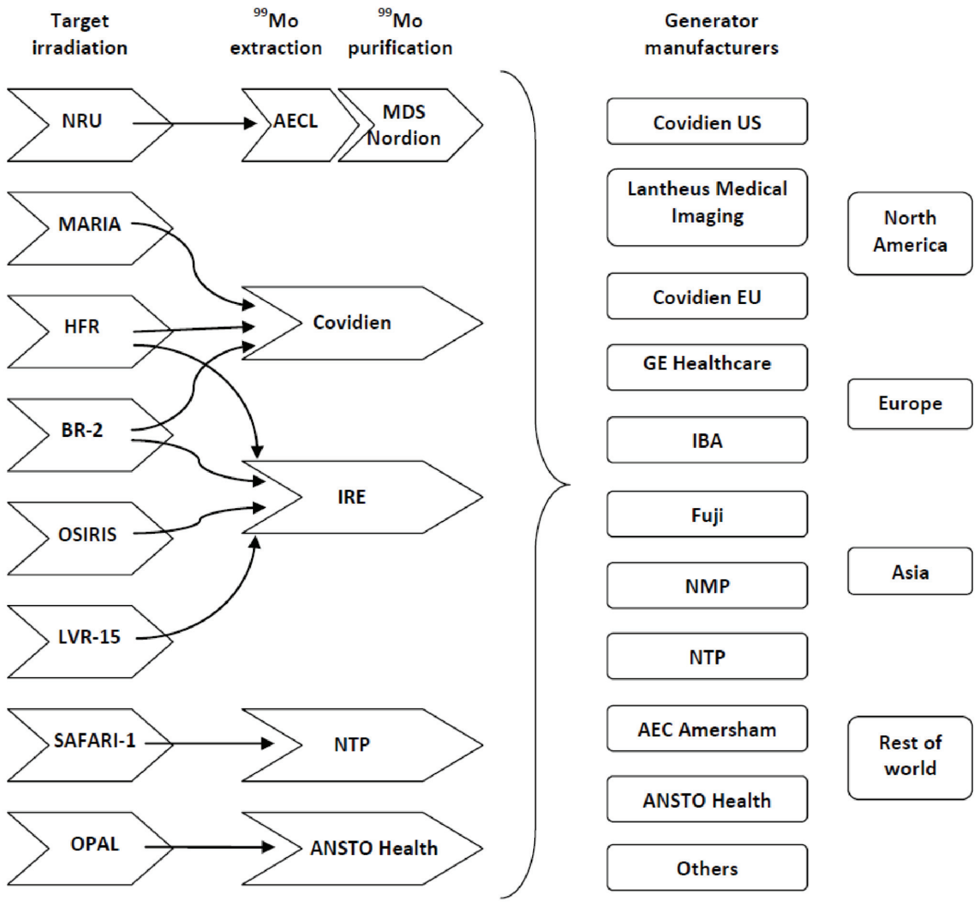
The important question is: are the processing facilities capable of meeting the world's demand or are there constraints that could reduce the reliability of the supply of ^{99}Mo even if there is sufficient reactor capacity?

3.2 Current situation

There are four main processors that supply the global market: MDS Nordion (Canada); Covidien (the Netherlands); the Institute for RadioElements (IRE, Belgium); and NTP Radioisotopes (South Africa). In addition, ANSTO (Australia) and CNEA (Argentina) currently produce bulk ^{99}Mo for their domestic markets and expect to be or are exporting smaller amounts. The unique situation in Canada must be pointed out here; AECL irradiates the targets and also does the initial extraction of the ^{99}Mo from the irradiated target. This extracted ^{99}Mo is then shipped to MDS Nordion for purification. Figure 3.1 provides an overview of the full supply chain.

Prior to the NRU shutdown, MDS Nordion supplied approximately 40% of the world market; Covidien, 29%; NTP, 18%; IRE, 12%; and ANSTO about 1% (Vanderhofstadt, 2009). After the shutdown of the NRU, MDS Nordion's supply was not available and the other processors stepped in to partially fill the gap. Although estimates vary on actual percentages, it is clear that Covidien, NTP and IRE all increased their market share during the shortages, albeit of a smaller total supply. After the return to service of the NRU and the HFR reactors, Nordion was able to return to the market but the new market breakup is not currently available.

Figure 3.1: ^{99}Mo supply chain major participants and distribution channels (as of June 2011)



This supply chain is becoming much more complicated as generator manufacturers are diversifying their sources of bulk ^{99}Mo and therefore most processors are supplying multiple generator manufacturers. The "others" box in Figure 3.1 is to indicate that most of the producers sell bulk ^{99}Mo to other smaller generator manufacturers that supply their local markets (such as in Brazil, China, Israel, Poland, Turkey, etc.).

If one were to only look globally at the available capacity of the processing facilities, it would appear that there were no concerns related to the processing capacity. Table 3.1 provides the available processing capacity and one project that is currently under development. Table 3.2 provides two demand scenarios: one based on the NEA future demand study, with an approximated annual growth rate of about 2% (see Chapter 5) and the other based on 5% global growth in demand. From these two tables, it is clear that the available global capacity greatly exceeds current world demand for ^{99}Mo and will continue to exceed capacity for more than a decade even with a continuous increase in demand. However, based on the 5% growth scenario, processing capacity will not be sufficient by 2021.

Table 3.1: Processing capacity

Processing facility	Location	Processing capacity six-day curies EOP/wk[1]
ANSTO	Australia	> 1 000
Covidien	Netherlands	> 3 500
CNEA Ezeiza Atomic Centre	Argentina	>600
IRE	Belgium	> 3 000
MDS Nordion	Canada	> 7 200[2]
NTP	South Africa	> 3 000
NTP – under construction	South Africa	2 625[3]
Total		>21 425[2]

1. A common unit measure used in the industry is the six-day curie, defined as the radioactivity of ^{99}Mo six days after the end of processing component of the supply chain (EOP).

2. Adjusted from Vanderhofstadt, 2010, based on MDS Nordion's ability to process AECL production, that can reach a maximum of 60% of global demand or 7 200 six-day curies EOP per week.

3. The capacity is currently meant to serve as back-up and not to be used immediately for production. Capacity value is estimated by NEA and represents a modification from Vanderhofstadt, 2010.

Source: Based on information from Vanderhofstadt, 2010, with modifications.

Table 3.2: Demand scenarios for ^{99}Mo

Demand growth (%)	2010	2013	2015	2017	2020	2025
~ 2	12 000	12 700	13 185	13 690	14 490	15 680
5	12 000	13 890	15 315	16 885	19 545	24 950

However, this global capacity overview does not recognise the complexities of the ^{99}Mo supply chain and the implications of these complexities creating capacity limitations at the regional level, affecting the ability to supply the global market. There are a number of factors that reduce the effective processing capacity, including regional limitations, differences between target designs in use, potential processing failures and the potential impacts of the conversion to LEU targets. These issues can exacerbate global shortages and are discussed in the remainder of this chapter.

3.3 Constraints on processing

Location requirements

One of the key limitations to processing capacity is the location requirements of processing facilities – they should be located close to the reactor. Irradiated targets have to be shipped to the processing facility in secure containers that weigh approximately four tonnes. These containers can only be transported at reasonable costs and under current regulations via road transportation. In order to minimise the decay of the ^{99}Mo that would occur during transportation, the processor should be located as close to the reactor as possible. Recognising the time required for transportation, 1 000 km (on land) was considered to be the maximum acceptable distance for transporting irradiated targets from the reactor to the processing facility (with much shorter distances being preferred).

Transportation via roads is required, as air transportation would not be cost effective and would require dedicated cargo airplanes. In addition, there are no containers that are widely licensed for transporting irradiated targets via air and it is expected that it would be a challenge to license such containers. Currently there is no air transportation of irradiated targets for the production of ^{99}Mo.

In terms of limitations, if the processing facility was further away than 1 000 km, the decay of the ^{99}Mo during transportation time would create a significant loss of product. This would result in an overproduction of material, resulting in an increase in radioactive waste volumes and increased waste management costs, increased use of valuable reactor fuel and an increase in safety risks as more radioactive material is required to be handled and transported than would otherwise be necessary.

In addition, the further away that processing facilities are located from reactors, the more complicated the transportation logistics and regulatory requirements. For example, crossing multiple jurisdictions requires approval from all the jurisdictions that are transited. There is also an increased risk of delays (regulatory delays, etc.).

However, the benefits of a processing facility being located close to the reactor must be balanced with the benefits of locating further away but being better positioned to obtain irradiation services from multiple reactors. This latter situation would allow the supply chain to minimise impacts of a failure at one reactor and increase supply reliability.

As a result of these issues, transportation is a significant barrier to flexibility, limiting possibilities for locating processors and for using reactors that could produce ^{99}Mo.

Current regional limitations

As noted in Section 3.2, globally there is sufficient processing capacity. However, there are limitations when one compares the reactor capacity and the corresponding processing capacity that can be used to process irradiated targets from those reactors. For example, the total peak reactor ^{99}Mo production capacity in Europe is greater than 18 000 six-day curies EOP per week, while the processing capacity is around 6 500 six-day curies EOP per week. In addition, when either the BR-2 or HFR reactor are operating alone and irradiating their full capacity of targets, each reactor alone will more than occupy the full processing capacity of Europe.

Of course, not all the reactors operate at the same time, nor do they all operate all year round. Theoretically, Europe's reactors could produce up to 604 000 six-day curies EOP annually. However, processing capacity in Europe is only sufficient to manage about 338 000 six-day curies EOP annually. It is clear from these numbers that processing, more than reactor capacity, is a limiting factor in Europe.

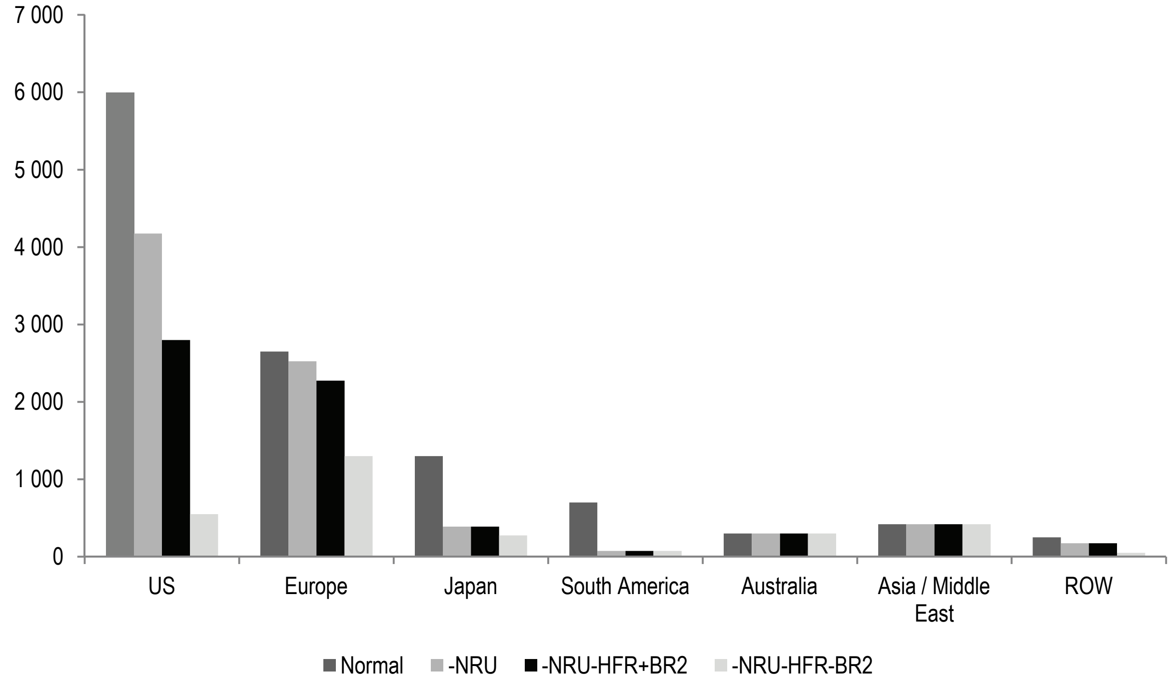
This situation is the same in Australia, where ANSTO's OPAL reactor could theoretically produce half of the world's demand of ^{99}Mo when operating (about 6 000 six-day curies EOP per week) but the limiting factor is its processing facility, which has the capacity to handle a maximum of 1 000 six-day curies EOP per week. In addition, there are some regions where there are no processing facilities for ^{99}Mo, such as in Japan, the United States and in some parts of South America.

The current processing capacity in those regions where processing exists is sufficient to supply demand in those regions. For example, European processing capacity is around 6 500 six-day curies EOP per week and demand in Europe is about 2 600 six-day curies EOP per week. Hence, these processing facilities are also important for supplying the broader global market.

This regional processing capacity limitation is important to consider when discussing possible new reactor supply; it is not useful to have reactors that can supply ^{99}Mo if there is not sufficient capacity to process it. This limitation is especially important when there are problems with reactor availability. The ideal situation when one reactor is down for extended maintenance (either planned or unplanned) is for another reactor or reactors to step in and irradiate additional targets to fill in the supply gap. However, regional processing capacity limitations reduce the ability of reactors to increase production to fill in the supply gap. For example, during the ^{99}Mo supply shortages of the later part of 2009 and early 2010 European reactors were not operating at full capacity because there was not enough processing capacity to handle the full reactor potential. Some European reactor operators indicated that during some of the shortage period, they were only running at 50 to 60% of theoretical capacity because their customers (the processors) were not able to process any additional irradiation services. This restricted level of production meant that the global market remained 20 to 30% under supplied.

For those regions with no processers, this regional capacity limitation can translate to a larger impact during a disruption of the supply chain (e.g. when a reactor is down for extended repair). Figure 3.2 shows the expected impact on various world regions when one or more of the major irradiating reactors are not able to contribute to the global supply chain. As can be seen, those regions without their own reactor and processing capacity are the hardest hit during a reactor outage.

Figure 3.2: Supply availability impacts of reactor unavailability



Source: Vanderhofstadt, 2009.

Another concern is that the lack of processing capacity in some regions can limit the possibility to produce ^{99}Mo from regional reactors. This has been a limiting factor for some short-term ^{99}Mo production proposals in the United States, where there was a reactor that could potentially produce ^{99}Mo but no processing facility. This means that supply for these regions must continue to be transported from other regions, with the corresponding safety and security risks faced by long-distance transportation, as well as greater decay of the product. The new projects being discussed in the United States have realised this limitation and the necessary processing facilities are part of projects.

This lack of regional processing capacity and the possible impacts are becoming a larger issue as the growth in nuclear medicine imaging techniques is expected to be most significant in those countries where the techniques are currently not widely used and ^{99}Mo is not currently produced (e.g. Brazil, China and India).

Risk of processing capacity failure

Processing plants are less susceptible to long downtime. However, there is the possibility that the processor can face an unexpected shutdown, as occurred with the incident from August to

November 2008 at the IRE facility. In such a case, processing capacity to fill the gap would have to come from another processor as the entire facility would be closed. Alternatively, there could be a situation where one production line of hot cells becomes unavailable due to some mechanical failure. In this case, if there is redundant capacity within the facility (a second line of hot cells) this capacity could continue to be used.

In a situation where there is a single reactor serving a single processor or where the regional reactor supply is greater than the remaining processing capacity, an outage at the processing facility would create a significant disturbance in the ability to supply ^{99}Mo. If the regional network is supported by processors that use different target designs, an outage at one of the processors may not be able to be compensated for by the other processor. This results in a supply chain with weak supply reliability.

Impact of LEU conversion on processing capacity

As discussed in the chapter on reactor capacity, conversion to LEU targets for the production of ^{99}Mo has been agreed to by most governments for security and non-proliferation reasons. As noted in that section, in order to produce the same amount of ^{99}Mo with LEU there may need to be a significant increase in the ^{235}U density in the targets or an increase in the number of targets irradiated.

In the cases where the density cannot be increased sufficiently to offset the lower ^{235}U content, there will be impacts resulting from increased target irradiation and processing to maintain the same amount of final production in a given period of time. For the processor, this will mean some degree of:

- increase in processing facility capacity (such as additional hot cells) and staff and processing activity;
- regulatory approval to process additional targets;
- increase in waste volumes and possibly additional waste management infrastructure.

Where the density can be increased to levels that do not result in the need for increasing the number of targets irradiated, there will not be a need for additional production infrastructure. The industry is working towards this outcome. However, even with denser plate targets there will be an increase in waste volumes. If, however, the proposed new foil targets were developed to a stage where they could be used commercially, this could lead to lower liquid waste volumes.

If these issues cannot be resolved, there could be an effective reduction in processing capacity in some regions until additional capacity can be developed and regulatory approvals received to process additional targets. Any required increase in processing capacity or activity to produce the same amount of ^{99}Mo would result in an increase in cost per six-day curie produced. However, reduced physical protection costs as a result of dealing with LEU instead of HEU may help to offset any potential cost increases of using LEU targets.

The industry is currently working to increase the density of the targets, including determining any possible changes required to the process and the processing facility. The barrier to be overcome is that the use of LEU targets has been demonstrated for smaller scale production (i.e. at the OPAL, RA-3, and BATAN [Indonesia] reactors) and only recently started to be used for commercially-viable, large scale production at the South Africa reactor and processing facilities.

One dilemma will be how to set up LEU irradiation in tandem with HEU production to ensure a continuous, reliable supply of ^{99}Mo to the global supply chain and to ensure continued revenue for processors and reactor operators. This may require additional investment in capacity. NTP has been able to undertake the LEU conversion process without stopping production given that they had sufficient hot cells available.

The NTP experience has revealed interesting information on the impacts on yield from their conversion from HEU (45% of ^{235}U) to LEU targets. They used LEU targets with a density 85% greater than the HEU targets and therefore only saw a decrease in yield per target in the range of 10 to 15% (Ball, 2010).

As noted in Chapter 2, at this time there is not yet an established body of knowledge as to the comparative yield, waste management costs, development costs, capital requirements and the related economic impacts that would be observed for a major ^{99}Mo producer using targets of higher enrichment (greater than 90% ^{235}U) wishing to undertake conversion. However, even with the uncertainty on the costs of conversion, it is clear that the conversion to LEU targets is necessary but not currently financially supported by the market (NEA, 2010a).

3.4 Barriers to the development of processing facilities

Costs

The market is characterised by significant barriers to entry. Extracting and processing the ^{99}Mo is a very capital intensive process, with a new large processing facility anticipated to cost about USD 200 million (NEA, 2010a). This is a significant investment to be made for an industry where there is uncertainty around reliability of irradiation services and a revenue stream that does not currently support the economic sustainability of the industry.

Historical prices have not been sufficient to support the development of significant new investment in some cases (NEA, 2010a). For example, one reason why larger processing facilities in Australia have not been developed is because the historical prices for bulk ^{99}Mo have not been high enough to justify the construction of a larger facility.

This cost barrier is exacerbated by the uncertainty in the current supply chain, which can greatly affect the expected return on investment. For example, if the major supplying reactor to the processing facility gets shut down for an extended period, the processing facility is making no revenue unless they find an alternative source for target irradiation or bulk ^{99}Mo from another supplier to continue to support their clients.

In addition, the necessary conversion to using LEU targets creates uncertainty on the final cost of production (and hence profits) that is expected for a major ^{99}Mo producer. Conversion will likely have some effect on the payback of investments in the processing capacity, possibly creating higher costs per unit of production.

Complex process

In addition to cost barriers, there are knowledge barriers to the development and use of additional processing capacity. Processing of ^{99}Mo is a knowledge-intensive procedure, with each processor having their method for extracting and purifying the ^{99}Mo and managing the waste developed through the process. Given its complexity, it has sometimes been described as an art, not a science.

The knowledge capacity is even more important as regulations and consumer expectations on the quality of the bulk ^{99}Mo are becoming more demanding in some countries. In some cases, radiochemicals are being tested for impurities at radiopharmacy levels even though the product is bulk ^{99}Mo and not the final radiopharmaceutical product. These increased demands on purity levels increase the value of the knowledge and skill of the processing company and its employees.

As well, given that bulk ^{99}Mo is transported around the globe and has a short half-life, there is important logistics knowledge that can make a difference between a successful processor and an unsuccessful one. A key addition of value at the processor component of the supply chain is the handling of the complicated logistics to get the bulk ^{99}Mo to generator manufacturers in as short a time as possible; for every hour of shipment approximately 1% of the remaining ^{99}Mo is lost due to decay.

The knowledge required to extract, process and then deliver bulk ^{99}Mo is therefore essential to being able to reliably participate in the supply chain. However, this knowledge is well protected as it provides a competitive advantage.

Waste issues

As with the operation of reactors, there is a concern among national governments and citizens that processing facilities in their country are producing waste that must be dealt with domestically, while the ^{99}Mo produced is being exported at prices that do not necessarily cover the long-term waste management costs. The developers of new processing capacity first have to be able to convince regulators and the public that ^{99}Mo processing is important and the waste can be managed in a responsible and economic manner. In addition, some current processing facilities are being faced with limitations to their current waste management facilities. These current limitations are also relevant when discussing LEU conversion as there may be additional waste volume to manage.

3.5 Conclusions

Global processing capacity is sufficient for at least the next decade but regionally there are immediate and longer-term concerns. The challenges related to regional processing capacity raise issues for the long-term reliability of the supply chain, having an impact on the ability of the industry to respond to such events as unplanned outages and meeting future demand growth. Reserve reactor capacity cannot effectively be used if the product cannot be processed and delivered to the global market. The location of reserve reactor capacity also imposes limits upon where additional processing capacity is located and vice versa.

Given the issues presented here, the ^{99}Mo supply chain could consider:

- Taking into account regional processing capacity limitations when examining possibilities for investments to ensure a correlation between reactor and processing capacity. A better geographical spread of reactor and/or processing capacity over different continents, including for emerging markets, would strengthen reliability in those countries currently greatly affected.

- Working towards a pricing structure that would ensure sustainability in processing capacity, including new investment, where required.

- Collaborating on LEU conversion efforts, including on target design and processing, with a goal of developing a common target design (or at least a common approach to new target approval) that can be used and processed by all supply chain participants. Realising this goal would increase the availability of reliable reserve capacity. This may raise some commercial confidentiality issues that would have to be recognised and worked through.

These issues are reflected in the HLG-MR policy approach to improving security of supply (see Chapter 10).

Chapter 4

Enhanced Communication between Suppliers and Consumers

4.1 Introduction

One issue that was identified as a key area of vulnerability was that in the event of unplanned shortages, the users of nuclear medicine were not receiving sufficient or timely information on supply availability to take measures to adjust. In addition, generator manufacturers had difficulty in getting information on when supply would be available. This lack of information was seen during the extended shortages, but has the strongest impact when an unexpected event first occurs. Hence, improving communication is especially important when that event has the potential to affect the supply of ^{99}Mo through the supply chain and therefore of the delivery of ^{99m}Tc to the patient. This chapter provides a discussion of the communication protocols created and implemented by the industry to inform the necessary communities of an unexpected event.

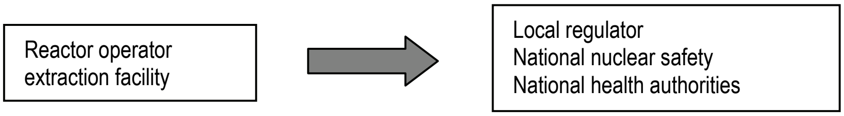
The chapter also provides a brief overview of actions being taken by the supply chain to provide better information to the health community on supply availability during shortage situations. It should be noted that behind this communication from generator manufacturers and radiopharmacies to their customers is the co-ordination of reactor schedules and the provision of the related information to the upstream supply chain. This co-ordination was discussed in Chapter 2 and is important as it was the foundation for communication to the health community during the 2009-2010 shortages.

4.2 Communication protocols

Following the first HLG-MR meeting, the HLG-MR asked the AIPES to work with the industry to encourage the adoption of best practices related to communicating supply concerns to the health community. The AIPES agreed to undertake this task and developed communication protocols for the industry to follow in the event of unexpected shutdowns. These protocols have been adopted by the industry and integrated into individual company procedures as of January 2010.

For an event that does not affect the supply of ^{99}Mo and only has a local effect, the reactor operator would communicate with regulatory authorities and undertake internal communication as required. This protocol is demonstrated in Figure 4.1.

Figure 4.1: Event requiring local communication

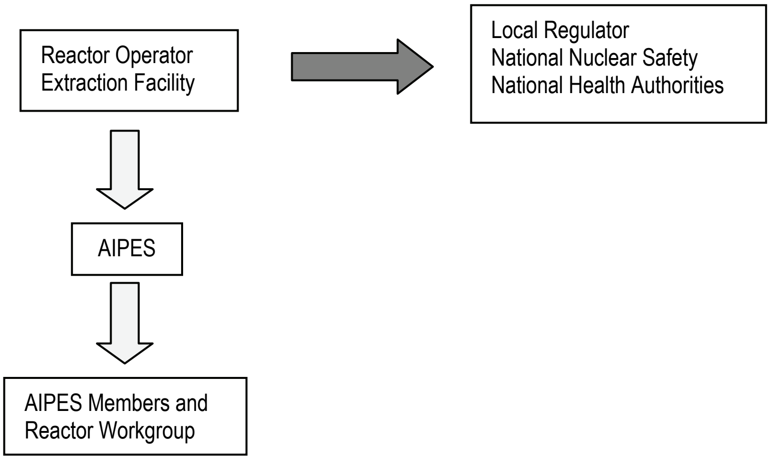


Source: Gheeraert, 2010.

In the case of an event that affects the maintenance schedule of the reactor, but does not have an immediate impact on the supply of ^{99}Mo, the reactor operator would communicate with regulatory authorities, utilise internal communication and work with AIPES. This last step would involve working with the AIPES members and the reactor workgroup to share information about the event and its impact and to update the maintenance schedule. This protocol is demonstrated in Figure 4.2.

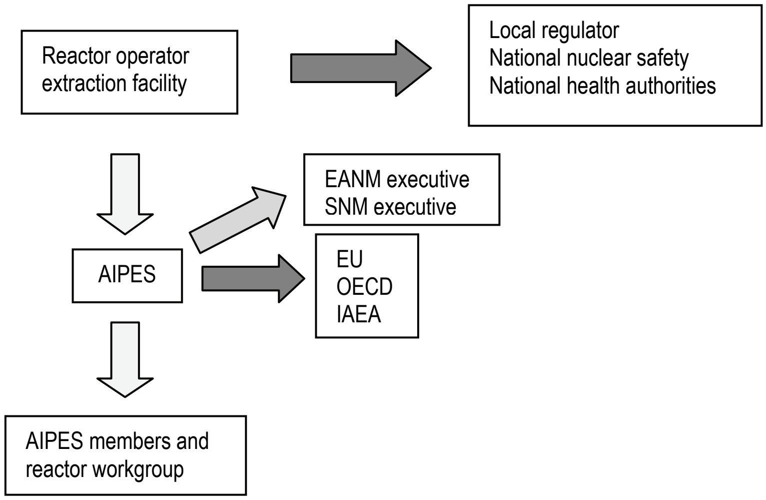
In the case of a more serious event, where attention and/or support is required from local and/or international authorities, the reactor operator would follow the steps outlined in the last protocol and AIPES would work with the nuclear medicine community and international organisations to address the impact of the event. Specifically, the AIPES would contact the executives of the European Association of Nuclear Medicine (EANM) and the Society of Nuclear Medicine (SNM), as well as officials from the European Union, the OECD/NEA and the International Atomic Energy Agency (IAEA). The AIPES would provide a warning to these bodies of any possible future difficulties in ^{99}Mo supply arising from the event and any support required by these bodies. It would also share on-going information with these international bodies to ensure proper communication about the event and its impacts. This protocol is demonstrated in Figure 4.3.

Figure 4.2: Event requiring reactor workgroup communication



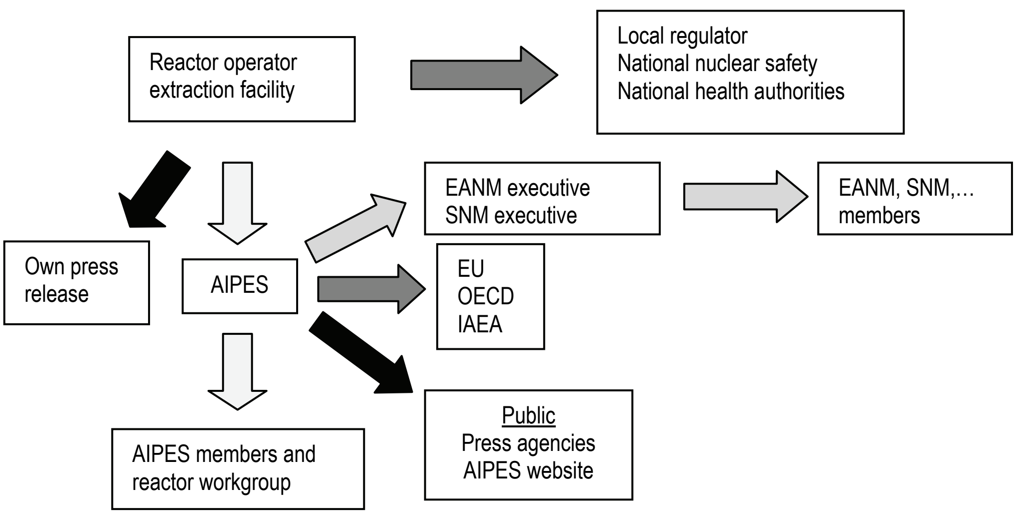
Source: Gheeraert, 2010.

Figure 4.3: Event requiring stakeholder communication



Source: Gheeraert, 2010.

Figure 4.4: Event requiring general public communication



Source: Gheeraert, 2010.

If a more serious incident occurs, one that would affect the supply of ^{99}Mo/^{99m}Tc in the near future, the reactor operator and AIPES would follow the steps outlined for less serious incidents, as well as also communicating with the broader nuclear medicine community and the general public. This broader communication would take the form of reactor operators and AIPES releasing their own press releases and the executives of the EANM and the SNM informing their members. This information would provide details on the event, a warning to the public on the expected impacts of the event, and ongoing information on the evolution of the incident and its ramifications. This protocol is demonstrated in Figure 4.4.

These protocols have been tested since June 2009 by AIPES members and experience has indicated that they have worked well.

4.3 Communication on supply availability to the health community

In addition to communication protocols for unexpected outage events, the HLG-MR requested that the industry provide better communication to the health community on expected available ^{99}Mo/^{99m}Tc supply. The industry associations indicated that the global nature of the supply chain and its related product decay made it difficult to provide a definitive prediction on available supply to the end customer. As a result, they concluded that it was the role of the individual generator manufacturers and distributors to inform their customers of their supply situation and any possible shortages.

The HLG-MR called on generator manufacturers to provide clients in the health community with projected supply levels for extended future periods (such as 90 days out) in its second rolling action plan. Being aware that supply availability can change on short notice, it was understood that these supply projections could be updated and refined through regular, ongoing dialogue with clients.

At the second meeting of the HLG-MR, the efforts by the industry to increase communication during the 2009-2010 shortage period were recognised by the nuclear medicine community, although it was also acknowledged that information was not consistent among suppliers or between regions. The HLG-MR also recognised that the industry had made efforts to improve communication with end users and was looking to the industry to voluntarily “standardise” its communication.

Figure 4.5 below provides an example of a future projection, provided by Covidien on their website (taken on 1 June 2010) and distributed to end users via a letter. Other generator manufacturers provide similar types of projections and communications to their customers. This example provides a colour-coded projection on available Covidien generator supply, indicating those days where no generators are expected to be delivered; Covidien has developed an iPhone application that also provides this information to their customers. This communication projection model was replicated further down the supply chain by Cardinal Health, a major radiopharmacy in the United States (http://nps.cardinal.com/nps/supplychaininfo/index.asp).

Figure 4.5: Example of available ^{99}Mo supply communication

Updated May 2010							June 2010						
1	M	T	W	T	F	S	S	M	T	W	T	F	S
						1			X	X	3	X	X
2	3	X	X	6	X	8	6	7	8	9	10	11	12
9	10	11	X	X	X	15	13	14	15	16	17	18	19
16	X	X	X	20	21	22	20	21	22	23	24	25	26
23	X	X	X	X	28	29	27	28	29	30			
30	31												

	Generator standing orders met with some extra
	Majority of generator standing orders met but no extra
	Generator standing orders shortage resulting in size reductions, ^{99m}Tc shortage
	Significant shortage to generator standing orders, severe ^{99m}Tc shortage
X	No ^{99}Mo supply expected. Generator production cancelled

Source: Covidien, 2010.

Communication efforts across the entire supply chain have improved drastically during the 2009-2010 shortage period. Co-ordination efforts and the related communication on the part of AIPES, reactor operators and processors (as discussed in Chapter 2), communication protocols for unexpected outages and ongoing supply updates to end users have resulted in a more transparent supply chain. These efforts have provided for a greater understanding within the full supply chain (including end users) of the available supply and allowed for all members of the supply chain to make efforts to reduce the impact of the supply shortages. This information has, for example, enabled medical practitioners to take steps to manage their demand for ^{99m}Tc procedures, maximising the use of the available supply. Without these communication efforts, the 2009-2010 shortage would have had a much larger negative impact on the health system. These communication efforts continue to be important as reactors face expected but longer than normal shutdowns for maintenance work.

Chapter 5

Demand for Molybdenum-99/Technetium-99m

5.1 Introduction

Understanding future demand

Understanding the future demand of ^{99}Mo/^{99m}Tc is essential when discussing the need for new ^{99}Mo producing reactors and related infrastructure, especially given the required level of investment. Decision makers need to have information to allow them to assess whether or not the investment will be used in the future, at least for a period long enough to make the investment worthwhile.

Some earlier studies on future demand have taken past growth and extrapolated continued growth. At that time, this may have provided a reasonable forecast. However, there are many uncertainties as to what the demand forecast should be now given the shortages of these isotopes seen in 2009-2010 and the associated changes in the use of ^{99m}Tc that occurred during the shortages. In addition, there are other external factors at play that serve to change historical demand, such as changing reimbursement rate policies in key markets or increasing wealth in emerging markets. It is important to understand these factors and their long-term effects on the demand for ^{99m}Tc and ^{99}Mo.

There is currently a significant degree of uncertainty in the industry as to the future of ^{99}Mo/^{99m}Tc with some supply chain participants expecting continued or increasing growth, while others predict growth to a saturation point then levelling off, and others predicting a decrease in demand. As a result of the uncertainty and the lack of a long-term comprehensive demand overview that includes recent changes in the supply chain, the HLG-MR sought to better understand future demand for ^{99}Mo/^{99m}Tc and related nuclear medicine procedures.

Earlier long-term demand estimates

There have been a few studies in the recent years that include a discussion on the global future demand for ^{99}Mo/^{99m}Tc; however these outlooks rarely went out to 2020 or beyond. This time frame is relevant when discussing new investments, as the development of a new reactor can take longer than eight years. Some of these past studies can be accessed through the NEA medical radioisotope website, www.oecd-nea.org/med-radio.

One of the longest period forecasting studies was released in November 2008, the AIPES *Report on Molybdenum 99 Production for Nuclear Medicine 2010-2020*. The report (AIPES, 2008) provided forecasts of future demand for ^{99}Mo and acknowledged that these forecasts could be overestimated given the possible impacts of the supply shortages that were being seen in the industry at the time of the report's release. These estimates were based upon expert opinion of interviewees and not the result of detailed surveys. The report indicated that ^{99m}Tc would remain a major radionuclide for nuclear medicine at least for the next 20 years. However, it noted that the strong growth experienced since the early 1970s was not expected to continue from 2010 onward. A forecasted annual growth rate of 1-2% indicates that the previous period of fast development will now be followed by consolidation. The report indicated that this growth rate could become higher in case of fast growth of single-photon emission computed tomography/computed tomography (SPECT/CT) systems or lower if a substitution in favour of positron emission tomography (PET) radionuclides or other imaging technologies takes place on a large scale.

Reasons for uncertainty on future demand

There are a number of factors that continue to support assessments of increasing growth in the market. For example, ageing populations and increasing obesity levels and the increase in related ailments in some developed countries could result in increased demand for nuclear medicine imaging, including ^{99m}Tc procedures. In addition, there is significant potential for growth in emerging economies as additional wealth leads to better health care supported by increased nuclear medical imaging.

However, the 2009-2010 shortage has led to a number of changes in the delivery and use of ^{99}Mo and ^{99m}Tc that may have a lasting impact on the demand for these medical radioisotopes. In addition, there have been discussions of other potential changes that could further impact the future demand, such as new software that facilitates reduced ^{99m}Tc dose requirements. On top of the changes from the shortage, there are other external factors in play that could impact demand, such as reimbursement rate levels.

In the past there have been some practices that have led to the potential overproduction of ^{99}Mo, given an economic structure that resulted in underpricing of ^{99}Mo (NEA, 2010a). In some cases, this has resulted in a supply chain that has not used the produced ^{99}Mo in the most efficient manner, allowing for significant product decay to occur in the supply chain. With the 2009-2010 shortage, many supply chain participants have worked to improve their processes and logistical arrangements to minimise product loss. For example, generator manufacturers have been altering production schedules to prepare and ship product as soon as possible once the bulk ^{99}Mo has been received.

In terms of radiopharmacy preparation practices, there have been some preparation and delivery practices that may be suboptimal because of the historical economic structure. For example, hospitals may receive a generator and not elute in a manner that maximises the use of the ^{99m}Tc produced. In some cases, patient doses were prepared a number of hours in advance, requiring additional ^{99m}Tc to be eluted to account for the decay of the product, instead of eluting the ^{99m}Tc closer to the time of the actual procedure. These practices were normal and accepted at the time as they sought to minimise other input costs (e.g. labour) and provide regular scheduling to medical practitioners and patients. With proper pricing (see NEA, 2010a), the optimality of these practices could be established. Regardless of the assessment, it is clear that some of these practices have changed during the recent shortages.

These potentially suboptimal practices along the full supply chain have resulted in the need to irradiate more targets, produce more bulk ^{99}Mo and transport more radioactive material than necessary. This overproduction also resulted in related radioactive waste management requirements. In addition, the need to handle more radioactive material than necessary could be contrary to the ALARA (as low as reasonably achievable) principle on radiation exposure. Under this principle, radiation exposure must be as low as reasonably achievable, economic and social factors being taken into account. However, this must be balanced with the increased exposure to radiopharmacy staff from eluting generators more efficiently.

Some radiopharmacies, hospitals and physicians changed these historical practices during the recent shortage period to deal with a reduced supply. For example, Covidien created its "Tc-99m Conservation Program" that encourages more thoughtful unit dose ordering practices by its customers to maximise the availability of ^{99m}Tc. According to Covidien, this programme freed up enough ^{99m}Tc to serve about 10% more patients each day during the 2009 shortages (Haynes, 2009).

In addition, some hospitals have reduced their ^{99m}Tc orders during the shortage and have instituted practices to use the available supply more efficiently. For example, many hospitals have altered the scheduling of their scans to periods when ^{99}Mo is available and to maximise the use of that available ^{99}Mo, including on weekends and evenings. In addition, some are finding ways to reduce ^{99m}Tc doses when possible. During the shortages, some hospitals did not expect to return to their full previous order quantities even when more supply becomes available (Urbain, 2010), and some market participants have indicated reduced demand following the shortage period.

To support these efforts, a number of medical organisations and governments have developed guidelines for the health community on efficient use of available ^{99}Mo/^{99m}Tc supplies during a substantial or extended medical isotope shortage. For example, the SNM and the Government of Canada have separately published guidelines, which are available on the NEA medical radioisotopes website (www.oecd-nea.org/med-radio). The communication efforts undertaken by the supply chain discussed earlier in this report have contributed to the effectiveness of these demand management actions as practitioners are able to plan around expected future available supply.

It must be recognised that some of the demand management actions have been reported to have a detrimental effect on staff morale in some cases, as work schedules are irregular and there is added stress. In addition, some changes were not necessarily cost effective. As will be seen later in this chapter, these negative effects affect the acceptability of adopting some of the demand management actions on a permanent basis during times of normal supply availability and the supply chain has generally seen these actions stopped once supply returned to normal.

In addition to demand management actions, there are a number of advances in studies, software and technology that indicate possible significant reductions in the use of ^{99m}Tc from current practices. For example, a study was undertaken that found that for SPECT myocardial perfusion imaging study of a patient, the at-rest component is unnecessary if the results of the patient's stress SPECT are normal; the impact is a reduction of the ^{99m}Tc required by as much as 61% for those patients (Miller, 2010). In addition, there are a number of software applications and technologies that are being developed and promoted by the industry that reportedly would reduce the amount of ^{99m}Tc needed per patient scan (UltraSPECT, 2009; Spectrum Dynamics, 2010). As well, computer algorithms have been developed and piloted to help determine the appropriateness of using SPECT procedures for patients, based on appropriate use criteria. In the pilot, SPECT testing was deemed to be inappropriate on about 15% of the sample body, which had all received SPECT testing (Dalton, 2009). These advances, if widely adopted, could result in reduced demand for ^{99}Mo and reduce radiation exposure to patients and medical practitioners, respecting the ALARA principle discussed above.

As well, there are some external factors at play that could impact the future growth of ^{99}Mo. One of these factors is the development and growth of alternative imaging modalities and isotopes that could potentially serve to replace or reduce the demand for ^{99m}Tc, especially given the recent supply concerns. There are also activities going on related to changing reimbursement rates and government concern on overuse that could have an impact on future demand for ^{99}Mo/^{99m}Tc.

Of course, there are many cases where there are currently no clear substitutes for ^{99m}Tc based SPECT imaging tests and any substitution possibilities that do exist would depend on whether the technicians were trained on the new modalities and if health approvals were received for substitute tracers. In addition, SPECT has significant advantages over other technologies, with high resolution, low radiation doses and transportation logistics of isotopes that allow a wide distribution, which will support its continued use (Plan Nuclear, 2009).

In addition, some governments are concerned about radiation doses from nuclear medicine sources (both diagnostic and therapeutic). In February 2010, for example, the United States House of Representatives' Committee on Energy and Commerce, Subcommittee on Health, held a hearing entitled *Medical Radiation: An Overview of the Issues*. This hearing examined the potential benefits and risks of the use of radiation in medicine. In addition, the California Senate passed a law requiring medical facilities to record radiation doses in patients' medical files (Associated Press, 2010). Although concern is mostly directed towards higher radiation-dose techniques (such as X-rays and CT scans), SPECT procedures could also be affected. With this increased scrutiny, there could be a push towards an overall reduction of nuclear medicine procedures, but it could also lead to an increase in SPECT procedures given the value of the procedures and that radiation doses from SPECT are lower than doses from some other alternative modalities.

NEA future ^{99m}Tc demand study

The HLG-MR, working with the Technopolis group, undertook a study to develop a future demand scenario for ^{99m}Tc, recognising differences in mature and emerging markets and building on available studies. As part of the project, an expert advisory group (EAG) was created and a global survey was conducted. The EAG consisted of nine experts (see Appendix 9) with an in-depth understanding of medical imaging and from diverse geographical and experience backgrounds.

The global on-line survey obtained data to increase understanding of future demand for medical imaging, various modalities and ^{99m}Tc. Data were collected from the survey over two months between January and March 2011. From there, the data obtained were analysed and the EAG, Technopolis and the NEA developed and verified the future demand scenario. The HLG-MR verified the findings and the developed demand scenario.

The concise results of the study are presented in this chapter. The full report on the demand study provides a comprehensive overview of the results and is available on the HLG-MR website (www.oecd-nea.com/med-radio).

Justification

Forward-looking exercises often consist of a range of methods, including iterative consultation rounds, interviews, surveys, etc. Two components are at the core of this study: a forecast, based on expert-consultation through interviews and survey; and a review of the results by the HLG-MR. The importance of forecasting is that it retrieves knowledge that can be used to anticipate and respond in a timely manner to developments that have yet to take place, but have a reasonable probability of occurring. This is particularly important for problems that may have far-reaching consequences and a large time span before solutions may be realised. In the case of the medical radioisotope ^{99m}Tc, shortages of radiopharmaceuticals could cause great difficulties that would take years to remedy. The main difficulty is the reduction of diagnostic procedures in clinics, for instance for cardiovascular diagnostics, oncology, bone scans, etc.

In this forecast study the future time span of 2020 and 2030 has been chosen. Even though projecting out to 2030 seems long, and therefore reliability less certain, the 2030 time horizon forces respondents to think beyond the lifespan of existing research reactors for radioisotopes. The study is meant to provide an indication of direction and degree of changes in demand in a timeframe that would be meaningful for new ^{99}Mo producing infrastructure (e.g. research reactors and processing facilities). Given the uncertainty that exists when looking out so far into the future, the results should be taken as indicative of long-term trends and not as absolute figures.

The forecast study has a global focus. This has implications for the way in which the survey was spread and for the response rates from the different countries. Results from one jurisdiction cannot simply be extrapolated to other jurisdictions as the access to and availability of the various imaging technologies may differ between countries in different parts of the world. As a result, survey questions were focused on the respondent's national situation, reflecting the assumption that respondents may not be able to accurately comment on demand and use in other jurisdictions.

The survey was developed with the audience of imaging specialists, nuclear medicine experts, as well as referring physicians in mind. Even though there were many different types of specialists who answered the survey, respondents were predominantly nuclear medicine experts, as they had the most relevant knowledge on expected future use.

5.2 Survey results

Information on response sample

The survey consisted of 15 questions in an online questionnaire. It was distributed globally through official medical professional organisations and personal contacts of the EAG and the HLG-MR. The survey obtained 713 responses from 52 different countries. From these, almost 50% came from North America (United States and Canada); more than one-third from Europe and the remaining responses (96) from the rest of the world. Even though the response was not high in the rest of the world, it does however reflect the actual use of ^{99m}Tc, which is highest in the United States, Canada and Europe. The responses in South America, Africa and Asia (excluding Japan and Korea) are considered as emerging markets for nuclear medicine as opposed to mature markets. In the following sections, the emerging markets opinions are derived from 43 respondents (6% of the respondents).

The professional background of the respondents is dominated (40%) by medical doctors that are imaging specialists using nuclear medicine. Adding the nuclear medicine technologists to this group creates the "nuclear medicine" group, representing 60% of all respondents. The remaining 40% has a diverse professional background, including radiologists, cardiologists, oncologists, internists, pharmacists, medical physicists and others.

The descriptor, "nuclear medicine background" does not discriminate between technetium-99m based modalities (conventional planar and SPECT modalities) and PET modalities. Therefore we also asked respondents to identify their specific expertise (^{99m}Tc-based, PET-based, or other expertise). Almost 90% of respondents have expertise with ^{99m}Tc-based imaging modalities. Of these, one-third has only SPECT or planar-based expertise (i.e. ^{99m}Tc-based imaging), while almost two-third has expertise combined with other modalities. A group of 36 respondents (5%) has no SPECT or PET expertise: they only work with other modalities.

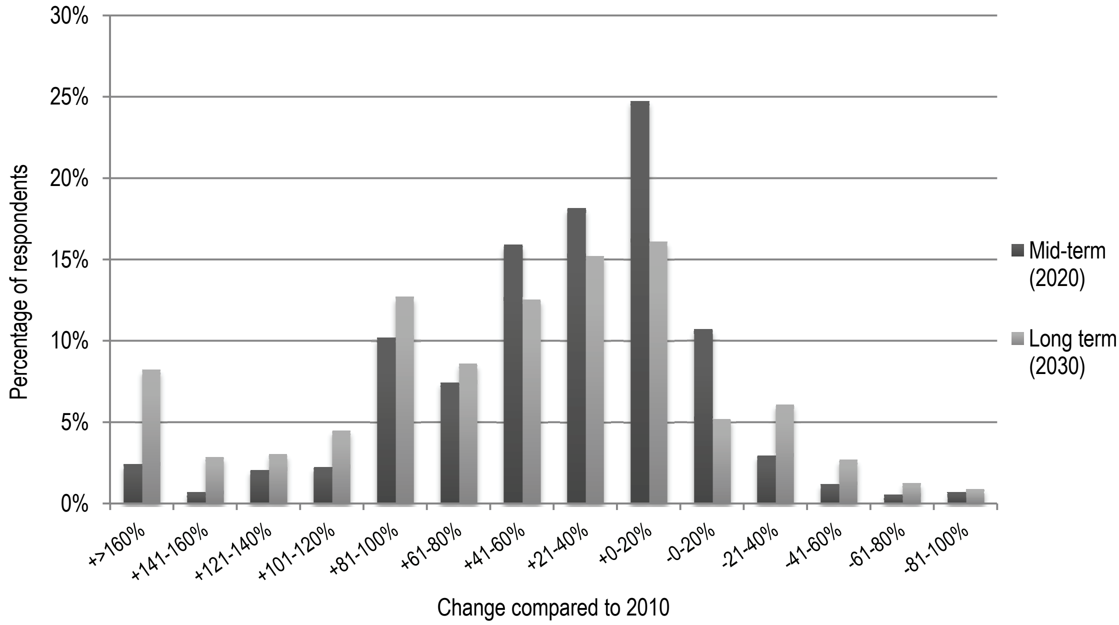
In the analysis of the responses to the survey, we additionally analysed the sensitivity of geographical location, mature/emerging markets, and/or for specific SPECT or non-SPECT expertise, when appropriate.

Expectations: forecast of future use

Expectations on the future of diagnostic imaging

Figure 5.1 shows that the majority of respondents expect a growth in the total number of imaging procedures (all types). Overall, the respondents expect the total number of imaging procedures to increase by about 35% by 2020 to 50% by 2030, when compared to the current use. This assumes an average annual growth rate of between 1.1% and 3.0%.[1]

Figure 5.1: Increase in diagnostic imaging compared to 2010



Interesting deviations from the average expectations on the future use of diagnostic imaging are to be observed between emerging and mature markets. On average, respondents from the emerging markets expect a much larger growth – 50% by 2020 and 70% by 2030 compared to 35% and 50% in mature markets; the median for the longer term is even higher for emerging markets (see Table 5.1). Emerging markets expect a growth in imaging procedures of up to 100% by 2030, which can be explained by the increasing wealth in these countries and consequently better access to health care. However, the results from the emerging markets show more extreme expectations (both positive and negative) – the standard deviation is higher.

[1] Average annual growth rates: 2020: 3.0% followed by annual growth of 1.1% between 2020 and 2030; when assuming linear growth up from 2010 to 2020 and 2020 to 2030.

Table 5.1: Average expected growth in imaging procedures in mature and emerging markets

	Mid-term average	Long-term average	Mid-term median	Long-term median
Mature markets	~ +35%	~ +50%	+21-40%	+41-60%
Emerging markets	~ +50%	~ +70%	+41-60%	+81-100%

Expectations on the future demand of ^{99m}Tc

The expected growth of ^{99m}Tc-based procedures is lower than the expected growth of diagnostic imaging procedures overall, as demonstrated in Table 5.2 (compared to Table 5.1). On average, respondents expect an increase of 20% by 2020 from 2010 levels, while they foresee an increase of 25% by 2030.[2] Again, respondents from the emerging markets expect a larger growth on average – 2020: 40% and 2030: 50% – than respondents from mature markets (see Table 5.2). When comparing the responses from people working only with SPECT (i.e. working with ^{99m}Tc-based imaging only) to the respondents having combined expertise and to the respondents having other expertise, no major differences are observed. This demonstrates that there is no observed bias based on the medical expertise of the respondents (Table 5.3). Therefore, from the survey we can conclude that ^{99m}Tc demand is expected to grow around 1-2% per year to 2030.[3] The expert advisory group endorsed this result.

Table 5.2: Average expected growth in ^{99m}Tc demand in mature and emerging markets*

	Mid-term average	Long-term average	Mid-term median	Long-term median
Mature markets	~ +20%	~ +25%	+0-20%	+0-20%
Emerging markets	~ +40%	~ +50%	+21-40%	+41-60%

* Please note that the median is a range, as the survey provided answer categories.

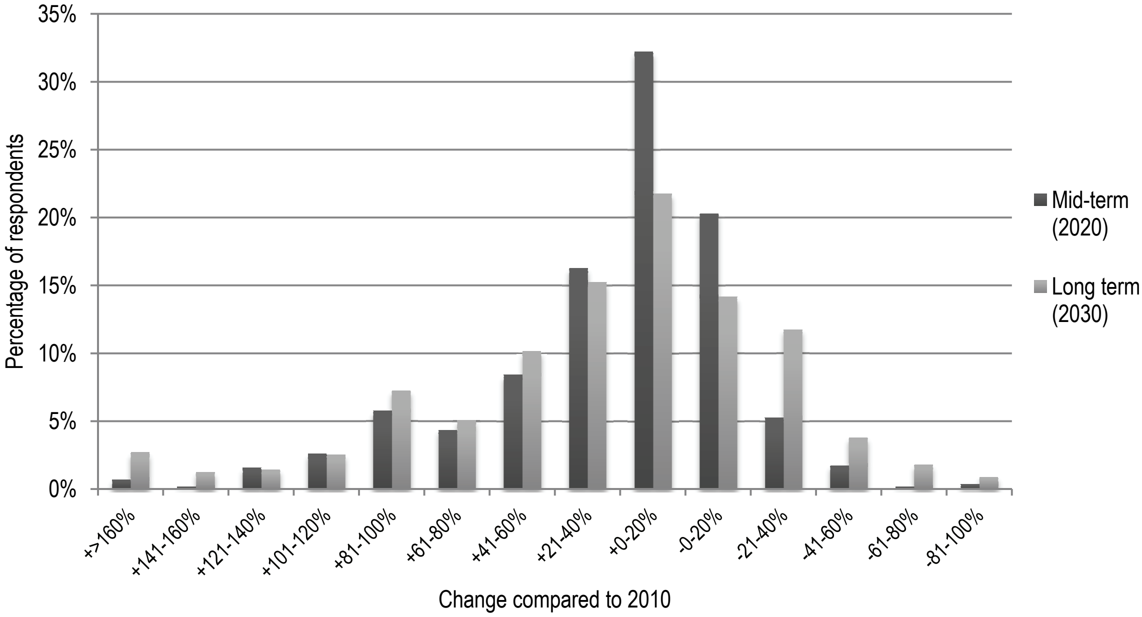
Table 5.3: Average expected growth in ^{99m}Tc demand in mature and emerging markets, by specialisation

	Mid-term average	Long-term average	Mid-term median	Long-term median
SPECT specialised	~ +23%	~ +24%	+0-20%	+0-20%
SPECT combined with other modalities	~ +21%	~ +23%	+0-20%	+0-20%
Only other modalities	~ +22%	~ +23%	+0-20%	+0-20%

2 Representing an annual growth rate of 1.8% between 2010 and 2020 followed by an annual growth of 0.41% between 2020 and 2030; assuming linear growth.

3 It should be noted that the survey questions focused on the time points 2020 and 2030, therefore the actual growth path to those dates is unknown. It is possible (and likely) that growth is not linear.

Figure 5.2: Expected future demand of ^{99m}Tc in 2020 and 2030 compared to 2010



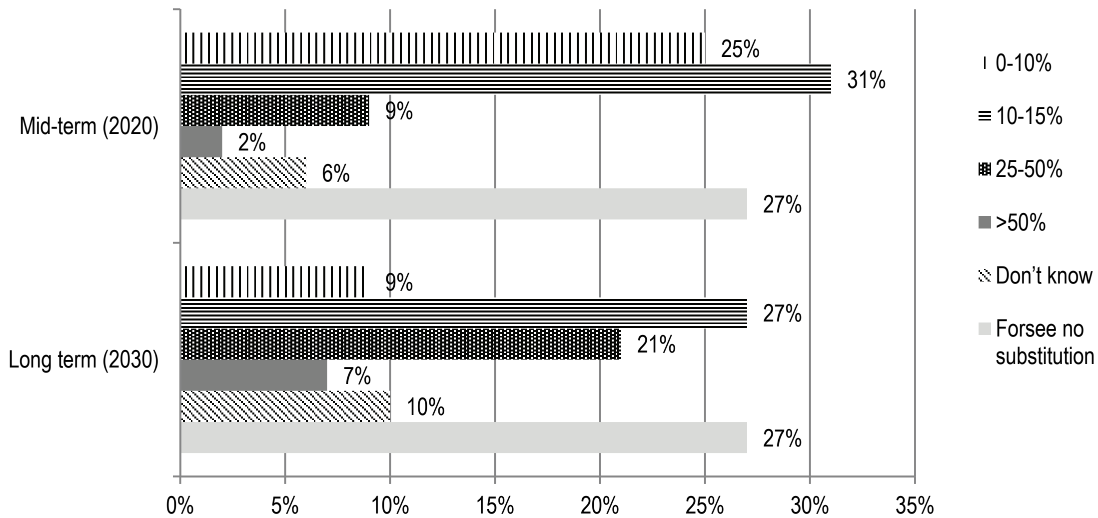
Expectations with regard to substitution of ^{99m}Tc modalities

External factors could impact the future growth of ^{99m}Tc/^{99}Mo as well. One of these factors is the development and growth of alternative imaging modalities, such as PET and combined modalities such as PET/CT or PET/MRI. Respondents were asked whether they expect a trend of other modalities substituting for ^{99m}Tc-based imaging by 2020-2030. According to 73% of the respondents, ^{99m}Tc-based imaging procedures will be substituted, at least partially, by PET-based technology (see Figure 5.3). However, as discussed later in this chapter, this substitution will likely come in the form of growth of alternative modalities replacing some growth of ^{99m}Tc-based SPECT imaging.

PET-based technology is superior in functional imaging quality, but is more expensive per procedure, requires investment in hardware infrastructure and highly skilled personnel. Therefore, it is not surprising that emerging markets foresee less substitution (only 62% of respondents). Likewise, respondents only working with SPECT – being convinced about the functionality of this technology – foresee less substitution (65%). On the other hand, 93% of respondents working only with other modalities foresee substitution. Substitution of ^{99m}Tc is expected to grow over time: by 2020 11% of the respondents expect that greater than 25% of ^{99m}Tc-based procedures will be substituted by other modalities; by 2030 28% of the respondents expect a substitution of greater than 25% of procedures.

In terms of modalities that are expected to replace ^{99m}Tc-based imaging, respondents expect that PET/CT will probably grow largest and PET/MRI and MRI will experience a relative growth on the longer term. Respondents did not expect that SPECT using an alternative isotope would replace the use of ^{99m}Tc.

Figure 5.3: Substitution of ^{99m}Tc by other modalities



Perceptions on stability and coping strategies

Stability of supply

The majority of respondents (~90%) indicated that they have suffered from the recent ^{99m}Tc-shortages. These effects were most notable in Asian countries, and least experienced in Oceania. However, even with this experience, over 60% of all respondents still expect that the ^{99m}Tc supply will be stable. A number of respondents indicated that it was difficult to predict long-term stability (20% had no opinion), but over 60% of respondents felt positive about the stability of future ^{99m}Tc supply; while about 40% of the respondents expect it to be relatively unstable in the period 2011-2020. Interestingly, the expected stability increases over time: for the period 2021-2030 more people expect the supply to be relatively stable. This assumes a growth of the supply capacity of ^{99m}Tc.

Coping strategies

One potential impact of the current shortage on future demand is that many supply chain participants have worked to improve their processes and logistical arrangements to minimise product loss, and have implemented demand management practices to use the available product in the most efficient way possible. In addition, there are a number of advances in cameras and software that promise significant reductions in the use of ^{99m}Tc from current practices.

Survey respondents indicated that efficient patient scheduling and reduction of doses were the most applied strategies for dealing with the shortages, however respondents indicated that most of the changes were not permanent. Of the changes seen, more efficient elution from generators and more efficient patient scheduling are the more permanent; the latter has turned to routine in 12% of the cases.

Figure 5.4: Expected stability of ^{99m}Tc supply, excluding no-opinion responses

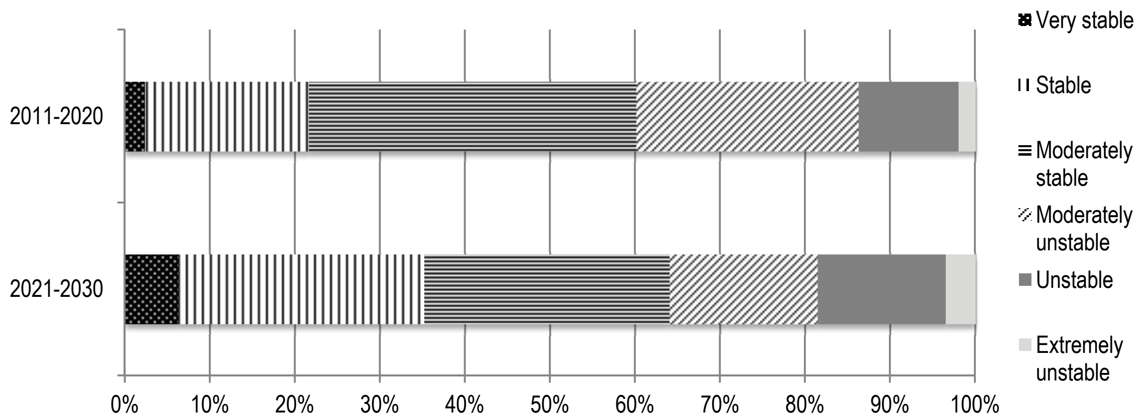
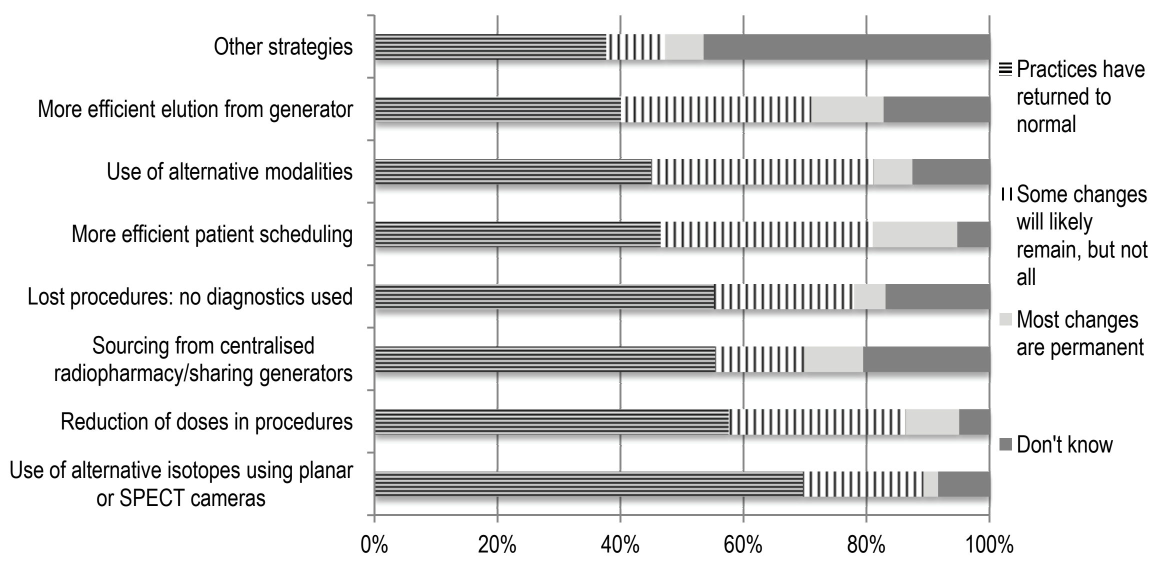


Figure 5.5: Coping strategies for the ^{99m}Tc shortage are mostly not permanent



5.3 Determinants of change

Expectations of surveyed experts

Apart from strategies to cope with the shortages in ^{99m}Tc, there are more general drivers that can influence future demand. In collaboration with the expert advisory group an extensive list of possible drivers was put together. These include categories such as: cost of ^{99m}Tc and alternatives, supply availability and reliability, alternative modalities, medical demand, policy and technology. Respondents were asked which drivers they thought would increase or decrease demand.

It is clear from the top five drivers (see Table 5.4) that increased demand depends on availability of ^{99m}Tc, improved technology or more efficient use. Both growing wealth and lower costs of ^{99m}Tc-based imaging were identified as potential demand increasers. The importance of the last two drivers comes partly from the current situation that ^{99m}Tc-based procedures are much cheaper (as much as ten times cheaper) than PET-based imaging.

Table 5.4: Top five drivers of increased/decreased demand

Increased demand	%	Decreased demand	%
Availability of improved technologies for ^{99m}Tc-based modalities	81	Development of radiopharmaceuticals/contrast agents for alternative modalities that would substitute for ^{99m}Tc-based imaging	78
Stable availability of ^{99m}Tc in future	77	Increase in ease of use or quality of other modalities compared to ^{99m}Tc-based imaging	70
Increased efficiency of use of ^{99m}Tc in clinic/radiopharmacies	60	Changes in cost of technetium-99m-based imaging	52
Changing use of diagnostics due to growing wealth in national economy (patients can afford diagnostics)	41	Availability of hardware and infrastructure replacing ^{99m}Tc-based imaging	50
Changes in cost of technetium-99m-based imaging	41	Government policies	44

Changes in cost are also perceived as a relevant driver for decreased demand. If the cost of ^{99m}Tc-based procedures increases in the future, this could drive a shift towards the more expensive PET-based procedures (more on this below). The first and second drivers for decreased demand are the development of alternative imaging modalities in general and of new radiopharmaceuticals for PET in particular. This shows that respondents have primarily chosen technological drivers, rather than non-technological drivers, as the key variables in encouraging decreased demand.

In relation to the driver on the demand impact of changing costs, we sought further information through the survey on how the respondents see price as influencing their choice. We asked them at what price increase of a ^{99m}Tc-based radiopharmaceutical (of which the ^{99m}Tc is often only a minority component) they would decide to move to alternative modalities. The responses indicated that a price increase of 230% of the radiopharmaceutical would lead to

1/3 decrease in ^{99m}Tc-based radiopharmaceuticals compared to current demand, while a 500% price increase would result in a 2/3 decrease, and a 1 000% increase would be necessary to decrease demand for ^{99m}Tc-based procedures to zero. From these results, ^{99m}Tc demand appears to be quite inelastic – meaning that changes in price have smaller changes in the overall demand of the product.

However, we recognise that these figures should be treated with care, as a more elaborate study would be required to accurately determine the price elasticity of ^{99m}Tc demand. Such a study may be directed at a different audience that was not well represented in this survey, i.e. the economic decision makers within hospitals, clinics, insurance companies, medical directors, CFOs, administrators, etc.

Global trends

Drawing from the results of the global survey, the EAG analysed in more detail some key drivers that represent a wider trend. The aim of this discussion was to establish the potential impact of these trends on the future ^{99m}Tc demand and the probability of the impact occurring, in order to validate the survey results. Since the mature and emerging markets are different with respect to these trends, they will be discussed separately when appropriate.

Trend 1: growing population, urbanisation and wealth increases

According to the United Nations, the world population is projected to reach around eight billion by 2023, from approximately seven billion today (UN, 2011). Asia currently accounts for over 60% of the world population with more than 4 billion people; China and India together have about 37% of the world's population. The growing population is expected to lead to an increase in diagnostic imaging, assuming that access to medical care will not decrease.

This growing population coincides with a growing urbanisation and increasing growth of wealth in low- and middle-income countries (World Bank, 2006). Urbanisation generally indicates increased development and growing wealth: by 2030 the middle-class population is expected to grow to 1.2 billion people (currently 400 million). However, it is expected that mature markets have already seen the greatest impacts of urbanisation and growing wealth while emerging markets will be most affected by this trend. Therefore the expected impact of urbanisation and growing wealth on ^{99m}Tc demand in emerging markets is a high increase, while mature markets would see a low increase.

The EAG has strong confidence that these impacts will occur. From this, the EAG validates the survey results indicating expectations of increased diagnostic imaging. The EAG also indicates that this supports the expectations of a small increase in ^{99m}Tc demand in mature markets, with a larger increase in emerging markets. The EAG does caution that in mature markets this increase in demand for diagnostic tests may also support substitution to new modalities in the long run; however building infrastructure for PET imaging is much more expensive and complicated than ^{99m}Tc-based imaging (see Trend 4 below).

Trend 2: ageing population and changing prevalence of medical conditions

This second trend is partly related to the previous one, but here we focus on the medical consequences of demographic change. In the mature markets, ageing is an important societal challenge, especially with regards to health care impacts. Coupling the effect of ageing populations with effective health care systems means that one could expect an increased need for patient care as an ageing population will likely see increased prevalence of cancer or cardiac diseases and a corresponding increase in treatment.

Since more people will need diagnostic imaging and the vast majority of these procedures are currently based on ^{99m}Tc-based SPECT scans, the EAG expects a medium positive impact in the mature markets on ^{99m}Tc demand, with a medium to high probability. In emerging markets, ageing is not such a challenge as yet, explaining the expectations of a low impact at first (with high probability). However, looking at 2030, the emerging markets' younger populations will have aged (UN, 2009) and therefore it is expected that there will be a large impact in the long run. By 2030, both ageing and wealth will have increased significantly in emerging economies. Consequently, more imaging procedures can be expected for diagnostic scans, which would drive an increase in demand for ^{99m}Tc.

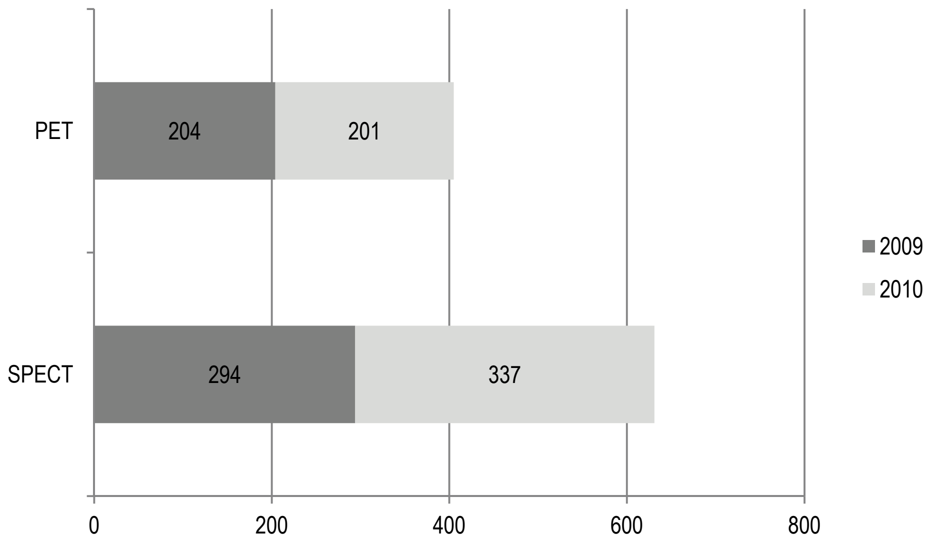
Trend 3: availability of cameras

Use of ^{99m}Tc depends on cameras for imaging. The present sales and expected trends of imaging hardware thus serve as good indicators for both the SPECT/PET shift as well as for whether emerging markets will skip the use of SPECT completely. In general, one could assume that sales of cameras serves as a proxy for demand for radiopharmaceuticals; the more cameras available the more sales will be seen in the related radiopharmaceuticals.

In China and India PET is on the increase, but similar numbers of SPECT cameras are sold as well. India, for instance, bought 20 PET cameras and 30 SPECT ones. Worldwide, there are approximately 2 000 PET or PET/CT cameras compared to about 22 000 SPECT cameras. In addition, since 2008 the sales of PET or PET/CT cameras are declining, because the market seems to be saturated – at least until replacements after the first life cycle. At the same time, there currently is a growth in SPECT/CT cameras, which is mainly replacement of older SPECT cameras. The view of the EAG is that SPECT cameras are not replaced by PET cameras but rather replaced by a new SPECT or SPECT/CT.

A key consideration related to the ongoing availability and growth of SPECT cameras is cost. The costs for PET cameras (EUR 1-2 million) are substantially higher than for SPECT cameras (EUR 400 000-800 000) – second hand SPECT cameras are also available, and even cheaper (EUR 150 000-300 000). It is expected that cardiac PET cameras will remain expensive for some time.

Figure 5.6: Estimated sales of PET and SPECT cameras in the world, except North-America (in number of units)



Note: Based on turnover data provided by COCIR – estimation by Technopolis, assuming average cost PET: EUR 1.5 million and SPECT: EUR 0.6 million.

In addition, PET cameras have specific infrastructural requirements, as they typically operate with tracers with a very short half-life. In order to be economically viable, a cyclotron needs to be serving four to five PET scanners. This is not much of a problem in denser and wealthy populations, but it is a barrier in more remote and rural areas (i.e. the emerging markets).

As a result of the cost difference and the time required to increase the availability of cameras, provide training and develop the medical infrastructure, the EAG expects that the availability of SPECT cameras will provide a high increase for ^{99m}Tc demand in emerging markets. The cost impact will be important as SPECT is still the cheapest option and emerging markets (as well as mature markets) are trying to manage the costs of health care. Given uncertainties about the long-term changes, the expected high increase remains for 2030, but with less certainty about the expectation.

For mature markets there is already a significant number of SPECT cameras in the market; there is a smaller number of PET cameras but purchases are taking place. With the understanding that SPECT cameras are generally replaced by SPECT or SPECT/CT cameras, but with PET cameras resulting in some replacement of SPECT procedures, the EAG expects an on-going medium growth impact on the use of ^{99m}Tc, but with certainty of this expectation at only a medium level. One key point that leads to additional uncertainty on the impact is that as new SPECT cameras are installed, they will likely be more efficient and thus lead to reduced demand for ^{99m}Tc for the same number of procedures.

Trend 4: SPECT/PET shift

One of the major issues in the discussions on future demand of ^{99m}Tc is whether PET will substitute for ^{99m}Tc-based procedures. From the survey, the top two drivers for decreased ^{99m}Tc demand are related to the use of substitutes (radiopharmaceuticals/contrast agents and modalities). More than 75% of the survey respondents expect that PET and combined PET modalities will eventually be more dominant and will replace SPECT procedures.

The EAG believes that PET modalities will substitute for some SPECT procedures between now and 2020/2030, although the level of substitution is expected to be low. However, they do indicate significant uncertainty around this prediction as there are a number of factors that could impact the substitutability of modalities.

Although the expectation of low substitutability is slightly contrary to the survey results, the EAG provided a critical analysis of the issues facing potential substitutions, which are discussed below. In addition, they recognised that a key uncertainty is related to the timing and pace of substitution; therefore substitution may occur, but likely at a pace slower than predicted by the survey respondents.

There are a number of factors that would prohibit or hinder the substitution of SPECT procedures by other modalities in the next decade or so. The first is that SPECT infrastructure and procedures are generally much cheaper than PET infrastructure and procedures. In addition, PET based infrastructure requires a larger team at the hospital or clinic compared to SPECT infrastructure. Related to this is the level of education and training that is available; in general there is a large SPECT installed base and much experience whereas PET still has a small installed base and therefore there is less experience with the technology. This will encourage the on-going use of SPECT procedures and the infrastructure, especially in emerging markets.

In addition, there are only a few PET radiopharmaceuticals approved for use, and the EAG indicated that the development and approval process of new radiopharmaceuticals is difficult and expensive. Coupling this restriction with the fact that not all the current SPECT procedures can be replaced by currently available PET radiopharmaceuticals, again supports the view that substitution of SPECT procedures will not be rapid.

In general, the EAG noted that SPECT provides high quality scans, so there is not an obvious incentive for a quick replacement with other, some currently not-available, PET procedures.

The EAG did recognise that the medical community is looking towards PET as a key modality for the future, but other imaging techniques such as MRI and stress-echo, and functional imaging with PET/CT, are key modalities as well. However, it is expected that all these techniques will be used in a balanced way. PET will replace some SPECT procedures, but will not be able to replace all. PET and other modalities will likely supplement the current SPECT procedures, moving into different areas, but not replacing directly SPECT. In addition, they recognise that some of the PET growth will capture the expected growth in overall diagnostic imaging, meaning that SPECT will have a smaller share of the overall market, but will not see an overall decline in absolute terms.

A note of caution to this assessment is the fact that stability of radiopharmaceutical supply is key to ongoing support for using a certain technology or radiopharmaceutical. If the ^{99}Mo/^{99m}Tc supply faces challenges like they have faced recently, this could increase the pace towards technology substitution. A perception of long-term unreliability could have the same effect; however, the survey indicated that most respondents indicated a confidence in having stable supply moving forward.

Taken these issues together, substitution of SPECT by PET would have a negative effect on ^{99m}Tc demand, but in the context of the different issues above the impact will be low.

However, all it takes is one paradigm shift; and the system could completely change. If new PET-based radiopharmaceuticals can come onto the market, or if there is a breakthrough in the costs of PET infrastructure, there could be a significant substitution of SPECT. For this reason, the EAG noted that there was a great deal of uncertainty related to the issue of substitution and they provided a low certainty related to their prediction of low substitutability.

Trend 5: new radiopharmaceuticals

As indicated by the respondents, the development of new radiopharmaceuticals for PET for studies that are currently done by SPECT or planar, could have a significant negative impact on ^{99m}Tc demand. This expectation is partly based on the fact that there has not been any development of new radiopharmaceuticals based on ^{99m}Tc, while there has been a lot of attention related to the development of new PET tracers. PET always had a different approach: since the early 1990s there has been considerable development of tracers.

However, the actual uptake of new radiopharmaceuticals could be quite limited as health regulatory approvals take time and are seen to be quite difficult. Taking a radiopharmaceutical to the market reportedly takes up to EUR 15 million in investment and not many players are willing to take such a risk. This may explain why from the 20 tracers that were in development 10 years ago none has made it to the market. Now only a few are in development, one of which is a PET tracer for cardiac disease that is now in clinical trials phase 3. If this is approved, there could be a shift to PET for cardiac perfusion. Since this PET tracer, no new radiopharmaceutical has entered the clinical phase. In addition, in some jurisdictions it is difficult to get new radiopharmaceuticals approved for reimbursement through health care systems, supporting the ongoing use of ^{99m}Tc-based radiopharmaceuticals that have already been approved.

The development of other new radiopharmaceuticals, such as for the detection of Alzheimer disease, might increase demand. However, there is still significant uncertainty as to whether radiopharmaceutical companies will invest the necessary funds to develop and approve new radiopharmaceuticals, especially if they are only for detection and not for therapy of the conditions. In addition, there is significant uncertainty as to whether the new radiopharmaceuticals will be based for SPECT or other modalities (e.g. PET).

Taken together, the EAG expects a negative impact of new (PET) radiopharmaceuticals on ^{99m}Tc demand, having a medium probability up to 2020, which is related mainly to the new cardiac PET tracer. In the long run, the development of new PET-based radiopharmaceuticals would significantly reduce demand for ^{99m}Tc in mature markets; however, there is still significant uncertainty on whether new radiopharmaceuticals will actually be developed and approved. In emerging markets, the effect of new radiopharmaceuticals is expected to have less of a negative impact on ^{99m}Tc demand between now and 2030 as mature markets are expected to lead the development of new radiopharmaceuticals, with emerging markets picking up the product later.

Assessment of global trends

The EAG made an assessment of the impact and the probability (or certainty) of the five major trends having the impact predicted on the demand for ^{99m}Tc. The impacts and probabilities differ largely in different jurisdictions, especially between emerging and mature markets. Table 5.5 summarises the assessment of the experts for mature markets; Table 5.6 for emerging markets.

For mature markets, the EAG expects ageing and prevalence of associated health issues and availability of (improved) SPECT cameras to have a medium positive effect on ^{99m}Tc demand, with medium/high certainty by 2020-2030. Availability of new radiopharmaceuticals may have a large negative impact on ^{99m}Tc demand, but the certainty is rather low as the actual amount and type of new PET tracers are unknown. A shift from SPECT to PET is considered to be unlikely and low impact. New imaging technologies are expected to be an add-on to the existing set of imaging procedures, rather than replacements for established (and cheaper) technologies. Growing wealth and ongoing urbanisation are expected to have a minor positive effect on demand in mature markets, as they are already reasonably wealthy and urban.

Table 5.5: Global trends and the expected impacts on ^{99m}Tc demand in mature markets

	Mature markets			
Trend	2020		2030	
	Impact	Probability	Impact	Probability
Growing wealth and urbanisation	+ Low	High	+ Low	High
Ageing prevalence	+ Medium	Medium/high	+ Medium	Medium/high
Availability cameras	+ Medium	Medium	+ Medium	Medium
SPECT/PET shift	- Low	Low	- Low	Low
New radiopharmaceuticals	- Medium	Medium	- High	Low

Note: 2011 EAG workshop: *impact* indicates weight (high, medium, low) as well as direction (+/-) that EAG expects the trend to have on ^{99m}Tc demand if it were to occur; *probability* represents the degree of certainty that the predicted impact will occur.

In emerging ^{99m}Tc markets, the EAG expects global trends to have more impact. Demographic changes, such as growing population, urbanisation and ageing are important trends with a positive effect on the demand for ^{99m}Tc. Growing wealth and urbanisation will certainly have a large positive impact on ^{99m}Tc demand. In the longer term, a high positive impact of ageing and the increased prevalence of related diseases will amplify this predicted growth, with medium probability. The growing availability of cameras (both new and second hand)[4] will have a large impact on the ^{99m}Tc demand by 2030, with a high degree of certainty. A low impact is expected from a shift from SPECT towards PET cameras and use of new radiopharmaceuticals in emerging markets by 2030; for the former, the EAG has low certainty on the prediction while they have more certainty on the latter prediction.

Table 5.6: Global trends and the expected impacts on ^{99m}Tc demand in emerging markets

	Emerging markets			
Trend	2020		2030	
	Impact	Probability	Impact	Probability
Growing wealth and urbanisation	+ High	High	+ High	High
Ageing prevalence	+ Low	High	+ High	Medium
Availability cameras	+ High	Medium	+ High	High
SPECT/PET shift	0	Low	- Low	Low
New radiopharmaceuticals	- Low	Medium	- Low	Medium

Note: 2011 EAG workshop: *impact*: indicates weight (high, medium, low) as well as direction (+/-) that EAG expects the trend to have on ^{99m}Tc demand if it were to occur; *probability* represents the degree of certainty that the predicted impact will occur.

5.4 Demand scenario

Discussion

In this document we have gathered the expectations of over 700 experts in diagnostic imaging. The results from the survey and the views of the expert advisory group have allowed for an educated analysis of the long-term future demand for ^{99m}Tc. The EAG analysis of the key drivers of change has validated the survey results, recognising the significant uncertainty when discussing future demand almost 20 years out.

[4] The shift from single SPECT cameras to multiple modality cameras (i.e. SPECT/CT and SPECT/MR) may play a significant role in the emergence of a second hand market. An EAG participant stressed that even today second-hand cameras with relatively high quality can be obtained.

The EAG was not able to arrive at unanimous agreement on whether ^{99m}Tc would be completely replaced in the very long run. However, given the uncertainties around substitution, the expert panel believes that the pace of change is slow and before 2030 there will not be substitution at such a level to actually reduce ^{99m}Tc demand. In addition, the other external factors potentially affecting ^{99m}Tc demand will slow historical growth, but will not remove its overall demand.

Another key element of the survey results, and one agreed to by the EAG, is the conclusion that the majority of the actions taken during the 2009-2010 shortages will not be permanent. The exception seems to be some few cases where more efficient elution from the generator and more efficient patient scheduling may remain. Again, these results may be changed in the future if there is pressure from tightening reimbursement rates or increased costs, where better use of generators may result in cost savings. However, expectations today are that the majority of changes have or will return to pre-shortage practices.

Given its analysis, the EAG endorsed the results of the survey, and found it probable that ^{99m}Tc demand will grow approximately 20% between 2010 and 2020, and 25% between 2010 and 2030, in mature markets; 40% between 2010 and 2020, and 50% between 2010 and 2030 in emerging markets. This represents an average annual growth rate of approximately 1.1 to 1.85% in mature markets and 2 to 3.42% in emerging markets, assuming straight-line growth from 2010 for both 2030 and 2020 (respectively). Incorporating the two points in the same growth line provides a representative annual growth for the mature markets as 1.84% from 2010 to 2020 followed by annual growth of 0.4% from 2020 to 2030; for emerging markets, this is 3.42% to 2020 followed by 0.69% between 2020 and 2030.

The EAG furthermore concluded that unexpected changes of any kind could have large effect on demands, especially if changes take place in jurisdictions where demand is currently large (i.e. Europe and North America). The EAG recognised the importance of costs of ^{99m}Tc with regard to this, and emphasised that reimbursement rates for technetium-based procedures and competing imaging modalities play a crucial role.

With regard to the results concerning subsets of the total survey sample size, it should be noted that the results of smaller subsets of respondents, i.e., emerging markets and division towards expertise are subject to higher uncertainty, because of smaller sample size. Therefore, correlations between answers of different populations in the sample were not significant.[5]

Scenario of ^{99m}Tc demand

To construct a quantitative future demand scenario based on the results of the survey and the input of the EAG, we would require a solid baseline on use in the various regions in the world. Although efforts were made, data on ^{99m}Tc consumption were not available for all regions. Various

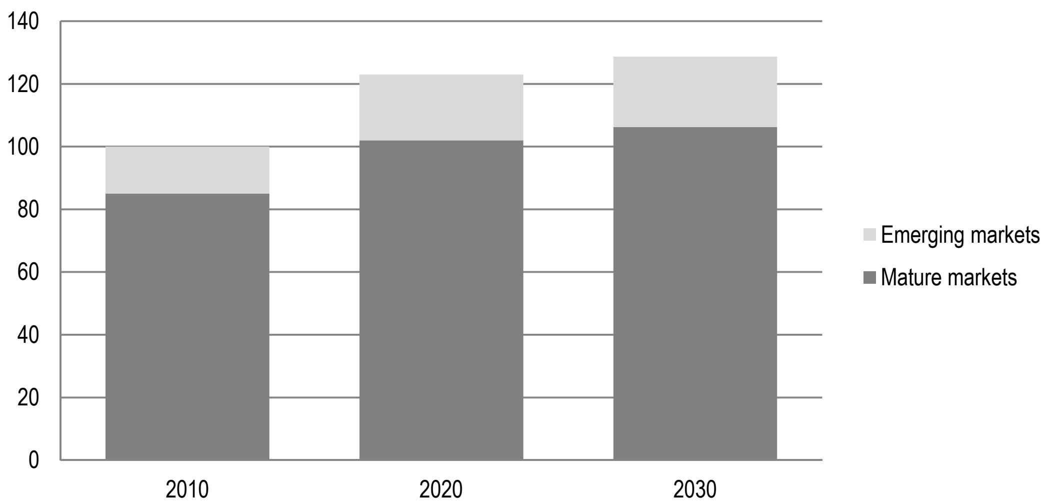
[5] See background report for more information.

(sometimes conflicting) figures exist on the number of procedures undertaken annually, however these are not provided for all the various regions examined in this global survey.

However, recognising the uncertainties inherent in a long-run future forecast, a general direction and size of changes in demand are sufficient. The scenario below provides that direction and size of change taking 2010 as 100 and then applying the growth rates from the survey: approximately 20% between 2010 and 2020, and 25% between 2010 and 2030, in mature markets; 40% between 2010 and 2020, and 50% between 2010 and 2030 in emerging markets. These growth rates were applied based on data that mature ^{99m}Tc markets represent 85% of the total market and emerging ^{99m}Tc markets represent 15%.[6]

The scenario below does not provide a growth path for ^{99m}Tc demand as the survey only provided data on two distinct points: 2020 and 2030. We did not want to provide a growth path in this document that may be misleading to readers.

Figure 5.7: Expected future demand of ^{99m}Tc, 2010 = 100



Scenario of ^{99}Mo demand

The original purpose of the overall project was to understand the impacts of future demand on the need for new ^{99}Mo producing infrastructure. This question is important given the required level of investment and decision makers need to have information to allow them to assess whether or not the investment will be used in the future, at least for a period long enough to make the investment worthwhile.

[6] Derived from data presented by Natural Resources Canada during NEA workshop on Security of Supply of Medical Isotopes, 29-30 January 2009, and updated with information on Australian demand.

From the results, it is clear that there will be an ongoing demand for ^{99m}Tc at least until 2030. Although views among survey respondents varied, the overall results show continued, albeit slow, growth. The share of ^{99m}Tc-based procedures within the overall imaging diagnostic market is expected to fall, but the absolute demand for ^{99m}Tc will not decrease between now and 2030.

Given that the majority of global ^{99m}Tc supply comes from ^{99}Mo produced in research reactors, we can derive a reasonable idea of the expected future need for ^{99}Mo from our results. Based on the survey results, we can assume that the same amount of ^{99}Mo is required to produce the ^{99m}Tc used globally (i.e. elution efficiencies are not sufficiently applied to result in less ^{99}Mo being required for the same amount of ^{99m}Tc).

Prior to the 2009-2010 shortages, the global demand for ^{99}Mo for ^{99m}Tc production was approximately 12 000 6-day curies per week. Although revised demand numbers are not currently available, it has been reported that following the shortages, world demand was approximately 9 000 6-day curies per week. More recent information from the supply chain has indicated that demand may be returning closer to pre-shortage levels. Looking at both a 12 000 and 9 000 starting point, the following figures show the forecasted demand of ^{99}Mo for 2020 and 2030.

Figure 5.8: Forecasted demand of ^{99}Mo

2010 demand = 12 000 6-day curies of ^{99}Mo per week

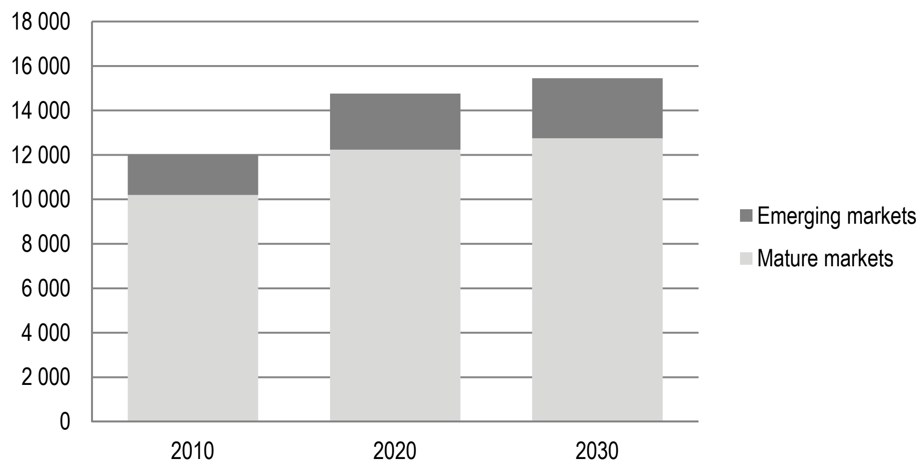
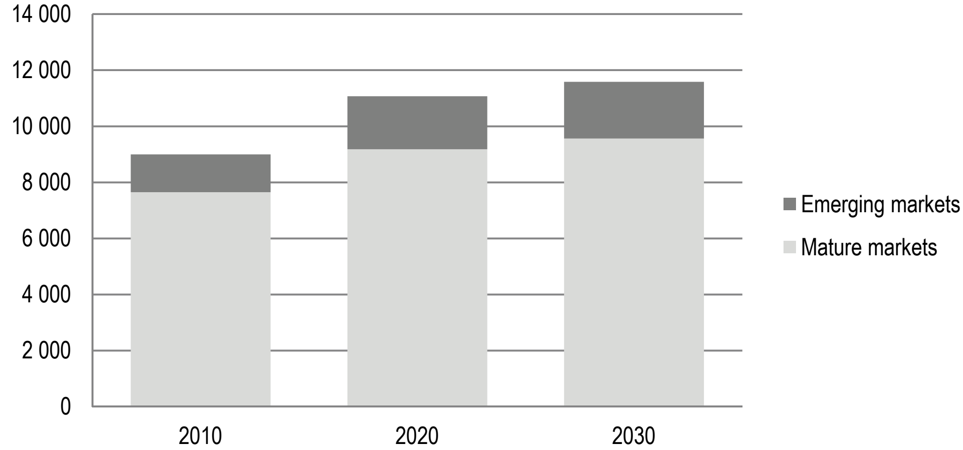


Figure 5.9: Forecasted demand of ^{99}Mo

2010 demand = 9 000 6-day curies of ^{99}Mo per week



5.5 Conclusions

The HLG-MR requested that a demand study be undertaken to provide an indication of the long-term demand for ^{99}Mo/^{99m}Tc. This request was based on significant uncertainty in the industry as to the future of these isotopes, with supply chain participants suggesting different futures.

The uncertainty came from whether changes in ^{99m}Tc use during the 2009-2010 shortages would remain after supply returned to normal. In addition, there are a number of recognised external forces that could affect future demand, including the development of other modalities, emerging ^{99m}Tc markets, the effects of changing reimbursement rates in some jurisdictions, expectations of future stability of ^{99m}Tc supply and demographic trends.

The results from the survey and the EAG analysis have provided a better understanding of the possible long-term effects of these changes, resulting in an expected steady growth of ^{99m}Tc demand, at a slow pace. Demands are expected to grow faster in emerging markets, but from a smaller base. The results show that substitution of ^{99m}Tc-based procedures by alternative modalities or isotopes will likely have an impact on the overall share of ^{99m}Tc in diagnostic procedures, but will not reduce the absolute amount of ^{99m}Tc being demanded.

This forecast for ^{99m}Tc growth translates reasonably to a similar situation for ^{99}Mo demand. If the changes seen during the 2009-2010 shortage related to efficient use of ^{99m}Tc were predicted to continue, there would have been a greater impact on ^{99}Mo demanded. However, survey results indicate that most of the pre-shortage practices were returned to after the shortages ended. Based on these results, it is reasonable to predict that ^{99}Mo demand will continue to grow at levels equal to approximately 2% annually until 2020 and then levelling off to a growth rate of less than 1% annually until 2030.

Chapter 6

Transportation and Procurement Issues

6.1 Introduction

Throughout the mandate of the HLG-MR, the transportation and procurement logistics have been raised as a key vulnerability within the supply chain. There is a need for efficient and effective transportation and related regulations to ensure optimal supply; issues can arise at every step of the chain:

- sourcing and transporting enriched uranium;
- transporting fabricated targets to research reactors;
- transporting irradiated targets from the research reactors to the processing facility;
- transporting bulk ^{99}Mo from the processor to the generator;
- transporting generators to hospitals or radiopharmacies.

In many instances the transportation crosses international boundaries. All parts of this transportation network need to work well for the supply chain to function properly and for there to be security of supply.

This chapter looks at the process and regulations affecting procurement and transportation. The discussion is directed towards those organisations that participate in, or regulate, this part of the supply chain. The chapter seeks to provide clarity on the major processes and the issues around those processes and provides recommendations to increase reliability and consistency.

This section considers the transport issues for the supply chain from the purchase of uranium through to generator delivery to hospitals or radiopharmacies. At each stage, there are issues to do with approvals for transport routes and containers. In most cases, these are covered by existing transport regulations, based on the *Regulations for the Safe Transport of Radioactive Material – 2009 Edition,* IAEA Safety Standards Series (TS-R-1) (IAEA, 2009), but other regulations relating to handling nuclear materials are also invoked in various stages of this process (including security and safeguards). The 2009-2010 shortages have put pressure on these processes and revealed some areas where additional processes may be needed to minimise delays. This is especially true for operators wishing to open up new routes.

6.2 Procurement and transport of enriched uranium

Issues

The key issues related to procurement and transportation of enriched uranium for use in targets by the reactor are the potentially long process involving multiple United States[1] agencies and the need for separate approvals to purchase and to export enriched uranium. These processes relate primarily to controls to prevent proliferation of nuclear material.

Discussion

Purchase of special nuclear material for civilian use will usually require that a bilateral safeguards agreement between the supplier and purchasing country (or equivalent) be in place beforehand. The export of HEU or LEU from the United States, which is the principle global supplier, requires a licence issued by the US Nuclear Regulatory Commission (NRC). The licence application requires that a contract with Y12 for the supply of the enriched material be in place.

NRC Regulations 10CFR Section 110.42 permit export of HEU to be used as a fuel or target in a nuclear research or test reactor, provided:

- There is no alternative LEU nuclear reactor fuel or target that can be used in that reactor.
- The proposed recipient of the uranium has provided assurances that whenever an alternative LEU nuclear reactor fuel or target can be used in that reactor, it will be used in lieu of HEU.
- The United States Government is actively developing an alternative nuclear reactor fuel or target than can be used in that reactor.

Other requirements for export approvals include provision of a letter of assurance from the recipient country. The export licence also identifies intermediate and ultimate consignees (person, organisation or government which prepares a consignment for transport) and any other parties involved.

The approval for the license to export HEU requires a multi-agency process involving the NRC, the National Nuclear Security Administration and the Department of State. The Department of State leads a United States government interagency review of the export licence application. In

[1] The United States is the principal supplier of enriched uranium for the major molybdenum-99 producers.

addition to this interagency review, there is a minimum 30-day public review period of the export licence application. The interagency review examines whether the amount of HEU requested is appropriate, verifies that the government assurances are in place, verifies physical security at the receiving facility and determines if the export of HEU is appropriate for the requested use. The interagency review provides a recommendation to the Department of State which then informs the NRC. The NRC then seeks NRC Commission approval for the export licence. Once the export licence is granted, the recipient import licence process is initiated. Assuming no physical protection upgrades at the recipient site, no public intervention and that government assurances and other required agreements are in place, the process typically takes at least 18 months.

Section 134 of the Atomic Energy Act of 1954 (42 U.S.C. 2160d) was amended by Section 630 of the Energy Policy Act of 2005 (Pub. L. 109-58, 8 August 2005, 119 Stat.594) allowing for the United States to continue exporting HEU to Belgium, Canada, France, Germany and the Netherlands solely for the production of medical isotopes on certain conditions, including that the countries supply an end-use assurance, and that the HEU will be irradiated in a reactor that uses LEU fuel or commits to convert to LEU fuel when it is available.

However, the American Medical Isotopes Production Act of 2011 (S.99) was introduced in the United States Senate in January 2011. This act seeks to set a time limit on continued export of HEU for the purposes of ^{99}Mo production (seven years after the enactment of the act), provided the United States domestic supply can be ensured within that timeframe. Department of Energy funding for the establishment of United States commercial LEU ^{99}Mo production is a provision in this bill. As of May 2011, this bill had not yet been approved by the United States Senate. A similar bill was passed in the House in 2010 (the American Medical Isotopes Production Act of 2009) but it was never passed by the Senate.

The other main source of HEU and LEU is the Russian Federation. No information was obtained on what the arrangements are for approvals.

Recommendation

In general, this is not the highest priority issue, since the purchases are infrequent but, nevertheless, there are opportunities for streamlining the process. The length of this regulatory approval process becomes a concern when there are shortages of available HEU for the production of targets. The use of longer-term contracts with appropriate approvals would have advantages in shortening the transport and procurement process.

6.3 Transport of uranium and target plates (to and from manufacturer)

Issues

There are a number of issues that make the transportation of uranium and target plates difficult:

- Multiple approval processes (for storage, security and safety purposes) from multiple regulators in each country concerned by the shipment are needed; the concerned countries are the ones through or into which the transport is taking place, and sometimes the ones over-flown. For example, the notification of shipments (for safety) and the certification of routes and means of transport (for security) are required from different regulators in the same country.

- Approved package designs (from safety regulators) may not always be available for one or more country on the itinerary.

- The transport of fissile material requires a multilateral approval which potentially can lead to longer approval processes.

- There can be a potential misalignment between countries in regards to the applicable transport regulations, with the implementation of different editions of TS-R-1 and in regards to its application. This would result in a more stringent review of the package design safety case performed by one of the countries concerned by the shipment.

- The recent shortages required countries to seek alternative supply routes and therefore required package designs and new routes to be approved by the competent authorities concerned by the transport.

Discussion

To transport uranium and unirradiated target plates requires compliance with safety, safeguards and security regulations, recognising the nature of the material as both a radioactive substance and nuclear material subject to security and non-proliferation requirements. Most organisations use a transport agent experienced in the export process, given the need for an export licence from the supplier country, an import licence from the importing country and transport route approvals, including in any countries where the uranium will be processed (e.g. made into targets, etc.). This expertise is also required for sending manufactured target plates to the reactor operator.

In addition to the safety transport regulations, security requirements, usually based on INFCIRC/225/Rev4 (currently being updated to Rev5) are recommended for IAEA Member States. An understanding of each "transit" country's regulatory framework and degree to which INFCIRC/225 and TS-R-1 have been adopted is necessary.

Depending on the level of enrichment of the uranium, there are different security categorisations of shipments, requiring different measures to be followed by the transporter. Categorisation of shipments is described in Table 6.1 and determines physical protection requirements during transport and storage. Fuller details are found in the relevant regulations.

The range of measures required for multi-country transits for shipment of Category 1 material are complex. This complexity is compounded if regulations applying to safety, transport modes and physical protection during transport of radioactive materials are not aligned between countries.

Table 6.1: Categorisation of uranium for shipments

Unirradiated ^{235}U	**Cat I**	**Cat II**	**Cat III**
Uranium enriched to 20% or more	5 kg or more	Less than 5 kg More than 1 kg	1 kg or less but more than 15 g
Uranium enriched to 10% but less than 20%	n/a	10 kg or more	Less than 10 kg but more than 1 kg
Uranium enriched above natural but less than 10%	n/a	n/a	10 kg or more

For multi-country transits, the consignor must notify the competent authority in the country of origin of the shipment and the competent authorities of each country through or into which the consignment is to be transported. Transport may be by road, sea or air but there are different requirements for transport containers:

- Competent authority country of origin certification is required for the transport cask.
- Competent authority validation of country of origin certification required for all transit or overflight countries.

Recommendation

This is a medium priority issue, since there are other reactors entering the supply chain and there will be a need for fabrication and transport of targets. Common adoption of best practices by regulators on package design approval could shorten and harmonise the authorisation/approval process and make more routes available to alleviate worldwide shortages.

6.4 Transport of irradiated targets

Issues

The issues concerning the transportation of irradiated targets are related to:

- Transport through multiple countries requires approvals from multiple national regulators.
- In many cases, these countries do not apply identical requirements for safety cases and package design approvals.

- Only transport by road is currently approved and economical and this creates a regional limitation.

Discussion

To be transported, irradiated material requires either a type B(U) or B(M), B(U)F or B(M)F package design, depending on the maximum mass of transported fissile material. A type B(U) package design does not require validation in every country concerned by the shipment (i.e. those through or into, and sometimes the ones over, which the transport is taking place) if already validated in one concerned country. A type B(M) package design requires a multilateral approval, meaning that the package design approval must be validated by all the countries concerned. A package design with a content of more than 15 g of ^{235}U (fissile material) is required to comply with type F requirements. The type F package, like the type B(M), requires multilateral approval. Given the lower content of ^{235}U in LEU targets, greater quantities of LEU targets than HEU ones can be transported in one package.

Transport of irradiated targets using B(U)F packages by road is now done in Europe. Most recent additions to the transportation routes has been for the transport of targets from the MARIA reactor in Poland to Covidien's plant in the Netherlands and for the transport of targets from the LVR-15 reactor in the Czech Republic to IRE in Belgium. These packages are generally able to be docked into the hot cell at the receiving area. Due to the significant decay that takes place and the potential requirements for multiple drivers and vehicles, a maximum distance of 1 000 km is considered the limit for transporting irradiated targets.

For transport of irradiated targets through multiple countries, approvals are required from multiple national regulators, based on similar but not identical requirements for safety cases and package design approval. Again, some form of standardisation of approval processes, including *de facto* mutual recognition, would seem to offer the potential for shortening the approval time. Such moves are already underway in Europe and North America but not elsewhere in the world.

Transport by air requires adapted packages and related approvals, but this mode of transport for irradiated targets is unlikely because of concerns by the various air carriers and transit countries and the costs of transporting large packages by air. However we note that the Russian Federation has transported spent fuel from Romania by air and that the detailed safety case was approved by the regulator. A dedicated plane was used for the shipment.

It has been proposed by the transport community to increase the fissile excepted threshold of ^{235}U to 45 g. This change is unlikely to come into force before 2013, since this kind of content requires multilateral approval.

Recommendation

This is a medium priority issue as it is linked to increasing the number of reactor sources. Mutual agreements between regulators in shipment countries could shorten the approval and validation process and make more routes available to alleviate any possible future worldwide shortages. However, this would need to involve both safety and security regulators. The development of common targets may also streamline the safety approval process, since it would increase experience and sharing of information among regulators.

6.5 Transport of bulk ^{99}Mo and generators overseas

Issues

In addition to the issues shared with the transportation of enriched uranium and targets, the issues specifically related to the transport of bulk ^{99}Mo and generators are:

- The time taken to do dangerous goods checking (between four and six hours when a dangerous goods qualified person is available) makes it difficult and expensive to ship the short half-life products. This time requirement remains even when the same products are shipped very regularly.

- Some countries or territories require import permits five days in advance even though the product is only transiting.

- Transport companies have concerns related to the transportation of radioactive materials leading to the denial of shipments. For example, there have been problems with return of spent generators because some shippers do not understand the difference between an "excepted package of radioactive material" and a radioactive package.

Discussion

Transport of ^{99}Mo either in bulk or in generators involves the same issues faced by the transport of the enriched uranium and the irradiated targets:

- Approval of package designs or validation for shipment is required by the countries concerned by the shipment (i.e. those through or into, and sometimes the ones over, which the transport is taking place).

- Certification of transport routes is required, meaning that a package design approved for transport on one route may not be approved on a different route.

- Package design approval or route certification processes are often different in different countries.

- In many countries several agencies are involved in the approval process and there may not be adequate co-ordination internally or a single process available to the licensee.

- Between countries, there may be no acceptance of another country's approval and therefore it often requires additional approvals that can have quite lengthy timeframes.

An additional concern related specifically to the transport of bulk ^{99}Mo and generators is the denial of shipment for ^{99}Mo transport that occurs in all parts of the world, with the greatest problems appearing to be in Canada, Japan and the United States. These denials may be exacerbated by the labelling of ^{99}Mo as radioactive material – a class which covers a full range from medical isotopes to large activity sources – without any distinction of its medical nature.

There was some discussion during the last five years regarding a new classification for medical isotopes currently under the Class 7 designation. It received very mixed reviews from regulators, the International Air Transit Association (IATA), the International Civil Aviation Organization (ICAO) and the International Steering Committee (ISC) members and has not been taken forward. Nevertheless, some groups involved in medical isotope transport are raising this possibility again. Although it sounds reasonable and may help to differentiate medical isotopes from other radioactive material, there are both practical considerations (i.e. definition, labelling, etc.) and timeframe (i.e. could take years to move it through the necessary process) issues. Another possible approach is to work with IATA to address the wording on the aircraft manifest; this could be taken up by the IAEA.

From a denial perspective, the ISC is aware of, and working to mitigate, issues in Europe where airlines such as KLM and BA have restrictions that create challenges for ^{99}Mo movement into and from the region. There are also ongoing issues where medical isotopes get off-loaded regularly from scheduled flights due to misinformation, lack of education of pilots or airlines, misinterpretation of the regulations, etc. The ISC has seen medical isotope shipments off-loaded when live animals, biological samples or human remains are on board the aircraft, when the pilot deems this other cargo to be a higher priority. The latter may be resolvable through education and awareness.

Of all the tools the industry and ISC have available, education and awareness of the products' uses, time criticality, patient impact, safety in packaging and shipment, and safety and security track record is the most effective and most needed. There is an IATA/CORAR video which was widely distributed to air carriers, pilot associations, etc., to be used for education purposes. This had a positive effect and it is this type of effort that needs to be continued throughout the rest of the world.

Recommendations

This is a high priority issue, since it relates directly to the transport of ^{99}Mo and generators that are designed to provide doses for patient treatments.

As with the shipment of enriched uranium and targets, harmonisation by regulators on package design approval could shorten the approval and validation process and make more routes available to alleviate any potential future worldwide shortages. This is occurring currently in Europe and could be extended to other countries. The IAEA could provide a helpful role in assisting regulatory authorities to either utilise the competency of another regulator or encourage development of codified design standards that can be easily checked to establish the ability of a package design to meet its purpose.

In order to facilitate the dangerous goods checking process, especially in the case of regular shipments, a standard licence for carriers of radioactive material should be pursued, similar to that expected to be proposed by the European Commission in 2011. This accreditation of shippers could allow for the process to move more quickly.

To deal with the issue of denial of shipments, more work on producing educational materials may alleviate concerns by transport companies. An updated education and awareness programme addressing the shortages and the priority need to expedite shipments should be considered by the shippers of ^{99}Mo.

For both of these last two issues, further examination of the use of different labelling may help reduce the incidence of denial of shipments and speed up the dangerous goods checking process. In addition, changing the wording of some of the descriptions used for the radioactive material could facilitate these processes.

6.6 Summary

The key issues in transport are the need to streamline and gain greater harmonisation in approval processes, and to tackle denials of shipment. The IAEA would be the appropriate organisation to work with international bodies and national regulators on common approaches to package design approval and route certification and the HLG-MR encourages the IAEA to take forward this issue as a matter of priority.

Chapter 7

Molybdenum-99/Technetium-99m Supply Chain Economics

7.1 Introduction

Consistent with early realisation that appropriate economic information and signals were critical to the pursuit of the security of supply of medical radioisotopes for the medium to long term, the HLG-MR requested that the NEA Secretariat undertake an economic analysis of the supply chain, from the irradiation of targets in research reactors to the delivery of the radiopharmaceutical to patients. Such an economic analysis had never been conducted before.

The report (NEA, 2010a) provides a good overview of economic factors affecting the supply chain historically and sets out a range of approaches to promote conditions for medium- to long-term security of supply. The report can be accessed through the NEA medical radioisotope website, www.oecd-nea.org/med-radio.

7.2 The supply chain and historical implications

Historically, only five reactors have been producing 90-95% of global ^{99}Mo supply, all of which are over 45 years old and subject to longer and more frequent planned and unplanned shutdowns. All the major producers irradiate targets using multipurpose research reactors, which were originally constructed and operated with 100% government funding, mainly for research and materials-testing purposes. When ^{99}Mo production started, the reactors' original capital costs had been paid or fully justified for other purposes. As a result, ^{99}Mo was seen as a by-product that provided another mission for the reactor that could generate extra revenue to support research. This resulted in:

- reactor operators originally only requiring reimbursement of direct short-run marginal costs;
- ^{99}Mo prices not covering any significant share of the costs of overall reactor operations and maintenance, or of capital costs or allowances for replacement or refurbishment costs;
- the by-product status remaining with no substantive pricing changes even as the importance of ^{99}Mo production increased among reactor operating activities.

As a result, prices paid to the reactor operator were too low to sustainably support the portion of reactor operations attributable to ^{99}Mo production, did not even cover short-run marginal costs in some cases, and did not provide enough financial incentive to support the replacement or refurbishment of ageing reactors.

The processing component, originally funded by governments, was commercialised in the 1980s and 1990s. Commercialisation was originally thought to be beneficial to all parties; however, contracts were based on historical perceptions of costs and pricing. This resulted in long-term contracts with favourable terms for commercial processing firms, with no substantial change to the prices for irradiation. Once these contracts were established, they set the standard for new processors and reactors that entered the market.

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

A complicating factor was the historical existence of excess capacity of irradiation services. Some excess capacity is necessary to provide back-up at times when reactors are not operating, or when unexpected or extended shutdowns occur. However, operators were not compensated for maintaining reserve capacity, creating an incentive for them to use the capacity to gain revenue rather than leaving it idle, driving down the prices of irradiation services further, reducing reliability and perpetuating processor market power.

Further downstream, pricing strategies of generator manufacturers were focused on encouraging sales of their cold kits. These strategies had a feedback effect upstream, with profits not flowing back through the ^{99}Mo supply chain and limiting the flexibility to absorb proposed upstream price increases.

The question that arises is: if the supply chain pricing structure was such that the irradiation services were economically unsustainable, why did reactors continue to irradiate targets? The answer is related to the social contract between governments and the medical imaging community. Governments subsidised the development and operation of research reactors and related infrastructure, including radioactive waste management. Using part of this funding, reactor operators irradiated targets to produce ^{99}Mo. In return, citizens would receive an important medical isotope for nuclear medicine diagnostic procedures.

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

Governments are re-examining their subsidies

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

Prices must increase, but the impact on end users will be small

Starting from a representative cost and pricing structure developed by the NEA, and based on information from supply chain participants, levelised unit cost of ^{99}Mo (LUCM) calculations were carried out to determine the magnitude of the price changes needed for economic sustainability. Their impact, based on various capital investment scenarios, was also examined. These scenarios range from using existing reactors to building a fully dedicated isotope reactor and processing facilities. Under all the scenarios, prices must increase. The analysis of the current economic situation found that, for existing reactors, the marginal revenue from production was lower than the marginal costs, with reactors facing a loss on every unit of ^{99}Mo produced.

The LUCM calculations indicated that significant price increases are necessary in the upstream supply chain in order for the latter to become economically sustainable. Reactor irradiation service prices would need to increase from EUR 45 per six-day curie (calculated from end of processing) to a range of approximately EUR 55 to 400. However, the analysis also finds that there is very little effect on the prices per patient dose. The reactor share in the final reimbursement rates would increase from approximately EUR 0.26 per procedure at pre-shortage prices to between EUR 0.33 and EUR 2.39 (see Table 7.1).

At pre-shortage prices, the irradiation price from the reactor (the EUR 0.26) is less than one-fifth of 1% of the final reimbursement rate (calculated as 0.11%). Even at the most extreme price increase from the reactor, the value of irradiation would increase to only 0.97% of the final reimbursement rate. The impact of the higher final radiopharmacy price on the reimbursement rate is minimal, increasing from 4.42% of the reimbursement rate to a maximum of 5.69%.

Table 7.1: Impact of price increases at hospital level

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

The analysis indicates that, while prices will increase for the downstream components, these should be able to be absorbed. However, this issue may require further study and possible assessment by hospitals and medical insurance plans, especially in the context of continued downward pressure on reimbursement rates or in cases where the health system provides fixed budgets to hospitals for radioisotope purchases.

Conversion to LEU would also have small effects on end users

The proposed conversion of targets normally containing between 45% and 93% ^{235}U (high enriched uranium – HEU) to targets containing less than 20% ^{235}U (low enriched uranium – LEU) for the production of ^{99}Mo has been agreed to by most governments for security and non-proliferation reasons. Even with uncertainty over costs of conversion for a major ^{99}Mo producer, it is clear that the current pricing structure provides insufficient financial incentive for the development and operation of LEU-based infrastructure.

However, in terms of the supply chain economics, the impact on the end user of converting to LEU targets is estimated to be quite small, even though the upstream price impact could be significant. Simulating conversion in a situation where the density of the uranium in the targets could not be increased significantly, the radiopharmacy price went from 5.06% to 5.58% of the final reimbursement rates and the share of the irradiation services increased from 0.35% to 0.86%.

7.3 Recommendations and options

The study makes a number of recommendations and investigates options to assist decision makers in restructuring the supply chain. These recommendations supported the HLG-MR development of the recommended policy approach presented in Chapter 10 of this report.

Government role in supporting the industry

Governments must first assess their role in the industry, especially as related to the level of subsidisation provided to the upstream ^{99}Mo supply chain (reactors and in some cases the processors). This is fundamentally a policy decision rather than an economic one.

The options for defining the social contract are based on the expected role of the government and the degree of financial support it is willing to provide. The government can choose to fund all capital and operating costs, with reactors charging only for direct marginal costs; to fund all infrastructure costs but require operations (including maintenance, upgrades, share of total reactor operating costs/overheads and waste) to be funded commercially; or to require all ^{99}Mo-related capital and operating costs to be covered by market prices. A transition period could be considered to allow time for the market to adjust to any new pricing paradigm. However, the first two options may create distortions in the international market.

The commercial model does not result in the government abdicating any health care responsibilities. Governments may decide to continue to pay for the use of ^{99m}Tc through increasing health insurance reimbursement rates. This is considered a more appropriate subsidy as it ensures the continued supply of ^{99m}Tc without specifying how it is produced. This would enable alternative technologies, if they are economic and efficient, to enter the market freely.

Paying for the full costs of ^{99}Mo

Regardless of the definition of the social contract, the reactor operator must be remunerated for the full costs of ^{99}Mo production. In addition, reactor operators must be compensated for maintaining reserve capacity. Where this remuneration will come from depends on the national social contract.

If governments decide to continue to provide financial support for ^{99}Mo production and reserve capacity, they need to commit to long-term, increased, ongoing remuneration to reactor operators, including dedicated funding for reserve capacity. They then need to decide if their support is to be only for their domestic market or for exports as well. In the latter case, they need to be aware that they have effectively entered into a social contract with the global supply chain. Government funding, in this case, could take the form of unilateral or international funding arrangements, with funding coming from either general taxes or charges applied to the ^{99}Mo/^{99m}Tc supply chain. An export tax could potentially be used to help reduce the amount of funds required from the general tax base.

Under a social contract of increased commercial funding, more appropriate market prices will be required to cover full costs. Reactor operators will need to require a substantial increase in prices, with commercial-based pricing becoming the norm in industry contracts over time.

For reserve capacity, end users should demand reliable supply and be willing to support it through a "reliability premium". This demand and remuneration should flow back through the supply chain, resulting in the upstream providing reserve capacity and being paid for it. However, it is possible that there may be a role for government intervention, requiring minimum levels of reserve capacity.

The challenge will be to develop a harmonised framework across producing countries that will allow a transition to full-cost remuneration in a period during which there are both old and new reactors, some with HEU and some with LEU targets. If new suppliers enter the market following the historically unsustainable remuneration model, this could result in commercial-based reactors not being able to sustain their current operations and new LEU-based ^{99}Mo production infrastructure not being constructed or maintained without government assistance. Without harmonisation, long-term supply reliability would be threatened, with the new sources of supply only postponing pending supply shortages. One option for harmonisation would be for an expert panel to review the market and to provide a view on whether producers are applying the agreed-upon social contract.

Changes must occur to secure long-term supply

The current economic structure of the ^{99}Mo supply chain does not provide sufficient financial incentive to economically support ^{99}Mo production at existing research reactors, let alone to develop new LEU-based production and processing capacity. It also does not recognise the economic value of reserve capacity. The lack of investment has resulted in a system reliant on older, less-reliable reactors. The shortage seen in 2009 and 2010 is a symptom of this economic problem.

It is clear that without ongoing financial support from governments, commercial pricing is required for the continued supply of reactor-based ^{99}Mo in the medium to longer term and the conversion to LEU-based production. Changes are necessary to achieve a ^{99}Mo/^{99m}Tc supply chain that is economically sustainable and reliable. Even as short-term supply has stabilised, it is important to stress that the symptom has been addressed but the underlying problem – the unsustainable economic structure – has not.

From the lessons learnt through the economic study, it was the hope of the HLG-MR that the supply chain would recognise the need to move towards economically sustainable pricing following the return to service of the NRU and HFR reactors. While the economic study was not reproduced, reports from market players have indicated that while some changes have occurred, the pressure on prices and the pricing structures that were seen prior to the shortage have predominately remained in place. This highlights the importance of implementing the recommendations presented in the HLG-MR policy approach (see Chapter 10). Without these changes, the unsustainable economic structure will remain, affecting the necessary infrastructure investment and setting the stage for the next shortage.

Chapter 8

Technologies for Producing Molybdenum-99/Technetium-99m

8.1 Background

As a result of shortages of ^{99}Mo produced within the uranium fission route (yielding almost all ^{99}Mo currently produced), quite a few alternative ^{99}Mo/^{99m}Tc production methods have attracted the attention of stakeholders. Some of these technologies are known but not used at large scale, others are basic theoretical concepts.

One of the actions requested by the HLG-MR was a review of existing and potential methods of producing ^{99}Mo, of which the two main methods are reactor-based and accelerator-based. The main aim of the study was to produce a state-of-the-art report on technologies for producing ^{99}Mc/^{99m}Tc. The full report can be accessed through the NEA medical radioisotope website, www.oecd-nea.org/med-radio.

8.2 Considered technologies

The technologies considered in this report have been divided into three classes: short-term, mid-term and long-term availability at significant scale. Depending on national priorities, the research and development on each mid- and long-term isotope production technologies could potentially be accelerated, and the proposed categorisation is therefore only indicative and essentially based on the amount of information available today.

Short-term is defined as potentially available in the time frame 2010-2017 (7 years is an estimate of the order of magnitude for a time needed to build a new research reactor from tendering). For these ^{99}Mo/^{99m}Tc production methods, the base technologies are already available and in most cases they are already used (or advanced tests of feasibility have been performed) for ^{99}Mo/^{99m}Tc production.[1] For the most widely used technologies, physical details and the economic data are available from industry. The list of technologies in the "short-term" category includes:

- uranium fission in research reactors (HEU[2] and LEU targets);

[1] Only uranium fission route is currently used for large-scale production.

[2] The assessment of the HEU fission route was performed for benchmarking other methods.

- solution reactor technology;
- neutron activation of ^{98}Mo in a nuclear reactor;
- direct ^{99m}Tc production with cyclotrons.

The *mid-term* technologies are expected to be available in the period 2017-2025. For these methods, preliminary feasibility tests have been performed, and for some of them the construction of experimental facilities is planned. Some economic projections are available. The list of technologies in the "mid-term" category includes:

- photofission route using an electron accelerator;
- photonuclear reaction ^{100}Mo(γ,n)^{99}Mo using an electron accelerator.

The *long-term* methods are expected to become available in a time frame beyond 2025. For those technologies, only some very general technical information is available, and no economic assessment is currently possible. The list of technologies in the "long-term" category includes:

- neutron fission using spallation neutron sources;
- technology using ^{100}Mo (n,2n)^{99}Mo reaction.

8.3 Assessment criteria

The study has established criteria used for the assessment of the short-, medium-, and long-term technologies listed above (see the first column of Table 8.1). The development of criteria for evaluating the identified technologies has involved considering both physical and economic characteristics of the production processes. It is important to use both the technical and economic assessments in comparing technologies, since, for example, a technology with more favourable economics may have significant technical challenges.

The physical characteristics that were used to build the assessment criteria cover a range of factors including physical properties of the corresponding nuclear reactions that can be objectively evaluated (such as production rate, yield and efficiency) and characteristics of the production processes (such as specific activity, isotope co-production, technical difficulty, safety and transport), as well as other issues that were considered important in assessing the ability to meet the market need. These physical characteristics of ^{99}Mo/^{99m}Tc production technologies were aggregated to a list of general characteristics to make the assessment of the technology easier to carry out.

As with the physical criteria, a range of economic factors (discussed in the report) were considered before arriving at a final set of economic criteria. These economic criteria are considered representative of the main differences between technologies.

However, no weighting for the assessment criteria has been proposed. Such weighting could not be universal because it strongly depends on national political and economical factors.

8.4 Assumptions on data

For uranium fission in research reactors, the data were provided by ^{99}Mo supply chain participants. It is the same data that were used in the NEA study on the economics of the ^{99}Mo supply chain (issued in September 2010).

For other technologies, data from published sources of information have been used. The data on these technologies (especially those at a conceptual stage but not yet realised on an industrial scale) are, therefore, sometimes based on estimated values and must be viewed accordingly, since there is no direct industry experience to verify the information provided.

It should be recognised that the technologies being assessed are at very different states of maturity and knowledge from well established to theoretical and, while the report recognises technical maturity as one of the criteria, it does not make any examination of the risks associated with the path to development. Neither development costs nor the corresponding risks to development are assessed in the report. Also, the costs associated with the ultimate waste management and its final disposal have not been analysed due to the lack of information for all technologies.

8.5 Methodology and assessment summary

Each criterion was assessed on a three-point grading system: high – ***, medium – **, low – *. A score of "high" is the most positive outcome and "low" is the least positive outcome.

For each criterion, a definition of "high", "medium" and "low" has been developed and explained in the report. These definitions are used to assess technical and economic data on each technology and to provide a rating.

The assessment of the HEU fission route in research reactors (currently used for about 90% of the world production of ^{99}Mo) is used to benchmark all the other technologies. However, the HEU route is not considered as an alternative technology since there is an international effort currently underway to reduce and eventually eliminate the use of HEU targets, given that they contain weapons-grade materials.

The summary of the results of the assessment of considered technologies is presented in Table 8.1, each rating is discussed in detail in the main text of the report.

Table 8.1: Summary of technology assessment results

		Short-term technologies				Mid-term technologies		Long-term technologies	
Assessment criteria	HEU in research reactors - Reference	Current LEU targets[a] in research reactors	LEU solution reactor	^{98}Mo activation in research reactors	$^{100}Mo \rightarrow {}^{99m}Tc$ in cyclotron	$^{238}U\ (\gamma,f)$ photofission	$^{100}Mo\ (\gamma,n)\ ^{99}Mo$	LEU fission with spallation neutrons	$^{100}Mo\ (n,2n)\ ^{99}Mo$
Technology maturity	***	***	**	**	**	*/**	*	*	*
Production yield	***	**	**	*/**	*/**	*	***	*/**	**
Available irradiation capacity	***	***	*	***	*	*	*	*	*
Distribution range and logistics	**	***	***	*	*	***	**	***	**
Simplicity of processing	*	**	**	***	***	**	***	**	***
Waste management	*	*	**	***	**/***	*	**	**	**
Proliferation resistance	*	***	***	***	***	***	***	***	n/a
Potential for other isotopes co-production	***	***	**	*	*	*	*	***	*
Normalised capital costs	**	**	***	**	**/***	*	**	n/a	n/a
Commercial compatibility	***	**	**	*	*	n/a	n/a	n/a	n/a
Estimated levelised unit cost	***	**	**	*/**	**	*	n/a	n/a	n/a
Ease of nuclear regulatory approval	***	***	**	**/***	***	**	**	*	*
Ease of health regulatory approval	***	***	**	**/***	**	*	*	*	*
Units required to supply world market	***	***	**	*/**	*	*	*/**	n/a	**

a. Aluminide dispersion targets.

Note: The technologies are assessed using a three-grade rating system. A score *** is the most positive outcome and * is the least positive outcome, n/a – not available.

8.6 Conclusions

Short-term technologies

The use of low enrichment uranium (LEU) targets has the following advantages over HEU:

- proliferation resistance;
- easier availability of the target material;
- easier compliance for target transportation and processing.

However, it currently has lower production yield than HEU and may require more targets to be irradiated with correspondingly increased volumes of waste. Increasing the uranium content of the targets (e.g. of the existing high density LEU targets, or using metallic foil targets) to counteract the lower production yield will be a key factor for LEU-based production, but there are no technological or economic reasons not to deploy this technology.

Solution reactor technology (using LEU) appears to have many favourable characteristics in terms of yield, production rate and, potentially, costs but has yet to reach full technological maturity and acceptance by regulators and users. Hence the technology development risk and its impact on final costs are unknown.

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

Neutron activation in a nuclear power reactor seems feasible but is currently not attractive for commercial users or power plant operators as it competes with their primary purpose (of generating power) and would require a detailed safety case and potentially long approval process.

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

Mid-term technologies

The main advantage of the photofission route for ^{99}Mo production (photon-induced fission of depleted uranium) is that the processing of the target and ^{99}Mo separation is the same as is currently used in the reactor fission routes. However, the irradiation part of this technology is currently not mature, and the predicted production yield is low. Because of this, the photofission route seems to have potential only as a small-scale ^{99}Mo production route.

The technology based on the photonuclear reaction ^{100}Mo(γ,n)^{99}Mo has high production yield, but has the same difficulties as the reactor-based neutron activation technology. This technology requires highly enriched molybdenum targets and would require recycling to improve economics. The predicted specific activity of molybdenum from this route is not sufficiently high to use in existing technetium generators. Rather, a gel generator or other types of generators would be needed, as in the neutron activation route.

Long-term technologies

While some general assessments have been made, it is not possible to draw significant conclusions on the two long-term technologies considered in the report due to lack of information (particularly on production yields and economics).

8.7 Further work

From this analysis, future work is required in the following areas:

- The costs of waste management and its final disposal should be accurately evaluated and included in the price of ^{99}Mo. This would allow a more complete assessment of the technologies according to the life-cycle costs of produced ^{99}Mo/^{99m}Tc.
- For the LEU fission route, further research and development is required on dense LEU targets and the associated processing technology. A final disposal route for waste from processing these targets should also be developed (also required for the current HEU route).
- The economics of solution reactors should be analysed in more detail, as they have many potential benefits, if the technology development and licensing is successful.
- The possibility of using metallic targets for neutron activation should be examined, and the cost of its processing and recycling should be evaluated.
- Additional research and development on the production and recycling of highly enriched molybdenum targets is needed. This is important for both direct ^{99m}Tc cyclotron production and the neutron activation technologies.
- Technical and economical aspects of portable gel generator technology (used in the neutron activation route) should be evaluated for large-scale capacity and licensing potential. Additionally, the use of other generator systems that can provide large generators with high concentrations of ^{99m}Tc from low-specific activity ^{99}Mo should be investigated.
- Decisions will be needed on funding the required research and development for the two long-term technologies necessary to determine if there is potential for their use in the future supply of ^{99m}Tc.
- There would be value in updating the report as new information becomes available.

Chapter 9

Iodine-131 Supply Situation

Following its second meeting, the HLG-MR asked representatives from Covidien, CORAR (Council on Radionuclides and Radiopharmaceuticals) and DRAXIMAGE to identify the bottlenecks in the supply chain for iodine-131 (^{131}I). The issue of a shortage of ^{131}I in North America was raised during discussions at the meeting. These representatives agreed to this work and presented their findings at the third meeting of the HLG-MR. This chapter is based on that presentation (Brown, 2010).

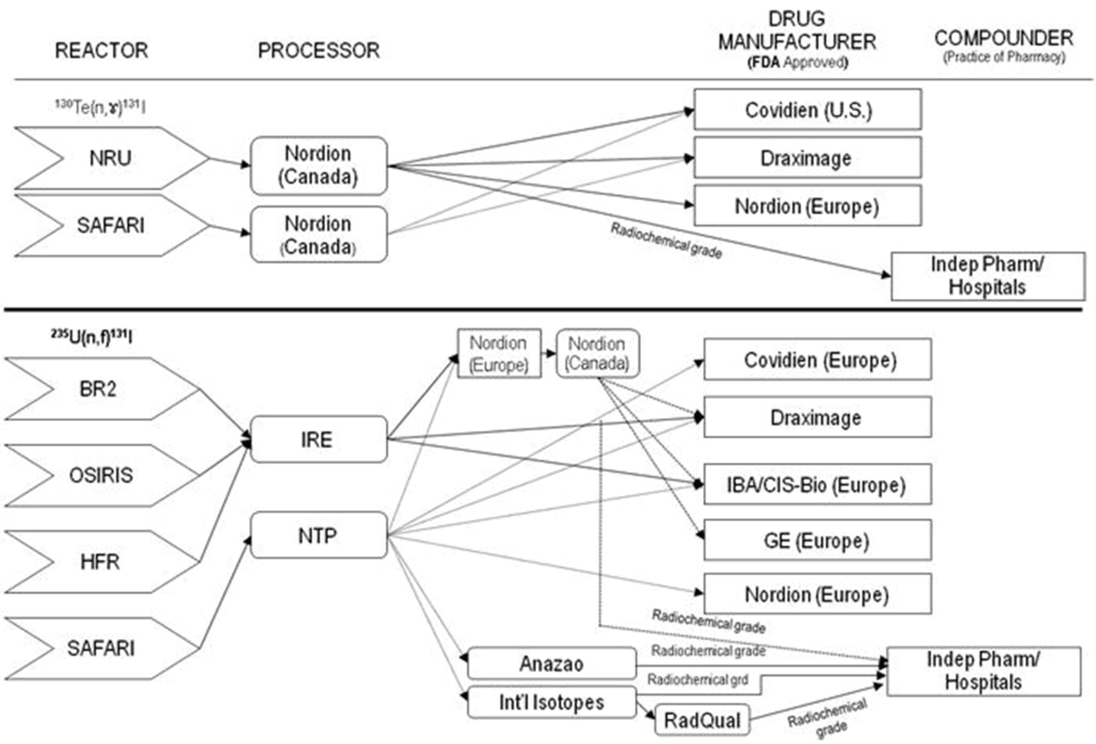
There are two methods that are used for producing ^{131}I for the global market: irradiation of tellerium-130 (^{130}Te) in a nuclear reactor and as a by-product of the irradiation of ^{235}U for ^{99}Mo production. Both of these methods are used by the major suppliers to the United States market. In 2009, the United States market was served by DRAXIMAGE (66%), Covidien (26%) and MDS Nordion (8%). Figure 9.1 shows the supply chain for the United States and European markets for each of these processes.

The identified shortfall of ^{131}I in the North American market came from the shutdown of the Canadian NRU reactor that was producing ^{131}I from ^{130}Te; Covidien was only able to obtain 70% of their needs from their supplier as they were only using ^{130}Te-derived ^{131}I. At the same time, there was an excess global supply of ^{131}I based on the ^{235}U fission process. Given the use of ^{235}U-derived ^{131}I in Europe, there were no supply shortages experienced.

In order to use alternative suppliers of ^{131}I and alternative methods for deriving ^{131}I, it is required to obtain approval from the relevant health authorities. Since the North American shortage began, Covidien has been working to qualify ^{235}U-derived ^{131}I, coming from alternative suppliers. In addition, during the shortage, NTP increased their supply of ^{130}Te-derived ^{131}I to compensate for the disruption in North American supply. With the NRU back on line and Covidien seeking regulatory approval to use alternative sources, the supply situation should be stabilised.

The shortage of ^{131}I highlights that the ageing reactor fleet has an impact beyond the supply of ^{99}Mo. Although ^{99}Mo supply is the key concern given its short half-life, the limited number of reactors that have the neutron flux required to produce it and its importance in medical diagnosis, these research reactors produce many other isotopes for medical and industrial needs and are essential for important research.

Figure 9.1: North American and European ^{131}I supply chain



Source: Brown, 2010.

Chapter 10

Policy Approach

10.1 Introduction

The work of the HLG-MR and the medical isotope stakeholders who have participated in this effort have identified a number of key challenges to developing a long-term secure supply of medical radioisotopes. As a result of the work undertaken to date, the OECD Nuclear Energy Agency (NEA) has released three reports under the new *The Supply of Medical Radioisotopes* series, subtitled:

- *An Economic Study of the Molybdenum-99 Supply Chain.*
- *Interim Report of the OECD/NEA High-level Group on Security of Supply of Medical Radioisotopes.*
- *Review of Potential Molybdenum-99/Technetium-99m Production Technologies.*

Issues identified in the reports that need to be addressed by changes to the market structure are:

- *Pricing structure*: The current pricing structure does not sufficiently remunerate the costs of the current research reactors, and the processors in some cases, that provide production capacity for the supply chain nor does it encourage investment in new infrastructure or conversion to using low enriched uranium (LEU) targets for ^{99}Mo production.
- *Reserve capacity*: Research reactors do not operate 100% of the time and when there is an unexpected or extended shutdown, reserve capacity in another reactor or production source is required to counter the lost production capacity. However, this reserve capacity was traditionally not paid for by the supply chain. In addition, the size of the reserve capacity needs to be determined and supported by effective co-ordination of the operating schedules of reactors to ensure efficient use and to support a sustainable market environment.
- *Transparency*: The pricing principles and market structure are not sufficiently transparent to ensure that appropriate costing/pricing is occurring, or to ensure sufficient capacity.

- *Role of government*: Governments' role in financially supporting the industry is not clear in all cases.

- *Consistency of policy approaches*: Policy approaches need to be consistent across jurisdictions to avoid creating market distortions that could have impacts for the long-term security of supply.

These issues are discussed at length in *The Supply of Medical Radioisotopes* reports.

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

The HLG-MR policy approach discussed below seeks to establish the framework to address the problems and issues identified in the reports, moving beyond the actions already undertaken. This approach should be applied by all countries that have an impact on the global market, either as producers or as consumers of ^{99}Mo/^{99m}Tc. It is meant to provide a comprehensive, consistent and coherent policy approach covering all the key issues and challenges. There are important linkages between the various policy components of the full approach. If one policy component is not included, it could affect the success of the other components; as a result, governments and industry need to consider any action within the context of the entire range of issues addressed by the HLG-MR policy approach.

This policy approach was developed by the HLG-MR after intensive examination of the key areas of vulnerability that threaten the long-term security of supply of ^{99}Mo/^{99m}Tc. During the examination of the areas of vulnerability and the development of this policy approach, external stakeholders were consulted and their viewpoints taken into account. For two specific areas, that of full-cost recovery and the supply of outage reserve capacity, working groups were formed to undertake a detailed examination of the best manner for implementing the related policy principles. The results of the work of these two working groups have been ratified by the full HLG-MR.

As with any good policy approach, the HLG-MR policy approach is meant to address problems that currently exist or that could develop as a result of suggested supply chain changes. It does not try to change parts of the supply chain that are working well; rather it seeks to build on those parts (e.g. the efficient transport logistics for bulk ^{99}Mo and generators).

Change is never easy. The changes that would occur during the implementation of this policy approach could have effects on some supply chain participants, for example, by reducing profits or requiring changes from past practices. This cannot be avoided if the market is to restructure for long-term effectiveness and it is noted that changes are already occurring in the supply chain because of recent supply disruptions. However, it is the view of the HLG-MR that these changes are necessary and the policy approach seeks to minimise the negative impact on any one stakeholder group, assigning responsibility for change where it is most appropriate and feasible.

This policy approach is meant to provide an international consensus agreement on the best approach to address the challenges threatening the security of $^{99}Mo/^{99m}Tc$ supply. The HLG-MR recommended policy approach described below is fundamentally a voluntary approach that is aligned with common interests in encouraging and ensuring a long-term secure supply of $^{99}Mo/^{99m}Tc$. Supply chain participants and governments are encouraged to apply this approach when implementing the principles of economic sustainability, ensuring that individual actions are consistent with this approach.

10.2 Policy option

From the reports completed and research undertaken to date, the HLG-MR has established its "central pillars of reform". These pillars recognise the problems being faced by the industry and are the key high-level reforms that the policy approach seeks to address. The central pillars are:

- market economics need to be improved;
- structural changes are necessary (diversity/contracts);
- government role has to be clearly defined;
- an effective co-ordinated international approach is necessary.

In developing the policy approach to address the central pillars, the HLG-MR started from the premise that market-based approaches, where possible, should be the basis for policy action to address the market and policy failures that exist in the current economic structure and supply chain. Recognising, however, that the failures are complex, it is clear that there is an essential role for governments to ensure the proper setting in which the problems can be addressed.

The "Economic Study" (NEA, 2010a) indicates that the first thing that needs to be done is a definition of the social contract – the agreement (informal or formal) between governments and its citizens, medical community and research reactor operators related to their involvement in the supply of ^{99}Mo. The policy approach sets that social contract along the following lines:

- Market participants should implement the necessary reform, but there are limits to what may be possible.
- Governments have an essential role in supporting market operations by ensuring the proper environment and addressing market failures, while recognising the commercial nature of the supply chain.

- International collaboration is necessary, particularly to avoid policy approaches at the domestic and regional levels that could negatively affect global ^{99}Mo/^{99m}Tc supply security.

- Transparency of market operation is important to ensure that the market continues its evolution to an economically sustainable system.

The issues embedded in each of these topics are all intertwined. As a result, the policy approach does not have a "starting point"; all the components are important and thus all need to be implemented. Implementing only part of the policy approach could result in an ineffective policy approach.

The policy approach discussed below includes principles and supporting recommendations. The principles are the actions that are fundamental to setting the supply chain on the right path to long-term security of supply. The supporting recommendations provide additional detail on the implementation of each of the principles. In some cases, the supporting recommendations represent changes that are already being implemented; these changes or actions are included in order to highlight their importance. In these cases further change may not be necessary; all that may be required is the on-going application of the change already taking place.

Market participants should implement the necessary reform

Governments from all major ^{99}Mo producing nations have indicated that they are no longer interested in subsiding its production at historical levels (or at all), and the "Economic Study" explains why there are no clear economic arguments for governments to subsidise research reactors to produce ^{99}Mo; it is clear that market participants should play a key role in supporting reliable supply. To move to an economically sustainable supply chain that delivers a secure long-term supply of ^{99}Mo, market participants have to be responsible for:

- paying for the full-cost of production;

- co-ordinating operating schedules to ensure appropriate use of available technologies, including research reactors;

- sourcing and paying for outage reserve capacity.

The participation of all market players in these activities will be important in achieving long-term economic sustainability of the ^{99}Mo supply chain. In order for market participants to have the incentive to take on these responsibilities, governments and research reactor operators will have to adopt commercially-based policies and practices related to the supply of ^{99}Mo/^{99m}Tc (see later section on government role to support and supplement market operations). These actions at the top of the supply chain will need to feed further down the supply chain to respond to the changing role of governments in ^{99}Mo/^{99m}Tc production. Without changes to the responsibilities of market participants, there will be no security of supply.

Paying the full cost of production

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

The "Economic Study" clearly demonstrated that the pricing structure from reactors prior to the most recent supply shortage was not economically sustainable. The cost of producing ^{99}Mo was traditionally subsidised by host nations. With a move by these host nations away from subsidising production that often benefits foreign nations or foreign companies, pricing must recover the full cost of production to ensure economic sustainability and a long-term secure supply. Appropriate pricing would also encourage an efficient use of the product, reducing wasted $^{99}Mo/^{99m}Tc$ and thus reducing excess production and the associated radioactive waste.

A full-cost recovery methodology should be implemented that would guide traditional non-commercial research reactor operators and other $^{99}Mo/^{99m}Tc$ production technology operators to realise full-cost recovery within their pricing of ^{99}Mo irradiation services. This costing methodology identifies the essential elements that should be included when determining the full cost of ^{99}Mo irradiation services and how these elements should be allocated between various missions in the case of multipurpose facilities. The application of the costing methodology at all the $^{99}Mo/^{99m}Tc$-producing research reactors and other production technology facilities within the global supply chain would ensure a consistent approach to full-cost recovery.

A consistent costing methodology appears only necessary for reactors and other $^{99}Mo/^{99m}Tc$ production technologies as processors and generator manufacturers already set prices based on their costs given their commercial nature (they generally receive no government subsidies).

The full-cost recovery methodology is not a price-setting mechanism; it defines the cost elements and allocation methods, but it does not dictate the value of those costs nor prices that would be expected or required under full-cost recovery. Given varying costs and ownership structures and national competition laws, international pricing-setting regulation would be difficult or impossible to implement. Nor is price-setting necessarily desirable; a full-cost recovery methodology would still allow for downstream stakeholders to benefit from improvements in efficiencies that lower production costs through offering lower prices (where sustainable).

Applying the full-cost recovery methodology ensures that there are no hidden subsidies directed towards ^{99}Mo production. The costing methodology is flexible, recognising different situations at different reactors, but identifies the key cost elements that need to be included in the pricing of ^{99}Mo irradiation services. It should be noted that the full-cost recovery methodology suggested below should be applicable to all production technologies; however, it was written based on experience with research reactors and thus some elements may need to be adapted slightly for alternative production technologies. The full-cost recovery methodology includes the following cost elements, which would be attributed to ^{99}Mo irradiation services:

A. Capital costs:

- refurbishment costs that would be depreciated (to distinguish from maintenance): amortised over the remaining life of the production technology;
- new infrastructure: amortised over the life of the infrastructure (e.g. 40 years for a research reactor), including any financing costs.

B. General overhead costs:

- general or shared administration: human resource management, financial and accounting services, legal services, IT, government relations, etc;
- site infrastructure support: roads and grounds, site and facilities maintenance.

C. General operational costs:

- reactor operation and maintenance staff, safety staff, centralised engineering, design and manufacturing services, etc;
- reactor fuel (or equivalent with alternative technologies) and other generic consumables;
- utilities: energy, water, etc;
- waste management: management of full waste streams from the reactor (or other production technology) up to, but not including legacy waste or final disposal (see discussion below for more detail);
- licensing and regulatory requirements, quality control;
- security, including staff.

D. Decommissioning costs:

- annual provisions for the decommissioning of the research reactor or alternative production technology.

E. Specific ^{99}Mo irradiation costs:

- irradiation device (e.g. rigs): design, construction, operation, maintenance, dismantling; specific costs associated with the device to be recouped if they were not already paid by the processor;

- handling of irradiation targets:
  - reception, storage, loading-unloading, conditioning;
  - “ex-works truck loaded” services, where provided (e.g. shipping, providing shipping containers, provision of targets); specific costs associated with these services to be recouped if they are not already provided by processor;
  - administration: specific staff, insurance, security.

The provision of outage reserve capacity is not included in the full-cost recovery methodology as this product could be offered separately from irradiation services. However, it is expected that the principle of full-cost recovery would be applied to any outage reserve capacity services provided. This issue will be discussed further in the section below on outage reserve capacity.

It should be noted that this full-cost recovery methodology provides for a level playing field between older reactors and new reactors. While new research reactors will require significant capital investments, these investments will be amortised over 40 years. An older reactor that is fully depreciated will likely require capital investments regarding ageing management of the reactor. While these investments may be smaller than investment costs of new infrastructure, they would have to be amortised over the remaining life of the reactor – much shorter than 40 years. Therefore, a new research reactor requiring EUR 250 million (for example) for the portion of the costs attributed to ^{99}Mo production and amortised over 40 years would face a similar cost structure to an older reactor requiring EUR 31 million in investments for life extensions, to be recouped over a period of five years.

At this present moment, it is not reasonable to include a cost premium for LEU conversion within the full-cost recovery methodology. First, the end-user receives no specific benefit from using LEU-based ^{99}Mo and thus there is limited market justification to pay a higher price. Second, if a price premium were included, there is no guarantee that the premium will be used for conversion since different operators are moving towards conversion at different paces. As a result, there is still a role for governments to support conversion efforts to LEU (see later section on role of government). In the future, once most ^{99}Mo production is achieved using LEU targets or there has been a market justification created (again, see later section on role of government), the market price (and the full-cost recovery methodology) should adjust to cover all operating or infrastructure costs of using LEU targets for the production of ^{99}Mo.

Any ^{99}Mo production facility that serves multiple purposes, such as the majority of the irradiating research reactors, will need to attribute a certain proportion of the general or shared costs to ^{99}Mo production, with the remaining portion of the costs being attributed to the other missions within the facility. This means that the full-cost recovery methodology would take the elements above and apply the following equation:

$$wA + xB + yC + zD + E = \text{full cost}$$

A proportion methodology would define the way to estimate the value(s) of the variables w, x, y, z. Cost element "E" requires no proportion because these are costs specific to ^{99}Mo irradiation services and therefore would be attributed 100% to the costs of ^{99}Mo irradiation services. The full-cost working group of the HLG-MR discussed many options on what that proportion methodology could be (e.g. by business activity, by some weighted measurement of space within the reactor, etc.). However, the group realised that additional work was required to determine the best methodology for the various components. For the purposes of this policy approach, a precise solution is not necessary at this time; however, the full-cost working group will develop a "guidance document" on how to proportion common costs for release end-2011.

It is important, at this point, to clarify the issues concerning waste management costs, since the full-cost recovery methodology excludes costs related to legacy wastes and final disposal. Legacy wastes are the wastes from a research reactor and processing facilities from the past. The HLG-MR recognises that these wastes need to be dealt with; however, they are also aware that it would be realistically impossible to ask the supply chain to pay for waste developed from past production. It is logical that full-cost recovery would be applied to those waste costs that are incurred from this point forward, but not for those wastes developed in the past.

The HLG-MR also determined that the costs related to final disposal of waste should not be included in the full-cost recover at this time. Currently, the disposal of spent fuel is part of a national policy, which varies in degree of implementation between countries. Given the differences between countries and the fact that the cost to a specific reactor is often difficult to determine within a national plan, it is unreasonable to ask the supply chain to pay an undefined cost. However, the HLG-MR recognises that once final disposal plans are defined and specific costs determined, these should be incorporated into the full-cost recovery within the waste management costs.

A final point on wastes needs to be made. The full-cost methodology is for reactors and alternative production technologies; it was not the intent of the HLG-MR to develop a full-cost recovery methodology for downstream supply chain participants who tend to be more commercially based. However, if we are to achieve full-cost recovery, it will be necessary to ensure that any government subsidisation of waste management related to the wastes produced from the processing of ^{99}Mo irradiated targets would become the responsibility of the supply chain, following the notion of full-cost recovery.

To implement full-cost recovery within the supply chain, government owners will have to require reactor operators (and other production technologies) to apply the full-cost identification methodology and to fully recover these costs within their pricing for ^{99}Mo irradiation services. Given the role of governments regarding nuclear activities, including the operations of their research reactors, governments generally have significant influence on the financial direction of the reactors. As a result, governments should have some form of influence with reactor operators to ensure that full-cost recovery is being undertaken at the reactor for ^{99}Mo irradiation services. Depending on the specific situation in each jurisdiction, the respective governments will have to determine the best approach to encourage reactor operators to move to full-cost recovery for ^{99}Mo irradiation services (e.g. regulations, policy directive, etc.) in their jurisdiction.

The HLG-MR agreed that governments should set a transition period for the implementation of full-cost recovery. This was done in recognition of the fact that the supply chain will require some time to prepare to move to full-cost recovery, including the time to adjust contracts within the system. This time would also allow the health community to become informed of the changes and to examine reimbursement rates and the effect of full-cost recovery on the costs of ^{99m}Tc based medical tests. The HLG-MR recognised that the transition period cannot be too long as it could affect the ability of providers of ^{99}Mo irradiation services to survive; no timeline will be perfect, but longer periods will affect sustainability and security of supply. In light of these considerations, the HLG-MR recommends that governments set a target of three years to implement full-cost recovery at reactors, starting from June 2011.

During the transition period, governments and reactor operators should discuss the new financial situation of full-cost recovery for ^{99}Mo irradiation services and the role this new financial situation will have on any funding support being provided to the reactor. For example, funding could be directed to the other missions within the reactor.

Any commercial-based reactors or alternative production technologies would, by definition of their status as commercial-based reactors, already be implementing full-cost recovery.

In order to ensure transparency and trust within the supply chain, the international expert panel (discussed later in section on transparency of implementation) would monitor and confirm that full-cost recovery is being undertaken.

The price increases that would be expected by the application of a full-cost recovery methodology should flow through the supply chain and should be reflected in the costs of the final medical procedure, to be reimbursed appropriately by the health care systems. Again, this is a normal market operation when the price of one input into a product increases. An input price increase may be absorbed in the short term but final product prices will eventually adapt to the increased costs. Market participants require that the revenue of a product cover the full costs of that product in order to remain in business.

As shown in the “Economic Study”, the final impact on end users of implementing full-cost recovery should be reasonably small. Any price increase should be acceptable in the supply chain as there is an increased recognition of the need to increase remuneration to irradiating reactors. This is a different situation than a few years ago, as supply chain participants should now realise that they are facing an untenable situation and it must be rectified. However, this may mean that some current contracts between supply chain participants need to accommodate this move towards economic sustainability. In addition, there may be a role for health insurance systems to ensure that they accommodate necessary prices increases (see later section on role of government for further discussion on this point).

A full-cost recovery methodology and the increased role of the market would not result in nuclear-related safety concerns being held “hostage” to commercial interests. None of these changes would alter the importance of compliance with health and safety regulations and commercial companies would need to continue to give the highest priority to compliance with all appropriate safety, security, safeguards and health regulations.

In addition, the move to full-cost recovery would not result in health care systems being victimised by ever increasing prices that they have no control over. Demand for ^{99}Mo/^{99m}Tc is not perfectly inelastic – if prices rise, there will be a point where changes in use patterns will reduce the amount of product demanded. These possibilities were seen during the recent shortage, for example with changes to how generators are eluted, how patients were scheduled and even what isotopes were used; these changes may in fact more than compensate for any increases that could occur as a result of implementing full-cost recovery. If prices rise too high (beyond what is justified by cost-efficiency calculations) insurers will encourage the use of substitutes where feasible and the market will develop other substitutes where none exist today.

To enable the acceptance of any price increases, it will be important for ^{99}Mo/^{99m}Tc producers (reactor and alternative technology operators), processors, generator manufacturers and radiopharmacies to improve communications around any forecasted price increase to help the health care providers and the health care systems plan budgets and manage expectations.

It should be noted that implementing full-cost recovery is in line with market economics; a commercial enterprise cannot survive very long if the price of the product it is selling is less than the costs to manufacture that product, including the necessary infrastructure to produce the product and bring it to market. As a result, the move to full-cost recovery will bring the current reactors into the commercial sphere regarding ^{99}Mo irradiation services. Producers that seek to negotiate the lowest prices possible for irradiation services, again, in line with normal market actions, will be faced with a new pricing paradigm. Nonetheless, they will be able to negotiate within the framework of fully paying for the services they receive.

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

Ensuring adequate capacity

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

In addition to paying for production capacity through the full-cost recovery methodology, the supply chain should also be responsible for the appropriate use of that capacity, including ensuring adequate reserve capacity. When one looks at all the available reactor and alternative technology capacity, there should be more than 100% of the required demand for the year. This capacity, sometimes referred to as peak capacity, includes the capacity of all reactors without taking account of their operational schedules or availability for isotope production. As a result, the term peak capacity actually hides two different types of capacity: weekly reserve capacity (WRC) and outage reserve capacity (ORC).

The first term (WRC) is the capacity that exists within the system to account for the fact that research reactors do not operate 100% of the time. As a result, there has to be enough capacity so that over the year, the total fleet of reactors and $^{99}Mo/^{99m}Tc$ alternative production technologies can provide sufficient irradiation services to produce the required amount of $^{99}Mo/^{99m}Tc$.

The second term (ORC) is the capacity that exists within the system to account for the fact that research reactors sometimes have unplanned or extended shutdowns. As a result, there needs to be on-call capacity that can be used during these events.

These two types of capacity and the policy option to address them will be discussed separately as they are very different types of capacity requiring different actions.

Weekly reserve capacity

Proper and effective co-ordination of reactor and alternative technology operation schedules should theoretically reduce WRC to zero on an annual basis – there should only be enough operating capacity in a year to meet the required demand, with no excess producing capacity. Any excess producing capacity is inefficient and could result in increased social and private costs (from over investment in capacity).

Currently, reactor operators and processors participate in co-ordination efforts organised by the Association of Imaging Producers and Equipment Suppliers (AIPES). During the recent shortages, these co-ordination efforts reduced the impacts of the shortage by working with reactors and processors to move production cycles where possible to balance out times of significant shortages. These efforts should continue and become more sophisticated to ensure more efficient scheduling.

To make co-ordination more effective, increased information sharing related to production capacity should be made available to the co-ordination group. This would allow for an assessment of whether the capacity is in excess of what is required in the market and could be part of outage reserve capacity (see next section).

In addition, "rules of engagement" could be developed that would describe the principles of co-ordination. These principles should recognise the need for a minimum level of production at all reactors. This minimum level is required to ensure that available $^{99}Mo/^{99m}Tc$ producers (reactors and alternative technologies) have the ability to produce $^{99}Mo/^{99m}Tc$, that they have some financial remuneration for production, that they are able to maintain the expertise to produce ^{99}Mo, and that the regulatory approval to produce and use their ^{99}Mo exists. This volume sharing would be encouraged through the provision of outage reserve capacity (see next section).

As part of these rules of engagements, reactors should agree to adjust operating programmes where feasible, working in good faith to ensure effective co-ordination.

To support these efforts towards effective co-ordination and the ability to maintain flexibility in the system, contracts between reactors and processors should provide for open access, removing any contractual provisions that may prevent diversity of supply sources and thus security of supply. Open access has also been recommended by the Council of the European Union.

Given the role of demand management actions during the most recent shortage, it is essential to recognise the important role that these actions could play for short periods where co-ordination efforts still result in a shortage.

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

To support effective co-ordination, contracts between ^{99}Mo/^{99m}Tc producing facilities and processors should allow for open access to ^{99}Mo irradiation services.

Demand-management options should be encouraged as they could support effective co-ordination efforts.

Outage reserve capacity

The "Economic Study" indicated that ORC should be funded from the supply chain via a "reliability price premium", with those stakeholders that do not pay the premium not receiving ^{99}Mo during any shortage situation. However, many stakeholders indicated that they did not see such a system as acceptable since they felt that distribution in times of a shortage should be "fair". They did, however, agree that it was the responsibility of the supply chain to source and pay for outage reserve capacity.

In order to recognise the need for fair distribution in times of shortage and still create the incentive for the supply chain to pay for the reserve capacity, it is necessary to set a minimum amount of outage reserve capacity that needs to be maintained by the supply chain and increase end-users' prices appropriately. This would require transparency and some verification of the amount of reserve capacity being held within the supply chain to ensure that the payments being received were used to increase reliability.

After examining many options, the HLG-MR agreed that ORC should be provided through incremental capacity options. For ease of implementation, and recognising the pivotal role of processors in the supply chain, processors should be responsible to hold at every point in time ORC options equal to at least the largest source in their supply chain. This is referred to as the n-1 criterion, where the supply chain should be able to absorb the loss of the largest unit in the chain. The HLG-MR Outage Reserve Capacity Working Group considered other levels of ORC, but determined that a level greater than n-1 would be too onerous and not necessary. It did recognise, however, that the n-1 level should be evaluated after some experience to determine if there was a need to change the recommended level (either to make stricter or more lenient).

A capacity option is a contract that provides the opportunity, but not the obligation, for Party A to access product from capacity that Party B sets aside in case Party A requires it. Party A would pay Party B for the opportunity; when Party A excises the option, requiring product from the capacity, they would pay Party B for the production.

In order to be useful, ORC should be available in a short-time frame when needed – within 48 hours from the moment of requesting the irradiation service.

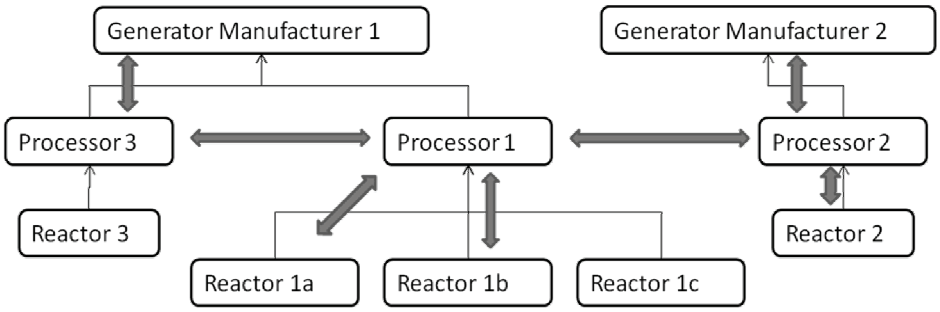
This does not mean that processors should be the sole supply chain actors dealing with ORC. ORC can come from all levels of the supply chain and should be paid for in the end price. This reserve capacity can come from idle reactor capacity, but also from generator manufacturers and/or hospitals that provide a credible, reasonable and incremental demand management plan (e.g. schedule shifting, priority setting, etc), or other processors (who would be required to account for these responsibilities in their own n-1 calculations). As a result, options contracts would be offered by individual providers based on their availability, and through private contracts between parties. Box 10.1 provides an illustrative example of how the ORC capacity option system could function, including for those supply chains that are not based on multiple regional research reactors.

Outage reserve capacity options would have to be based on credible, reasonable, incremental and available outage reserve capacity. For example, reactors offering ORC should be producers of ^{99}Mo that leave some irradiation channels idle. This ensures that they have the experience and regulatory approval in place to fulfil ORC requirements when necessary.

In order to ensure that reactor based ORC options are credible and available, the reactor will have to be operated some minimum amount within the previous three- to four-month period. As noted above, if a reactor does not provide some minimum level of ^{99}Mo irradiation services on a quarterly basis, they may not have the expertise, personnel, experience or ability to provide outage reserve capacity if it was required. Where a reactor is not requested by a processor to provide this minimum amount of irradiation services in a preceding three-month period, they should not be considered to be a credible and available source of outage reserve capacity.

This provision of credible and available outage reserve capacity from a reactor, coupled with the n-1 criterion, supports the necessity to have some "volume sharing" of production among reactors without dictating which reactors processors would have to buy from. The n-1 criterion would encourage volume sharing as a concentrated share of production at one reactor would increase the need for ORC within the system.

Box 10.1: An example of how the ORC system could work



- P2, in a single source supply chain, holds ORC options contract with:
  - P1 to supply product if R2 down;
  - GM 2 to implement demand side management (DSM) downstream to address shortage condition.
- P1 holds ORC options contracts with:
  - R1a, R1b and P2 in enough quantity to address if reactor in supply chain down;
  - P2 then must hold ORC within R2 at amount offered to P1.
- P3 holds ORC options contracts with:
  - GM 1, which can implement DSM downstream to use supply from P1 more efficiently during shortage period;
  - P1 to provide supply if R3 goes down;
  - P1 then must hold additional ORC from R1a, R1b to amount offered to P3.

A further requirement to ensure that ORC options were credible, incremental, and available would be the need to include provisions for enforceability within the ORC options contracts. These provisions would be some form of penalty clause that would be triggered if the ORC was not available when required, or if it was determined that the ORC sourced was actually being sourced by two or more parties.

Valuing and paying for ORC

Processors would negotiate private ORC options contracts with their partners in the supply chain. The prices of the ORC options contracts would be settled in the market, recognising that options contracts prices should allow for full-cost recovery. This would allow for clear price signals on the need for additional or less ORC capacity. If there is excess capacity in the market above and beyond ORC needs, prices will fall and some players will be forced to leave the ORC market and use their capacity for other purposes; if there is not enough ORC supply, prices will rise and additional ORC will be offered.

In terms of full-cost recovery, the price paid for options contracts should logically cover the transaction costs and fixed costs (capital and operating) of ORC providers. When the option is exercised, the processor would have to pay additional variable costs based on the actual production capacity used. Governments should clearly indicate that they will not subsidise ORC at reactors and therefore costs will have to be fully recovered through ORC contracts. However, how that pricing is presented should be up to the supplier of the ORC options contract (e.g. whether bundled with irradiation services or priced as a product separate from irradiation services).

While processors would be expected to pay for ORC options contracts, they would recuperate the costs through ^{99}Mo/^{99m}Tc prices to their customers and further downstream. In essence, these downstream prices would include a non-optional reliability premium. End users should be made aware of the need for reliability provisions and the fact that their payments include some portion to ensure a secure supply of these vital medical radioisotopes by supporting reserve capacity. End users should also clearly include provisions in their contracts with suppliers related to reliability that would be triggered in the event of non-deliverability of product, encouraging upstream reliability measures.

A key feature of this recommended ORC provision system is that those processors that are currently dependent upon one single reactor for their supply will be able, and responsible, for sourcing and paying for ORC. This situation was demonstrated in the figure above where an isolated processor sourced ORC through an agreement with another processor. In this manner, this approach recognises the global nature of the supply chain, but allows for regional organisation and opportunities for the provision of ORC.

Again, to increase trust and transparency within the system, the international expert panel would review the provision of ORC within the system to determine that processors were holding the required level of ORC. This would provide an additional incentive for processors to voluntary hold ORC, otherwise the international expert panel would report that they were not providing the recommended level of reliability.

Recognising that time will be required within the supply chain to become informed and then prepare for the ORC provision system being recommended by the HLG-MR, a transition period is recommended before full implementation is required. In addition, the health community will require some time to examine the effects of sourcing and paying for ORC within the supply chain. Again, however, a transition period that is too long may mean that ORC is not provided in sufficient amount, affecting the economic sustainability of the provision of ORC and thus the security of supply. The HLG-MR recommends a target of three years from June 2011 to fully implement the proposed outage reserve capacity system.

Supporting recommendations: Processors should voluntarily hold at every point in time ORC equal to their largest supply (n-1 criterion), which can come from anywhere in the supply chain as long as it is credible, incremental and available on short notice.

Reserve capacity options should be transparent and verifiable to ensure trust in the supply chain.

Reactor operators, processors and generator manufacturers should review the current contracts to ensure that payment for reserve capacity is included in the price of ^{99}Mo.

Continued communication efforts to downstream stakeholders

During the recent supply shortage, communication efforts to downstream users were improved greatly. Many generator manufacturers provided updates to their customers on generator availability. This information was very useful to hospitals and doctors as they could plan appropriate imaging schedules in advance and implement other demand-management actions. In addition, protocols developed by AIPES and put in place by their members for proper communication during the event of an unplanned outage are essential to ensuring a quick flow of information from reactors down to the end-users.

Even in the current situation of normal supply, these communication efforts are important to continue. They improve the transparency of the supply chain, increase levels of trust and their on-going existence means that they can be used again in short order in the event of any future shortage. In addition, the downstream communication allows for the improved ability of the medical community to exercise demand-management actions to reduce the effects of future shortages, effectively serving as reserve capacity.

Supporting recommendation: Communication efforts, providing three months advance notice to downstream stakeholders on generator supply should continue. In addition, industry communication protocols regarding unplanned outages should be implemented by all industry participants and remain active.

Government role to support and supplement market operations

In order for the market and the market players to be able to, and to have the incentive to, realise the policy approach described above, it is necessary that governments set the proper environment. Governments clearly have a role in establishing the framework in which markets can function properly, including addressing past policy failures and addressing market failures where they exist. To encourage a secure supply of ^{99}Mo and ^{99m}Tc, governments must clearly define their social contract and ensure that the proper tools are in place to realise that social contract.

In addition, governments have a clear and essential role to ensure nuclear safety and security, licensing and regulating nuclear facilities and nuclear-related activities along the full nuclear fuel cycle. Further, governments have a role in ensuring reliable medical care for their citizens. They are responsible for regulating all aspects of medical isotope production and use, including providing approvals related to the safety, efficacy and quality for patient use of medical isotopes. The role of governments also extends to ensure the development and implementation of environmental and non-proliferation policy goals and commitments. While the delivery of these roles may differ between countries, there is no question that these are key government responsibilities, and will continue to remain so.

The policy approach recognises these essential roles and also recommends actions (discussed below) which are critical for the market to be able to completely fulfil its expected role in ensuring long-term security of supply.

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

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

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

Requiring implementation of full-cost recovery methodology

Given that historical subsidies from governments to reactors have been a key issue related to the current economic unsustainability of the production of ^{99}Mo, governments must require research reactors and alternative production technologies to undertake full-cost recovery related to ^{99}Mo/^{99m}Tc production (including waste management, overhead and capital costs). This required move to pricing that reflects full-cost recovery at the reactor level will push changes through the entire supply chain, with the supply chain making the necessary adjustments in the market to fund the resulting price increases. Governments should avoid price-setting regulations, for the reasons already described in the "Economic Study", focussing rather on ensuring that full-cost recovery is applied (using the methodology described in the earlier section on paying the full cost of production).

It is essential that all producing reactors and alternative production technologies are required to implement the full-cost recovery methodology to avoid market distortions in the global market that could have negative implications for long-term security of supply.

In addition, governments must resist any temptation to intervene in the day-to-day ^{99}Mo market operations of research reactors or alternative technologies. It will be especially important for governments to resist pressure to address expected rising prices by removing the requirements to implement full-cost recovery. Removing these requirements would result in ^{99}Mo irradiation services continuing to be economically unsustainable and could result in severe distortions in the market between producers. As a result, such an intervention could easily hinder the long-term security of supply.

It is in governments' and citizens' self-interest to remove subsidies provided directly to reactors for ^{99}Mo production, not least because some part is currently supporting foreign health care systems and, in some cases, foreign companies. In addition, ^{99}Mo related subsidies may crowd out useful advancements of alternative technologies, other tracers and isotopes, or other modalities as a result of artificially low prices that distort the playing field. In addition, undue subsidies in parts of the global supply will distort the overall market, likely resulting in creating a certain barrier to achieving economic sustainability and thus, long-term security of supply.

In order to allow for a smooth, but not drawn-out, transition to full-cost pricing at the reactor stage, governments should set a target for reactor and alternative technology operators to implement full-cost recovery within three years (as discussed in the earlier section on paying the full cost of production).

By no means should the removal of government subsidies for ^{99}Mo production encourage any continued operation of reactors that do not meet the utmost safety and security standards. Any extension of operations of older reactors as a result of this policy change should be undertaken only where the reactor meets the required levels of security and safety. In addition, older reactors have been shown to be less reliable than new reactors. Any impacts on security of supply as a result of the extension of reactor lifetimes should be taken into account in the decision-making process.

It should be noted that this does not impact any current arrangements where governments fund the non-commercial activities of research reactors.

Responsibility to health care

In those nations where governments have a role in financially supporting health care systems, support for non-invasive medical imaging techniques should occur in an economically sustainable manner. Recognising the positive externalities of patient access to reliable nuclear medicine diagnostic procedures, governments have a responsibility to ensure that reimbursement rates or isotope budgets are sufficient to support necessary tests, even with possible increases in ^{99m}Tc prices to account for the move to full-cost recovery for ^{99}Mo irradiation services. Of course, support for medical imaging techniques based on ^{99m}Tc should be consistent with a broader, coherent framework for medical imaging, such that the most cost-effective imaging solutions may evolve in the marketplace and deliver the best care at the best price.

This principle would apply to private insurance companies as well, recognising the longer-term savings from accurate, prompt and non-invasive diagnosis of diseases. If this commitment from the payer community to accept increased costs of ^{99m}Tc is not forthcoming, the supply chain will continue to be economically unsustainable and supply will continue to be unreliable.

Although the “Economic Study” determined that there should only be a very small impact on final procedure costs at the patient level from the move to economically sustainable prices, there are some concerns that in practice prices will rise higher than determined in the study. For example, there have been reported changes in prices of generators resulting from the revaluation of ^{99}Mo in the market, shifting away from low-margin pricing, especially in the face of generic brands of key cold-kits entering the market. However, building on the analysis undertaken for the “Economic Study”, a tripling of generator prices within an economically sustainable price structure would result in the radiopharmaceutical pricing of the ^{99m}Tc representing approximately 7% of the average final imaging test cost per treatment instead of the 4.5% seen under the historical pricing structure.

It is clear that health insurance increases, if necessary, should not be the only reaction to any increase in market prices. As was seen during the last supply shortage, there are actions that can be used for more efficient use of ^{99}Mo/^{99m}Tc in the supply chain; these actions would also deliver cost-savings which have the potential to more than counter any upstream price increases as more efficient use means less product purchased. For example, as prices rise, there will be increased incentives to use ^{99m}Tc generators more efficiently through changing elution patterns, moving to centralised radiopharmacies, more “just-in-time” delivery of generators and radiopharmaceuticals, and/or changing historical patient scheduling patterns. In addition, there may be some cases where ^{99m}Tc procedures could be substituted by other isotopes or modalities; insurance plans should undertake cost/efficiency calculations to ensure that any substitutions are justified, including on patient dose received, and are not just a reaction to increasing prices.

Providing government support for ^{99m}Tc medical procedures through the medical system, rather than supporting production at reactors, is the logical place as it is provided directly to address the positive externality – the health benefits of nuclear medicine diagnostic imaging. In addition, it removes the market distortions of creating artificially low prices upstream allowing for more efficient use of the product and avoiding picking technology winners (isotopes, modalities or production technologies).

However, in order for governments, health care providers and private health insurance companies to determine if reimbursement rates or isotope budgets need to be increased within the health system, transparency needs to be improved regarding costs. Greater transparency regarding the price of ^{99m}Tc would be facilitated by separate pricing and reimbursement of the isotope from the radiopharmaceutical product, as well as from other diagnostic imaging procedure costs. This would provide an increased understanding among health insurance systems, governments and the health community of the real price of ^{99m}Tc and also allow for a better evaluation of cost/efficiency in regards to ^{99m}Tc price increases. For insurers, this would also provide for an increased understanding of what are reasonable price increases and the impact on final procedure costs.

Supporting recommendations: Governments should:

- **In co-operation with health care providers and private health insurance companies, monitor radiopharmaceutical price changes in order to support the transparency of costs.**

- **Periodically review payment rates and payment policies with the objective of determining if they are sufficient to ensure an adequate supply of ^{99m}Tc to the medical community.**

- **Consider moving towards separating reimbursement for isotopes from the radiopharmaceutical products as well as from the diagnostic imaging procedures.**

Weekly reserve capacity

As noted in the previous section, market players should participate in efforts to co-ordinate scheduling of reactor operating times related to ^{99}Mo production. The benefits of this co-ordination include ensuring continuous reliable supply, efficiency, market transparency, reduced social and private costs (through reducing over investment) and promoting economic progress (by facilitating economic sustainability and reducing government subsidies) and improving distribution of ^{99}Mo supply infrastructure/production. Recognising these benefits, governments should encourage producers (research reactors and ^{99}Mo/^{99m}Tc alternative production technologies) and processors operating in their jurisdiction to participate in good faith with the scheduling efforts being undertaken by AIPES or other global co-ordination efforts.

If reactor and processor operators in their jurisdiction do not participate in these scheduling efforts, governments could explore options to make participation mandatory. Currently, voluntary participation in scheduling efforts has been successful with all participants respecting (to the extent possible) their commitments; regardless, some jurisdictions may be interested in moving to making participation mandatory and could begin to explore tools for doing so, including enforcement if commitments are not met.

New producers and processors that enter the market should also participate in on-going co-ordination efforts.

Supporting recommendation: Governments should encourage continued supply chain participation in ^{99}Mo/^{99m}Tc production schedule co-ordination efforts, including making such participation mandatory if voluntary participation wanes or commitments are not respected.

Outage reserve capacity

Although the market should be solely responsible for sourcing and paying for outage reserve capacity, governments should monitor the levels of ORC, based on the information received by the international expert panel (see later section on transparency of implementation). It is possible, given historical involvement, that the supply chain will expect that governments will intervene in situations of shortage, thus reducing the incentive for supply chain participants to voluntarily maintain a set level of ORC. If this is the case, governments should consider addressing this free-rider problem by regulating minimum levels of ORC, as described in the "Economic Study".

Supporting recommendation: Governments should monitor levels of ORC maintained by the market and, if found to be below the n-1 criterion, consider regulating minimum levels.

Facilitating upfront investments in the face of uncertainty

Under a traditional market model, the commercial sector would finance upfront capital from its own savings or through borrowing. In some instances, high upfront costs coupled with a high risk profile for the project (for example, regulatory, technological or demand risks) can make the investment costs (e.g. interest rates) prohibitive to realising new investment opportunities. In these cases, there can be a role for government to facilitate upfront investments if the final product provides a societal benefit.

In an ideal situation, commercial companies would provide upfront capital funding for ^{99}Mo/^{99m}Tc related capital investments in new production infrastructure. In the case of a new multipurpose research reactor, these capital investments would likely represent at least 20% of the total investment costs of a key producing reactor. However, the large investment required (upwards of EUR 85 million for 20% of a new research reactor) prohibits commercial investment in many cases.

Another option would be for reactor developers and processors to seek private funding for the ^{99}Mo related capital investments, which would be paid back through future revenue streams from sales of ^{99}Mo irradiation services. However, private funding institutions require some form of certainty on expected revenues and are looking for long-term commitments (e.g. through contracts that contain take or pay agreements, etc). The difficulty for commercial players in the supply chain is that it is difficult to provide long-term commitments on purchasing ^{99}Mo irradiation services that would provide sufficient security to the private funder (e.g. in the realm of 15 years out) given the uncertainty on demand that far in the future.

The government could facilitate upfront investment by assuming the uncertainty risk of the investment in the ^{99}Mo related infrastructure. Governments could provide low-interest loans or loan guarantees to research reactors (and processors, where required) for ^{99}Mo related investments; they could also take an equity position in the commercial ^{99}Mo operations, or some other public-private partnership arrangement, supporting ^{99}Mo related investments. These financial actions should receive appropriate returns. If the government provides on-going financial support to the research reactor for other public-good missions, payment could be provided by subtracting ^{99}Mo related revenue from budgeted support to the reactor over the operational period.

By definition, these actions could be seen as subsidies provided by governments to new ^{99}Mo/^{99m}Tc production facilities (e.g. research reactors). However, they are not inconsistent with the notion of implementing full-cost recovery. Any government support provided through these financial arrangements would have to respect the principle of full-cost recovery, with the government receiving appropriate returns over an appropriate time period. As a result, the pricing of the ^{99}Mo irradiation services would still be based on full-cost recovery, with the government acting as a form of investor that requires appropriate returns. This support would enable investment in new infrastructure that otherwise may not occur.

Governments would have to ensure that there was sufficient expected demand for the ^{99}Mo producing infrastructure so that they do not encourage over building. If this were the case, excess capacity would be developed (beyond required reserve capacity) and prices would be expected to fall below economically sustainable levels and the returns of the project would be threatened. One way to minimise this risk is to establish shorter-term public-private partnerships where commercial companies could provide short-term commitments related to production. In addition, governments are able to hedge the risk of excess capacity development or reduced future demand through the multipurpose nature of research reactors; they may be able to shift production to another isotope if ^{99m}Tc demand wanes. A downstream commercial entity does not have this production flexibility if it is beyond its scope of normal business.

Supporting recommendation: Governments should, where required, support financial arrangements to enable investment in ^{99}Mo/^{99m}Tc infrastructure using various forms of public-private partnerships with appropriate returns.

Capacity planning

While governments should not be involved in the actual payment of ^{99}Mo capacity, they do have a role in supporting the non-commercial missions of multipurpose research reactors that have clear public functions. As a result, governments have a clear role in capacity planning for these research reactors. One of the considerations when making overall investment timing decisions should be the available capacity for ^{99}Mo production and the need for new available capacity.

If a reactor were to come on line earlier than required for ^{99}Mo production (as a result of other timing decisions), the government could "hold" that capacity and only release it on the market once it is required. Conversely, they may consider bringing forward planned research reactor infrastructure if ^{99}Mo capacity is required.

Supporting recommendation: Governments should consider ^{99}Mo/^{99m}Tc production capacity requirements when planning multipurpose research reactors to ensure that the required capacity is available. However, the funding of the ^{99}Mo-related capacity development should be supported through the commercial market.

Conversion to using LEU targets

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

The HLG-MR is aware that the conversion to using LEU targets for the production of ^{99}Mo has been agreed to by all major ^{99}Mo-producing nations, most recently through the work plan of the Washington Nuclear Security Summit. These commitments were made by governments given their importance for ensuring non-proliferation and supporting nuclear safety. However, these commitments impose an economic cost on the producers and users of $^{99}Mo/^{99m}Tc$ which are an externality to market participants. It is clear that the current economic structure of the supply chain does not provide the economic incentives or resources to convert to LEU targets. In addition, there are requirements for additional research and development related to increasing yield.

At the moment, there is no market justification for most ^{99}Mo producers to undertake conversion; end users (doctors, patients, health insurance systems) see no difference between ^{99m}Tc produced from HEU targets and ^{99m}Tc produced from LEU targets. As a result, the move to producing ^{99m}Tc from LEU targets provides no direct benefits to the end users, but would impose a cost. Conversion is to be undertaken as part of work towards meeting non-proliferation goals. As a result, governments should encourage R&D efforts and provide financial support to these efforts. In addition, given the production price differences (related to yield and potential waste management costs) governments should consider providing financial support in the short- to medium-term through start-up grants for LEU production or addressing the price differential through paying a production incentive.

Joint R&D efforts are currently underway through work at the International Atomic Energy Agency (IAEA). The IAEA has a number of activities underway to foster the use of LEU targets as well as encouraging the development of new indigenous capabilities to produce $^{99}Mo/^{99m}Tc$ in smaller markets. For example, the IAEA and interested member states have already collaborated extensively through the Coordinated Research Project (CRP) on "Developing techniques for small scale indigenous ^{99}Mo production using LEU fission or neutron activation". This CRP has encouraged potential facilities to become producers using LEU targets. Beyond the CRP, the IAEA is in the process of establishing an international working group on conversion planning for ^{99}Mo production facilities from HEU to LEU. This working group comes out of a meeting held with major ^{99}Mo producing reactors, processors and generator manufacturers and is expected to provide a multilateral and collaborative forum to identify and progress actions related to conversion efforts worldwide. Governments could consider working with the IAEA on these or related projects.

The path and time frame for conversion from HEU to LEU targets may differ among stakeholders. The HLG-MR recognises the need to secure sufficient global supply of enriched uranium in order to avoid the risk of ^{99}Mo supply disruptions during and after conversion.

In the future, governments should consider taking measures that would provide a market justification to using LEU targets, creating a level playing field regarding conversion and providing an incentive to convert. For example, once LEU targets are being used in most ^{99}Mo producing technologies, governments could consider implementing an HEU-tax on users of ^{99}Mo produced from HEU targets or they could impose import limitations on ^{99}Mo produced from HEU targets.

The US government action to encourage the development of LEU-based ^{99}Mo production for domestic uses is a good first step to creating a market in LEU-based ^{99}Mo. However, beyond creating pressure on domestic producers that do not participate in the programme, there is still not a market reason to pursue LEU-based production since it is not clear that it creates a market advantage at the end-user level.

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

Developing alternative technologies

Although multipurpose research reactors have distinct advantages related to the production of ^{99}Mo, there has been significant interest raised over the past number of years in alternative forms of medical isotope production. These alternatives provide certain advantages and certain disadvantages compared to each other. NEA (2010b) provides a good assessment of the various available technologies.

In general, the diversification of supply sources tends to increase reliability and security of supply. As a result, there could be benefits to continue to explore the development of alternative technologies that could be deployed if they are found to be economically and technologically viable.

Implementing a proper pricing structure for reactor-based ^{99}Mo production, based on the full-cost recovery methodology, including waste management costs, will level the playing field for the development of these alternative technologies. Once prices reflect the accurate cost of production, alternative technologies may be further encouraged, if economically viable. As well, any activity that creates market justification for using LEU over HEU targets (as recommended above) would also help to level the playing field for alternative, non-HEU technologies.

In addition, governments could facilitate diversification by setting the proper climate. This includes maintaining an appropriate regulatory framework and facilitating innovation. For example, they should ensure that the regulatory approval process for the production and medical application of isotopes from new technologies is developed to enable licensing in a timely manner, while ensuring the highest standards of safety and security, possibly in co-operation with international partners. In addition, governments could provide funding to R&D on alternative technologies (or tracers/isotopes) and encourage private investment in innovation. Further, increasing understanding of the economic parameters of alternative technologies would provide for a better assessment of their potential.

Again, the on-going efforts of the IAEA in encouraging the development of alternative technologies to enable indigenous capabilities to produce $^{99}Mo/^{99m}Tc$ in smaller or emerging markets are a good example of joint R&D. The CRP discussed above has established coalitions of interested nations related to the development of non-fission-based processes for developing $^{99}Mo/^{99m}Tc$. Significant progress has been seen through the CRP and the coalitions. Governments could consider participating in these IAEA efforts in encouraging alternative technologies.

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

Role for international collaboration

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

Over the past two years, the level of international collaboration dedicated to enabling the security of supply has increased greatly and has been instrumental in sharing information, determining the root causes of the crisis, minimising impacts of the shortage and working towards solutions. This collaboration has existed through many forums (AIPES, IAEA, NEA HLG-MR and the European Commission, for example). Given the global nature of the $^{99}Mo/^{99m}Tc$ supply chain, international collaboration has been, and will continue to be, important to dealing with the complex issues; unilateral action that only deals with a problem domestically could easily undermine the entire market. Ensuring reliable supply is a global problem requiring global solutions.

This is not to say that domestic or regional actions are not critical or necessary, as they are and will become even more important in delivering more concrete actions to increase security of supply. Domestic and regional policy approaches and actions should be examined where it is most efficient to do so, recognising the special considerations or legislative powers at these levels. Any such approach or action should be developed in a manner that is consistent with, and non-harmful to, supporting the proper functioning of the international market and the global supply of $^{99}Mo/^{99m}Tc$.

Domestic or regional networks need to be able to be linked to international markets in an effective way or else the global market will fail. This requires international collaboration to ensure a consistent direction to resetting the global ^{99}Mo supply chain to ensure long-term reliable supply. This collaboration is necessary to put in place the "rules of the game" that governments, industry and stakeholders can adopt to ensure quick and effective changes. For example, the HLG-MR developed this document to serve as an international consensus on the changes that need to occur in the supply chain to ensure long-term security of supply.

Without international collaboration and consistency in approaches, severe distortions could occur in the market, threatening long-term reliable supply. For example, all producing nations need to agree on the need for the irradiation full-cost recovery methodology and implement it; otherwise the supply will never be economically sustainable.

On-going international collaboration is necessary to review the progress made towards implementing an economically sustainable supply chain and to discuss any changes that may be necessary on the path forward. Finding the right balance and tools may take some time and a forum for discussion of ideas will strengthen and improve efforts.

For example, if the voluntary-based approach to outage reserve capacity does not deliver the expected outcome, governments may be best served by determining a common approach to regulating minimum required levels, especially since outage reserve capacity will be found globally.

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

There are on-going efforts that should be continued and possibly expanded related to international collaboration working towards consistent transportation regulation internationally. As discussed in the "Interim Report", this is a key action to ensure global access to vital medical diagnostic techniques.

In addition, there is on-going collaboration on using LEU targets for ^{99}Mo production. Additional efforts may be required, for example on R&D, on policies to encourage conversion and on harmonising targets. These efforts will continue to be most effective when involving international collaboration.

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

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

Transparency of implementation

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

To improve the functioning of the ^{99}Mo supply chain, to facilitate the capacity development required for long-term supply reliability and to ensure the application of the principles of economic sustainability, transparency needs to be made a central foundation of efforts to reset the supply chain. This is true of any supply chain that is seeking to become more market based in its delivery mechanism. It is essential to be able to determine whether the principles of economic sustainability are being implemented.

In order to ensure that the implementation of economic sustainability succeeds, all stakeholders need to have confidence that the actions they are taking are being matched by all other players. This is necessary in regards to the application of the full-cost recovery methodology, sourcing and paying for outage reserve capacity, participating and respecting reactor scheduling efforts to ensure appropriate weekly reserve capacity, etc. This confidence can be bolstered by the availability of clear, open and transparent information.

Some information is obviously commercially confidential and therefore transparency measures should only apply to that information that is deemed necessary to ensure effective market operation and supports government involvement when necessary. Transparency measures that seek information only for "having transparency" are neither appropriate nor efficient. However, it is important that both private and public participants in the supply chain have access to sufficient information to understand the market situation, including available and planned capacity and progress in implementing full-cost recovery at the reactors.

Information on available and planned capacity and on future demand is essential so that proper investment decisions can be made. This information would allow market players to predict capacity needs with increased certainty (including understanding where there is overcapacity), determine when infrastructure investments are required and work to avoid bottlenecks in the supply chain.

Given the global nature of the supply chain, an international expert panel (IEP) could undertake a review of the supply chain through interviews with supply chain participants and reviewing available information. Based on this input, the IEP would then undertake an assessment on whether the market was moving in the required direction outlined in this policy paper. The panel could release, bi-annually, a report that provides its full assessment on the supply chain and whether:

- full-cost recovery from reactors is being implemented;
- voluntary co-ordination of reactor scheduling is working and is not being used to limit supply lower than demand intentionally (to increase prices);
- the appropriate amount of outage reserve capacity is being maintained;
- available and planned capacity will be sufficient to meet expected demand;
- other agreed-upon policy approaches are being followed.

The IEP and its review would have no regulatory powers, but the information provided could encourage all players to act in an economically sustainable manner. In this case, it would serve as a "labelling" (reporting) tool for the supply chain to know which players are acting in accordance with the agreed upon policy approach. In addition, it would serve to inform governments which could then take specific action if required.

Where the IEP finds one or more of these issues not being implemented as required, the international policy forum could also examine the issues and recommend the appropriate steps to address the issues. Participation in the IEP and its efforts to report on the status of the implementation of the policy approach within the market will be voluntary.

Transparency is also important for the end user. Under this proposed policy approach, end users are being asked to pay for reliable supply. As a result, there needs to be some indication to the end user that they are actually receiving the reliability for which they are paying. After its review, the IEP would be in a position to indicate whether the supply participants are maintaining the recommended levels of outage reserve capacity. This review could be a key indication to end customers of the reliability of their supply chain, providing a strong incentive to supply participants to maintain the necessary levels of outage reserve capacity.

The HLG-MR is in the process of developing the Terms of Reference for the IEP, including the suggested make-up of participants. The details of how the IEP will operate and obtain information are still under development. However, it is not expected that the IEP would request access to confidential financial accounts of companies. Rather, the assessments would be based on confidential discussions with supply chain participants and governments. The latter should generally have key insights into whether production technologies in their jurisdiction are implementing full-cost recovery. The details of the IEP will be discussed and confirmed by the HLG-MR.

Supporting recommendation: An international expert panel should be established to evaluate the ^{99}Mo/^{99m}Tc supply chain every two years.

10.3 Conclusions

The principles and supporting recommendations are essential to moving forward towards a long-term secure supply of ^{99}Mo. These recommendations take into consideration the need for the supply chain to become economically sustainable. Without these changes, secure supply will likely not be feasible in the long term.

It is clear that any changes to an established way of doing things can create challenges for some participants and the results may not be exactly as expected. This has been seen during the liberalisation of electricity markets, for example. Working towards an economically sustainable ^{99}Mo supply chain that provides for a long-term security of supply is no exception. While the HLG-MR feels that the policy approach suggested in this paper is the best direction for ensuring that change, finding the right balance and tools can take time. The provisions in this policy option for on-going review as the market changes occur should serve to monitor the market and adjust the policy as required.

Annex 10.A1: Principles and Supporting Recommendations

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

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

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

- Supply chain participants, both public and private, should both continue and improve annual co-ordination efforts through the Association of Imaging Producers and Equipment Suppliers (AIPES) or another similar mechanism to ensure the appropriate use of available capacity, recognising a minimum necessary volume level at all ^{99}Mo/^{99m}Tc producing facilities. New entrants to the supply chain should join these co-ordination efforts.
- To support effective co-ordination, contracts between ^{99}Mo/^{99m}Tc producing facilities and processors should allow for open access to ^{99}Mo irradiation services.
- Demand-management options should be encouraged as they could participate to support effective co-ordination efforts.
- Processors should voluntarily hold at every point in time outage reserve capacity equal to their largest supply (n-1 criterion), which can come from anywhere in the supply chain as long as it is credible, incremental and available on short notice.
- Reserve capacity options should be transparent and verifiable to ensure trust in the supply chain.
- Reactor operators, processors and generator manufacturers should review the current contracts to ensure that payment for reserve capacity is included in the price of ^{99}Mo.
- Communication efforts, providing three months advance notice to downstream stakeholders on generator supply should continue. In addition, industry communication

protocols regarding unplanned outages should be implemented by all industry participants and remain active.

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

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

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

Governments should:

- In co-operation with health care providers and private health insurance companies, monitor radiopharmaceutical price changes in order to support the transparency of costs.
- Periodically review payment rates and payment policies with the objective of determining if they are sufficient to ensure an adequate supply of ^{99m}Tc to the medical community.
- Consider moving towards separating reimbursement for isotopes from the radiopharmaceutical products as well as from the diagnostic imaging procedures.
- Encourage continued supply chain participation in ^{99}Mo/^{99m}Tc production schedule co-ordination efforts, including making such participation mandatory if voluntary participation wanes or commitments are not respected.
- Monitor levels of outage reserve capacity maintained by the market and, if found to be below the n-1 criterion, consider regulating minimum levels.
- Where required, support financial arrangements to enable investment in ^{99}Mo/^{99m}Tc infrastructure using various forms of public-private partnerships with appropriate returns.
- Consider ^{99}Mo/^{99m}Tc production capacity requirements when planning multipurpose research reactors to ensure that the required capacity is available. However, the funding of the ^{99}Mo-related capacity development should be supported through the commercial market.

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

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

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

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

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

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

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

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

- An international expert panel should be established to evaluate the ^{99}Mo/^{99m}Tc supply chain every two years.

Chapter 11

Conclusion

Over the past few years, there has been a shortage of molybdenum-99 (^{99}Mo) and its decay product, technetium-99m (^{99m}Tc), which is used in almost 80% of all nuclear medicine diagnostic procedures. The OECD/NEA established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in 2009 to examine the underlying reasons for the shortage and to develop a policy approach to ensure their long-term security of supply.

During the two years of its mandate, the HLG-MR has been able to examine the major issues that affect the short-, medium- and long-term reliability of ^{99}Mo/^{99m}Tc supply. The HLG-MR, working with medical isotope stakeholders, has completed a comprehensive assessment of the key areas of vulnerability in the supply chain and an identification of the issues that need to be addressed. It has examined the supply chain, undertaken a full economic analysis of the supply chain, and also reviewed potential ^{99}Mo/^{99m}Tc production technologies. This work has resulted in the release of a number of reports detailing the findings from these studies under the *Supply of Medical Radioisotopes* series.

Through the work of the HLG-MR and its stakeholders, significant progress has already been achieved on improving the supply situation through increased communication, co-ordination of research reactor schedules and a better understanding of demand-management opportunities. Although the current supply situation of ^{99m}Tc has stabilised with the return to service of two of the world's five main supplying research reactors, the underlying problem – that of an unsustainable economic structure – remains to be adequately addressed. The market has not restructured sustainably and thus, the long-term supply situation is no more stable or secure than it was during the shortage periods.

The HLG-MR developed a policy approach that provides recommendations detailing the essential steps to be taken by governments, industry and the health community to address the vulnerabilities within the supply chain, including changing an economic structure that does not support or reinforce reliable supply. The recommendations include ways to send strong price signals across the supply chain, to ensure international co-ordination of supply availability, to improve communication and demand-side management and to establish a mechanism for periodic international review.

The recommended changes should be applied by countries exporting to or influencing the global market; they are necessary to achieving change and realising secure supply. As individual countries take actions to increase the security of supply of these important medical isotopes in their own jurisdictions, it is important that their approaches are consistent with this international policy approach; the supply chain is global in nature and an inconsistent approach may have a negative impact on security of supply. The HLG-MR encourages decision makers to closely examine the information in this report and to consider implementing the principles for market reform.

The release of this report in June 2011 concludes the mandate of the HLG-MR.

At the request of its member countries, the NEA will continue its work in the field of medical radioisotopes, focussing on encouraging the implementation of the recommendations and ensuring long-term supply security of ^{99m}Tc. Participation in these new efforts will involve the NEA member countries and, as with the HLG-MR, some non-NEA countries that affect the global supply chain.

References

AIPES (2008), *Report on Molybdenum 99 Production for Nuclear Medicine 2010-2020*, Association of Imaging Producers and Equipment Suppliers, November, AIPES-eeig Editor, see www.vrom.nl/Docs/milieu/200902_AIPESMolySupplyReport.pdf.

AECL (2009), *2009 Annual Financial Report*, Atomic Energy of Canada Limited, downloaded from www.aecl.ca/NewsRoom/Reports/Annual.htm.

Associated Press (2010), *California Could Require Recording of Radiation Doses*, 28 March 2010, www.mercurynews.com.

Ball, G. (2010), "Experiences of HEU to LEU Mo-99 Production Conversion: NTP", presented at the IAEA meeting on Conversion Planning for Mo-99 Production Facilities from HEU to LEU, Vienna, Austria, 24-27 August 2010.

Brown, R. (2010), "I-131 Supply Update", presentation at the 3rd Meeting of the OECD/NEA HLG-MR, 24-25 June 2010, OECD, Paris, France.

Cabocel, J.-P. and G. Turquet de Beauregard (2010), "Update on the Current 2010 Schedule", presentation at the 3rd Meeting of the OECD/NEA High-level Group on the Security of Supply of Medical Radioisotopes, 24-25 June, OECD, Paris, France.

Covidien (2010), *Covidien Mo99 Calendar Update 5-5-10 EMEA*, accessed 1 June 2010. www.covidien.com/imageServer.aspx?contentID=17216&contenttype=application/pdf,

Dalton, K. (2009), "Some Patients Get Inappropriate Nuclear Stress Tests", *The Source for Interventional Cardiovascular News and Education*, 9 December 2009, from www.tctmd.com.

Gheeraert, M. (2010), "AIPES", presentation at the Meeting on the Security of Supply of Medical Radioisotopes in EU Member States, 4-5 May 2010, Luxembourg.

Haynes, E. (2009), "Supply Shortage Management and Communication Efforts", presentation at the 2nd Meeting of the OECD/NEA HLG-MR, 14-15 December 2009, OECD, Paris, France.

Health Imaging (2009), *ACR: Medicare Cuts May End Non-hospital Imaging*, 3 November 2009, accessed 3 November 2009, www.healthimaging.com/index.php?option=com_articles &view=article&id=19366:acr-medicare-cuts-may-end-non-hospital-imaging.

IAEA (2009), *Regulations for the Safe Transport of Radioactive Material, 2009 Edition,* International Atomic Energy Agency, Vienna, Austria, www-ns.iaea.org/ standards/documents/default.asp.

IAEA (2010), *Nuclear Technology Review 2010*, IAEA, Vienna, Austria.

Miller, R. (2010), "Additional Rest SPECT Test Found Unnecessary in Patients with Normal Stress SPECT", www.heart.org, accessed 8 January 2010.

NEA (2010a), *The Supply of Medical Radioisotopes: An Economic Study of the Molybdenum-99 Supply Chain*, OECD, Paris, France.

NEA (2010b), "Review of Potential Molybdenum-99/Technetium-99m Production Technologies", OECD, Paris, France, forthcoming.

Plan Nuclear (2009), "The Future of Spect and Spect Pricing", *Nuclear Medicine and Nuclear Imaging: Business and Strategy*, posted 1 September 2009, http://plannuclear.com/ 2009/09/01/the-future-of-spect-and-spect-pricing,

Ponsard, B. (2010), "Mo-99 Supply Issues: Report and Lessons Learned", presented at the 14th International Topical Meeting on Research Reactor Fuel Management (RRFM 2010), Marrakech, Morocco, 21-25 March 2010, published by the European Nuclear Society, ENS RRFM 2010 Transactions.

Spectrum Dynamics (2010) "D-SPECT Camera Brings Dramatic Dose Reductions to Nuclear Cardiology", downloaded from www.spectrum-dynamics.com/products/index.html, posted 20 May 2010.

UltraSPECT (2010), "Ultraspect Reconfirms its Clinically proven FDA-Cleared Dose-Reduction solutions to the Technetium Shortage", downloaded from www.ultraspect.com posted 10 February 2010.

UN (2009), "World Population Ageing 2009", United Nations, New York, United States.

UN (2011), "World Population Prospects: The 2010 Revision", United Nations, New York, United States.

Urbain, J. (2010), University of Western Ontario, Conversation on 20 April 2010.

Vanderhofstadt, J.M. (2009), "Medical Radioisotope Processing Sector: Key Issues and Challenges", presentation at the 2nd Meeting of the OECD/NEA High Level Group on the Security of Supply of Medical Radioisotopes, 14 December, OECD, Paris.

Vanderhofstadt, J.M. (2010), "Status and Future Challenges for the Mo-99 Supply from Europe", presentation at the Meeting on the Security of Supply of Medical Radioisotopes in EU Member States, 4-5 May, European Commission, Luxembourg.

World Bank (2006), "Global Economic Prospects: Managing the Next Wave of Globalisation", The World Bank, Washington, D.C., United States.

Appendix 1

HLG-MR Members

Argentina	Pablo CRISTINI Manager of Radioisotope Production Ezeiza Atomic Center National Commission of Atomic Energy
Australia	Ron CAMERON[1] (Vice-Chair 2009) Executive General Manager Strategy, Government and International Relations Australian Nuclear Science and Technology Organisation (ANSTO)
	Adrian (Adi) PATERSON CEO Australian Nuclear Science and Technology Organisation (ANSTO)
	Ian TURNER[2] General Manager, ANSTO Radiopharmaceuticals and Industrials (ARI) Australian Nuclear Science and Technology Organisation (ANSTO)
Belgium	Leo SANNEN Director of the Institute of Nuclear Materials Science SCK•CEN
	Jean-Michel VANDERHOFSTADT CEO – General Manager Institut des Radio-Eléments (IRE) The National Institute for Radioelements

[1] Succeeded by Adrian PATERSON.

[2] Succeeded by Adrian PATERSON.

Canada	Meena BALLANTYNE[3] Assistant Deputy Minister, Health Products and Food Branch Health Canada
	Serge DUPONT (Chair) Deputy Minister Natural Resources Canada
	Paul GLOVER Assistant Deputy Minister, Health Products and Food Branch Health Canada
European Commission	Remigiusz BARANCZYK European Commission, Directorate-General for Energy Directorate D – Radiation protection
France	Daniel IRACANE Directeur de l'Énergie Nucléaire du Commissariat à l'Énergie Atomique (CEA), Saclay
Germany	Ingo NEUHAUS[4] Forschungsneutronenquelle FRM II Technical University Munich
	Winfried PETRY Scientific Director FRM II Technical University Munich
	Jochen SÜSSENBERGER Bundesministerium für Wirtschaft und Technologie
Italy	Sandro SANDRI ENEA – CR Frascati

[3] Succeeded by Paul GLOVER.

[4] Succeeded by Winfried PETRY.

Japan	Takayuki FUJIYOSHI Director, Office for Quantum Radiation Research Basic and Generic Research Division Ministry of Education, Culture, Sports, Science and Technology (MEXT)
	Tatsuo IDO Executive Director of Japan Radioisotope Association
	Hiroki TAKAYA[5] Director, Office for Quantum Radiation Research, Basic and Generic Research Division, Ministry of Education, Culture, Sports, Science and Technology (MEXT)
Korea, Republic of	SunJu CHOI Director, Radioisotope Research Division Reactor Utilization & Development Center Korea Atomic Energy Research Institute
	Prof. Jong Kyung KIM[6] Hanyang University
Netherlands	Harrie SEEVERENS (Vice-chair 2009-2011) Ministry of Health, Welfare and Sport (VWS) Department of Pharmaceutical Affairs and Medical Technology
	Rob J. STOL Managing Director Nuclear Research & Consultancy Group (NRG)
Russian Federation	Liudmila ANDREEVA-ANDRIEVSKAYA Chief Expert, Department of International Cooperation State Atomic Energy Corporation “Rosatom”

[5] Succeeded by Takayuki FUJIYOSHI.

[6] Succeeded by SunJu CHOI.

	Svyatoslav MAKAROVSKY[7] Director, Department of Foreign Economic Relations Joint Stock Company "V/O IZOTOPE"
	Pavel TERENTIEV Director on Foreign Trade Joint Stock Company "V/O IZOTOPE"
South Africa	Don ROBERTSON Managing Director, NTP Radioisotopes Nuclear Energy Corporation of South Africa (Necsa)
United States	Mary Lisa MADELL Director of the Office of Europe and Eurasia Office of Global Health Affairs Department of Health and Human Services
	Parrish STAPLES Director of European and African Threat Reduction Office of Global Threat Reduction, US Department of Energy

OBSERVERS

IAEA	Natesan RAMAMOORTHY[8] Director, Division of Physical and Chemical Sciences International Atomic Energy Agency (IAEA)
	Meera VENKATESH Director, NAPC Division of Nuclear Sciences and Applications

7 Succeeded by Pavel TERENTIEV.

8 Succeeded by Meera VANKATESH.

Appendix 2

Delegated Participants

The following have participated with, or for, the HLG-MR member at more than one meeting.

Belgium	Bernard PONSARD Head of Unit, Radioisotopes and Silicon Production SCK•CEN/BR-2 Reactor
Canada	Cécile CLÉROUX Assistant Deputy Minister AECL Restructuring Natural Resources Canada
	Sylvana GUINDON Director Nuclear Energy Division Natural Resources Canada
	Alexander McEWAN Minister of Health's Special Advisor on Isotopes (Government of Canada) Medical Director, Cross Cancer Institute Professor and Chair, Dept. Oncology University of Alberta
France	Alain ALBERMAN Commercial and Project Manager Commissariat à l'Énergie Atomique (CEA)
Japan	Shoichi HASEGAWA Technical Advisor Ministry of Education, Culture, Sports, Science and Technology Research Promotion Bureau, Office for Quantum and Radiation Research

	Keiko SHIOTSUKI Manager, Radiopharmaceuticals and Radioisotopes Japan Radioisotope Association
Netherlands	Kevin CHARLTON Commercial Manager Irradiations and Development Nuclear Research & Consultancy Group (NRG)
South Africa	Piet LOUW Operations Director, NTP Radioisotopes Nuclear Energy Corporation of South Africa (Necsa)
United States	Rilla HAMILTON Office of Global Threat Reduction US Department of Energy

Appendix 3

OECD Secretariat

Thierry DUJARDIN
Deputy Director, Science and Development

Ron CAMERON
Head, Nuclear Development Division

Alexey LOKHOV
Nuclear Development Division

Chad WESTMACOTT
Nuclear Development Division

Appendix 4

Terms of Reference and Outline Work Programme

High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) under the Auspices of the OECD Nuclear Energy Agency

Background

On 29-30 January 2009, the OECD Nuclear Energy Agency hosted a workshop *Security of Supply of Medical Radio-isotopes*. The purpose of the workshop was to discuss the challenges facing the reliable supply of technetium-99m (^{99m}Tc), a key medical isotope derived from molybdenum-99 (^{99}Mo), and to identify measures that should be taken to ensure reliability of supply.

Workshop participants placed priority on challenges relating to the management of existing capacities and maximisation of these capacities in times of shortages, on the economic validity of the current model, on flexibility and efficiency of the supply chain, on regulatory impediments and demand side management. They identified the need to develop, deepen and share, as appropriate, contingency plans for future supply disruptions. They also focused on the longer term and on the need to engage the health authorities to reduce uncertainties regarding long term demand and the means by which to encourage more investment in production and greater redundancy in the system.

Participants identified the following measures to enhance short-term supply security:

- Reactor owners and operators should continue to share information and to enhance co-ordination of reactor maintenance schedules, with a view to ensuring an uninterrupted global supply of isotopes.

- Options for increasing production from existing reactors in times of global shortage should be further explored and encouraged.

- Current economic conditions for irradiation services should be reviewed to provide better incentives to reactor operators, including where the main mission is research in support of national nuclear energy or scientific programmes.

- Unnecessary impediments to the distribution of medical isotopes, such as restrictions in transport capabilities and denial of shipment by airline companies, should be removed.

- Anticipative actions to avoid the dilemma between meeting nuclear safety requirements or meeting health care needs should be encouraged; in this regard, participants were pleased to be informed of the outcome of the nuclear regulators meeting held in Paris three weeks earlier.

- Radiopharmacies, hospitals, health product regulators and the medical community should explore options for more efficient patient scheduling and utilisation of $^{99}Mo/^{99m}Tc$ generators to make best use of currently available supplies of ^{99}Mo and/or other potential alternatives.

There was unanimous support for the establishment of a working group to carry forward the agenda of the workshop, also involving the IAEA.

Establishment of the High-level Group

Mandate from the meeting of the NEA Steering Committee, 28-29 April 2009

On 29 April 2009, the NEA Steering Committee held a policy debate on the isotopes issue, during which they reviewed the outcome of the workshop, heard presentations from four invited speakers and discussed the way forward. The Steering Committee endorsed the proposal for a high-level group on the Security of Supply of Medical Isotopes under the auspices of the NEA to carry forward the agenda of the workshop and to identify the practical measures that should be taken.

The Steering Committee discussion covered the following points:

- In order to cover the supply side and demand side of the issue, a high level group consisting of 8 to 12 members would be established and that will consist of senior representatives nominated by interested member governments; several countries indicated at the Steering Committee meeting that they would nominate a representative to sit on the group.

- Countries represented on this high level group should be ready to consider, subject to their agreement to the work programme, to share the burden of providing resources in order that the work can proceed.

The group will approve its terms of reference and action plan at its first meeting and to facilitate an early meeting, the NEA will send out letters to all member countries asking if they have a senior representative whom they wish to nominate to the group.

It is anticipated that the group will sustain engagement on this issue; it will ensure co-ordination of the above efforts and foster transparency and accountability; it will give due recognition to the fact that governments have the responsibility for establishing an environment conducive to the private and/or public sector investments that may be required; that the conversion to low enriched uranium is a common goal and the feasibility and timing of implementation should be weighed against impact on the vulnerability of the supply chain.

Terms of reference

To review the total ^{99}Mo supply chain from uranium procurement for targets through to patient delivery, indicating the areas of vulnerability and identifying issues to be addressed, and mechanisms to address them, to strengthen the reliability of supply. The group should consider the immediate issues, the medium term issues (two to five years) and the longer term issues (greater than five years) in arriving at their conclusions and recommendations.

- The HLG-MR will report to the Steering Committee of the OECD Nuclear Energy Agency.
- The NEA will provide the Secretariat to the HLG-MR.
- The NEA may also undertake specific studies within its area of expertise, as requested.
- HLG-MR members will identify necessary resources to enable this work to proceed.
- The HLG-MR will have a two-year mandate. This will only be extendable by consent of the members and endorsement by the Steering Committee.
- The HLG-MR will establish an action plan at its first meeting, compatible with the available resources, to be approved by the Steering Committee. The action plan will contain specific deliverables, allocation of responsibilities and timing of deliverables.
- The NEA Steering Committee will be invited to approve the terms of reference and the action plan prior to its next meeting in October 2009.
- The action plan will be developed in close co-operation with the IAEA and key international organisations and institutions that are well positioned to propose and implement the necessary changes.
- Specific HLG-MR members will be responsible for obtaining early and clear commitments from key international organisations and institutions to provide support in the development and implementation of the action plan and will report on progress at each subsequent HLG-MR meeting.

Roles and responsibilities

The following provides a breakdown of roles and responsibilities to be further refined in consultation with key international organisations. As such, the roles and responsibilities listed below must be considered as indicative only. The HLG-MR will refine them as required.

Lead organisation	***Roles and responsibilities***
OECD/NEA	- Review the value chain for ^{99m}Tc with emphasis on the economics of the upstream segment of the market. - Explore and advise on the role of government in the commercial market. - Assess options to fund back-up capacity to ensure security of supply; assessment of market or other mechanisms to fund back-up capacity. - Assess and identify solutions to supply chain inadequacies; development of a mathematical model system reliability.
AIPES/isotope industry	- Co-ordinate existing reactor schedules used to produce medical radioisotopes to enhance supply response. - Establish a mechanism to assess the production of ^{99}Mo over the coming short, medium and long term and the ability to meet demand. - Establish an arrangement whereby additional production capacity can be brought into action as needed in times of emergency. - Establish communications protocols for early warning for unanticipated events.
Reactor owners/ operators	- Assess and implement options for increasing production in times of shortages. - Define their maximum output capacity and the time it would take to ramp up capacity. - Assess the viability of existing reactors used to produce medical radioisotopes. - Assess the options for expanding/introducing production in existing reactors used to produce medical radioisotopes.
IAEA	- Assess the possibilities of utilising existing reactors, not currently being used to produce medical radioisotopes, for ^{99}Mo production, the timescale and the measures that would be needed to enable this to happen.

Lead organisation	*Roles and responsibilities*
	- Assess transport impediments and identify measures to remove impediments. - Assess capability and requirements of smaller countries and the option of regional centres for irradiation and production. - Assess the stage-wise needs, timelines and economics of large scale ^{99}Mo production using LEU and final waste management aspects. - Assess the capabilities of alternative (non-reactor) technologies for the production of ^{99}Mo and the likely impact as well as the need for new reactor production capacity.
INRA/ASN	- Facilitate standardisation/licensing of transport packages and other regulatory issues. - Streamline inter-country agreements on approval processes for transport and certification of packages.
Health community (SNM, HC)	- Develop options for efficient patient scheduling and utilisation of available supplies - Assess potential alternatives to procedures using ^{99}Mo, for employment in shortage situations - Assess long-term demand for ^{99m}Tc including the impact of alternative procedures and new technologies - Enhance contingency plans and information sharing on contingency plans; establish communication protocols for early warning for unanticipated events.

NEA Secretariat

The NEA will form a small Secretariat, supported by voluntary contributions, to support the work of the HLG-MR; the Secretariat will arrange and host meetings/workshops, co-ordinate efforts with the organisations noted above, prepare necessary documentation (agendas, reports of meetings).

In addition, as noted above, the NEA may undertake specific studies as requested by the HLG-MR, subject to the resources being made available.

Appendix 5

Meetings of the HLG-MR

During its mandate, the HLG-MR held five meetings, along with a number of conference calls. A representative group of medical isotope stakeholders, including representatives of the nuclear regulation community, the medical isotope industry and the nuclear medicine community were invited to the first part of the meetings. This format provided a useful information and idea sharing opportunity, allowing the HLG-MR to obtain insights from industry and the medical community.

At the first meeting (17-18 June 2009, in Toronto, Canada) the Terms of Reference for the group (provided in Appendix 4) and the first instalment of the HLG-MR rolling action plan (provided in Appendix 6) were agreed upon. The plan included undertaking an economic analysis of the supply chain, increasing useful and regular communications to users about ^{99}Mo and ^{99m}Tc supply availability, developing protocols to inform stakeholders of unanticipated events and co-ordinating reactor schedules. The action plan also included assessing options to increase short-, medium- and long-term production. These options include demand-side management (e.g. promoting efficient patient scheduling, using alternative procedures) and producing ^{99}Mo via alternative reactors or technologies. In terms of bringing new supply to market, the action plan included work to identify regulatory issues, especially those related to the transportation of ^{99}Mo and ^{99m}Tc, and measures to address these issues.

At the second meeting of the HLG-MR (14-15 December 2009, Issy-les-Moulineaux, France) participants welcomed the positive actions that had been taken up to that time, such as the progress on the economic study, the development of communication protocols and the co-ordination and communication of reactor schedules. The presentations and ensuing discussions highlighted the complexity of the issues affecting the reliable supply of medical radioisotopes, especially those related to the economics of the supply chain.

Participants agreed to a list of actions to further improve the management of the 2009-2010 shortage and to work towards increasing security of supply – the second instalment of the rolling action plan (provided in Appendix 7). This list included developing and implementing communication protocols, sharing guidelines with the global health community on the efficient use of available supplies of ^{99}Mo and ^{99m}Tc and examining opportunities for securing longer-term medical radioisotope supply.

The HLG-MR held their third meeting (24-25 June 2010, Paris, France). At that meeting new actions to produce medical radioisotopes from Argentina, Brazil and the Russian Federation were discussed. As well, two NEA studies, undertaken for the HLG-MR by the NEA Secretariat, were presented: one on the economics of the $^{99}Mo/^{99m}Tc$ supply chain and one that examined a wide range of current and emerging $^{99}Mo/^{99m}Tc$ production technologies. Along with finishing these two studies, the third instalment of the rolling action plan (provided in Appendix 8) included items related to enhancing supply, improving regulation and communication, optimising use, supporting nuclear non-proliferation and studying future demand.

The fourth meeting (27-28 January 2011, Paris, France) was focused on the development of the policy approach to address the issues affecting the long-term security of supply. Input was received from medical isotopes stakeholders on a draft policy approach. The HLG-MR reached agreement on the necessary aspects of the policy approach, including a set of principles that should apply to countries exporting to or influencing the global market. For two specific areas working groups were formed to undertake a detailed examination of the best manner for implementing the related policy principles.

At the fifth meeting (23-24 June 2011, Paris, France) of the HLG-MR, this report was released. Part of the meeting was dedicated to a "Conference on the Global Security of Supply of Medical Radioisotopes". This conference provided an opportunity for the HLG-MR to share its work with important decision makers from the health and nuclear communities. During the other components of the meeting, participants discussed the implementation of the policy approach and the next steps for the NEA regarding its continued efforts in the field of medical radioisotopes supply security.

Appendix 6

First Instalment of Rolling Action Plan

From the 1st Meeting of the HLG-MR, 17-18 June 2009, Toronto, Canada.

- The NEA will undertake analysis of the economic considerations of the upstream isotope supply and provide preliminary findings for the next face to face meeting.

- The chair of the HLG will write a letter to the AIPES asking them to confirm actions related to upstream and downstream communication on supply availability, including reactor schedules and information by members to the health care system.

- The chair of the HLG will write a letter to the SNM requesting an assessment of the demand for ^{99m}Tc and the impact of alternative procedures and new technologies in the long-term. The letter will also confirm that they will undertake analysis of the current supply shortage and ways to optimise use of supply.

- The IAEA will advise on the scope for increasing production from new producing countries over the medium term, constraints such countries are facing, and actions that might be taken by the IAEA or member countries to overcome such barriers.

- The IAEA will advise on the current regulatory requirements governing the transportation of irradiated products and how such requirements would best be met.

Appendix 7

Second Instalment of Rolling Action Plan

From the 2nd Meeting of the HLG-MR, 14-15 December 2009, Issy-les-Moulineaux, France.

Action plan from the open session

SNM, EANM and Health Canada will provide guidelines for the health community on the most efficient use of available $^{99}Mo/^{99m}Tc$ to the NEA for public availability by end of January.

- AIPES and its members will continue efforts to co-ordinate reactor scheduling and to implement the agreed communications protocol, including an early warning protocol for unexpected supply disruptions. Correspondingly, generator manufacturers will provide clients in the health care community projected supply levels for periods of 90 days, to be updated and refined through regular, ongoing dialogue with clients and contingency planning for unexpected shortages.

- The IAEA through countries involved in its activities will continue the work to examine opportunities for production of ^{99}Mo from additional sources, including non-fission methods, and how and when these additional opportunities could be brought to market. This work will culminate in final reports in 2011, serving as a basis for further action by countries.

- Processors will continue efforts to diversify their sources of supply by crystallising opportunities for irradiation of materials in other research reactors, subject to resolution of funding and regulatory issues.

- The HLG-MR will detail the regulatory impacts on the supply chain, in particular related to transportation and target supply, and provide guidance on how harmonisation and greater co-operation can be encouraged and accelerated.

- The IAEA, in conjunction with the NEA, AIPES, and CORAR will support the work with regulators to address regulatory issues affecting the supply chain, with priority to be given to standardisation of containers for intermediate products and their approvals. Operators and industry participants will continue to supply information to the IAEA on different transport-related issues as they arise. The HLG-MR will facilitate the agreement on responsibilities and time lines for these issues.

- The HLG-MR will produce a mid-term diagnostic report in mid-2010, as well as the economic study on the supply chain, and will discuss next steps related to the key issues and challenges facing the medical radioisotope supply chain.

- To contribute to the economic study, nuclear medicine societies will provide information on the scope and level of reimbursements by health authorities or insurance plans and how these may affect demand and the ability to absorb increases in ^{99m}Tc prices, which in turn will influence the capacity for adjusting the price of ^{99}Mo.

- AIPES will work to define the units of measurement of ^{99}Mo in order to ensure effective communication among stakeholders.

- Covidien and CORAR will work to identify the bottlenecks in supply for ^{131}I.

Additional specific HLG-MR actions

- NEA Secretariat, with ongoing input from other HLG-MR members and stakeholders, will complete the economic study and publish results mid-2010. If deemed necessary from the economic study, the HLG-MR will examine options for infrastructure funding models and international financing mechanisms.

- The HLG-MR, working closely with the IAEA, will articulate criteria and details of the most promising reactor opportunities for securing ^{99}Mo production in the short, medium, and long term to provide information to decision makers in order to accelerate appropriate decisions.

- NEA Secretariat, in co-ordination with the IAEA and with input from other HLG-MR members and stakeholders, will produce a state of the art report on alternative technologies (non-fission and non-reactor methods) for producing ^{99}Mo.

- The transportation sub-group will complete its work on transportation issues; this work will be incorporated into the mid-term and final reports.

- The HLG-MR will examine issues related to processing capacity for incorporation into the mid-term and final reports.

- The HLG-MR will convene a group to provide guidance to the HLG-MR on future demand scenarios for ^{99m}Tc, recognising differences in developed and developing countries, which will be incorporated into the mid-term and final reports.

Appendix 8

Third Instalment of Rolling Action Plan

From the 3rd Meeting of the HLG-MR, 24-25 June 2011, Paris, France.

Enhancing supply

AIPES and its members will continue efforts to co-ordinate reactor scheduling, even once the short-term shortage situation has been passed. Following its meeting in September, AIPES will disseminate the 2011 schedule. As part of their on-going coordination role, efforts will be made by AIPES and its members to determine how best to address coordination in a situation of surplus supply to ensure the availability of reserve capacity, and how best to communicate levels of available reserve capacity as an indicator of supply reliability.

The IAEA through countries involved in its activities will continue the work to examine opportunities for production of ^{99}Mo from additional non-HEU sources, including non-fission methods, and how and when these additional opportunities could be brought to market. This work will culminate in final reports in 2011, serving as a basis for further action by countries.

Governments and supply chain participants will continue efforts to foster the development of long-term non-HEU supply options, taking into account technological, economic, regulatory, and other relevant factors, including funding models and timelines for potential deployment.

Improving regulation

The IAEA, in conjunction with the NEA, AIPES, and CORAR will develop a guidance document for regulators on approval processes for containers for intermediate products, supporting on-going work with regulators to address regulatory issues affecting the supply chain.

CORAR, with the support of the NEA and AIPES, will continue discussions with the IAEA on how to improve communication to the shipper of the medical nature of the shipment of ^{99}Mo, both in bulk and in generators. Possible options to be pursued include developing a new UN shipping classification for the medical isotope shipment, more information on the aircraft manifest, or adding a new label on the container to provide additional information.

Operators and industry participants will continue to supply information to the IAEA on different transport-related issues as they arise, including denial of shipments. Systematic reporting of these issues should be done via the process laid out in *IAEA's Denial Network Handbook*, which can be found at http://ns-files.iaea.org/fileshare/rit/default.asp?fd=774.

Improving communications

Drawing on communication protocols developed by AIPES and its members, ^{99}Mo supply chain participants will continue to provide clients in the health care community projected supply levels for extended periods (such as 90 days), to be updated and refined through regular, ongoing dialogue with clients and contingency planning for unexpected shortages.

Optimising use

Nuclear medicine associations will continue efforts toward efficient use of ^{99}Mo and ^{99m}Tc through implementation of guidelines for product-use optimisation and continued promotion of such guidelines even once the short-term shortage situation has passed.

Any documentation of efforts or experience will be provided to the NEA for posting on its website to encourage sharing and the on-going integration of demand management practices even when the short-term situation returns to normal. This documentation will include, but is not limited to, surveys done on the effects of the medical isotope supply disruption on health system practitioners by the Canadian Institute for Health Information (the CIHI study) and the Society for Nuclear Medicine, as well as upcoming studies being done in France and the United Kingdom.

The EANM will consider undertaking a study to determine the effects of the shortage on medical practitioners in Europe. If this study is undertaken, its results will be posted on the NEA website with a goal of sharing lessons learned.

Supporting nuclear non-proliferation

Governments, reactor operators and processors should continue to collaborate on LEU conversion efforts, including on target design and processing, with a goal of developing standardised approaches to conversion that can be used by all supply chain participants in order to increase reliable and available reserve capacity.

Supporting sustainable future economic conditions

The NEA Secretariat will draft an executive summary and appropriate disclaimer and finalise the economic study based on comments received and publish results by September 2010. HLG-MR members will provide any additional comments on the draft economic study by 15 July.

The NEA will develop a series of background papers to support the discussions of policy options at the next HLG-MR meeting in January 2011. These papers will follow up on the findings of the economic study and will look at different market models and approaches to ensure sufficient capacity, including reserve capacity.

Additional specific HLG-MR actions

The NEA Secretariat will redraft the state of the art report on technologies for producing $^{99}Mo/^{99m}Tc$ and provide to HLG-MR members for review before the end of July. Comments from the HLG-MR will be provided to the Secretariat by 20 August to enable publication of the study (via pdf on web) by September 2010. This report will include a discussion of criteria to be used when assessing promising reactor and non-reactor opportunities for securing ^{99}Mo production in the short, medium, and long term, providing information to decision makers in order to accelerate appropriate decisions.

HLG-MR members will provide comments on the existing draft of the Mid-Term Diagnostic Report to the NEA Secretariat by 29 July. The Secretariat will provide a final draft by mid-August for HLG-MR approval and publishing (via pdf on web) by September 2010.

The HLG-MR will convene an expert advisory group to provide guidance to the HLG-MR on future demand scenarios for ^{99m}Tc, recognising differences in developed and developing countries and building on available studies, which will be incorporated into the final report.

To support the demand scenario work, HLG-MR members will provide suggestions of experts for the advisory group by 20 August. The experts should provide for regional and professional diversity, including referring physicians (e.g. cardiologist, oncologist), nuclear medicine specialists and medical imaging technology experts (e.g. on software, camera advances).

The NEA will ensure governments of member countries are kept abreast of developments by disseminating reports and papers to the members of the NEA Steering Committee and by posting them on its website.

Appendix 9

Members of the Demand Project Expert Advisory Group and Technopolis Group Consultants

Maurizio DONDI	Head of Nuclear Medicine Section Division of Human Health International Atomic Energy Agency Austria
Richard J. FLANAGAN	Ex-CEO, Draximage Canada
Marc GHEERAERT	Philips Healthcare International, and President of AIPES The Netherlands
Tomio INOUE	Professor Department of Radiology Yokohama City University Graduate School Japan
Steven M. LARSON	Memorial Sloan-Kettering Cancer Center United States of America
Jörg MAHLSTEDT	Vorsitzender des Vorstandes des BDN Germany
Alexander McEWAN	Director of Oncologic Imaging at Cross Cancer Institute Professor and Chair, Dept. Oncology University of Alberta Canada

Richard UNDERWOOD	Professor of Cardiac Imaging Imperial College London United Kingdom
Fred VERZIJLBERGEN	European Association of Nuclear Medicine (EANM), and St. Antonius Hospital The Netherlands
Marijn KIEFT	Technopolis Group
Jon van TIL	Technopolis Group
Ingeborg MEIJER	Technopolis Group

Appendix 10

Further Reading

The NEA maintains a list of non-NEA documents on its medical radioisotope webpage www.oecd-nea.org/med-radio. This "external documents" list was developed in order to provide a central repository of the most recent, relevant studies, position papers and guidance documents related to ^{99}Mo and ^{99m}Tc. Links to the following documents can be found at the website.

External documents

Background information/non-NEA position papers

- IAEA article: "Breaking Bottlenecks, IAEA Tackles Transport Woes of Life-saving Radioactive Materials" (25 January 2011).
- IAEA article: "IAEA Helps to Close Radioisotope Production Gap, Vitally Important Diagnostic Isotope Used Once a Second Worldwide" (7 January 2011).
- Council of the European Union Conclusions "Towards the Secure Supply of Radioisotopes for Medical Use in the European Union" (6 December 2010).
- IAEA Coordinated Research Project on Production of Mo-99 from LEU or Neutron Activation.
- Annex to IAEA Nuclear Technology Review 2010 (September 2010) *Production and Supply of Molybdenum-99*.
- Proceedings from *Security of Supply of Medical Radioisotopes in EU Member States*, Luxembourg 4-5 May 2010 (September 2010).
- Communication from the Commission to the European Parliament and the Council on medical applications of ionising radiation and security of supply of radioisotopes for nuclear medicine (6 August 2010).
- Commission Staff Working Document, accompanying document to Communication from the Commission to the European Parliament and the Council on medical applications of

ionising radiation and security of supply of radioisotopes for nuclear medicine (6 August 2010).

- CEA, NRG, SCK•CEN and TUM (2010) Position Paper: *Scenario for Sustainable Molybdenum-99 Production in Europe* (13 April 2010).

- Government of Canada (2010), Response to the Report of the Expert Review Panel on Medical Isotope Production (31 March 2010).

- National Research Council of the National Academies Report (2009), *Medical Isotope Production Without Highly Enriched Uranium.*

- European Nuclear Society (2009), position paper, *The Medical Isotope Crisis.*

- Ramamoorthy, N. (2009), Editorial Commentary: *Supplies of Molybdenum-99: Need for Sustainable Strategies and Enhanced International Cooperation*, Nuclear Medicine Communications, 30:899-905.

- Council of the European Union (2009), *Conclusions on the Security of Supply of Radioisotopes for Medical Use* (15 December 2009).

- Canada's Expert Review Panel on Medical Isotope Production Report (30 November 2009).

- ANSTO (2009), *The Global Mo-99 Crisis: Australia's Unique Leadership Role*, Newsletter (November 2009).

- European Commission (2009), *Supply of Radioisotopes for Medical Use and Current Developments in Nuclear Medicine*, Ad Hoc Interservice Group Preliminary Report (30 October 2009).

- TRIUMF report: *Making Medical Isotopes: Report of the Task Force on Alternatives for Medical-Isotope Production* (2008).

Health community guidance documents/information

- "A Review of the Supply of Molybdenum-99, the Impact of Recent Shortages and the Implications for Nuclear Medicine Services in the UK", Administration of Radioactive Substances Advisory Committee (November 2010)

- Canadian Institute for Health Information report, Results of the National Survey on Medical Isotopes Supply Disruption (16 June 2010).

- European Medicines Agency: workshop on current use and future needs of radiopharmaceuticals labelled with radionuclides produced in reactors and possible alternatives (20 May 2010).

- Health Canada, *Guidance for Maximizing Supply of Technetium-99m (Tc-99m) during a Shortage* (November 2009).

- SNM, *Isotope Shortage Survey Results* (10 August 2009).

- SNM, *Recommendations for Dealing with the Isotope Shortage*.

Demand expectations

- Ministry of VROM (Netherlands) study, *Radioisotopes in Medicine: Foresight of the Use of Reactor Isotopes until 2015* (19 December 2008).

- AIPES, Report on Molybdenum 99 Production for Nuclear Medicine 2010-2020 (November 2008).

NEA PUBLICATIONS AND INFORMATION

Printed material

The NEA produces a large selection of printed material, part of which is on sale, and part of which is distributed free of charge. The full catalogue of publications is available online at www.oecd-nea.org/pub.

Internet and electronic products

In addition to basic information on the Agency and its work programme, the **NEA website** offers free downloads of hundreds of technical and policy-oriented reports.

For full access to all print and electronic products, see the OECD/NEA **Nuclear Energy iLibrary** at www.oecd.org/bookshop?16121s1.

An **NEA monthly electronic bulletin** is distributed free of charge to subscribers, providing updates of new results, events and publications. Sign up at www.oecd-nea.org/bulletin/.

You can also visit us on **Facebook** at www.facebook.com/OECDNuclearEnergyAgency.

OECD PUBLISHING, 2 rue André-Pascal, 75775 PARIS CEDEX 16
ISBN 978-92-64-99164-4

The Supply of Medical Radioisotopes: The Path to Reliability

The reliable supply of molybdenum-99 (^{99}Mo) and its decay product, technetium-99m (^{99m}Tc), is a vital component of modern medical diagnostic practices. Disruptions in the supply chain of these radioisotopes can delay or prevent important medical testing services. Unfortunately, supply reliability has declined over the past decade, due to unexpected or extended shutdowns at the few ageing, ^{99}Mo-producing, research reactors and processing facilities. These shutdowns have recently created global supply shortages.

This report provides the findings and analysis of two years of extensive examination of the ^{99}Mo/^{99m}Tc supply chain by the OECD/NEA High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR). It puts forth a comprehensive policy approach that would help ensure long-term supply security of ^{99}Mo/^{99m}Tc, detailing the essential steps to be taken by governments, industry and the health community to address the vulnerabilities of the supply chain, including its economic structure.

OECD Nuclear Energy Agency
12, boulevard des Îles
92130 Issy-les-Moulineaux, France
Tel.: +33 (0)1 45 24 10 15
nea@oecd-nea.org **www.oecd-nea.org**

ISBN 978-92-64-99164-4