Nuclear Development
November 2010

The Supply of Medical Radioisotopes

Review of Potential Molybdenum-99/ Technetium-99m Production Technologies

AEN NEA

NUCLEAR ENERGY AGENCY

The Supply of Medical Radioisotopes:

Review of Potential Molybdenum-99/Technetium-99m Production Technologies

NUCLEAR ENERGY AGENCY
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

1 FOREWORD

At the request of its member countries, the OECD Nuclear Energy Agency (NEA) has become 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 Steering Committee for Nuclear Energy established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in April 2009. 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. In order to reach this objective, the group has been reviewing the ^{99}Mo supply chain, working to identify the key areas of vulnerability, the issues that need to be addressed and the mechanisms that could be used to help resolve them. A report on the economic study of the ^{99}Mo supply chain was issued in September 2010.

Among the actions requested by the HLG-MR was a review of other potential methods of producing ^{99}Mo, of which the two main methods are reactor-based and accelerator-based. The HLG-MR requested both the development of a set of criteria for assessing the existing and proposed methods, as well as an analysis, where possible, of those methods using these criteria.

This report provides a set of criteria and an initial assessment of the situation at the present time, based mainly on published sources of information. The work is not regarded as comprehensive, nor does it attempt to rate the criteria for importance in performing the assessment. However it does provide a technological review and economic estimates of these methods. It also recognises that the expected ^{99}Mo production costs for several of the considered technologies (especially those at a conceptual stage but not yet realised on an industrial scale) can only be estimated and therefore must be viewed accordingly, since there is no direct industry experience to verify the information provided.

This report was prepared by the NEA Secretariat at the request of the HLG-MR. It is not presented as a consensus view of the HLG-MR but to enable discussions and further analysis among the members of the HLG-MR, other stakeholders and decision-makers. The individuals and organisations that contributed to the study are not responsible for the opinions or judgements it contains.

1.1 Acknowledgements

This report would not have been possible without input from a significant number of producers and stakeholders. As for the economic study, the input from the ^{99}Mo supply chain participants was essential for completing this study, and the NEA greatly appreciates the information provided by interviewees. Also, the NEA would like to thank Christine Poinot and Siegfied Douce (CEA, France), Brigitte Guérin (University of Sherbrooke, Canada), Tom Ruth and Timothy I. Meyer (TRIUMF, Canada) and P. Chakrov (INP, Kazakhstan) for their valuable inputs.

Drafts of this report were reviewed by members of the HLG-MR and participants who provided comments and suggestions on several occasions. In addition, valuable comments were received during the presentation of the findings at the Third Meeting of the HLG-MR.

This report was written by Alexey Lokhov of the NEA Nuclear Development Division. Detailed review and comments were provided by Ron Cameron and Chad Westmacott of the NEA Nuclear Development Division, with other reviews and input from Natesan Ramamoorthy and Edward Bradley from the IAEA.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

2 EXECUTIVE SUMMARY

2.1 Background

For many years, the isotope molybdenum-99 (^{99}Mo) has been supplied to the medical community, and its decay product technetium-99m (^{99m}Tc) is one of the most used diagnostic imaging agents.

Due to recent shortages of supply of ^{99}Mo production, the NEA was asked by its member countries in April 2009 to establish a High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) to help address the shortages and work towards increasing the reliability of supply in the short, medium and long term.

Because 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 current study was to produce a state of the art report on technologies for producing ^{99}Mc/^{99m}Tc.

2.2 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);
- 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

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.

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 $^{100}Mo(\gamma,n)^{99}Mo$ 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.

2.3 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 ES1). 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.

2.4 Assumptions on data

For uranium fission in research reactors, the data was provided by ^{99}Mo supply chain participants. It is the same data that was 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 has been used. The data on these technologies (especially those at a conceptual stage but not yet realised on an industrial scale) is, 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 this 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 this 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.

2.5 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 ES1, each rating is discussed in detail in the main text of the report.

Table ES1: Summary of technology assessment results

		Short-term technologies				Mid-term technologies		Long-term technologies	
Assessment Criteria	HEU in research reactors - Reference	Current LEU targets[3] in research reactors	LEU solution reactor	^{98}Mo activation in research reactors	^{100}Mo → ^{99m}Tc in cyclotron	^{238}U (γ,f) photofission	^{100}Mo (γ,n) ^{99}Mo	LEU fission with spallation neutrons	^{100}Mo (n,2n) ^{99}M
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	**

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.

---

3. Aluminide dispersion targets.

2.6 Conclusions

2.6.1 Short-term technologies

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

   a. Proliferation resistance;

   b. Easier availability of the target material;

   c. 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.

2. 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.

3. 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.

4. 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.

5. 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.

2.6.2 Mid-term technologies

6. 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.

7. The technology based on the photonuclear reaction $^{100}Mo(\gamma,n)^{99}Mo$ 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.

2.6.3 Long-term technologies

8. 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).

2.7 Further work

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

1. 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 $^{99}Mo/^{99m}Tc$.

2. 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).

3. 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.

4. The possibility of using metallic targets for neutron activation should be examined, and the cost of its processing and recycling should be evaluated.

5. 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.

6. 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.

7. 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.

8. There would be value in updating this report in approximately one year as new information is expected to become available over this period.

3 INTRODUCTION

For many years, molybdenum-99 (^{99}Mo) and its decay product technetium-99m (^{99m}Tc) have been supplied to the medical community through irradiation of uranium targets in reactors and processing of the irradiated targets in dedicated processing facilities. This has been a mature and effective supply process, which has been capable of supplying the world market and coping with the growth in that market for more than 30 years. The reliability of the industry has allowed widespread use of ^{99m}Tc as a diagnostic imaging agent and around 30 million procedures are performed each year.

However, the supply has relied on reactors that are now ageing and recently both unanticipated and planned shutdowns of the main reactors have caused shortages in supply throughout the world. As a result of the shortages, the NEA was asked by its member countries in April 2009 to establish a High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) to help address the shortages and work towards increasing the reliability of supply in the short, medium and long term.

One of the actions requested by the HLG-MR was for the NEA Secretariat to undertake a review of other potential methods of producing ^{99}Mo, of which the two main methods are reactor-based and accelerator-based. The HLG-MR requested both the development of a set of criteria for assessing the existing and proposed methods, as well as an analysis, where possible, of those methods using these criteria.

This report provides a set of criteria and an initial assessment of the situation at the present time, based mainly on published sources of information. The work is not regarded as comprehensive, nor does it attempt to rate the criteria for importance in performing the assessment. However it does provide a technological review and economic estimates of these methods, which it is hoped will be helpful for decision-makers in deciding further investment. It also recognises that the expected ^{99}Mo production costs for several of the considered technologies (especially those at a conceptual stage but not yet realised on an industrial scale) can only be estimated and therefore must be viewed accordingly, since there is no direct industry experience to verify the information provided. Clearly more in-depth work will be needed to examine the methodologies and the IAEA is currently compiling a more comprehensive report on the potential technologies, which will add to the information presented here. In addition, estimating costs has been difficult in several of the cases due to sparse data.

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 this report recognises technical maturity as one of the criteria, it does not make any examination of the risks associated with the path to development. Development costs are therefore not included in the economic analysis.

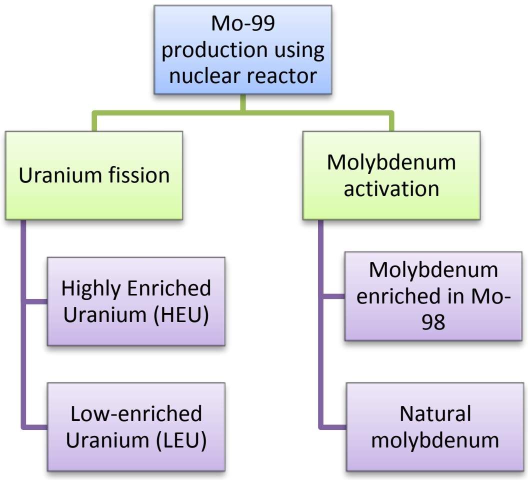
This report provides a review of known and potential ^{99}Mo/^{99m}Tc production technologies. However, it is recognised that decisions on technology choices will depend on national approaches and policies towards domestic and/or global production and other priorities for technology development.

4 LIST OF TECHNOLOGIES

4.1 Reactor-based methods of ^{99}Mo production

The nuclear reactor ^{99}Mo production technologies can be divided into two subsets: Uranium fission-based and neutron activation of molybdenum-98 (Figure 1).

Figure 1: Summary of reactor-based ^{99}Mo production technologies



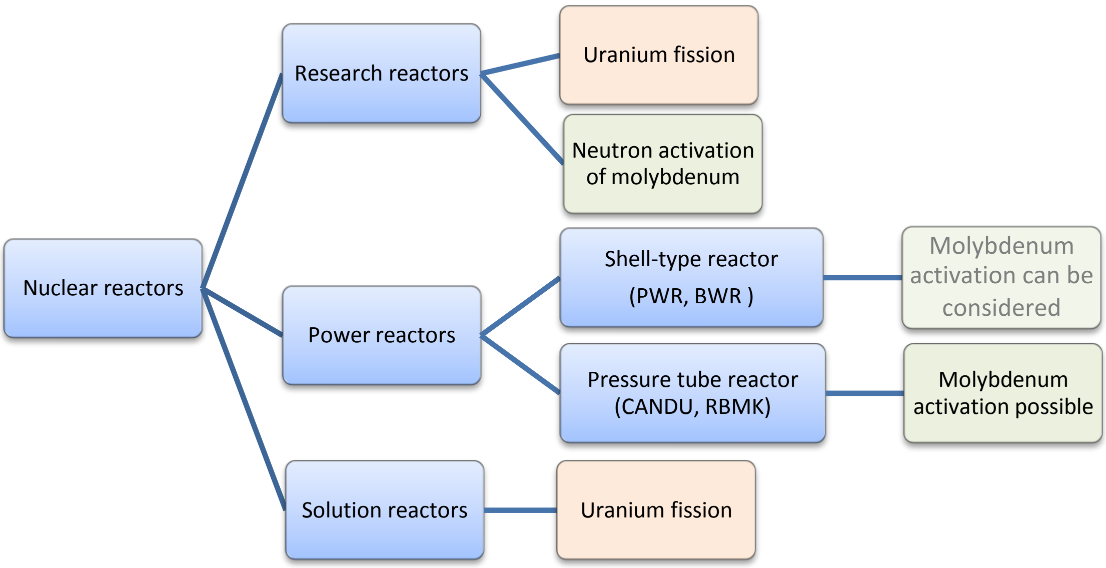
In the fission route (NA, 2009), ^{99}Mo is recovered from the fission of ^{235}U (the cumulative yield of ^{99}Mo is 6.13% of fission products, IAEA/NEH). Two types of fission targets are in use today: highly enriched uranium (HEU) typically containing more than $90\%_{mass}$ of ^{235}U and low-enriched uranium (LEU) with less than $20\%_{mass}$ of ^{235}U. Presently, most of the ^{99}Mo is produced from HEU targets.

In the activation process, ^{99}Mo is produced from naturally occurring ^{98}Mo (abundance 24.13%) by neutron capture. Both natural and enriched molybdenum can be used for this purpose. The efficiency of the activation route is less than in the fission route. The specific activity of the molybdenum in the activation route is very low (more than 500 times lower than in the fission route), and a dedicated technetium purification step is sometimes needed before the latter is usable for medical diagnostics. However, recent progress in low specific activity gel generators (portable or centralised) and simple waste management (compared to the fission route) have renewed interest in further investigating this technology.

Both fission- and activation-based technologies can be realised in research reactors (see Figure 2) where irradiation rigs are easily accessible. In principle, molybdenum activation could also be performed in pressure tube power reactors[4]. The irradiation of molybdenum in the instrumentation channels of the most common shell-type power reactors (PWRs or BWRs) is technically possible but has more technical and safety case challenges compared to the use of pressure tube reactors.

4. This has been tried in the past, for example see Zykov *et al.*, 2001.

Figure 2: Potential molybdenum-99 production in different types of reactors



The ^{99m}Tc production chains for fission and activation methods are summarised in Table 1. Although the major steps for both routes are quite similar, the underlying complexity of the treatment is considerably different. For example, the irradiated target in the fission route is highly radioactive and its transport to the processing facility requires careful management, in compliance with regulatory and transport requirements. On the contrary, in the activation route the irradiated target transport is in principle easier because it is less radioactive but the volumes are considerably larger (because of low specific activity of the activation ^{99}Mo) and suitable large certified containers are not available.

In order to get quantitative evaluation criteria for the whole process, all the production steps need to be analysed in detail. The report concentrates on the irradiation and processing steps of the chain, but does not look at the financial issues concerning bringing the technologies to maturity, final waste disposal and logistics.

Table 1: Summary of the ^{99m}Tc production chains for fission and activation routes in a nuclear reactor

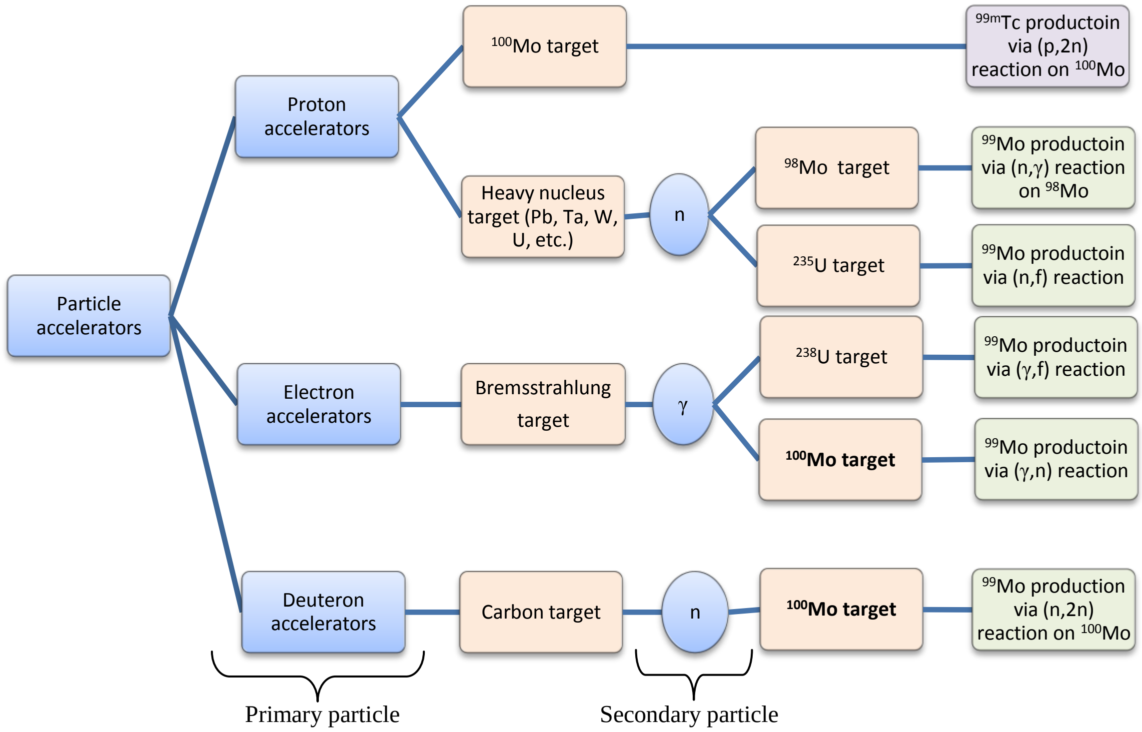
^{99}Mo production by fission process	Issues	^{99}Mo production by activation process	Issues
HEU/LEU target fabrication	Dense LEU targets fabrication	Molybdenum target fabrication: Natural/Enriched molybdenum	For MoO_3 targets: Availability, purity and price of enriched molybdenum, recycling of enriched molybdenum Metallic targets: Fabrication and qualification, plus the same issues as for MoO_3 targets if enriched molybdenum is used
Target transport to the reactor	Security of HEU target transportation	Target transport to the reactor	
Target irradiation	Safety and regulatory issues	Target irradiation	
Irradiated target transportation to the processing facility	Safety and regulatory issues	Irradiated target transportation to the processing facility	Large container currently not available Safety and regulatory issues
Processing	Availability of processors Safety risks of operation High technical complexity for new entrants Waste management (including security issues if HEU used)	Processing	Availability of processors and recycling facilities
Transportation to the technetium generator manufacturer	Denial of shipment	Transportation to the centralised technetium extraction facility or gel generator manufacturer	Large amounts of low-activity Mo transportation, denial of shipment
Technetium generator fabrication		Technetium generator fabrication[5]	Development and large-scale fabrication of gel generator Possible additional Tc purification
^{99m}Tc generator shipment to the radiopharmacy or hospital	Denial of shipment	^{99m}Tc gel generator or ^{99m}Tc doses shipment to the radiopharmacy or hospital	Gel generator or other extraction facility certification Denial of shipment

5. This step only applies to manufacturing of portable gel or other type of generators.

4.2 Accelerator-based methods of ^{99}Mo/^{99m}Tc production

The most widely discussed accelerator-based routes of ^{99}Mo or ^{99m}Tc production are summarised in Figure 3. In some accelerator-based technologies the ^{99}Mo or ^{99m}Tc is produced directly via the interaction of bombarding particles with the target material. In other accelerator-based technologies the primary accelerated charged particles (electrons, protons, deuterons, etc.) are used to produce energetic secondary particles (photons, neutrons) that then interact with the target material to produce ^{99}Mo. The indirect production is intrinsically more complicated than the direct one.

Figure 3: Summary of potential accelerator-based ^{99}Mo/^{99m}Tc production technologies



4.2.1 *Reaction ^{100}Mo(p,2n)^{99m}Tc*

In this route ^{99m}Tc is directly produced for immediate use, via the reaction of an accelerated proton with a ^{100}Mo nucleus yielding ^{99m}Tc and two neutrons. This is only useful for a local production because ^{99m}Tc is a short-lived radioisotope.

4.2.2 *Reaction ^{238}U(γ,f)^{99}Mo*

The photo-fission of depleted uranium is induced by energetic gamma rays that are produced via bremsstrahlung (i.e. deceleration radiation) of high-energy electrons provided by an accelerator. The processing of irradiated targets is similar to the one in the reactor-based fission routes.

4.2.3 Reaction $^{100}Mo(\gamma,n)^{99}Mo$

Molybdenum-99 may be produced through the photon-to-neutron reaction (γ,n) on a molybdenum target with enriched ^{100}Mo. Photons for this reaction are provided, as in the previous technology, from the electrons deceleration radiation.

4.2.4 Reaction $^{100}Mo(n,2n)^{99}Mo$

Molybdenum-99 is produced through the ^{100}Mo(n,2n)^{99}Mo reaction using an enriched ^{100}Mo target. High-energy neutrons for this reaction are provided by energetic deuterons bombarding a natural carbon target.

4.2.5 Reaction $^{235}U(n,f)^{99}Mo$ using spallation neutron sources

In this route neutrons are generated by spallation reactions induced by energetic protons bombarding a heavy metal target. These neutrons are used for fissioning the uranium nuclei in a target, as in a nuclear reactor. The process works in the same way as the reactor-based fission production route, but the system remains subcritical and can be operated by changing the proton beam intensity. This kind of solution is very close to the concept of an accelerator driven nuclear reactor (ADS – accelerator driven system).

4.2.6 Other routes

4.2.6.1 Reaction $^{96}Zr(\alpha,n)^{99}Mo$

The reaction ^{96}Zr(α,n)^{99}Mo allows selective production of ^{99}Mo by bombarding the zirconium target with accelerated helium nuclei (Schenter, 2006). High specific activity molybdenum would then be separated from the target. The α-particle accelerators are fairly available, but their present beam currents are probably too low. This method has not been proven.

4.2.6.2 Reaction $^{98}Mo(n,\gamma)^{99}Mo$ using spallation neutron sources

In this route ^{99}Mo is produced by a neutron capture reaction by a ^{98}Mo target. Neutrons are generated by spallation reactions induced by energetic protons bombarding a heavy metal target. The energy of the neutrons produced is high; they would therefore need to be slowed down to the ^{98}Mo resonances energy interval to optimise the yield of the reaction.

5 CRITERIA FOR ASSESSING THE TECHNOLOGIES

The development of criteria for evaluating the identified technologies has involved considering both physical and economic characteristics of the production processes. Physical criteria are discussed in Section 5.1, the economic criteria are discussed in Section 5.2, and the final list of the assessment criteria is given in the Section 5.3.

5.1 Aggregated physical criteria

The physical characteristics of $^{99}Mo/^{99m}Tc$ production technologies[6] were aggregated to a list of general characteristics to make the assessment of the technology easier to carry out. Each general characteristic presented in this section is 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.

5.1.1 Technology maturity

This criterion is an overall assessment of the technology's readiness. Some technologies are currently at a basic conceptual stage, others have been experimentally tested, and the most advanced are already used for commercial $^{99}Mo/^{99m}Tc$ production. The evaluation of the Technology maturity is performed using the following convention:

- If the technology is commercially used for substantial ^{99m}Tc production, the score is High (***).
- If the technology has been experimentally proven or already used for commercial production, but significant improvements are still needed, the score is Medium (**).
- If the technology is only a basic theoretical concept then the score is Low (*).

5.1.2 Production yield

The overall production yield of a technology is determined by actual production rates (if known) or using theoretical calculations if actual rates are not known or not available; the characteristics of the target and the specific activity of the product. Thus production yield is evaluated using the following rules:

- If the output of $^{99}Mo/^{99m}Tc$ (determined as above) is high compared to all the other technologies, then the score is High (***).
- If the production yield is intermediate compared to other technologies, then the score is Medium (**).
- Technologies with low output of $^{99}Mo^{/99m}Tc$ are scored with Low (*).

5.1.3 Available irradiation capacity

Depending on the $^{99}Mo/^{99m}Tc$ production method, the target's characteristics and the production rate, the theoretically available irradiation capacity was estimated:

- If a considerable part of the world demand for $^{99}Mo/^{99m}Tc$ can be satisfied using existing facilities then the score is High (***).

6. Physical characteristics used to build assessment criteria are discussed in an Appendix (Section 11).

- In the case where facilities exist, but their use for $^{99}Mo/^{99m}Tc$ production is limited or the number of facilities are limited, then the score is Medium (**).
- If no irradiation facility is currently available the score is Low (*).

5.1.4 *Distribution range and logistics*

The maximal theoretical distances between irradiation and processing facilities, generator manufacturer and hospitals determines the distribution range of the technology:

- If there are no physical constraints or regulatory issues restricting the long-range shipments of $^{99}Mo/^{99m}Tc$, then the score is High (***).
- In the case where some restrictions of shipment are imposed by physical reasons or foreseeable regulatory issues, the score is Medium (**).
- If the technology is only suitable for local $^{99}Mo/^{99m}Tc$ production the score is Low (*).

5.1.5 *Simplicity of processing*

This criterion reflects the processing safety of a technology, which depends on the type of process used, the physical and chemical form (including radioactivity) of the targets, and their residual power:

- If the process presents low potential risks of criticality, fire or leak, and no fissile, highly radioactive or hazardous materials are involved, then the score is High (***).
- If low quantities of radioactive or hazardous materials are involved, but the process involves some inherently hazardous features (e.g. hydrogen production), then the score is Medium (**).
- If large quantities of fissile, highly radioactive or hazardous matters are involved, or the process has high criticality, fire or leakage risks, then the score is Low (*).

5.1.6 *Waste management*

This criterion assesses the overall efficiency of waste processing, the volume and type of the waste, associated security risks and complexity of materials recycling:

- If the waste contains no fissile, highly radioactive or hazardous materials; and the recycling of materials could be easily implemented, then the score is High (***).
- If small amounts of fissile or radioactive materials are involved or there are moderate difficulties in active materials recycling, then the score is Medium (**).
- If the waste is highly radioactive, contains large amounts of fissile or hazardous materials, and their recycling or management is difficult, then the score is Low (*).

5.1.7 *Nuclear proliferation resistance*[7]

This criterion provides information on the risks associated with the deployment of the assessed $^{99}Mo/^{99m}Tc$ production method from the viewpoint of nuclear proliferation:

- If the method does not involve weapons-grade materials or technologies the score is High (***).

7. For this criterion a binary grading system is used.

– If weapons-grade fissile materials or technologies potentially directly usable for nuclear proliferation are explicitly involved then the score is Low (*).

5.2 Economic criteria to evaluate technologies to produce ^{99}Mo or ^{99m}Tc

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

5.2.1 Normalised capital costs

This criterion provides an indication of the ease of financing the proposed technology assuming that a mature stage of development has been reached, based on the size of capital investment required for a "Greenfield" facility of the various technologies. It is presented as an "overnight capital cost", meaning that time to development and financing charges are not included in the calculations. The higher the capital cost, the more difficulty in financing a project based on the technology as larger amounts of capital will need to be secured from public or private sources.

In order to ensure comparability between projects of various sizes and yields, the capital costs will be normalised based on the proportion of the overall project that would be attributable to ^{99}Mo or ^{99m}Tc production, recognising that some projects have co-product uses or other purposes (e.g. multi-purpose research reactors or cyclotrons). In addition, the capital costs will be normalised to a yield of 100% of annual world demand, or 624 000 6-day curies of ^{99}Mo (End of Processing) per year. Where ^{99m}Tc is produced directly, a division factor on activity will be used to "translate" usable ^{99m}Tc curies to ^{99}Mo 6-day curies, simulating a ^{99m}Tc generator[8] (see NEA, 2010a).

The following rules were used to attribute an assessment rating to the criterion of normalised capital cost:

- If the normalised capital costs are low compared to other production technologies, then the score is High (***).
- If the normalised capital costs have intermediate values, compared to other considered technologies then the score is Medium (**).
- If the normalised capital costs have high values, compared to other considered technologies then the score is Low (*).

5.2.2 Potential for co-production of other isotopes

This criterion provides an indication of economic sustainability, demand-risk mitigation and the ability to avoid creating other isotope shortages. If co-production of other isotopes is possible, then the project may be more economically sustainable, being able to derive revenue or provide other services

---

8. Dividing ^{99m}Tc activity by 12.75 gives the activity of ^{99}Mo 6-day curies (EOP) necessary based on the amount of curies of ^{99m}Tc that are able to be eluted from a ^{99m}Tc generator when eluted 3 times a day starting one day after calibration, and then translating ^{99}Mo calibrated curies to 6-day curies (from end of processing) of ^{99}Mo.

   This methodology (for details see NEA, 2010a) allows for comparison of capital costs related to production between different technologies, regardless of how they produce ^{99m}Tc. There is only one exception, that of ^{100}Mo(p,2n)^{99m}Tc, which may be more equivalent to only one elution on the first day. This requires addition input on proper methodology.

from these co-products. In addition, the ability to produce other isotopes reduces the risk from potential declining demand for ^{99}Mo or ^{99m}Tc before the end of the project's lifespan (often greater than 30 years) as the facility could be used for other purposes including for the future development and production of other isotopes. Finally, the investment in facilities to produce ^{99m}Tc should not result in shortages of other essential isotopes by replacing technologies that co-produce other isotopes.

The following rules were used to attribute an assessment rating to the criterion potential for co-production of other isotopes:

- If the technology under study allows co-production of other useful isotopes, or the facilities can be reoriented for production of other isotopes, then the score is High (***).
- If the co-production of other useful isotopes is possible but the conversion is technically complicated, the score is Medium (**).
- If the technology under study can only be used to produce ^{99}Mo or ^{99m}Tc and no conversion to other isotopes production is possible then the score is Low (*).

5.2.3 Commercial compatibility

This criterion is defined as the interest of commercial supply chain players, who have expertise in the production and transportation supply logistics of the shipment of ^{99}Mo or ^{99m}Tc (i.e., processors and generator manufacturers). Without the interest of these stakeholders, the production of ^{99}Mo or ^{99m}Tc will be much less effective as there will be no developed supply chain to deliver the product to the end user.

The determination of the value of this criterion will be based on the known and publicly expressed interest of current *or credible potential* supply chain players. If the criterion were only based on current supply chain stakeholders, there is the potential for a biased positive assessment of current technologies, given their invested capital and experience with certain technologies.

The following rules were used to attribute an assessment rating to the criterion commercial compatibility:

- If the technology under study can use existing processing facilities and it is compatible with the existing generator manufacturing specifications, then the score is High (***).
- If the development of the technology assessed would need considerable changes in the processing facilities or generator manufacturing, then the score is Medium (**).
- If the technology under study is incompatible with the existing generator's specifications and a new type of generator should be developed, or if a new type of processing facilities should be built, then the score is Low (*).

5.2.4 Estimate of the levelised unit cost (ELUCM)

This criterion provides an estimate of final production costs for different technologies, per unit of the isotope produced. This criterion is an important addition to the capital cost criterion for a number of reasons, as levelised unit cost also accounts for:

- The fact that some technologies with high capital costs may produce substantially more quantities of ^{99}Mo or ^{99m}Tc, thereby having a higher net present value;
- The time required to construct facilities based on specific technologies;

- The operational costs of the technology, including the costs for waste management if necessary (and if known)[9];
- The expected usable lifespan of the technology.

To estimate the production levelised unit costs, the costs and revenues of the producing facility are discounted to a common year, and normalised to ^{99}Mo 6-day curies (end of processing), based on the following formula:

$$\mathrm{ELUCM_{prod}} = P_{99\mathrm{Mo}} = \frac{\sum_t \left(\frac{\mathrm{Investment_t} + \mathrm{O}\&M_t + \mathrm{Decommissioning_t}}{(1+r)^t}\right)}{\sum_t \left(\frac{^{99}\mathrm{Mo}_t}{(1+r)^t}\right)}$$

Where:

$^{99}Mo_t$: The amount of ^{99}Mo produced in year "t" in 6-day curies (EOP);

P_{99Mo}: The constant price of ^{99}Mo in 6-day curies (EOP);

$(1+r)^{-t}$: The discount factor for year "t";

Investment: Investment costs in year "t";

$O\&M_t$: Operations and maintenance costs in year "t";

Decommissioning: Decommissioning cost in year "t". For the purpose of this report, the decommissioning was <u>not included</u> in ELUCM estimates due to poor data availability for all the reviewed technologies.

For the O&M costs, this includes the attributable portion of any O&M related to "common" infrastructure if it is multipurpose, including a portion of staff salaries, fuel and repairs. When comparing technologies, this criterion does not include the costs of the logistics of supply delivery as that is very location-specific. However, when comparing specific projects in any one country, O&M should include logistic costs.

For the economic criterion used here, the ELUCM presented is calculated at the stage where the ^{99m}Tc will be available. For example, for reactor-based production the ELUCM presented and compared will be presented as the ELUCM of a 6-day curie of ^{99}Mo at the generator component of the supply chain. In order to arrive at that point, the ELUCM for each upstream stage of the supply chain will be calculated, with the ELUCM of that stage being used as an input cost in the downstream component of the supply chain. As a result, the calculations for ELUCM for the processing and generator are calculated using the same formula as noted for the production level, using the ELUCM for the production level as an input cost.

9. As in the NEA study of the ^{99}Mo supply chain (NEA, 2010), there is no specific variable for waste costs. For reactor fission, interviewees have indicated that short-term waste management costs were included in O&M.

For the purposes of this study, information on costs for generator manufacture (for reactor-based production) was not publicly available. As a result, a proxy ELUCM at the generator stage was created, using the price difference between the current cost of a 6-day curie of ^{99}Mo at the processing stage and the calculated ELUCM at the processing level. This difference is then assumed to be passed through to the generator, increasing the current cost of a 6-day curie of ^{99}Mo at the generator stage. This final cost will serve as the proxy for the ELUCM at the generator level.

Costs for several of the considered technologies (especially those at the basic concept stage but not yet realised on an industrial scale) can only be estimated, since there is no industry experience, and it is not always possible to independently verify the claimed costs used for the estimate.

The following rules were used to attribute an assessment rating to the criterion estimated levelised unit cost (ELUCM):

- If the value of ELUCM is low compared to other routes then the score is High (***).
- If the value of ELUCM is intermediate (compared to other routes) or if the uncertainty on ELUCM is high then the score is Medium (**).
- If the value of ELUCM is high compared to other routes or if it is unknown, then the score is Low (*).

5.2.5 Ease of nuclear regulatory approval

This criterion provides an indication of the development risk for the various technologies related to regulatory barriers that could impede development. For example, unproven technologies may require regulatory approval, but the licensing system may not yet be in existence or is very complicated; or the use of a certain technology in a facility created for another purpose may create uncertainty as to whether the regulatory approval will be forthcoming.

If there were significant regulatory hurdles or uncertainties, this would increase the economic costs to the technology, given the higher "risk premium" attached to the technology. A high risk of a technology not being realised will clearly reduce the economic attractiveness of the technology (or the project).

The following rules were used to attribute an assessment rating to the criterion ease of nuclear regulatory approval:

- If the licensing procedure for the technology is well known and the duration of its issuing may be estimated, then the score is High (***).
- If the licensing procedure is known but is not fully transparent, or if the duration of licensing is not predictable, then score is Medium (**).
- If the licensing system does not exist for the technology under study or significant regulatory barriers to development may be foreseen, then the score is Low (*).

5.2.6 Ease of health regulatory approval

This criterion provides an indication of the radiopharmaceutical and drug approval risk for the various technologies related to regulatory barriers that could impede development. Molybdenum-99 or ^{99m}Tc produced by some unproven technologies will require new quality, purity and medical tests. The uncertainty associated with this process may reduce the economic attractiveness of the technology under study.

The following rules were used to attribute an assessment rating to the criterion ease of health regulatory approval:

- If the radiopharmaceuticals produced using the raw isotope obtained within the technology under study are proven to comply with the pharmacopoeia and good manufacturing practice (GMP) requirements, then the score is High (***).

- If the main tests on the purity and radiochemical compliance with the pharmacopoeia requirements have been successfully performed, then score is Medium (**).

- If no tests for pharmacopoeia or GMP requirements have ever been performed for the isotopes produced using the technology considered, then the score is Low (*).

5.2.7 Units required to supply world market

This criterion provides an indication of the ability of the technology to be used on a large scale for providing ^{99}Mo or ^{99m}Tc. This criterion will be defined as the minimum number of units that would be necessary to supply the entire world market, calculated using the theoretical output potential of a facility. For each of the technologies, the size of the facility will be defined (based on an accepted norm).

The following rules were used to attribute an assessment rating to the criterion units required to supply world market:

- If the number of units required to supply the world market is less than 10, then the score is High (***).

- If the number of units required to supply the world market is between 10 and 100, then score is Medium (**).

- If the number of units required to supply the world market is higher than 100, then the score is Low (*).

The criteria can be used to compare the current available infrastructure to provide an indication as to the magnitude of infrastructure development required to meet global needs.

5.3 Final list of assessment criteria

The final set of the assessment criteria includes:

- Technology maturity
- Production yield
- Available irradiation capacity
- Distribution range and logistics
- Simplicity of processing
- Waste management
- Proliferation resistance
- Potential for other isotopes co-production
- 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

In Chapters 6, 7 and 8 all the considered technologies are assessed according to the above set of criteria, using the three-grade rating system [Low (*), Medium (**) and High (***)].

The technologies considered for assessment have been divided into three classes: short-term, mid-term and long-term availability at significant scale (see Figure 4):

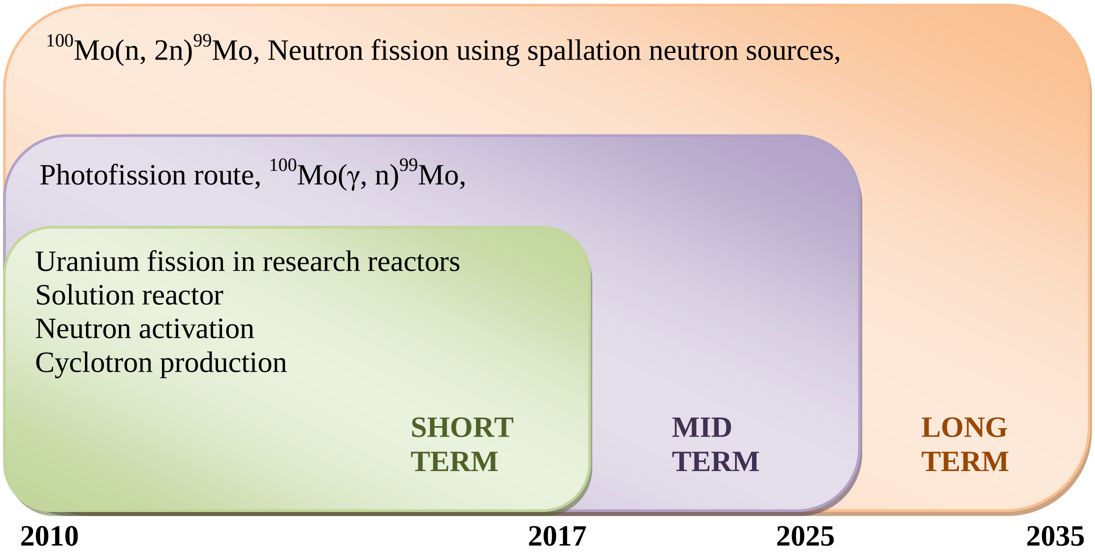
- Short term is defined as potentially available in the time frame 2010-2017 (7 years is an estimate of the time needed to build a new research reactor from tendering). These technologies are already available and in most cases they are already used (or advanced tests of feasibility have been performed) for $^{99}Mo/^{99m}Tc$ production. For the most widely used technologies economic data are available from industry (see NEA, 2010a for details).

- The mid-term technologies are expected to be available in 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 long-term methods are considered to become available after 2025. For those technologies, only some very general technical information is available and no economic assessment could be done at this time.

Depending on national priorities, the research on each isotope production technology could potentially be accelerated; hence the classification in the Figure 4 is only indicative and essentially based on the amount of information available today.

Figure 4: Classification of technologies used in the report and summary of the data availability



	Currently used for commercial ^{99}Mo production	Advances tests on feasibility performed	Preliminary tests on feasibility performed	Economic data available from industry	Economic inputs available from the literature
Uranium fission in research reactor	+	+	+	+	+
Solution reactor	-	+	+	+ (estimated)	+
Neutron activation	+ (small scale)	+	+	-	+
Cyclotron production of ^{99m}Tc	-	+	+	-	+
Photofission route	-	-	+	+ (estimated)	+
^{100}Mo(γ, n)^{99}Mo route	-	-	+	+ (estimated)	+
Neutron fission sin spallation neutron sources	-	-	-	-	-
^{100}Mo(n, 2n)^{99}Mo	-	-	-	-	-

6 ASSESSMENT OF SHORT-TERM TECHNOLOGIES

In this chapter the technologies that could be available for ^{99}Mo production before 2017 are discussed.

6.1 Fission route with uranium targets in a research reactor

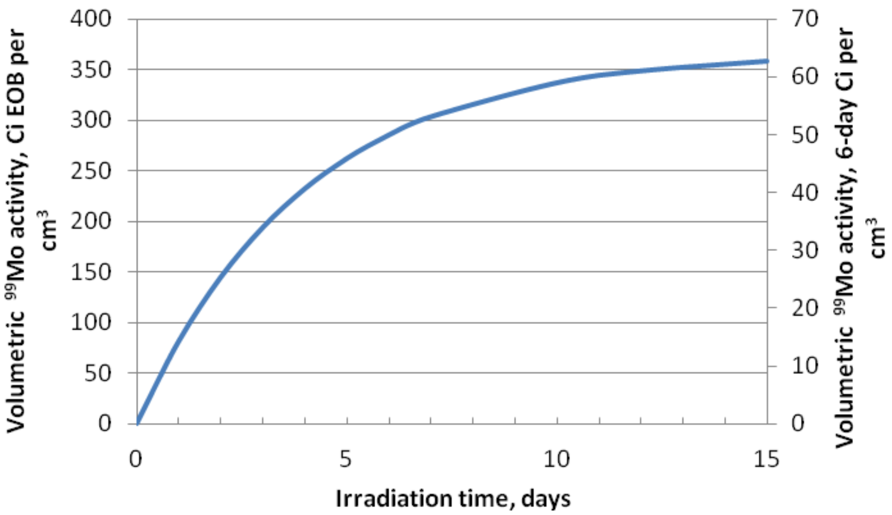
6.1.1 Targets with highly enriched uranium

Molybdenum-99 used by all major producers today (MDS Nordion, Covidien, IRE, NTP[10]) is generated using targets containing highly-enriched uranium (HEU). This maximises the ^{99}Mo production rate and minimises the quantity of minor actinides generated during the irradiation. Also, the high level of uranium enrichment minimises the volume of the effluents generated during the processing step.

However, an international effort is currently underway to reduce and eventually eliminate the use of HEU targets given that they contain weapons-grade uranium. International commitments to research and develop non-HEU technologies for isotope production make the initiation of new HEU-based production capabilities politically sensitive.

This section provides an assessment of the HEU fission route, which is subsequently used for benchmarking other methods.

Figure 5: Volumetric ^{99}Mo activity for a HEU target irradiated at 10^{14} neutrons cm^{-2} s^{-1} (thermal) flux



10. NTP Radioisotopes is in the process of converting to LEU targets at the time this study was undertaken.

Nuclear reactors are used to produce more than 40 activation products and 5 major fission product medical radioisotopes (^{131}I, ^{133}Xe, ^{89}Sr, ^{90}Y, ^{99}Mo). Currently, ^{131}I and ^{133}Xe are co-produced[11] with ^{99}Mo, with alkaline dissolution methods.

For ^{235}U, the thermal cross-section is $\sigma_f = 580$ barn. A typical HEU target contains 1.6 g/cm^3 of uranium enriched to 93% in ^{235}U. For a thermal neutron[12] flux of 10^{14} cm^{-2}s^{-1}, the saturated volumetric activity**[13]** of the irradiated target is about 365 Ci EOB per cm^3 (cf. Figure 5).

Typically, a target is irradiated for 5-7 days to reach optimal ^{99}Mo production level (around 71-82% of saturation concentration). Once the irradiation is over, the target is cooled for approximately 12-24 hours and then transported into the processing plant. After irradiation, the target is very radioactive. The high gamma radiation makes the target transport[14] and its processing complex and subject to detailed regulation.

There are two ways of separating ^{99}Mo from the irradiated uranium targets: An alkaline process and an acid process. Most of the major ^{99}Mo producers use the former process because it is well-adapted for aluminium-containing targets and allows co-production of ^{131}I. The processing of the targets is performed in hot cells[15] [shielding capacity of about 200-250 mm of lead equivalent (IAEA, 2003)] where the targets are dissolved in sodium hydroxide solution; the molybdenum is separated, purified, qualified and packaged.

Approximately 40-50 kg of HEU are used annually for medical radioisotope production (NNSA and ANSTO, 2007). After the processing step, more than 97% of the HEU contained in the targets ends up in the waste. In principle, it could be recovered from the waste and recycled but it has traditionally been assumed that buying fresh HEU is cheaper. Also, there is not an easily accessible route to reprocess this material. The annual amount of waste corresponding to the 12 000 6-day curie/week production rate (estimated world demand) using the HEU route can be estimated (using data from Vandegrift, 2006) as 43 kg of HEU uranium waste, 1.2 grams of ^{239}Pu and about 1.5 kg of fission products.

The separated molybdenum and resulting technetium are very pure. The main radionuclide impurities are ^{131}I and ^{103}Ru, their maximal concentration should not exceed 50 ppm. Today, the typical concentration of ^{131}I in the separated technetium is less than 3 ppm, and less than 0.2 ppm for ^{103}Ru (Duran, 2005).

The economic assessment of the HEU and LEU fission routes is based on the same statistical data (provided by reactor operators, processors and generator manufacturers) used in the NEA economic study of the ^{99}Mo supply chain (NEA, 2010a). Currently, five reactors and four processing facilities are currently needed to meet the world demand for ^{99}Mo. The capital cost of nuclear reactor

11. Alternatively, ^{131}I can be and is often produced from the activation of Te targets.

12. The average energy of the thermal neutrons is about 0.025 eV.

13. One has $A_S = Y_{Mo99}\,\sigma_f\,\varepsilon\,\rho_U/M_U\,N_A\,\varphi = 6.13\ 10^{-2}\cdot 580\ 10^{-24}\cdot 0.93\cdot 1.6/235.6.02\ 10^{23}\cdot 10^{14} = 13.9$ TBq/cm^3 = 365 Ci/cm^3, where Y_{Mo99} is the fission yield of ^{99}Mo, ρ_U is the uranium content, M_U is the molar mass of uranium, N_A is the Avogadro number, ε is the enrichment in ^{235}U and φ is the thermal neutron flux.

14. If the processing facility is located on the same site with the reactor, the transporting of irradiated targets is considerably simplified.

15. About 5 hot cells are needed for the alkaline process, according to the reported industry experience and (IAEA, 2003).

and processing facilities (for ^{99}Mo production) corresponding to 100% of the estimated annual world demand (624 000 6-day curies), and if starting from a Greenfield site, is about USD 1 380 million (see Table 2), USD 605 million for the reactor parts (the standard deviation is 30%) and USD 780 million for the processing parts (the standard deviation is 70%).

Table 2: Estimated levelised unit cost (ELUCM) calculation for fission HEU

Fission HEU	Reactor	Processing
Unit capital costs (USD 2009)	USD 605 m, σ = 30%	USD 195 m, σ = 70%
Number of units for 100% of the world demand in ^{99}Mo	5	4
Assumed percent for ^{99}Mo production[16]	20%	100%
Total world capital costs for ^{99}Mo production	USD 605 m, σ = 30%	USD 780 m, σ = 70%
General annual operating costs (USD 2009)	USD 36 m x 5	USD 32 m x 4
-Fuel		
-Target		
-Waste		
-Maintenance		
-Irradiated targets		USD 90 m
-Other		
Assumed percent for ^{99}Mo production	20%	100%
Total operating costs for ^{99}Mo production	USD 36 m	USD 220 m
ASSUMPTIONS		
Development time (yrs)	8	4
Development costs/yr	5% for first 3 yrs; 17% for next 5 yrs	25% for 4 yrs
Discount rates	5%	10%
Payback requirement (yrs)	20	20
	Costs at irradiation stage	**Costs at processing stage**
ELUCM results (USD 6-day curies EOP)	**USD 120 to 175** includes irradiation	**USD 380 to 670** includes irradiation and processing
Final generator price "ELUCM", in USD per 6-day curie EOP		
Costs at irradiation stage	**Cost at processor stage**	**Generator price "ELUCM" (USD 6-day curies EOP)**
USD 120 to 175	**USD 380 to 670**	**USD 555 to 850**

The estimation of the levelised unit cost of ^{99}Mo production, in USD per 6-day curie at the EOP (the technology is normalised to be able to provide 100% of the estimated annual world demand) is presented in Table 2. The final estimated price is about USD 555 to 850 per 6-day curie at the EOP (see Table 2 and NEA, 2010). This result is in agreement with the prices (ranging from about USD 300 to 900) reported by industry (see NEA, 2010a).

In Table 3 the technology is assessed according to the list of criteria defined in Section 5.3.

16. The same methodology as described in the Section 5.5.2 of the NEA economic study of the ^{99}Mo supply chain (NEA, 2010a) is used (see Section 5.2.4). For example, here it is considered that 20% of reactor construction cost should be attributable to ^{99}Mo production.

Table 3: Assessment of the reference HEU fission technology

Criteria	Score	Comment
Technology maturity	***	HEU fission in a nuclear reactor is the most widely used way of producing ^{99}Mo. It is a well established technology, with high production yield, high ^{99}Mo specific activity and very pure final product.
Production yield	***	The production yield in the HEU fission route is very high compared to other considered technologies.
Available irradiation capacity	***	Currently almost all the world's demand for ^{99}Mo is satisfied using existing facilities. Many of the existing research reactors can, in principle, be used for ^{99}Mo production via the fission route, but most of them are old, and thus one may expect a considerable shortage in the irradiation capacity in the coming years. (NEA, 2010b)
Distribution range and logistics	**	Although the logistics of the HEU targets and the separated molybdenum is challenging, there are no physically motivated constraints for world-wide shipment. However, the transport of the targets containing weapon-grade HEU to the reactor is heavily regulated from the security view point. The transport of highly radioactive irradiated targets to the processing plant (if not located on the same site) involves sophisticated containers with heat removal and heavy radiation protection. Denial of ^{99}Mo shipment is also an important factor.
Simplicity of processing	*	In the most-used alkaline process, hydrogen is produced. Because of the presence of HEU (potential criticality risk), the high residual power of the irradiated targets and the waste the Simplicity of processing criterion gets the lowest score (in comparison with other considered technologies).
Waste management	*	Highly radioactive waste is produced within the HEU route and it is not systematically recycled. A large quantity of weapon-grade HEU is contained in the liquid wastes (about 97% of HEU from the target). From the technical point of view the HEU in the waste could be recovered and reused, but there are no currently implemented solutions for the liquid wastes.
Proliferation resistance	*	HEU targets and wastes contain weapons-grade materials.
Potential for other isotopes co-production	***	Other medical radioisotopes (among which are ^{131}I and ^{133}Xe) are co-produced in the fission route. In general, many different radioisotopes (including medical) are produced in nuclear reactors.
Normalised capital costs	**	The estimated capital cost, normalised to 100% of the estimated world demand (624 000 6-day curies), is about USD 1 380 million.
Commercial compatibility	***	Today, the HEU fission route is the most commercially attractive option from the point of view of the current ^{99}Mo/^{99m}Tc supply chain.
Estimated levelised unit cost	***	The estimated levelised unit cost of the final product (including generator) is about USD 555 to 850 per 6-day curie of ^{99}Mo.
Ease of nuclear regulatory approval	***	The licensing procedure for the HEU route is well known.
Ease of health regulatory approval	***	The radiopharmaceuticals using ^{99m}Tc from HEU fission ^{99}Mo are already approved and used worldwide.
Units required for supply world market	***	Several reactors (five to ten, depending on size) would be enough to satisfy the world demand for ^{99}Mo.

6.1.2 Targets with low-enriched uranium

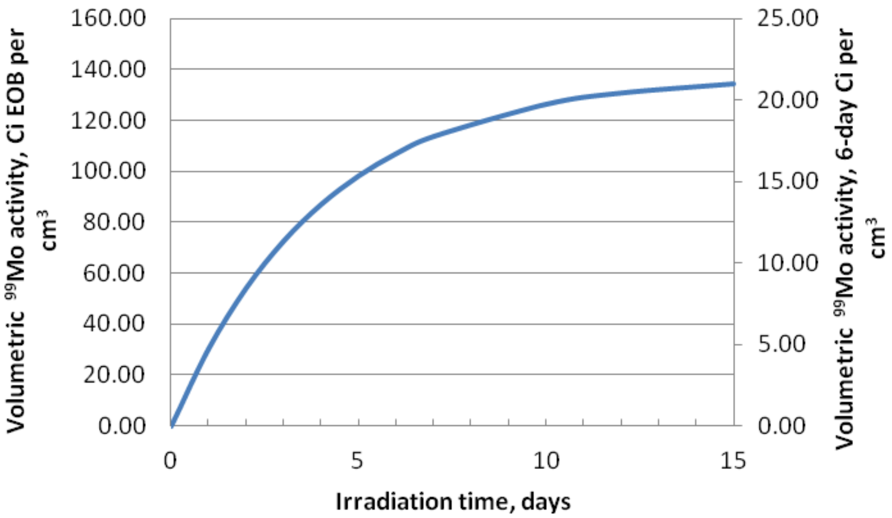
6.1.2.1 U-Al dispersion targets

Some of the ^{99}Mo producers use targets with low-enriched uranium (LEU), namely the South African NTP Radioisotopes[17], Argentinean CNEA and Australian ANSTO. These targets involve only proliferation-safe reactor-grade uranium enriched to less than 20% ^{235}U. Because of this, the targets can be supplied by several fuel manufacturers.

The main technological issue of the LEU route is the need for fabrication of dense targets (with high specific ^{235}U content) compatible with the well established ^{99}Mo separation process. Important progress has been made and further development is expected since the same kinds of materials are used for the fabrication of fuel for research reactors.

Currently available LEU U-Al dispersion targets contain approximately 2.9 g/cm^3 of uranium enriched to 20% in ^{235}U. For a thermal flux of 10^{14} cm^{-2}s^{-1}, the saturated volumetric activity of the irradiated target may be estimated as about 140 Ci EOB per cm^3 (cf. Figure 6).

Figure 6: Volumetric ^{99}Mo activity for a LEU target (19.75% of ^{235}U, 2.9 gU cm^{-3}) irradiated at 10^{14} neutrons cm^{-2}s^{-1} thermal flux



[17] Currently awaiting final regulatory approval.

Table 4: Estimated levelised unit cost (ELUCM) calculation for fission LEU aluminide dispersion targets[18]

Fission LEU	Reactor	Processing
Unit capital costs (USD 2009)	USD 605 m, σ = 30%	USD 195 m, σ = 70%
Number of units for 100% of the world demand in ^{99}Mo	5	4
Assumed percent for ^{99}Mo production[19]	50%	100%
Total world capital costs for ^{99}Mo production	USD 1 510 m, σ = 30%	USD 780 m, σ = 70%
General annual operating costs (USD 2009)	USD 36 m x 5	USD 32 m x 4
-Fuel		
-Target		
-Waste		
-Maintenance		
-Irradiated targets		USD 228 m
-Other		
Assumed percent for ^{99}Mo production	50%	100%
Total operating costs for ^{99}Mo production	USD 89 m	USD 390 m
ASSUMPTIONS		
Development time (yrs)	8	4
Development costs/yr	5% for first 3 yrs; 17% for next	25% for 4 yrs
Discount rates	5%	10%
Payback requirement (yrs)	20	20
	Costs at irradiation stage	**Costs at processing stage**
ELUCM results (USD 6-day curies EOP)	USD 300 to 430 includes irradiation	USD 560 to 930 includes irradiation and processing
Final generator price "ELUCM", in USD per 6-day curie EOP		
Costs at irradiation stage	**Cost at processor stage**	**Generator price "ELUCM" (USD 6-day curies EOP)**
USD 300 to 430	**USD 560 to 930**	**USD 735 to 1 100**

The volume of nuclear wastes and effluents generated during the processing of the irradiated targets is considerably increased relative to HEU. The annual amount of waste corresponding to the 12 000 6-day curie/week production rate (estimated world demand) using the LEU route depends on

18. The difference from the HEU route depends simply on the enrichment and density ratios of the target. These calculations use 93% and 20% enrichment of the uranium and comparative uranium content of 1.6 and 2.9 g cm^{-3}. No account has been taken of the impact of foil targets with higher densities.

19. The same methodology as described in the Section 5.5.2 of the NEA economic study of the ^{99}Mo supply chain (NEA, 2010) is used (see Section 5.2.4). For example, here it is considered that 50% of reactor construction cost should be attributable to ^{99}Mo production if LEU targets are used because the production yield is lower than in the reference HEU case.

the type of the target, but can be roughly estimated[20] as 215 kg of LEU uranium waste (using data from Vandegrift, 2006), 25 grams of ^{239}Pu and about 1.5 kg of fission products. The main issue with the LEU processing is the management of the increased volume of intermediate- and low-level liquid waste (increased compared to HEU). According to the ANSTO experience (Cameron, 2009) the annual amount of liquid waste corresponding to the 12 000 6-day curie/week production rate using the LEU route could be estimated as ≈2 600 litres/year of ILLW[21] and the same amount of LLLW[22]. ANSTO is currently implementing a technology allowing solidification and significant reduction of the liquid waste storage volume (Cameron, 2009).

The separated technetium is very pure. The main radionuclide impurities are ^{131}I and ^{103}Ru and their maximal concentration should not exceed 50 ppm. Today, the typical concentration of ^{131}I in the separated technetium is less than 0.3 ppm, and less than 0.02 ppm for ^{103}Ru (Duran, 2005).

With currently used LEU aluminide dispersion targets, the highest theoretical ^{235}U content is about 2.6 times less than with 93% enriched HEU. To account for this difference, the ELUCM is calculated by increasing the required irradiation capacity to produce the same amount of ^{99}Mo/^{99m}Tc. As a result, the capacity required in the representative research reactor increases from 20 percent in the HEU case to 50 percent in the LEU case. We assume that the processing capacity would be the same as in the HEU case (the same equipment is thus adapted to handle more targets).

The capital cost of nuclear reactors and processing facilities, normalised to 100% of the estimated annual world demand (624 000 6-day curies), is estimated at about USD 2 290 million (see Table 4 and NEA, 2010), USD 1 510 million for the reactor parts (the standard deviation is 30%) and USD 780 million for the processing parts (the standard deviation is 70%). The increase for the reactor stage is a simple function of the number of targets to supply the same amount of ^{99}Mo.

The estimation of the levelised unit cost of ^{99}Mo production, in USD per 6-day curie at the EOP (the technology is normalised to be able to meet the estimated annual world demand) is presented in Table 4. The final estimated cost is between USD 735 and 1 100 per 6-day curie at the EOP (see Table 4 and NEA, 2010). In Table 5, the technology is assessed according to the list of criteria defined in Section 5.3.

20. Converting from the assumed annual use of HEU of about 45 kg (enriched to 93%) to LEU enriched to 19.75%.

21. ILLW – Intermediate-level Liquid Waste.

22. LLLW – Low-level Liquid Waste.

Table 5: Assessment of LEU fission technology using aluminide dispersion targets in research reactors

Criteria	Score	Comment
Technology maturity	***	LEU fission ^{99}Mo production is used in Argentina and Australia, and awaiting routine operational approval in South Africa. Although the technology is well established, the fabrication of dense LEU targets with high ^{235}U is an issue, and the processing may need to be optimised. Nevertheless, LEU fission route has high production yield, high ^{99}Mo specific activity and pure final product.
Production yield	**	The production yield in the LEU fission route is lower than in the case of HEU fission route, because the ^{235}U content of currently used dense LEU targets is lower than in HEU targets.
Available irradiation capacity	***	The situation is similar to the HEU route, but more irradiation rigs would be needed with the LEU targets, because the ^{235}U load per target is currently lower with LEU than in HEU, or more reactors would be required.
Distribution range and logistics	***	The transport of LEU targets with no weapon-grade uranium is easier than in the case of HEU. However, the issues related to the transport of highly radioactive irradiated targets to the processing plant remain the same as with HEU targets.
Simplicity of processing	**	The processing of LEU targets is slightly safer than that of HEU targets, because the ^{235}U concentration is lower.
Waste management	*	Highly radioactive waste is produced within the LEU fission route (larger volume compared to the HEU route). The amount of plutonium in the waste is increased compared to the HEU route, but it does not affect the waste management process.
Proliferation resistance	***	No weapons-grade materials are involved in the LEU fission route. The equipment is unlikely to be divertible for weapon-grade materials production.
Potential for other isotopes co-production	***	Other medical radioisotopes (among which are ^{131}I and ^{133}Xe) are co-produced in the fission route. In general, dozens of different radioisotopes (including medical) are produced in nuclear reactors.
Normalised capital costs	**	The capital cost, normalised to 100% of the world's estimated demand, is about USD 2 billion.
Commercial compatibility	**	LEU fission route currently has lower commercial attraction than the HEU route.
Estimated levelised unit cost	**	The estimated levelised unit cost of the final product (including generator) corresponds to USD 735 to 1 100 per 6-day curie of ^{99}Mo.
Ease of nuclear regulatory approval	***	The licensing procedure for the LEU route is well known.
Ease of health regulatory approval	***	The radiopharmaceuticals using ^{99m}Tc from LEU fission ^{99}Mo are already approved and used in several countries.
Units required to supply world market	***	Several reactors and processing facilities (five to ten) would be enough to satisfy the world demand for ^{99}Mo.

6.1.2.2 *Dense foil targets*

The output per LEU target can be potentially improved by the use of a LEU foil target consisting of a metallic foil (about 135 µm thick) wrapped on an aluminium or nickel tube and encapsulated in an aluminium cladding (Wiencek *et al.*, 2008).

The use of LEU metallic targets could achieve yields of ^{99}Mo comparable to or even higher than in the current HEU with U-Al alloys (under the same irradiation conditions) because the density of metallic uranium is very high (~19g/cm^3) compared to the uranium content in a HEU U-Al target (~1.6 g/cm^3).

LEU-foil targets currently being developed (Wiencek *et al*., 2008) contain several grams of ^{235}U. The manufacturing process of the foil targets is currently being optimised to obtain high-quality regular foils.

Before the foil is dissolved for ^{99}Mo extraction, it is mechanically separated from the cladding, thus reducing the volume of acid needed for dissolution by ~10 times and therefore cutting waste volumes and increasing the efficiency of Mo recovery and purification process.

The uranium foil is currently not fully compatible with the most used alkaline route for the processing[23]. The acid process appears to be the most suitable for metallic foils.

Several research centres in Korea, Indonesia and the USA are currently working on the improvement of the LEU foil targets (NA, 2009), which could become an alternative to the currently used Al-U dispersion targets with LEU.

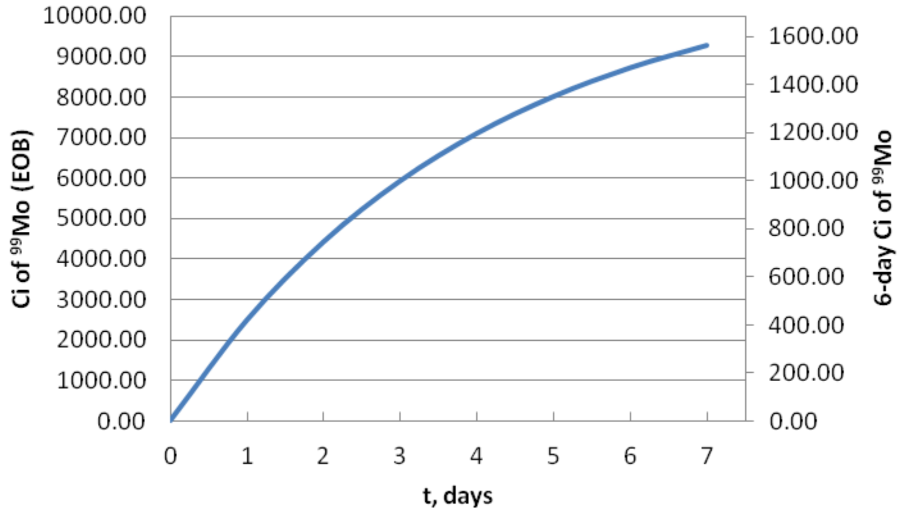
6.2 Fission route with low-enriched uranium solution reactor

Molybdenum-99 production using a solution nuclear reactor is promoted as a promising alternative to solid targets irradiation in research reactors (Ball, 1997; Ponomarev-Stepnoy *et al.*, 1999; IAEA, 2008 and NA, 2010). Solution reactors have been successfully operated by several countries in the past. Babcock & Wilcox Company, in association with Covidien, is currently developing a solution reactor for ^{99}Mo production. It is expected to be operational by 2014 (B&W, 2009).

The core of a solution reactor consists of a homogeneous fluid fuel (uranyl nitrate or uranyl sulphate). In the case of an LEU fuel enriched to 19.75% the volume of the core would be about 1 000 litres (Ball, 1997). The reactor operates at low power (about 200 kW_{th}). While operating, the fission products (including ^{99}Mo) are accumulated in the solution. After several days of operation, the reactor is shut down, and the solution is pumped through an extraction column that absorbs ^{99}Mo. The final step is the purification of the separated ^{99}Mo.

23. It would require an additional use of hydrogen peroxide, (Dong *et al.*, 1995), or electrochemical dissolution (Guelis *et al*., 2009), or dissolving in nitric acid followed by recovering the Mo on a titania sorbent then stripping it with an alkaline solution for feeding into the current alkaline process (Jerden, 2009) and (Stepinski, 2007).

Figure 7: Theoretical molybdenum-99 production in a solution nuclear reactor functioning at 200 kWth



Although there is significant experience with using solution nuclear reactors for research purposes (mainly for criticality studies), there are challenges to overcome to produce medical radioisotopes (see IAEA, 2008). Some of the challenges are to guarantee steady-state operation at constant power during several days and handle the changing isotope inventory of the fuel solution. Another important issue is the purification and recycling of the fuel solution.

A solution reactor operating at 200 kW could theoretically produce about 9 000 Ci (EOB) of ^{99}Mo per week or about 1 600 6-day Ci of ^{99}Mo per week (see Figure 7). The molybdenum separation process is considered to be faster than the corresponding process in the fission route with solid targets irradiated in a research reactor because there is no dissolution step. Theoretically around 10 solution reactors operating at 200 kW would be necessary to satisfy the world's demand for ^{99}Mo. Babcock & Wilcox Company has announced that 3 solution reactors would be enough to cover 50% of the USA demand in ^{99}Mo. Assuming that the USA demand is about 45% of the world demand in ^{99}Mo, about 13 solution reactors would be needed to satisfy the world demand.

The estimation of the levelised unit cost of ^{99}Mo production may be performed assuming the advertised unit solution reactor cost of USD 25 million (reactor and processing facility) and operating costs similar to other reactors. However, since this technology has not been constructed and operated (for ^{99}Mo production), these costs are not independently verifiable. Depending on the deployment strategy (4 sites of 3 units or 13 sites of 1 unit), the estimated ELUCM varies from USD 410 to 970 per 6-day curie at the EOP. However this is based on only one source of information[24] and hence it does not have high confidence level. In Table 6, the technology is assessed according to the list of criteria defined in Section 5.3.

24 Private communication. No other values yet published.

Table 6: Assessment of the fission route with low-enriched uranium solution reactor

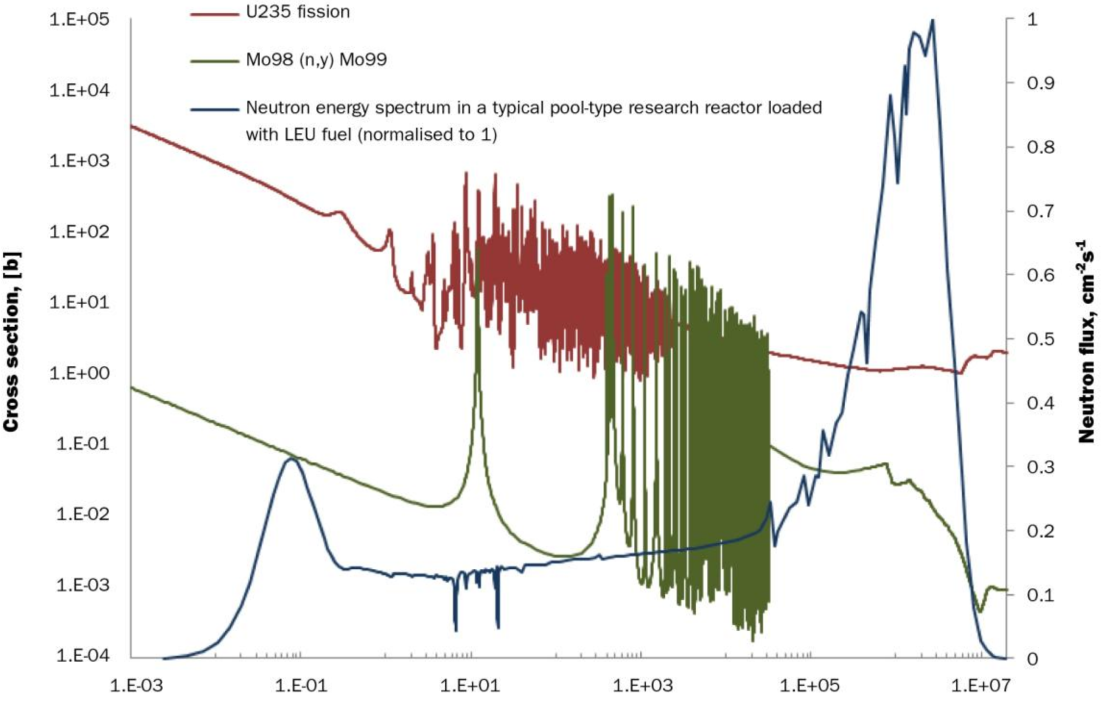
Criteria	Score	Comment
Technology maturity	**	Solution reactors were built in several countries, mainly for criticality studies (United States, France and Russia). Successful tests have been made in the ARGUS reactor (Russia) to produce pure ^{99}Mo (Ball, 1998). However, for the moment this technology is not used for ^{99}Mo production.
Production yield	**	The production yield in the LEU fission route should be high if the reactor is able to operate (continuously) at expected power level of 200 kW, product recovery is efficient and process losses are not too high.
Available irradiation capacity	*	No LEU solution reactors are currently available for ^{99}Mo production.
Distribution range	***	The solution is processed on-site and the separated ^{99}Mo could be shipped worldwide.
Simplicity of processing	**	The processing is slightly safer than the alkaline process for solid targets (no hydrogen produced). However, there are risks of criticality and leaks of highly radioactive solution.
Waste management	**	The use of LEU is significantly optimised within this route. However, the amount of highly radioactive fission product waste is comparable to the one in the LEU route with solid targets.
Proliferation resistance	***	The targets and the equipment are unlikely to be divertible for weapon-grade materials production.
Potential for other isotopes co-production	**	Other fission product radioisotopes (among which are ^{131}I and ^{133}Xe) could in principle be co-produced using solution nuclear reactors.
Normalised capital costs	***	The reported capital cost for one solution reactor (and processing facility) is about USD 25 million, this totals to about USD 325 million if normalised to 100% of the world's demand for ^{99}Mo.
Commercial compatibility	**	LEU solution reactors have a large potential interest for the existing ^{99m}Tc generator manufacturing industry.
Estimated levelised unit cost	**	The estimated levelised unit cost of the final product (including generator) is estimated to be USD 410-970 per 6-day curie of ^{99}Mo. However this estimate is based on only one source of information and hence it does not have a high confidence level.
Ease of nuclear regulatory approval	**	Similar facilities have been licensed in the past (but not for commercial production of isotopes).
Ease of health regulatory approval	**	Basic tests of the purity of ^{99}Mo produced have been successfully performed using existing solution reactors, but there is no regulatory experience.
Units required to supply world market	**	At least 13 solution reactors of 200kW$_{th}$ would be needed to satisfy the world demand in ^{99}Mo.

6.3 Molybdenum-99 production via the neutron activation of ^{98}Mo

6.3.1 Neutron activation in a research reactor

The activation process is based on the neutron capture reaction with ^{98}Mo nuclei. This process has been known for many years but is being reconsidered following the current shortage. Natural molybdenum contains 24.13% of ^{98}Mo. The microscopic cross section for the thermal neutrons is approximately equal to 0.14 b, and the resonance integral (neutrons with intermediate energies) ^{98}Mo is of 7.2 b, i.e. more than 50 times higher than the thermal neutron absorption cross section (see Figure 8). Thus the neutron energy spectrum in the irradiation device can significantly influence the yield of ^{99}Mo (Ryabchikov *et al.*, 2004).

Figure 8: Microscopic cross section of ^{98}Mo(n,γ)^{99}Mo and ^{235}U fission, and a neutron energy spectrum for a typical pool-type research reactor with LEU fuel.



Cross sections source: ENDF/B-VII.0

In order to compare the efficiency of the neutron activation route to the neutron fission one (used here as reference), it is necessary to average cross sections with the same neutron energy spectrum. The ^{235}U fission and ^{98}Mo activation cross sections were averaged using a spectrum representative for a pool-type research reactor[25] (see Table 7 and Figure 8). Using these results, macroscopic cross sections (taking in account the concentration of the target nuclei) can be compared. This allows comparison of the reference HEU fission route to the activation route with different targets in the same irradiation conditions.

25. The neutron energy spectrum and weighted cross-sections were provided by CEA/SERMA (France). The neutron spectrum was obtained from a cell-type modelling (using the APOLLO2 code) of a representative pool-type research reactor. *Used with permission*.

The macroscopic cross sections for the neutron activation process were calculated for two types of targets (MoO_3 and metallic molybdenum), and for two enrichments in ^{98}Mo [natural and high enrichment (98% of ^{98}Mo)]. The targets currently used are MoO_3. The results are given in Table 8. For a reference value, a macroscopic cross section for a typical HEU target (with 1.6 gU per cm^3) was calculated. The corresponding volumetric specific activities (for different molybdenum targets and a thermal neutron flux of 10^{14} $cm^{-2}s^{-1}$) are given at Figure 9.

Table 7: Uranium-235 fission and molybdenum-98 activation microscopic cross sections weighted by a representative neutron energy spectrum (pool-type research reactor) [26]

Cross-sections averaged with a neutron spectrum typical for pool-type research reactors with LEU fuel	Energy interval: 0 – 20 MeV
$^{235}U(n,f)$ fission cross section	59.5 b [27]
$^{235}U(n,f)^{99}Mo$ effective cross section **The cumulative yield of ^{99}Mo is 6.13%**	3.65 b
$^{98}Mo(n,\gamma)^{99}Mo$ cross section	0.212 b

In the case of dense metallic targets with highly enriched molybdenum, the macroscopic cross section of the activation route is ~90% of the effective macroscopic cross section for ^{99}Mo production with the HEU fission route. For molybdenum trioxide targets with natural/enriched molybdenum (technology currently employed), this ratio is about 14 and 3.4, respectively. However, even in the most efficient case the specific activity of ^{99}Mo remains below some tens of Ci/g.

The processing of the irradiated targets is done in sealed tong boxes provided with a shield of 100 mm of lead equivalent (IAEA, 2003). Currently only targets with MoO_3 are irradiated and processed[28]. In the tong boxes, the cans with MoO_3 are opened and the target is dissolved in NaOH. The solution is then filtered to remove the non-dissolved impurities.

The specific activity of molybdenum is low and thus the standard technetium generator technology (with alumina column) cannot be effectively used. Instead, a large centralised generator or ^{99m}Tc separating facility (“extraction generator”) has been proposed that would produce technetium for local use (Zykov *et al.*, 2001).

The only current possibility to provide portable technetium generators is to use gel generators in which the MoZr mixture is used as column matrix itself. Several countries (India, Kazakhstan, Uzbekistan and some others) use this technology for regional ^{99}Mo production (very often using centralised ^{99m}Tc extraction facilities). Significant research and development is being done to improve the technology of technetium generators from low- and medium-activity molybdenum (Saraswathy *et al.*, 2007; Sarkar, *et al.*, 2009).

---

26. Provided by CEA/SERMA (see footnote 25).

27. The cross sections are averaged (using the neutron energy spectrum) in the energy interval 0-20MeV. These values differ significantly from the values in the thermal region. For example, for thermal neutrons with an average energy of 0.025 eV the fission cross-section of ^{235}U is about 580 b, but the value of the same cross section averaged in the interval 0-20 MeV is about 59 b.

28. In the case of metallic targets an additional calcination step should be included to use the same process.

Table 8: Calculated macroscopic cross sections for molybdenum neutron activation process and comparison to the reference HEU fission

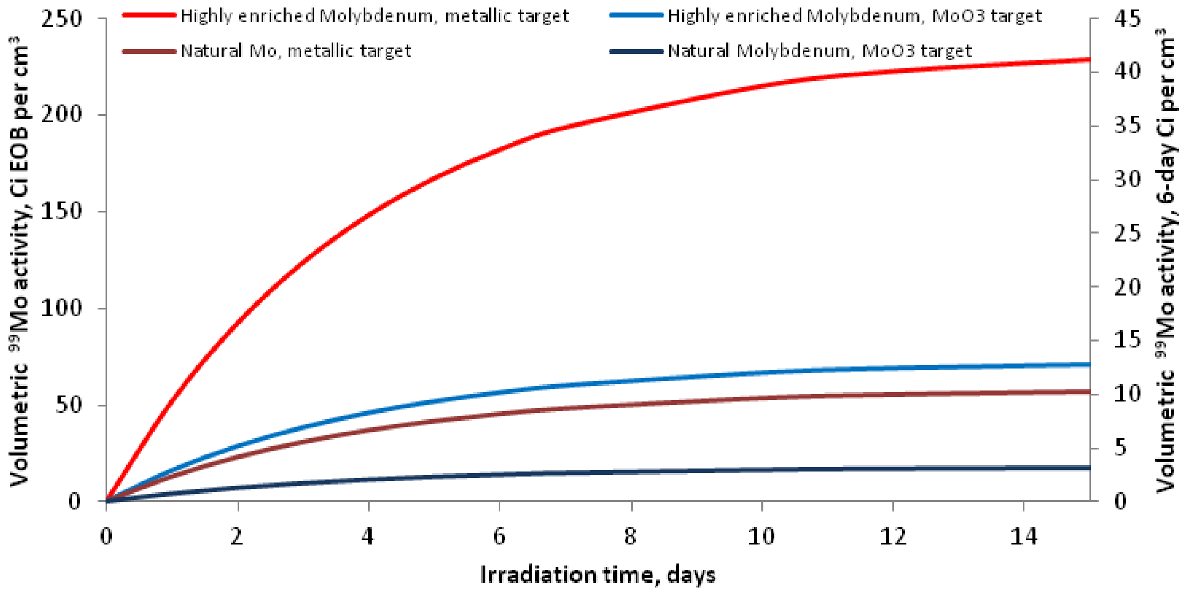
	MoO_3 target, natural molybdenum	**MoO_3 target, highly enriched molybdenum (98% of ^{98}Mo)**	**Metallic target, natural molybdenum**	**Metallic target, highly enriched molybdenum (98% of ^{98}Mo)**
	MoO_3 targets are used		***Metallic targets are not used***	
Macroscopic cross section: $\varepsilon\, \rho / M\, N_A\, \sigma$ One-group microscopic cross sections σ from Table 7)	^{98}Mo abundance: ε=24.13% Molar mass of MoO_3: M=144 g/mol Density of MoO_3: ρ=4.7g cm^{-3}	^{98}Mo enrichment: ε=98% Molar mass of MoO_3: M=144 g/mol Density of MoO_3: ρ=4.7g cm^{-3}	^{98}Mo abundance: ε=24.13% Molar mass of MoO_3: M=96 g/mol Density of MoO_3: ρ=10.3 g cm^{-3}	^{98}Mo enrichment: ε=98% Molar mass of MoO_3: M=98 g/mol Density of MoO_3: ρ=10.3 g cm^{-3}
Macroscopic ^{99}Mo production cross section for a typical HEU target 1.6 gU per cm^3	$1.4{\cdot}10^{-2}$ cm^{-1}			
Macroscopic ^{99}Mo production cross section for molybdenum targets	$1.0{\cdot}10^{-3}$ cm^{-1}	$4.1{\cdot}10^{-3}$ cm^{-1}	$3.3{\cdot}10^{-3}$ cm^{-1}	$1.3{\cdot}10^{-2}$ cm^{-1}
Relative yield compared to HEU reference case HEU efficiency is 100%	**7.1%**	**29%**	**23%**	**92%**

The radiochemical purity of ^{99m}Tc produced from modern portable gel generators (Chakrov, 2010) is higher than 99%, the final product contains less than 0.02% of ^{99}Mo, a value five times lower than the European Pharmacopoeia limit of 0.1%. The concentration of Al, Mo and Zr inactive impurities is also lower than the European Pharmacopoeia specifications, and the final product is sterile.

The estimation of the levelised unit cost of ^{99}Mo production, in USD per 6-day curie at the EOP was performed using the same data for the reactor and processing facilities as in HEU/LEU fission routes and the following hypothesis:

- The required irradiation capacity is increased proportionally to the ratio of yields in the HEU route and in the assessed activation route (see Table 8). Thus, in the case of natural molybdenum MoO_3 targets, the irradiation capacity would need to be increased by a factor of 14 compared to the HEU fission route; in the case of metallic targets with highly enriched molybdenum this factor would be 1.09.

Figure 9: Theoretical volumetric ^{99}Mo activity for different molybdenum targets irradiated with 10^{14} neutrons $cm^{-2}s^{-1}$ thermal neutron flux (neutron energy below 0.625 eV)



- The cost of processing (for the same number of targets) is assumed to be 1/5th of the one in the HEU route, i.e. the equivalent cost share of one hot cell of the five[29] typically used in the HEU route. A hot cell is not actually required but a tong box would be sufficient. Thus the required processing capacity is obtained from the one corresponding to the HEU fission route by multiplying it by the same factor as the irradiation capacity and dividing by five.

- The price of the highly enriched molybdenum (> 98% of ^{98}Mo) is assumed to be USD 4 200 per gram (Mushtaq, 2009). No other referenced data were found for this material.

- For metallic targets with enriched molybdenum, the annual quantity needed is estimated to be about 315 kg/year. This figure is obtained by conversion from the HEU fission route: The annual consumption of HEU to satisfy the world demand for ^{99}Mo is about 45 kg (NNSA and ANSTO, 2007), the corresponding volume of the targets is 45 kg/1.6 $g{\cdot}cm^{-3} = 2.8{\cdot}10^4\ cm^3$. The enriched metallic molybdenum has a density of 10.3 $g{\cdot}cm^{-3}$, and with this type of target the efficiency is theoretically 1.09 times lower than in the HEU fission route. Thus one obtains $2.8{\cdot}10^4\ cm^3 \times 10.3\ g{\cdot}cm^{-3} \times 1.09 \approx 315$ kg of molybdenum per year.

Similar calculations for MoO_3 targets with highly enriched molybdenum give ~460 kg/year for the annual quantity of ^{98}Mo.

- If the enriched molybdenum is not recycled its cost is taken into account every year.

- If the enriched molybdenum is recycled[30], the cost of molybdenum needed for one year of functioning (315 kg × USD 4.2 million per kg = USD 1 325 million) is included in the capital cost needed for molybdenum production.

---

29. See footnote 15 on the page 24 and (IAEA,2003).

30. According to (Mushtaq, 1995) up to 90% of the target material can be recycled.

- The costs of recycling of enriched molybdenum were estimated by doubling the cost of the gel generator manufacturing used to recover Mo from the gel. The price of a gel generator (per 6-day Ci of ^{99}Mo) was assumed to be the same as in the fission route. However it is not clear if these generators can be returned, reprocessed and re-used in the same way as is done currently.
- In the case of a centralised facility for separating ^{99m}Tc from low-activity molybdenum the costs associated with the generator manufacturing were omitted (because the doses of ^{99m}Tc are manufactured on-site) and the reported cost is the value of ELUCM at the processing stage. The centralised facilities are only suitable for local production.

Table 9: Estimated levelised unit cost (ELUCM) calculation for the neutron activation route for different types of targets and deployment strategy (centralised or distributed)

Scenarios	MoO_3 target, natural molybdenum	MoO_3 target, highly enriched molybdenum (98% of ^{98}Mo)	Metallic target, natural molybdenum	Metallic target, highly enriched molybdenum (98% of ^{98}Mo)
	MoO_3 targets are used		*Metallic targets are not used today. Data provided for comparison.*	
1. Portable gel generator used **2. No enriched Mo recycling**	USD 1 245 – 2 140 /6-day Ci	USD 3 740 – 3 960 /6-day Ci -About 85% is the cost of enriched Mo - About 460 kg of ^{98}Mo per year	USD 510 – 850 /6-day Ci	USD 2 480 – 2 550 /6-day Ci -About 85% is the cost of enriched Mo - About 315 kg of ^{98}Mo per year
1. Portable gel generator used **2. Full recycling of enriched Mo** **The cost of one year of enriched Mo consumption included into the capital costs**		USD 1 400 – 1 630 /6-day Ci		USD 1 130 – 1 200 /6-day Ci
Centralised facilities for ^{99m}Tc extraction (only suitable for local production)				
1. Centralised extraction of ^{99m}Tc **No generator costs included** **2. Full onsite recycling of enriched Mo** **The cost of one year of enriched Mo consumption included into the capital costs**	USD 1 100 – 1 970 /6-day Ci	USD 560 – 780 /6-day Ci	USD 330 – 610 /6-day Ci	USD 290 – 360 /6-day Ci

The results for the estimated levelised unit cost (ELUCM) calculations for different types of target (oxide or metallic form), enrichment (natural or highly enriched) and the deployment strategy (distributed with portable gel generators or centralised ^{99m}Tc separating facility) are presented in Table 9. As in the previous ELUCM calculations for the fission route, the interval for the values corresponds to a standard deviation of 30% on the capital cost of reactor and 70% on the processing facility.

Several observations could be made on the basis of the ELUCM calculation summarised in the Table 9:

- The use of dense metallic targets may allow significant reduction of the costs of ^{99}Mo production. However, currently only MoO_3 targets are used;
- The recycling of targets with highly enriched molybdenum has a very strong influence on the cost of the final product. With the assumption on the cost of one gram of enriched molybdenum, the share of target material in the ELUCM is about 85% if the targets are not recycled;
- Centralised separation of ^{99m}Tc has costs considerably less for the final product than in the case of portable gel generators. However, given the short half-life of the final product, centralised separation of ^{99m}Tc can only provide local needs. As a result, a large number of ^{99m}Tc separating facilities would be required to meet the world demand, and thus this technology would probably not be suitable to supply global needs.

The main benefits of the activation process are the following:

- Molybdenum-containing targets are not fissile and thus their irradiation could be done in almost any reactor with sufficient neutron flux;
- The radioactivity of the irradiated activation target is considerably lower than that of irradiated uranium target;
- The amount of wastes generated during the irradiation and processing is relatively low.

The main issues for the activation route are:

- The very low specific activity of molybdenum, complicating the generator technology;
- The cost, availability and recycling of highly enriched molybdenum (if this is used).

In Table 10, the molybdenum activation in research reactor is assessed according to the list of criteria defined in Section 5.3.

Table 10: Assessment of ^{98}Mo neutron activation technology

Criteria	Score (1-4)	Comment
Technology maturity	**	^{98}Mo neutron activation is used for commercial production at small scales in India, Kazakhstan and some other counties. Although significant progress has been recently made in the production of portable gel generators with sufficiently pure ^{99m}Tc, large-scale production using the activation route is not envisaged in the near future.
Production yield	*/**	The yield of ^{99}Mo in the activation route is 50 times lower than in the fission route, if natural molybdenum targets are used. It can be theoretically increased if metallic targets with enriched molybdenum (in ^{98}Mo) are used but it is still 3.8 times less efficient than the fission route with HEU.
Available irradiation capacity	***	Almost any research reactor and even some power reactors may be used for ^{98}Mo activation. A reactor with 10^{14} $cm^{-2}s^{-1}$ thermal neutron flux (fully-devoted to ^{99}Mo production) could in principle produce up to 500-1000 6-day Ci of ^{99}Mo. There are 25 medium flux ($3 \cdot 10^{13}$ to 10^{14} $cm^{-2}s^{-1}$) and 54 high flux (> 10^{14} $cm^{-2}s^{-1}$) research reactors distributed over the world.
Distribution range and logistics	*	The specific activity of the activated molybdenum is considerably lower than from the fission route. An outsize container would be needed to transport large quantities (e.g. 2 000 Ci of ^{99}Mo corresponding to 1kg of MoO_3 powder) of molybdenum from the irradiation facility to the generator manufacturer.
Simplicity of processing	***	No fissile materials are contained in the irradiated targets (thus no criticality risk). The process does not involve hazardous materials.
Waste management	***	Almost no radioactive waste is generated (except the non-used ^{99}Mo). If enriched molybdenum is used, recycling would be needed.
Proliferation resistance	***	No fissile materials are involved.
Potential for other isotopes co-production	*	No other medical radioisotopes are produced within the ^{98}Mo activation route. However, nuclear reactors may be used for production of other isotopes.
Normalised capital costs	**	The capital cost corresponding to the currently used option (highly-enriched MoO_3 targets, no ^{98}Mo recycling) corresponding to 100% of the world's demand is about USD 1.6 billion.
Commercial compatibility	*	In the current ^{99}Mo/^{99m}Tc supply chain, only some research reactors may be interested in developing a large-scale ^{99}Mo/^{99m}Tc production by the neutron activation route.
Estimated levelised unit cost	*/**	The estimated levelised unit cost of the final product is USD 3 740 to 3 960 per 6-day Ci for the currently used option and with the current assumptions (highly-enriched MoO_3 targets and no ^{98}Mo recycling). This cost could drop to USD 510 to 850 if dense metallic ^{nat}Mo targets were developed and used together with portable gel generators.
Ease of nuclear regulatory approval	**/***	Already used in some countries (India, Kazakhstan, etc.). Was used in Japan in the past.
Ease of health regulatory approval	**/***	Tests of the purity of ^{99}Mo produced have been successfully performed. Used in some non-OECD countries (India, Kazakhstan, etc.).
Units required to supply world market	*/**	Even in the optimal case more than 20 reactors (reasonably charged) would be needed.

6.3.2 Neutron activation in a power reactor

From the physical point of view, irradiation of ^{98}Mo in a pressure tube power reactor is similar to a research reactor and the targets can be recovered at any moment. Many of the pressure tube power reactors have irradiation channels that could be used for medical radioisotopes production (see Zykov *et al.*, 2001) with no negative effect on the power generation. Pressure tube reactors are operated in Canada (20 CANDU), Russia (11 RBMK), India (15 CANDU-type), South Korea (4 CANDU), Romania (2 CANDU), China, Taiwan and Argentina (1 CANDU each).

The irradiation of molybdenum in instrumentation channels of the most common shell-type power reactors (PWRs or BWRs) is technically possible but seems challenging compared to using pressure tube reactors. However, this route is being evaluated (GE-Hitachi, 2010).

Molybdenum-99 production in power reactors is technically possible. However, a centralised generator or ^{99m}Tc separating facility is preferred in this case (because of low molybdenum specific activity), or an advanced portable gel generator like those already used in India and Kazakhstan (Saraswathy *et al*., 2007; Sarkar *et al*., 2009; Chakrov, 2010). Given that these kinds of reactors are well distributed over the world, this option has technical merit.

However, most of the utilities have not shown any interest in medical radioisotopes production and the licensing procedure does not seem straightforward.

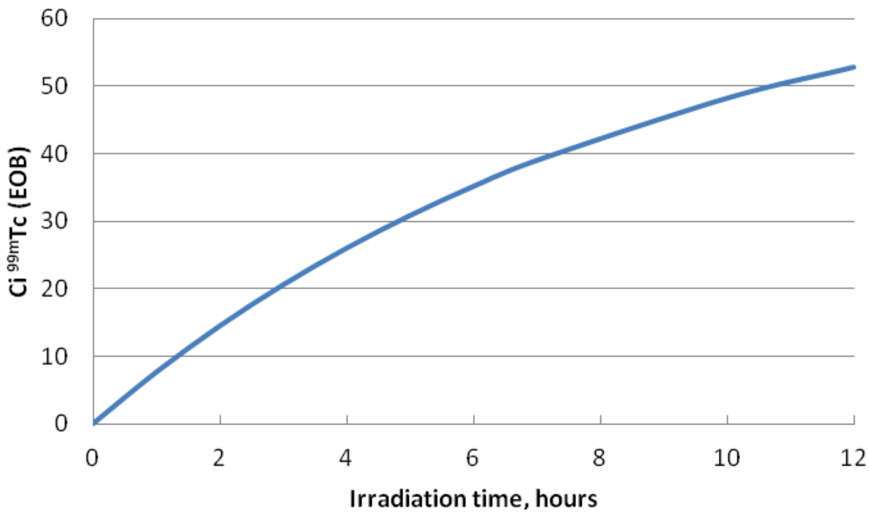
6.4 Direct cyclotron production of ^{99m}Tc via $^{100}Mo(p,2n)^{99m}Tc$ reaction

A beam of energetic protons from a cyclotron (about 20 MeV) can be used to produce ^{99m}Tc via the bombardment of a molybdenum target highly enriched in ^{100}Mo (> 99%).

Cyclotrons are used to produce 14 proton-rich medical radioisotopes, the most used are ^{18}F,^{15}O,^{11}C,^{13}N.

According to experimental data reported in (Scholten., 1999; Tacaks *et al*. 2003), the ^{99m}Tc production rate via the $^{100}Mo(p,2n)^{99m}Tc$ reaction is about 16 Ci mA^{-1} h^{-1} (Ci of ^{99m}Tc EOB) at 24 MeV. The corresponding saturated ^{99m}Tc activity is 141 Ci mA^{-1} (Ci of ^{99m}Tc EOB).

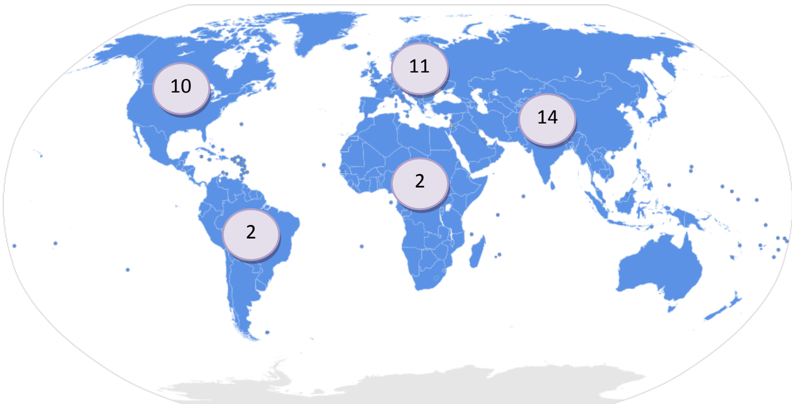
Figure 10: Direct ^{99m}Tc production in a 500 µA cyclotron at 24 MeV



As reported in (Guérrin *et al.*, 2010), a high-current medium-energy (500 μA, ~24 MeV) cyclotron may produce up to 70 Ci of ^{99m}Tc in two 6-hour bombardments (see Figure 10). Guérrin *et al.*, 2010 assumed that the processing losses of ^{99m}Tc would be of approximately 15%. Considering an average patient injection of about 25 mCi of ^{99m}Tc and 10 hours decay for processing, shipment and holding in the hospital, this amount would be enough to prepare 800 doses of ^{99m}Tc radiopharmaceuticals – 0.5% of the estimated current world daily demand (NA, 2009).

Thus about 200 high current medium energy (500 μA, ~24 MeV) cyclotrons devoted to ^{99m}Tc production would be needed to satisfy the world demand in ^{99m}Tc, and they would need to be appropriately located to satisfy the current demand globally. There are 39 cyclotrons with beam energy superior to 20 MeV in the world that could be used for ^{99m}Tc production (see Figure 11).

Figure 11: Distribution of cyclotrons with energies over 20 MeV for medical isotope productions (inputs from IAEA, 2010)



The processing of the irradiated targets could be done in several ways. In the most recent test described by Guérrin *et al.*, 2010, the targets were dissolved by electrochemical dissolution in HCl in the presence of hydrogen peroxide H_2O_2 and purified using the method of Chattopadhyay *et al.*, 2008. The radionuclide purity of the cyclotron-produced ^{99m}Tc is very high (> 99.99%), and the concentration of other technetium isotopes was more than 10 times below the US pharmacopoeia (USP) requirements.

Although Guérrin *et al.*, 2010 have not directly measured the content of the stable ^{99}Tc in the solution, the labelling efficiency was also more than 8% above the UPS requirements (of > 90%). The authors (Guérrin *et al.*, 2010) have performed in vivo experiments (on rats) with reactor- and cyclotron-produced ^{99m}Tc. The conclusion is that cyclotron-produced ^{99m}Tc is suitable for preparation of USP-compliant ^{99m}Tc radiopharmaceuticals.

The estimation of the levelised unit cost of equivalent ^{99}Mo production[31], in USD per 6-day curie at the EOP was done using the following assumptions:

- The costs of the cyclotrons and the processing facilities are assumed to be the same as currently available medical cyclotrons of the required size. According to the information

31. One cyclotron is assumed to produce 1/200 of the world demand of ^{99m}Tc corresponding to 3120 6-day Ci of ^{99}Mo per year. To obtain the ELUCM for the direct cyclotron production, the calculated annual costs of ^{99m}Tc were divided by 3120.

obtained from industry and reported in (JUPITER, 2005), the price of a 30 MeV medical cyclotron with 1 mA beam is about USD 11 million. The data for the processing part was taken from the economical study of the cost of positron emission tomography (Keppler and Conti, 2001). According to the information provided by industry representatives, this assumption is appropriate for the processing part.

- The price of the molybdenum highly enriched in ^{100}Mo (>99% of ^{100}Mo) is assumed to be the same as the price of molybdenum highly enriched in ^{98}Mo (also used in Section 6.3.1): USD 4 200 per gram (Mushtaq, 2009). However there is great paucity of data on this cost.
- According to the data presented in Guérrin *et al*. (2010), two 6-hour irradiations of enriched molybdenum targets are sufficient to satisfy 0.5% of the world daily demand in ^{99m}Tc. The reported weight of one target[32] is in between 0.1 and 0.4 g. The annual estimated consumption of enriched molybdenum is thus (0.1 to 0.4) × 2 targets × 365 days × 200 cyclotrons ≈ 15-58 kg per year (about 73-290 grams per cyclotron).

Table 11: Estimated levelised unit cost (ELUCM) calculation for one cyclotron capable to satisfy 1/200 of the world demand in ^{99m}Tc with no target recycling

Cyclotron direct ^{99m}Tc production	Cyclotron	Processing
Unit capital costs (USD 2009)	USD 11 m	USD 450 000
Assumed percent for ^{99}Mo production	100%	100%
Number of units for 100% of the world demand in ^{99m}Tc	*200*	*200*
Total world capital costs for ^{99m}Tc production	*USD 2 200 m*	*USD 90 m*
General annual operating costs (USD 2009)		
- Enriched molybdenum (73-290 g/year/unit)	USD 300 000 – 1 200 000	
- Electricity	USD 400 000	
-Staff	USD 1 000 000	USD 250 000
Total unit operating costs for ^{99}Mo production	USD 1.7 m – 2.6 m	
Total world annual operation costs for ^{99m}Tc production	*USD 340 m - 760 m*	*USD 50 m*
Development time (yrs)	3	3
Development costs/yr	33% for 3 yrs	33% for 3 yrs
Discount rates	5%	5%
Payback requirements, yrs	20	20
ELUCM results (USD 6-day curies ^{99}Mo equiv), targets not recycled	**USD 930 – 1 230**	
ELUCM results (USD 6-day curies ^{99}Mo equiv), targets recycled	**USD 850 – 900**	

The result of the ELUCM calculation (for one cyclotron) is given in Table 11. Within the assumptions listed above and if no recycling of enriched molybdenum target is implemented the ELUCM cost is about USD 930 – 1 230 of equivalent 6-day Ci. If the target material is recycled, the ELUCM cost theoretically decreases to ~USD 900 of equivalent 6-day Ci.

In Table 12, the direct ^{99m}Tc production technology is assessed according to the list of criteria defined in Section 5.3.

32. For a beam of protons (6 mm diameter) with 25 MeV and metallic molybdenum targets (density of ~10.3 g/cm^3), the total stopping power is of about 13 MeV/mm.

Given the short half-life of the final product, direct ^{99m}Tc production with cyclotrons can only provide local needs. As a result, a large number of cyclotrons would be required to meet world demand and they would need to be located proportionally to the demand. Thus this technology would probably not be suitable to supply global needs.

Table 12: Assessment of $^{100}Mo(p,2n)^{99m}Tc$ technology

Criteria	Score	Comment
Technology maturity	**	The direct ^{99m}Tc production via proton bombardment of enriched ^{100}Mo targets in a cyclotron has been tested experimentally.
Production yield	*/**	The production yield depends on the cyclotron energy and power. With today's technologies the yield is quite small compared to the fission route.
Available irradiation capacity	*	About 40 of the existing cyclotrons in the world could produce for ^{99m}Tc. The number of high-current cyclotrons needed to satisfy the world's demand for ^{99m}Tc is approximately 200.
Distribution range and logistics	*	The final product is ^{99m}Tc, a short-lived isotope. Thus, the clinics must be located near the cyclotron.
Simplicity of processing	***	The processing does not involve hazardous, explosive or fissile materials.
Waste management	**/***	Almost no nuclear waste is produced. Targets with expensive enriched and pure molybdenum (in ^{100}Mo) are used, and thus recycling would be necessary.
Proliferation resistance	***	Neither irradiation/processing facilities nor the materials involved could be diverted for nuclear weapons development.
Potential for other isotopes co-production	*	Cyclotrons may be used to produce other medical radioisotopes (^{15}O, ^{18}F, etc.). However, they could not be produced at the same time as ^{99m}Tc is produced. Currently two 6-hour irradiations per day could be envisaged.
Normalised capital costs	**/***	About USD 11 million per accelerator capable of satisfying about 0.5% of the world demand, about USD 2.3 billion for the world demand. For small markets the scalability of the capital costs is an important advantage.
Commercial compatibility	*	The current $^{99}Mo/^{99m}Tc$ supply chain has limited commercial compatibility in using cyclotrons for ^{99m}Tc production.
Estimated levelised unit cost	**	If no recycling of the target material is implemented, the estimated levelised unit cost of the final product corresponds to USD 930 to 1 230 per 6-day curie of ^{99}Mo (converted figures). With recycling the value of ELUCM is about USD 900.
Ease of nuclear regulatory approval	***	The radiological, safety and security risks are considerably below the ones of technologies involving nuclear reactors.
Ease of health regulatory approval	**	Tests of the purity of ^{99m}Tc produced have been successfully performed at small scale.
Units required to supply world market	*	This technology is not suitable for world-size scales of production. With today's technologies the world demand in technetium may be satisfied with 200 cyclotrons.

6.5 Summary for short-term technologies

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

- Uranium fission in research reactors (HEU and LEU-aluminide dispersion targets);
- Solution reactor technology;
- Neutron activation of ^{98}Mo in nuclear reactor (various deployment scenarios);
- Direct ^{99m}Tc production with cyclotrons.

The technologies considered in this report were assessed according to the set of criteria defined in Section 5.3, using a three-grade rating system [Low (*), Medium (**) and High (***)]. The summary of the assessment result is presented in Table 13.

Table 13: Summary of short-term technologies assessment results

	Technologies currently used for large scale (> 1 000 6-day Ci per week) production		Small-scale or potential short-term technologies		
	Reference HEU in research reactors	Current LEU targets (aluminide dispersion) in research reactors	LEU solution reactor	^{98}Mo activation in research reactors	^{100}Mo → ^{99m}Tc in cyclotron
Technology maturity	***	***	**	**	**
Production yield	***	**	**	*/**	*/**
Available irradiation capacity	***	***	*	***	*
Distribution range and logistics	**	***	***	*	*
Simplicity of processing	*	**	**	***	***
Waste management	*	*	**	***	**/***
Proliferation resistance	*	***	***	***	***
Potential for other isotopes co-production	***	***	**	*	*
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 summary of the estimates of the levelised unit cost of ^{99}Mo (in USD per 6-day curie) is given in Table 14 for technologies currently used for large-scale ^{99}Mo production (i.e. more than 1 000 6-day Ci per week), and in Table 15 for small-scale and potential short-term technologies. The width of the intervals is determined by the uncertainty in the data used for assessments.

Table 14: Summary of the estimates of the levelised unit cost of molybdenum (ELUCM) for technologies currently used for large-scale production (>1 000 6-day Ci of ^{99}Mo per week), calculated with the data and assumptions discussed in the report

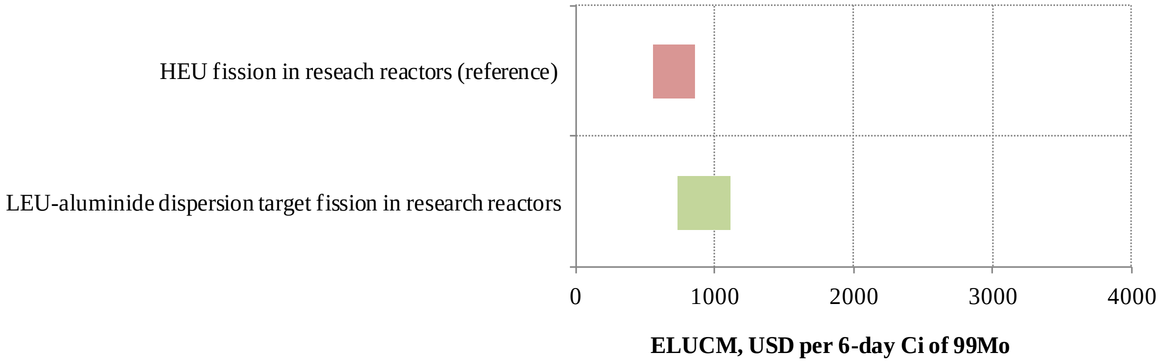
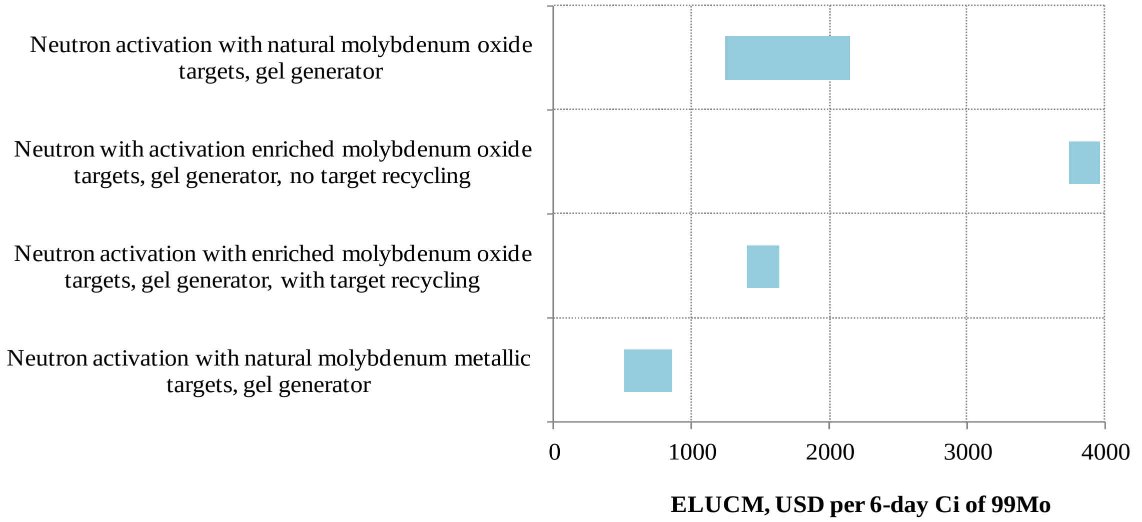
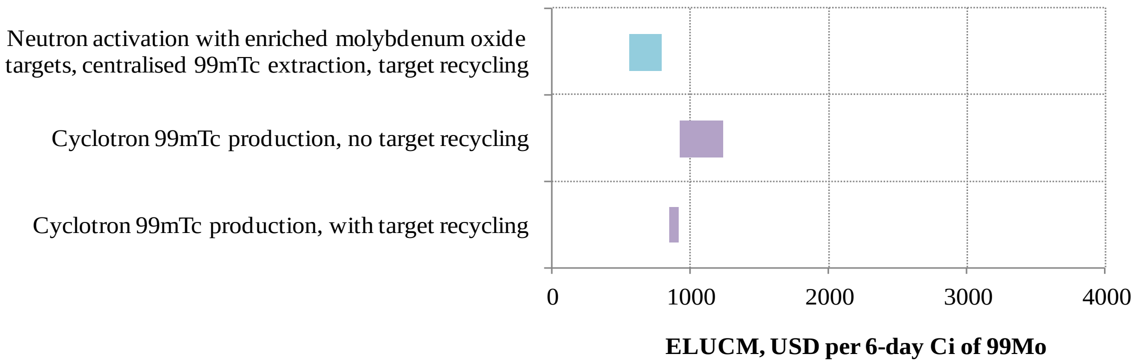


Table 15: Summary of the estimates of the levelised unit cost of molybdenum (ELUCM) for potential technologies, calculated with the data and assumptions discussed in the report

As noted in the text, some of these estimates are based on small amounts of data and a range of assumptions, which are not always possible to verify. Hence these values should be understood in this context.



Centralised ^{99m}Tc production technologies



Note: The uncertainty in the case of direct cyclotron ^{99m}Tc production with target recycling is smaller than the one with no recycling because the cost of the target material in the latter case is included in the capital cost and thus has small impact on the cost of the final product (compared to the case when the target material is not reused).

7 ASSESSMENT OF MID-TERM TECHNOLOGIES

In this section, the additional technologies (to those discussed in the previous chapter) that could be available for ^{99}Mo production after 2017 are discussed.

7.1 Molybdenum-99 production via the photofission route based on the $^{238}U(\gamma,f)^{99}Mo$ reaction

In this route the electrons from an accelerator are directed on to a converter target where they decelerate and emit gamma rays (bremsstrahlung). These gamma rays induce photofission of the ^{238}U in the target situated after the converter.

The fission yield of the uranium is a function of the energy of electrons (Oganessian, 2002). Below 10 MeV almost no fission occurs. The fission yield rises sharply between 10 and 30 MeV, and continues its growth above 30 MeV. In the photofission process of ^{238}U, ^{99}Mo is produced with similar yield to that of neutron-induced ^{235}U fission[33] (6.1%).

After irradiation, the uranium target is processed in the same manner as in the fission route, i.e. alkaline or acid dissolution and molybdenum extraction (solvent or ion-exchange) in a shielded hot cell.

According to the evaluation[34] done for the isotope production facility currently being realised (ARIEL, Canada), about 12 6-day Ci of ^{99}Mo could be produced after 7 days of irradiation of a typical target with a beam power of 500 kW. In the case of the ARIEL project, the proof-of-principle test will use a 25 MeV, 4 mA beam of electrons. For such a machine (beam power 100 kW) combined with a 15 $g{\cdot}cm^{-2}$ of ^{238}U target, one can envisage producing 2.3 6-day Ci after 7 days of irradiation.

The convertor in ARIEL will be made of Tantalum (Ta) with variable thickness to minimise the power density. Water flowing around the Ta and the U_3O_8 capsule provides the necessary cooling of the convertor and target. For example, at 50 kW, 25 kW will be dissipated into the convertor with 15 kW into the target. The rest of the power escapes the convertor and the target as photons, electrons, positrons and neutrons. The target will be made of U_3O_8 (density is 8.3 $g{\cdot}cm^{-3}$) ceramic disc encased into a zirconium alloy capsule. For the test, target geometry will be prepared that presents about 15 $g{\cdot}cm^{-2}$ to the incident photon beam. According to GEANT4 simulations done by TRIUMF, a 50 kW, 25 MeV electron beam with a convertor and target size described above yields $4.4{\cdot}10^{12}$ fissions per second.

ARIEL is expected to start operation[35] in 2015 and to reach its full power of 500 kW in 2017. The capital costs associated with the electron-accelerator-based photofission facility of ARIEL (civil construction, technical elements and labour to assemble the device) are roughly estimated by the ARIEL team as USD 45 million. The ongoing O&M are expected to be about USD 4 million per year (not including the target processing).

33. The photofission cross-section is below 0.15 b in the energy interval 10-30 MeV. The effective cross-section for ^{99}Mo is thus approximately equal to $6.1\ 10^{-2}{\cdot}0.15 \approx 9$ mb.

34. The data on the ARIEL project was provided by Tim Meyer (TRIUMF, Canada).

35. ARIEL is not intended to become a real-time production facility for commercial isotopes. It could only be used as an "emergency backup" facility for key isotopes that could be produced via the photofission route.

One can estimate the levelised unit cost (ELUCM) for the photofission route using the above technical and financial data for the irradiation part together with the data for the processing from the reactor fission route. The result is greater than USD 10 000 per 6-day Ci of ^{99}Mo, mainly due to the low production capacity considered (12 6-day Ci of ^{99}Mo per week).

In Table 16, the photofission ^{99}Mo production technology is assessed according to the list of criteria defined in Section 5.3.

Table 16: Assessment of the photofission $^{238}U\ (\gamma,f)\ ^{99}Mo$ technology

Criteria	Score	Comment
Technology maturity	*/**	The photofission technology has been tested experimentally. Although the ^{99}Mo separation in the case of photofission is identical to the one in the reactor-based fission routes, the whole ^{99}Mo production technology using photofission has not been tested.
Production yield	*	The yield of ^{99}Mo in the photofission reaction is almost the same as in the reactor-based fission route. But the energy consumed by the electrons accelerator is very high, and thus the overall production efficiency is considered as low.
Available irradiation capacity	*	High-energy electrons accelerators with high-power beams are not widely available.
Distribution range and logistics	***	(Same as in HEU/LEU reactor-based fission route.)
Simplicity of processing	**	Almost no fissile material is involved, thus the processing is safer than in the LEU fission route (no criticality risk).
Waste management	*	(Same as in LEU reactor-based fission route.)
Proliferation resistance	***	No enriched uranium involved and no significant quantities of fissile materials could be produced during the irradiation.
Potential for other isotopes co-production	*	Many other isotopes could be produced using electron accelerators but not simultaneously with ^{99}Mo.
Normalised capital costs	*	About USD 45 million would be needed to build an accelerator capable of producing 0.1% of the world demand in ^{99}Mo.
Commercial compatibility		*No data available.*
Estimated levelised unit cost	*	The very rough estimates suggest that the cost of ^{99}Mo produced would be very high.
Ease of nuclear regulatory approval	**	No fissile material involved, the regulatory risks are slightly lower than in the LEU reactor-based fission route. However, licensing of any first of a kind facility could be quite lengthy.
Ease of health regulatory approval	*	No tests performed.
Units required to supply world market	*	If deployed for large-scale production, hundreds of 500 kW units would be needed to satisfy the world demand for ^{99}Mo.

7.2 Reaction $^{100}Mo(\gamma,n)^{99}Mo$

The cross section of $^{100}Mo(\gamma,n)^{99}Mo$ reaction is approximately equal to 0.1 barn for the energy interval 12-17 MeV. Thus, one can imagine a 25-50 MeV electron accelerator generating gamma rays via bremsstrahlung in a converter (same as for the photofission route described in Section 7.1), and using them for the (γ,n) reaction on a ^{100}Mo target.

The advantage of the $^{100}Mo(\gamma,n)^{99}Mo$ reaction is that its macroscopic cross section is considerably larger than in the photofission route. Comparing the U_3O_8 targets envisaged for the photofission production with ARIEL and metallic molybdenum targets highly enriched in ^{100}Mo, this ratio[36] is more than 35.

The production yield and the specific activity of molybdenum strongly depend on the type and dimensions of the target and converter. According to the recent calculations and measurements (TRIUMF, 2008 and Bunatian *et al*., 2009), about 650 6-day Ci of ^{99}Mo could be produced after 7 days of irradiation with an accelerator like ARIEL (500 kW, see Section 7.1) and a target of 30 g of highly-enriched molybdenum. The specific activity of molybdenum in this case would be ≈20 Ci/g.

The ^{99}Mo production yield is higher in the $^{100}Mo(\gamma,n)^{99}Mo$ compared to the one in the photofission route. However, the maximum predicted specific activity would be of several hundred Ci of ^{99}Mo per gram of molybdenum (TRIUMF, 2008). This is low compared to the minimum specifications of about 1 000 Ci per g_{Mo} for existing commercial technetium generators[37]. Similar to the low- and medium-activity molybdenum from the neutron activation of ^{98}Mo targets, a system of distributed centres of centralised ^{99m}Tc production has been envisaged (Bennett *et al*., 1999).

In Table 17, the ^{99}Mo production technology based on the $^{100}Mo(\gamma,n)^{99}Mo$ reaction is assessed according to the list of criteria defined in Section 5.3.

---

36. The concentration of uranium nuclei in U_3O_8 target is about 1.9 10^{22} cm^{-3} and the ^{99}Mo production photofission cross-section is ~9 mb (see footnote 33), thus $\Sigma_{(\gamma,f\,Mo99)}$=1.7 10^{-4} cm^{-1}. For the $^{100}Mo(\gamma,n)^{99}Mo$ reaction (cross-section 0.1 b) with ^{100}Mo target (concentration 6.2 10^{22} cm^{-3}) $\Sigma_{100Mo(\gamma,n)99Mo}$=6.2 10^{-3} cm^{-1}. Thus $\Sigma_{100Mo(\gamma,n)99Mo}/\ \Sigma_{(\gamma,f\,Mo99)}$=36.

37. The specific activity of molybdenum in the fission route is 10^4 - $4.8 \cdot 10^5$ Ci per g_{Mo} (Ottinger and Collins, 1996; NA 2009).

Table 17: Assessment of the $^{100}Mo(\gamma,n)^{99}Mo$ technology

Criteria	Score	Comment
Technology maturity	*	^{99}Mo production via the $^{100}Mo(\gamma,n)^{99}Mo$ reaction has been tested experimentally. However, it is still on the stage of laboratory research.
Production yield	***	The theoretical production yield is quite high. However, the specific activity of molybdenum produced is not sufficiently high to be usable within the existing ^{99m}Tc generators.
Available irradiation capacity	*	High-energy electrons accelerators with high-power beams are not widely available.
Distribution range and logistics	**	(Same as in reactor-based ^{98}Mo neutron activation route.)
Simplicity of processing	***	(Same as in reactor-based ^{98}Mo neutron activation route.)
Waste management	**	Targets with pure and expensive ^{100}Mo used, recycling is needed.
Proliferation resistance	***	(Same as in reactor-based ^{98}Mo neutron activation route.)
Potential for other isotopes co-production	*	Many other isotopes could be produced using electron accelerators but not simultaneously with ^{99}Mo.
Normalised capital costs	**	Using the data for the ARIEL facility and the estimated production rate, about USD 900 million would be needed for the irradiation facilities, plus additional costs for the target material (highly enriched molybdenum).
Commercial compatibility		*No data available.*
Estimated levelised unit cost		*No data available.*
Ease of nuclear regulatory approval	**	Although the technology is not completely proven, as no fissile material involved. The regulatory risk may be considered as Medium. However, licensing of any first of a kind facility could be quite lengthy.
Ease of health regulatory approval	*	No tests performed.
Units required to supply world market	*/**	If deployed for large-scale production, about 20 high-power electron accelerators (500 kW) would be needed to satisfy the world demand in ^{99}Mo. With 100 kW accelerators the number of units is about 100.

7.3 Summary for mid-term technologies

The mid-term technologies are expected to be available in 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 $^{100}Mo(\gamma,n)^{99}Mo$ using an electron accelerator.

The technologies considered in this report are assessed according to the set of criteria defined in Section 5.3, using a three-grade rating system [Low (*), Medium (**) and High (***)]. The summary of the assessment result is presented in Table 18.

Table 18: Summary of assessment results for mid-term technologies

		Mid-term technologies	
	HEU in research reactors - Reference	^{238}U (γ,f) photofission	^{100}Mo (γ,n) ^{99}Mo
Technology maturity	***	*/**	*
Production yield	***	*	***
Available irradiation capacity	***	*	*
Distribution range and logistics	**	***	**
Simplicity of processing	*	**	***
Waste management	**	*	**
Proliferation resistance	*	***	***
Potential for other isotopes co-production	***	*	*
Normalised capital costs	**	*	**
Commercial compatibility	***	n/a	n/a
Estimated levelised unit cost	***	*	n/a
Ease of nuclear regulatory approval	***	**	**
Ease of health regulatory approval	***	*	*
Units required to supply world market	***	*	*/**

n/a – not available

8 ASSESSMENT OF LONG-TERM TECHNOLOGIES

In this section the additional technologies (to those discussed in two previous chapters) that could be available for ^{99}Mo production after 2025 are discussed. No economic assessments are currently possible for these technologies.

8.1 Reaction $^{235}U(n,f)^{99}Mo$ using spallation neutron sources

Spallation neutron sources produce intense neutron beams via a collision of energetic accelerated protons (with energies from dozens to hundreds of MeV) with heavy nuclei targets like lead, tantalum, tungsten, uranium etc. Each collision results in up to 20-30 fast neutrons (with energies mainly between 1 and 10 MeV).

Spallation neutrons are slowed down and provoke fission of ^{235}U nuclei. Basically, the ^{99}Mo process works like in a nuclear reactor but the system remains subcritical.

With today's PbBi targets a significant neutron yield may be achieved. In the MEGAPIE experiment the fission rate of ^{235}U is of about $3 \cdot 10^{-9}\ s^{-1}\ mA^{-1} at^{-1}$(Chabod, 2006; Panebianco *et al.*, 2007), and the proton current is approximately equal to 1 mA[38].

Thus, for a dense low-enriched (19.75% ^{235}U) uranium carbide target (density ~13.6 $g \cdot cm^{-3}$) and a proton current of 1 mA the volumetric yield of ^{99}Mo can be estimated[39] as 1.6 Ci $h^{-1}\ cm^{-3}$ (EOB), and about 135 Ci cm^{-3} (EOB) after 7 days of irradiation.

Today, there are 9 spallation neutron sources located in Argentina, Japan, Switzerland, the United Kingdom and the United States of America.

Molybdenum-99 production using spallation neutron sources is similar to reactor fission. The main difference is that the source of neutrons is not a nuclear reactor but an accelerator with a spallation target. Also, the chemical and physical form of the target is different. Spallation neutron sources are sophisticated and expensive machines designed for advanced scientific research. Their use for ^{99}Mo production does not seem optimal.

In Table 19, the ^{99}Mo production technology based on the ^{235}U fission with spallation neutrons is assessed according to the list of criteria defined in Section 5.3.

---

38. For example, the fission rate of ^{235}U in the reactor fission route is about $5 \cdot 10^{-8}\ s^{-1} at^{-1}$ (with a thermal neutron flux of $10^{14}\ cm^{-2} s^{-1}$). This is about 20 times higher than the fission rate measured in the MEGAPIE experiment (Chabod, 2006).

39. Using the formula for volumetric activity $Y_{Mo99}\ [\sigma\ \varphi]\ \ \varepsilon\ \rho_{UC}/M_{UC}\ N_A(1-e^{-\lambda t})$, where Y_{Mo99} is the fission yield of ^{99}Mo, M_{UC} is the molar mass of uranium carbide and ρ_{UC} its density, N_A is the Avogadro number, ε is the enrichment in ^{235}U, λ – the decay constant of ^{99}Mo and $[\sigma\ \varphi]$ the fission rate.

Table 19: Assessment of the fission route with spallation neutron sources technology

Criteria	Score	Comment
Technology maturity	*	This technology is a basic theoretical concept.
Production yield	*/**	The theoretical yield of ^{99}Mo in the spallation neutron induced fission reaction is almost the same as in the reactor-based fission route. But the energy consumed by the proton accelerator is very high and, thus, the overall production yield is considered as low.
Available irradiation capacity	*	Spallation neutrons sources are not widely available. Nine spallation neutron sources, mainly devoted to research, are located in Argentina, Japan, Switzerland, the United Kingdom and the United States of America.
Distribution range and logistics	***	(Same as reactor-based LEU fission route.)
Simplicity of processing	**	(Same as reactor-based LEU fission route.)
Waste management	**	(Same as reactor-based LEU fission route.)
Proliferation resistance	***	(Same as reactor-based LEU fission route.)
Potential for other isotopes co-production	***	(Same as reactor-based LEU fission route.)
Normalised capital costs		*No data available.*
Commercial compatibility		*No data available.*
Estimated levelised unit cost		*No data available.*
Ease of nuclear regulatory approval	*	The technology is not proven for ^{99}Mo production.
Ease of health regulatory approval	*	No tests have been done.
Units required to supply world market		*No data available.*

8.2 Reaction ^{100}Mo(n,2n)^{99}Mo

The cross section of ^{100}Mo(n,2n)^{99}Mo reaction is approximately equal to 1.5 barn for the energy interval 10-17 MeV. One can produce intense neutrons with average neutron energy of 14 MeV by bombarding a natural carbon converter with a 40 MeV deuteron beam. Neutrons can be used to produce ^{99}Mo via ^{100}Mo(n,2n)^{99}Mo (Nagai and Hatsukawa, 2009).

With a 5 mA 40 MeV deuteron beam (200 kW) one may obtain about 190 Ci of ^{99}Mo for 250 g enriched ^{100}Mo in two days of bombardment (Minato and Nagai, 2010). Such an accelerator (40 MeV 5 mA) is currently under construction in France to produce exotic neutron rich radioactive nuclei via the fission reaction of a natural uranium target for nuclear physics interests (Fadil *et al*., 2008).

After irradiation the metallic ^{100}Mo or $^{100}MoO_3$ targets are processed. One of the ways to process the target is to use a sublimation method.

The optimal deuteron energy allowing highest ^{99}Mo yield and lowest impurity generation is about 40 MeV.

In Table 20, the ^{99}Mo production technology based on the $^{100}Mo(n,2n)^{99}Mo$ reaction is according to the list of criteria defined in Section 5.3

Table 20: Assessment of the $^{100}Mo(n,2n)^{99}Mo$ technology

Criteria	Score	Comment
Technology maturity	*	This technology is a basic theoretical concept.
Production yield	**	The theoretical production yield is moderate compared to other alternative technologies.
Available irradiation capacity	*	A high-energy deuteron accelerator with high-power beams is under construction.
Distribution range and logistics	**	(Same as reactor-based molybdenum activation.)
Simplicity of processing	***	(Same as reactor-based molybdenum activation.)
Waste management	**	Targets with expensive enriched and pure molybdenum (in ^{100}Mo) are used and, thus, recycling is necessary. Sublimation method allows one to reuse irradiated ^{100}Mo samples.
Proliferation risk		*No data available.*
Potential for other isotopes co-production	*	High energy neutrons from accelerators could be used for co-production of other isotopes, but not at the same time.
Normalised capital costs		*No data available.*
Commercial compatibility		*No data available.*
Estimated levelised unit cost		*No data available.*
Ease of nuclear regulatory approval	*	The technology is not proven for ^{99}Mo production.
Ease of health regulatory approval	*	No tests have been done.
Units required to supply world market	**	At least 35 deuteron 200 kW accelerators would be needed to satisfy the world demand for ^{99}Mo.

8.3 Summary for long-term technologies

The long-term methods are expected to become available in the time frame 2025-2035. For those technologies, only some very general technical information is available, and no economic assessment could be done currently. 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.

The technologies considered in this report are assessed according to the set of criteria defined in Section 5.3, using a three-grade rating system [Low (*), Medium (**) and High (***)]. The summary of the assessment result is presented in Table 21.

Table 21 Summary of technology assessment results

		Long-term technologies	
	HEU in research reactors - Reference	**LEU fission with spallation neutrons**	**^{100}Mo (n,2n) ^{99}M**
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
Estimated levelised unit cost	***	n/a	n/a
Ease of nuclear regulatory approval	***	*	*
Ease of health regulatory approval	***	*	*
Units required to supply world market	***	n/a	**

n/a – not available

9 SUMMARY AND CONCLUSIONS

The main aim of the current study was to produce a state of the art report on technologies for producing molybdenum-99 / technetium-99m. As part of this process, the study has established criteria and assembled information on the most promising technologies for securing molybdenum-99 /technetium-99m production at large scale in the short, medium, and long term. The review is intended to provide information to assist decision-makers, but clearly decision-makers will apply their own national priorities on such choices. 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.

Various $^{99}Mo/^{99m}Tc$ production routes involving nuclear reactors or accelerator techniques have been assessed using a common set of criteria. 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. The non-ordered list of criteria includes:

- Technology maturity
- Production yield
- Available irradiation capacity
- Distribution range and logistics
- Simplicity of processing
- Waste management
- Proliferation resistance
- Potential for other isotopes co-production
- 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 technologies considered in this report are assessed according to the above set of criteria, using a three-grade rating system [Low (*), Medium (**) and High (***)]. A score of “High” is the most positive outcome and “Low” is the least positive outcome.

The technologies considered for assessment have been divided in three classes: short-term, mid-term and long-term availability at significant scale.

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[40]. For the most widely used technologies, physical details and the economic data are available from industry (see NEA, 2010a for details). The list of technologies in the "short-term" category includes:

- Uranium fission in research reactors;
- Solution reactor technology;
- Neutron activation of ^{98}Mo in nuclear reactor;
- Direct ^{99m}Tc production with cyclotrons.

The **mid-term** technologies are expected to be available in 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 $^{100}Mo(\gamma,n)^{99}Mo$ using an electron accelerator.

The long-term methods are expected to become available in the time frame beyond 2025. For those technologies, only some very general technical information is available, and no economic assessment could be done today. 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.

40. Only uranium fission route is currently used for large-scale production.

Table 22: Summary of technology assessment results

		Short-term technologies				Mid-term technologies		Long-term technologies	
	HEU in research reactors - Reference	Current LEU targets[41] in research reactors	LEU solution reactor	^{98}Mo activation in research reactors	^{100}Mo → ^{99m}Tc in cyclotron	^{238}U (γ,f) photofission	^{100}Mo (γ,n) ^{99}Mo	LEU fission with spallation neutrons	^{100}Mo (n,2n) ^{99}M
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	**

n/a – not available

41. Aluminide dispersion targets.

Depending on national priorities, the research and development on each mid- and long-term isotope production technology could potentially be accelerated; the proposed categorisation is therefore only indicative and essentially based on the amount of information available today. The summary of the results of assessment of these technologies is presented in Table 22.

The analysis of molybdenum-99/technetium-99m production technologies leads to the following conclusions and remarks.

Remarks

- The assessment of the reactor fission of highly enriched uranium (HEU) technology was performed as a benchmark only. This technology is currently used for about 90% of the world production of ^{99}Mo. However, an international effort is currently underway to reduce and eventually eliminate the use of HEU targets, given that they contain weapons-grade materials.

- The estimates of the cost of ^{99}Mo/^{99m}Tc production should be regularly revised. In this report, an attempt has been made to estimate the production costs based on the information available from industry interviews and open sources. Some of these estimates are based on small amounts of data and a range of assumptions, which are not always possible to verify.

- The costs associated with bringing a technology to maturity and the corresponding risk to development are not assessed in this report. Also, the costs associated with the ultimate waste management and its final disposal have not been analysed due to the lack of information.

Short-term technologies

1. The use of low enrichment uranium (LEU) targets has the following advantages over HEU:
    a. Proliferation resistance;
    b. Easier availability of the target material;
    c. 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.

2. 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.
3. 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.

4. 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.
5. 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

6. 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 for small-scale ^{99}Mo production.
7. The technology based on the photonuclear reaction $^{100}Mo(\gamma,n)^{99}Mo$ 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

8. 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).

Further Work

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

1. 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 $^{99}Mo/^{99m}Tc$.

2. 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).

3. 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.

4. The possibility of using metallic targets for neutron activation should be examined, and the cost of its processing and recycling should be evaluated.

5. Additional research and development on the production and recycling of highly enriched molybdenum targets is needed. This is important for both the direct ^{99m}Tc cyclotron production and the neutron activation technologies.

6. 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 evaluated.

7. Decisions will be needed on funding the required research and development for the two long-term technologies to determine if there is a potential for them in the future supply of ^{99m}Tc.

8. There would be value in updating this report in approximately one year as new information is expected to become available over this period.

10 REFERENCES

Ball, R. (1997), United States Patent Application, Pub. No.: US 1997/005596611A.

Ball, R. *et al*., (1998), "Present Status of the Use of LEU in Aqueous Reactors to Produce Mo-99", 1998 International Meeting on Reduced Enrichment for Research and Test Reactors. October 18-23, 1998, Sao Paulo, Brazil. Available at: www.rertr.anl.gov/Mo99-98/RBall.pdf.

Bennett, R.G. *et al*. (1999), "A System of 99mTc Production Based on Distributed Electron Accelerators and Thermal Separation", *Nuclear Technology*, Volume 126, Number 1, Pp. 102-121 April 1999.

Bunatian, G.G. *et al*. (2009), *On the Usage of Electron Beam as a Tool to Produce Radioactive Isotopes in Photonuclear Reactions*, Joint Institute for Nuclear Research preprint E6-2009-182, www1.jinr.ru/Preprints/2009/182%28E6-2009-182%29.pdf.

B&W (2009), "Medical Isotope Production System", www.babcock.com/library/pdf/PS-301-110.pdf.

Cameron, R. (2009), *Management of Wastes from the production of Mo-99*, Presentation at the OECD/NEA High Level Group on the Medical Radioisotopes meeting, December 2009.

Chakrov, P. (2010), *^{99}Mo/^{99m}Tc gel generator option: Kazakhstan experience*, Presentation at the IAEA Consultancy meeting on Medical Radioisotopes, March 2010.

Chattopadhyay, S. *et al*. (2008), "Recovery of ^{99m}Tc from Na_2 [^{99}Mo] MoO_4 solution obtained from reactor-produced (n,g) ^{99}Mo using a tiny Dowex-1 column in tandem with a small alumina column", *Appl. Radiat. Isotopes*, No. 66: pp. 1814-1817.

Chabod, S. *et al*. (2006), "Neutron flux characterisation of MEGAPIE target", *Nucl. Intr. And Meth.* A 562, pp. 618-620.

Christian, J.D. *et al*. (2000), "Advances in Sublimation Separation of Technetium from Low- Specific-Activity Molybdenum-99", *Ind. Eng. Chem. Res.*, Vol. 39, No. 9, pp. 3157-3168.

Dong, D. *et al*. (1995), "Processing of LEU Targets for ^{99}Mo Production – Dissolution of Metal Foil Targets by Alkaline Hydrogen Peroxide (A,P)", Proc. 1995 International Meeting on Reduced Enrichment for Research & Test Reactors, Paris, France, September, 1995. Available at: www.rertr.anl.gov/MO99/DONG95.pdf.

Duran, A. (2005), *Radionuclide purity of fission Mo-99 produced from LEU and HEU. A comparative study*, Presentation at the 2005 International RERTR Meeting, Boston, MA, November 6-10. www.rertr.anl.gov/RERTR27/PDF/S8-3_Duran.pdf.

Fadil, *et al*., (2008), *Nucl. Instr. Meth*. B 266, p. 4318.

Gelis, A. *et al.* (2009), *Alternative methods for digesting irradiated LEU foil targets to produce ^{99}Mo in alkaline media*, proceeding of the RERTP 2009 International Meeting, Beijing, China, 1-5 November, 2009.

Guérin, B. *et al*. (2010), "Cyclotron Production of 99mTc: An Approach to the Medical Isotope Crisis", *Journal of Nuclear Medicine*, 51: 13N-16N. http://jnm.snmjournals.org/cgi/reprint/51/4/13N.

GE-Hitachi (2010), *GE Hitachi Nuclear Energy to Deliver Life-Saving Medical Isotope Molybdenum-99 Using Alternative to Highly Enriched Uranium*, Press release, 25 January 2010. www.ge-energy.com/about/press/en/2010_press/012510.htm.

IAEA (2003), *Manual for reactor produced radioisotopes*, IAEA-TECDOC-1340. Vienna, Austria, www-pub.iaea.org/MTCD/publications/PDF/te_1340_web.pdf.

IAEA, (2008), *Homogeneous Aqueous Solution Nuclear Reactors for the Production of Mo-99 and other Short Lived Radioisotopes*, IAEA-TECDOC-1601, Vienna, Austria, www-pub.iaea.org/MTCD/publications/PDF/te_1601_web.pdf.

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

IAEA/NEH (2010), *Nuclear Energy Handbook: IAEA Handbook of Nuclear Data for Safeguards*, Section C. www-nds.iaea.org/sgnucdat/c3.htm#92-U-235.

Jerden, J.L. Jr. *et al*. (2009), *Optimisation and scale-up of a nitric-acid dissolver system fpr LEU-foil targets for a Mo-99 production*, proceeding of the RERTP 2009 international meeting, Beijing, China, November 1-5, 2009.

Jupiter (2005), Cost/*Benefit Comparison For 45 Mev And 70 Mev Cyclotrons*, Study conducted for the US Department of Energy by JUPITER Corporation to compare costs of high-energy medical cyclotrons. www.er.doe.gov/np/program/docs/Reports/CYCLOTRON%20REPORT-pdf%20format%20%285-24-05%29.pdf.

Koscielniak, S *et al*. (2008), "Accelerator Design for a ½ MW Electron linac for Rare Isotopes Beam Production", Paper presented at EPAC08, 11th European Particle Accelerator Conference Genoa, June 23-27 2008. Available at: http://legacyweb.triumf.ca/publications/pub/arch08/pp-08-06.pdf.

Keppler, J.S. and P.S. Conti (2001), "A cost analysis of positron emission tomography", *American Journal of Roentgenology*, Available at: www.ajronline.org/cgi/reprint/177/1/31.pdf.

Minato and Nagai, (2010), Article in preparation.

Mushtaq, A. (1995), "Desorption of Mo-99 from Spent Mo-99/Tc-99m Generator", *Journal of Radioanalytical and Nuclear Chemistry Letters*, 199, p. 89.

Mushtaq, A. (2009), "Can Enriched Molybdenum-98 Replace Enriched Uranium?", *The Nonproliferation Review*, 1746-1766, Volume 16, Issue 2, Pp. 285-292.

NA (2009), *Medical Isotope Production without Highly Enriched Uranium*, The National Academies Press, Washington, D.C., 2009. Available at: www.nap.edu/catalog.php?record_id=12569.

Nagai, Y. and Y. Hatsukawa, (2009), "Production of 99Mo for Nuclear Medicine by 100Mo(n,2n)99Mo", *J. Phys. Soc. Japan*. Vol. 78, No. 3, pp. 033201-1-4.

NEA (2004), *Beneficial Uses and Production of Isotopes – 2004 Update*, OECD, Paris, France.

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

NEA (2010b), *The Supply of Medical Radioisotopes – Interim Report of the OECD/NEA High-level Group on Security of Supply of Medical Radioisotopes*, OECD, Paris, France.

NNSA and ANSTO, (2007). *Global initiative to combat nuclear terrorism: Workshop on the production of Mo-99 using low enriched uranium*. 2-5 December, Workshop Report, 21 pages. Sydney, Australia.

Oganessian Y.T. *et al.* (2002), "RIB production with photofission of uranium", Nuclear Physics A Vol. 701, No. 1, pp. 87-95(9).

Ottinger, C.L., and E.D. Collins (1996), *Assessment of potential ORNL contributions to supply of molybdenum-99*, Oak Ridge National Laboratory, Report No. ORNL/TM-13184. Oak Ridge, Tennessee, www.osti.gov/bridge/servlets/purl/231363-twIdQO/webviewable/231363.pdf.

Panebianco *et al*. (2007), "Neutronic performances of the MEGAPIE target", International Conference on Nuclear Data for Science and Technology, : http://arxiv.org/ftp/arxiv/papers/0705/0705.1533.pdf.

Ponomarev-Stepnoy *et al*. (1999), *United States Patent Application*, Pub. No.: US 1999/005910971A.

Ryabchikov, A.I. *et al*. (2004), *Obtaining molybdenum-99 in the IRT-T research reactor using resonance neutrons*, Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms, Vol. 213, 5th Topical Meeting on Industrial Radiation and Radioisotope Measurement Applications, January 2004, Pp. 364-368.

Saraswathy, P. *et al*. (2007), *Tc-99m Generators for Clinical Use Based on Zirconium Molybdate Gel and (n,γ) Produced Mo- 99: Indian Experience in the Development and Deployment of Indigenous Technology and Processing Facilities*, 29th International Meeting on Reduced Enrichment Research and Test Reactors, www.rertr.anl.gov/RERTR29/Abstracts/S9-5_Saraswathy.html.

Sarkar, S. K. *et al*. (2009), *Update on Operational Experience of Zirconium Molybdate – ^{99}Mo Gel Generator Production in India*, 31st International Meeting on Reduced Enrichment Research and Test Reactors, www.rertr.anl.gov/RERTR31/pdf/S7-P4_Sarkar.pdf.

Schenter, *et al*. (2006), *United States Patent Application*, Pub. No.: US 2006/0023829 A1.

Scholten, B. *et al*. (1999), "Excitation functions for the cyclotron production of 99mTc and 99Mo", *Appl Radiat Isotopes*, Vol. 51, pp. 69-80.

Stepenski, D.C. *et al*. (2007), Assessment of Utility of Homogeneous Aqueous Solution Nuclear Reactors for the production of Mo-99 and other short-lived radioisotopes, 20-22 June 2007, Presentation at the IAEA Consultancy, IAEA, Vienna, Austria.

Takacs, S. *et al*. (2003), “Evaluation of proton induced reactions on 100Mo: new cross sections for production of 99mTc and 99Mo”, *J. Radioanal Nuclear Chem*. Vol. 257, pp. 195-201.

TRIUMF, (2008), “Making Medical Isotopes. Report of the Task Force on Alternatives for Medical-Isotope”, A. Fong, T.I. Meyer and K. Zala Production/Editors, AAPS Canada, TRIUMF 2008, www1.jinr.ru/Preprints/2009/182%28E6-2009-182%29.pdf.

Vandegrift, G. (2006), *HEU vs. LEU Targets for ^{99}Mo Production – Facts and Myths*, Technical Workshop, Oslo Symposium on the Minimisation of Highly Enriched Uranium in the Civilian Sector, 18 June 2006, www.nti.org/e_research/official_docs/labs/heu_vs_leu_facts.pdf.

Wiencek, T.C. *et al*. (2008), *Status and progress of foil and target fabrication activities for the production of 99Mo from LEU*, Presentation at the 2008 International RERTR Meeting, 5-9 October 2008, Washington, DC, www.rertr.anl.gov/RERTR30/pdf/S15-4_Wiencek.pdf.

Zykov, M.P. *et al*. (2001), “Use of Extraction Generator for Preparing a ^{99m}Tc Radiopharmaceutical”, *Radiochemistry*, Vol. 43, No. 3, May 2001, pp. 297-300.

11 APPENDIX

11.1 Physical characteristics used to build assessment criteria of $^{99}Mo/^{99m}Tc$ production technologies

The physical characteristics that were used to build the assessment criteria cover a range of factors including physical properties of the 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 characteristic are discussed below and in the text, where details on the assessed technologies are provided.

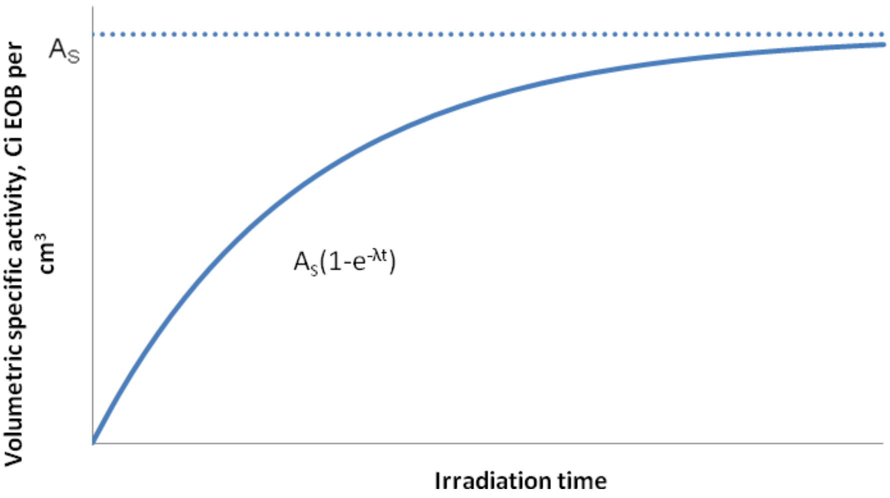
Based on the physical characteristics discussed below a set of assessment criteria is built in Section 5.1.

11.1.1 Molybdenum-99 or Technetium-99m production rates

The production rate is characterised by the cross section of the reaction and the flux of the incident particles. Because of the radioactive decay of the produced isotopes, the activity of the target becomes saturated with time[42] (see Figure 12).

42. Let φ the flux of incident particles, Σ - the macroscopic cross section and λ is the decay constant of the produced isotope. If the isotope produced is stable then the concentration n of the isotope produced grows with time as $n=\varphi\ \Sigma t$. If the isotope produced is unstable (like ^{99}Mo) then its concentration grows like $n = \varphi\ \Sigma/\ \lambda\times(1-\exp(-\lambda t))$. The saturated volumetric activity in this case $A_S= \lim \lambda n(t)= \varphi\ \Sigma$ (the decay rate is equal to the production rate).

Figure 12: Typical evolution of the target's (volumetric) activity during the irradiation



NB: A_S is the saturated volumetric specific activity and λ is the decay constant of the produced radioisotope.

The ^{99}Mo/^{99m}Tc saturated volumetric activity A_S is thus a general characteristic of the efficiency of ^{99}Mo/^{99m}Tc production, measured in [Ci (EOB) cm^{-3}] in the case of reactor-based production and in [Ci (EOB) mA^{-1}] in the case of accelerator-based production. It gives an estimate of the maximal quantity of radioisotopes that could be produced within the technology under study.

11.1.2 Target dimensions and type

This criterion determines the chemical form and the quantities of materials needed for target manufacturing.

It also gives some information on the ease of irradiation in a reactor or accelerator. The non-fissile targets are often less problematic to irradiate than the fissile ones. In the case of a fissile target, the safety parameters of the reactor may be impacted, and thus each case should be carefully evaluated.

If the fission cross section of the target material is high (as in the case of HEU or dense LEU targets), the target can influence the safety parameters of the reactor and need forced cooling. It can be interpreted as an indicator of the irradiation safety risk. The target composition is also a measure of the security risk (especially in the case of HEU).

11.1.3 Irradiated target power

The residual thermal power in an irradiated target is due to its α, β and γ radioactivity caused by the presence of the fission and, to a lesser extent, activation products. The corresponding specific powers are respectively P_α, P_β, P_γ [W/g]. The gamma power P_γ gives an idea on the shielding needed to transport the irradiated target and indirectly characterises the complexity of the processing line.

The power of the irradiated target together with other important physical characteristics (process type, chemical and physical form, etc.) can be seen as an indicator of the processing safety risk (consequences in case of a leak, criticality risks, etc.)

Also, the total thermal power determines the need for cooling during transportation.

11.1.4 Specific activity of the separated molybdenum

The specific activity of the molybdenum determines the type and size of the ^{99m}Tc generator. In the case of low and medium activity molybdenum, an additional purification of the eluted technetium is needed (in the case of a gel generator).

The specific activity is also important for the logistics issues. For example, if the specific activity of the separated molybdenum is low, an outsize container would be needed to transport large volumes of radioactive material. This could have negative consequences on the isotope distribution.

11.1.5 Type, volume and α-,β-,γ-power of the waste

The type, volume and activity of the wastes are very important and strongly depend on the method used for ^{99}Mo production.

In the case of HEU fission, the waste consists of large amounts of non fissioned weapon-grade uranium, fission products and higher actinides. If LEU is used, the total volume of waste is increased, but it does not contain weapon-grade uranium and the criticality risks in storing the waste are reduced. The management of chemical effluents (used in processing) is an important issue. Another important aspect is the amount of plutonium[43] (increased amount in LEU waste compared to HEU) and other actinides contained in the waste.

In the case of the activation route the waste management is simpler because no fission products or actinides are involved, which are radioactive wastes.

11.1.6 Technetium generator activity and dimensions

The technology of technetium extraction depends on the way the ^{99}Mo was produced and on its specific activity. In the fission route, compact column generators are commercially produced.

For low specific activity molybdenum from the activation route, several technologies are available. Some of them can only be realised in a form of centralised ^{99m}Tc separation facilities (involving ion-exchange or solvent extraction techniques). Other methods, especially the gel generators, may be used in centralised or portable schemes.

The generator dimensions and unit activity allow comparison of various ^{99}Mo technologies and identify possible limitations to its development.

11.1.7 Maximal possible distances between irradiation and processing facilities, generator manufacturer and the hospital

The transport of the targets to the irradiation facility, their shipment to the processing plant and finally the delivery of the separated molybdenum to the generator manufacturer strongly depend on the technology used. For example, the transport of the irradiated targets in the fission route is a complicated issue, but the transport of the separated molybdenum is now well mastered. On the contrary, the transport of the targets to the processing facility in the activation route is easy, but no

43. Still, the quantity of plutonium remains very small (see Section 6.1.2).

standardised container is available for long-distance shipment of large quantities of low-activity molybdenum to the gel generator manufacturer.

The range of the possible geographical extent of a ^{99}Mo production technology can be obtained from the maximal possible distances between the irradiation and process facilities, generator manufacturer and the clinics. These distances are determined by the physical characteristics of the production technology.