

**Securing a Supply of Critical Medical Isotopes for Canada
Using ZEUM Technology**

*An Expression of Interest Submitted to the
Expert Review Panel on Medical-Isotope Production*



Expression of Interest Cover Form

1. Project Title	Securing a Supply of Critical Medical Isotopes for Canada Using ZEUM Technology
2. Project proponent(s) (legal names of companies)	TRIUMF
3. Project partner(s) (legal names of companies, utilities, provinces)	MDS Nordion
4. Project start date: (year/month)	Dec 2009
5. Project completion date: (year/month)	Jun 2013
6. Project location(s):	Vancouver, BC, and Kanata, ON
7. Project summary	
<p>TRIUMF has a 30 year history with MDS Nordion producing medical isotopes for commercial use with accelerators. This proposal combines the strengths of both institutions, TRIUMF (an accelerator laboratory) with MDS Nordion (a medical-isotope company), to produce a uniquely Canadian solution to a worldwide crisis: the shortage of Mo-99. Medical isotopes have been produced using both accelerators and nuclear reactors for decades. Traditionally, certain critical isotopes (<i>e.g.</i>, Mo-99) could only be produced in useful quantities by reactors. Dramatic improvements in accelerator technology in the last decade are now very timely, since they primarily focus on high current applications. Small electron linear accelerators now operate with microamps of current. The feasibility of producing Mo-99 using low-current electron accelerator driven photo-fission has historically been dismissed because of the low yields and consequently no patent was ever submitted for photo-fission production of Mo-99. However it is now straightforward to accelerate 100 milliamps when using the latest superconducting radio-frequency technology (SRF), a gain of 100,000. This advance naturally leads one to reconsider a photo-fission accelerator solution.</p> <p>Accelerators have a role to play in any modern long term solution to the present Mo-99 crisis. Photo-fission permits the use of natural uranium targets and hence eliminates the concerns of proliferation. Accelerators are simple, easy to build and maintain, and can be readily licensed for use since they do not present significant environmental risk. SRF accelerator technology has already been transferred from TRIUMF to Canadian industry; these accelerators could be built in Canada for domestic use or export.</p> <p>One fortunate coincidence of nature is that the photo-fission yield of Mo-99 from natural uranium is the same as neutron-fission yield from highly-enriched weapons-grade uranium. The chemistry developed by AECL and MDS Nordion will apply equally well to either production method. Rather than one reactor dominating the Mo-99 supply chain, a single point of failure, we propose a new model where multiple streams feed the Canadian supply chain, ensuring a robust supply of Mo-99 for Canadians. Since these SRF accelerators are compact as well as scalable, the multiple streams can derive from several independent accelerators, providing backups for themselves. Of course the photo-fission Mo-99 can easily be combined with reactor produced Mo-99.</p> <p>The risk for building such accelerators is low. The primary challenge is two-fold: operation of a two-stage convertor and natural uranium target system with a MW of electron beam power, and a business model that is attractive to the private sector for producing Mo-99 with accelerators without government subsidies. This proposal will definitively address both issues.</p>	

8. Expected benefits	<p>Demonstrating ZEUM technology for deployment in Canada has the following benefits:</p> <ul style="list-style-type: none">• Is complementary to reactor-based solutions for making medical isotopes• Integrates smoothly with existing supply-chain and distribution systems to supplement and/or backstop existing and anticipated new Mo-99 producers• Avoids the use of enriched uranium, thus mitigating concerns about proliferation of nuclear material.• Employs accelerators which offer certain advantages in terms of siting, licensing, operating, and scaling.• Offers a Made-in-Canada solution for generating supplies of Mo-99 sufficient for Canadian domestic needs, thereby enhancing confidence in and security of supply.• Builds on Canadian strengths in nuclear science and technology and assure Canada a continued world leadership role in the future of medical isotopes and nuclear medicine.
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Attestations

By submitting this EOI, the project proponent attests that:

- It is acting on behalf of all partners and collaborators and has received written permission from them to do so.
- It agrees with the terms and conditions of the Panel Call for Expressions of Interest process as described in the Proponent’s Guide.
- Any proprietary or confidential information provided as part of the submission, by any party, is provided with the authorization of that party. Reviewers are bound by the requirements of the Access to Information Act and the Privacy Act regarding the treatment of confidential information.
- It understands and acknowledges that no liability and no commitment or obligation exists on the part of NRCan to make a financial contribution to the project, and, furthermore, that any costs or expenses incurred or paid by the proponent in the preparation of the Expression of Interest are the sole responsibility of the proponent, and no liability exists on the part of NRCan.
- It understands and acknowledges that NRCan reserves the right to alter or cancel the currently envisaged process at its sole discretion.
- The individual signing below attests that he/she has authority to sign on behalf of the proponent.

<p>Please sign below to confirm these attestations:</p>	
<p>Name of Duly Authorized Officer for Proponent: <i>Nigel S. Lockyer</i></p> <p>Title of Duly Authorized Officer for Proponent: <i>Director, TRIUMF</i></p>	<p>Date</p>

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1 Executive Summary

This proposal will demonstrate the feasibility of using accelerator-driven photo-fission of natural uranium (U-238) to produce significant quantities of high purity Molybdenum-99 (Mo-99). To meet Canada's domestic need would require roughly 5 MW total of electron-beam power impinging on a convertor with the subsequent photon beam directed onto U-238 targets. These high-power beams would be generated by linear accelerators employing the latest Superconducting Radio Frequency (SRF) accelerator technology developed by TRIUMF and now successfully transferred to Canadian industry. A single electron accelerator could deliver about 2 MW of beam power at 50 MeV with nearly "off the shelf" SRF technology (*e.g.*, 700 MHz). Canadian demand for Mo-99 could be met with a handful of MW-class accelerators for a total project cost of about \$200 million.

Photo-fission production of Mo-99 using electron accelerators and natural uranium has been internationally reviewed¹ and is now called ZEUM technology (Zero-Enriched Uranium Mo-99). We propose that a 100 kW test is sufficient to measure the Mo-99 yield efficiency and to demonstrate the feasibility of a MW-class machine as well as the more challenging convertor and target designs. We estimate that the 100 kW test will be completed by 2012 and that a pilot plant for commercial production could be complete and operational by 2015. We envision a supply chain for world production of Mo-99 with multiple input streams. A ZEUM production facility would complement other production mechanisms and would offer Canadians greater stability and security of Mo-99 supply during shortages and other interruptions. At other times, ZEUM technology would contribute to the world supply chain.

The proposed ZEUM technology demonstration would take advantage of a physics-driven SRF accelerator project already underway at TRIUMF. Prototype elements would be used to generate the 100 kW beam. After irradiation, the U-238 target would be transferred to MDS Nordion to perform the necessary chemical purification and analysis to measure the yield and demonstrate that the final product is equivalent (per drug master file definitions) to that presently delivered by MDS Nordion. In addition, a business model for commercial deployment of ZEUM will be constructed.

The accelerator-driven photo-fission method has several advantages. The accelerator is buildable, scalable, easily maintained, and a low safety risk and can therefore be licensed in a relatively short period of time. Mo-99 product from ZEUM technology would have equivalent purity (*i.e.*, specific activity) as that from reactors using highly-enriched weapons-grade uranium, eliminating need for significant changes to the chemical processing. The use of natural uranium eliminates any nuclear-proliferation issues. The ZEUM technology, once demonstrated, is simple and can be transferred to the private sector to build a pilot plant sufficient to supply all of Canada, thereby removing government from the supply chain of Mo-99.

¹*Making Medical Isotopes: Final Report of the Task Force on Alternative Medical-Isotope Production*, TRIUMF (2008).

We consider the construction of a MW-class electron accelerator by Canadian industry to be low risk. The target technology is challenging and thus convincingly demonstrating performance at 100 kW and the extrapolation to 1 MW (perhaps distributed over multiple targets) is moderate risk. The yield and purity is critical and so we assign medium risk. The deliverable from this proposal will be measured yield and purity of ZEUM-produced Mo-99 as well as a business model from which the viability of producing significant quantities of Mo-99 via accelerator photo-fission can be determined.

This proposal builds on the University of Victoria-led CFI-approved electron linear accelerator (e-linac at TRIUMF), the high power target technology experience of TRIUMF and MDS Nordion, as well as the chemical processing and business acumen of Nordion. This proposal requests \$7.7 million in funding to design and build the high-power targets, modify TRIUMF infrastructure for the test, and to perform the demonstration in 2012.

2 ZEUM Technology

Canada is facing a breakdown in the supply chain for Molybdenum-99 (Mo-99), a radioactive isotope in high demand for molecular-imaging procedures in nuclear medicine. The present-day Mo-99 supply chain can be described as shown in Figure 2.1. It can be grouped into three distinct stages:

- Physics: Making the isotope;
- Chemistry: Extracting and purifying the isotope and combining it with relevant molecules to form radiopharmaceuticals; and
- Biology: Injecting the radiopharmaceutical product into the patient and using imaging equipment to conduct a scan.

The real deliverable (in the hands of the physician and patient) from this supply chain is a three-dimensional image indicating where selected biochemical activity is taking place within the human body. This is the power of nuclear medicine: analyzing biological function (as opposed to anatomical structure) at the molecular level—in real time and non-invasively.

In preparing a forward-going strategy, the objective should be to improve the security, reliability, and effectiveness of the deliverable. The supply chain can be improved by enhancements to any of the three stages, although typically perturbations in one stage will affect the downstream stages. Combinations of changes to the chief stages can be considered; one needs to judge whether preserving the existing supply chain's integrity (see Appendix B) is important. For instance:

- The physics stage could be altered by using accelerators rather than nuclear reactors to produce the medical isotopes;
- The chemistry stage could be altered to use different types of “physics” inputs and still produce equivalent Tc-99m radiopharmaceutical products; or
- The biology stage could be altered by using other imaging modalities such as PET which relies on an entirely distinct and independent supply chain of “physics” and “chemistry” inputs.

A comprehensive strategy will need to address solutions over the short, medium, and long term. Phased implementation of modifications to the supply chain is the key to smooth transition and overall success.

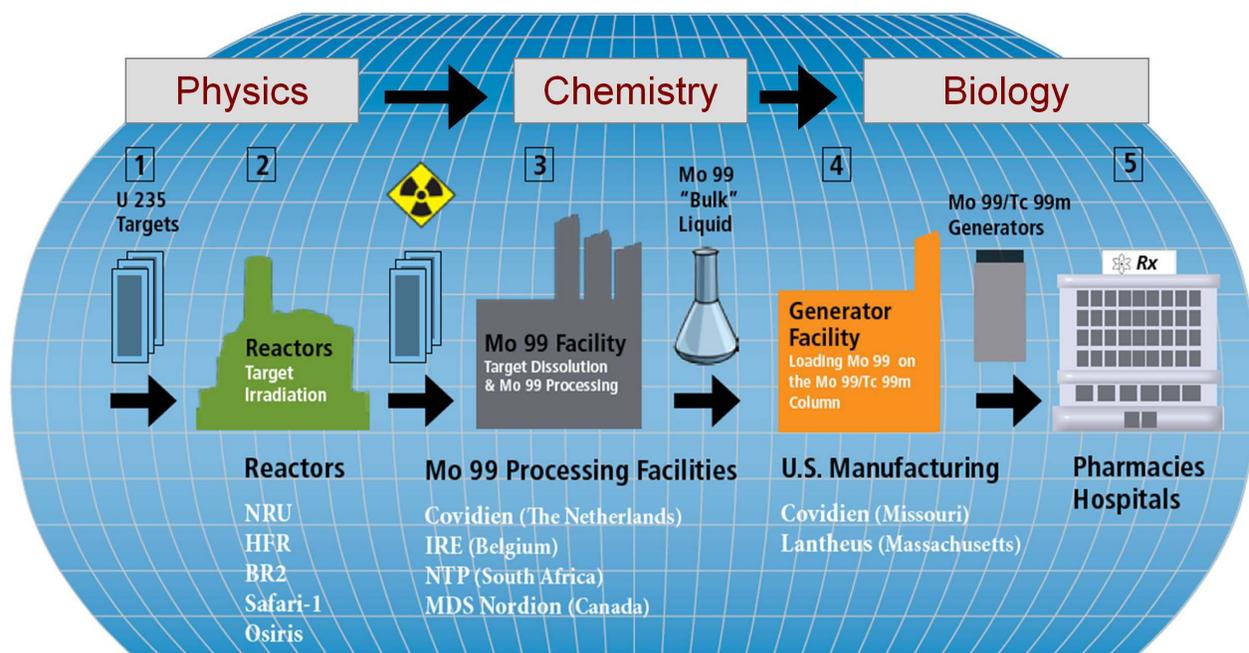


Figure 2.1. Present-day supply chain for Mo-99. The process can be separated into three steps: “physics” to produce Mo-99, “chemistry” to separate and purify the Mo-99 (and manufacture the generators) and “biology” where the Mo-99/Tc-99m radiopharmaceutical is used in the clinic with patients for molecular imaging.

As Canada’s national accelerator laboratory (see Appendix A), TRIUMF is examining alternatives to the “physics” step that involve accelerators instead of nuclear reactors (see Figure 2.2). Some of these alternatives have dramatic implications for the “chemistry” steps as well as the present-day networks for distribution and transport. This proposal discusses a technology using natural uranium called Zero-Enriched Uranium Mo-99 or ZEUM.

Accelerators have several attractive features:

- The accelerator can be turned on and off at will and without consequence.
- The accelerator does not produce radioactive waste from its operation.
- Accelerators can employ different “physics” and achieve useful Mo-99 yields without using weapons-grade uranium.
- The technology is scalable: additional accelerators can be built or turned on and off as needed.
- The licensing and decommissioning processes are straightforward, a few months or less compared to years.

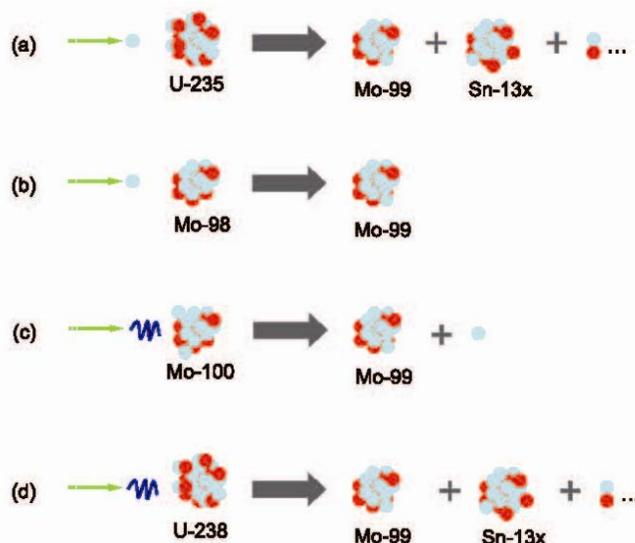


Figure 2.2. Selected physics mechanisms for producing Mo-99. (a) Neutron fission of U-235 (present-day reactor technique). (b) Neutron-capture process on Mo-98. (c) Photo-neutron process on Mo-100. (d) Photo-fission of U-238.

Moreover, as the principle employs the use of a linear accelerator rather than a nuclear reactor the concept is stand-alone with regards to dependence on existing aging nuclear infrastructure assets. Photo-fission of zero-enriched uranium Mo-99 targets offers an alternate option for supplementing the production capacity of Mo-99, thus lessening the reliance on only a few research reactors and securing a supply of medical isotopes for Canada. This proposal outlines a framework for development, proof-of-principle demonstration and a path to commercialization of this novel ZEUM technology.

Accelerator technology has advanced significantly in recent years and is now at a point where machines of sufficiently high power can be constructed to provide the primary engine driving a project of this nature. This initiative will build upon an emerging Canadian prowess in the new platform technology of SRF and will use photons—rather than neutrons—to produce Mo-99.

With the addition of novel technology elements developed specifically to convert a high-intensity electron beam into gamma rays and apply them effectively onto a U-238 target, commercial quantities of Mo-99 can be produced without the use of either nuclear reactors or HEU. These technical goals are all within reach and the resulting Mo-99 from ZEUM technology is expected to integrate well into the existing supply chain. Further refined to commercial practice, the technology would be scalable and modular in that multiple supply streams can be pooled to stabilize and supplement the current supply pattern and the business models that support them.

Canada has been a world leader in the supply of medical isotopes for decades. Centres of excellence exist with resources and capabilities well suited to the challenges of developing ZEUM technology into a viable option for medical-isotope production. In particular, this proposal will highlight the unique combination of existing technology elements, novel

development work, isotope-processing expertise, business and regulatory acumen now available to realize a more secure supply of medical isotopes for Canada.

In addition, this project is an opportunity for Canada to offer the world an innovative solution for regionally based Mo-99 supply while creating jobs in Canada, protecting existing global markets and securing domestic access to medical isotopes critical to the health of Canadians.

2.1 Project Details

The Zero-Enriched Uranium Molybdenum (ZEUM) technology is based on a high-power electron accelerator using superconducting radio-frequency cavities and natural uranium targets. This section overviews the ZEUM technology and outlines a pathway toward private-sector implementation without public subsidy.

2.1.1 Project Description and Technology Identification

Photo-fission has recently been proposed as a novel way to produce medical isotopes, in particular Mo-99, using natural or depleted non-fissile Uranium-238 targets.² The chief elements of the technology are:

- High-power electron accelerator for the production of an intense beam of electrons;
- Converter for the conversion of the beam of electrons into an intense beam of photons (*i.e.*, gamma rays);
- ZEU target struck by the photon beam to produce Mo-99 by photo-fission of U-238; and
- Physical and mechanical extraction and purification of the irradiated target to yield Mo-99 samples identical to those currently produced in a nuclear reactor.

Demonstrating this new technology and preparing it for commercialization is the purpose of this proposal. To do so, a 100 kW test is proposed that will measure the overall yield and efficiency of ZEUM-produced Mo-99. These results will be used to make the business case for a full-scale commercial facility with total beam power of several MW (perhaps spread over several accelerators and/or target assemblies) to meet Canada's domestic needs.

High-Power Electron Accelerator

The primary engine driving the proposed Mo-99 concept is a high power electron linear accelerator based on the well-established and broadly applied technology of superconducting radio-frequency (SRF) acceleration. The majority of modern accelerators are built using SRF technology for the acceleration of charged-particle beams. Accelerating structures called cavities provide high-amplitude microwave fields used for acceleration. The cavities are made of niobium which becomes superconducting when cooled below 9 K. As a result SRF cavities can produce high gradient fields at 100% duty factor very efficiently because of the extremely low

²*Making Medical Isotopes: Final Report of the Task Force on Alternative Medical-Isotope Production*, TRIUMF (2008).

ohmic losses dissipated on the cavity walls. In contrast, the use of normal conducting structures is limited to duty factors of a few percent or less due to the enormous power requirement; the large ohmic losses may easily heat the cavity material beyond the level at which it can be removed by water cooling. The SRF technology has already been applied to several large scale applications and its reliability has greatly improved in the recent years. With the right choice of parameters, SRF can be sufficiently reliable to be commercially viable.

The intrinsic power efficiency of SRF structures, along with their compactness and high-accelerating gradient capability, makes them a cost effective approach to a MW-class photo-fission driver. To generate sufficient supply of Mo-99 for the Canadian market, it is estimated that 5 MW of electron beam power at 100% duty factor is required (see *Making Medical Isotopes* report or Appendix D). The nominal electron linac parameters are 50 MeV electron energy and 100 mA beam current. There is a choice of frequencies of the accelerating structures based on presently available technology. The demonstration test proposed here will be conducted using 1.3 GHz technology as a match to other projects already in progress at TRIUMF. It is projected that the more popular 704 MHz would be the frequency of choice for a full-scale commercial plant because of somewhat lower capital costs.

For the 1.3 GHz option the approach taken at Cornell University can be considered where a 1.3 GHz Injector Linac was recently designed and constructed to provide 0.5 MW beam power. This linac is built from building blocks composed of a 100 kW klystron, two 50 kW input couplers and a 2-cell RF cavity driven at up to 10 MV/m gradient. The five SRF cavities are housed in a single cryostat. The energy gain is 1 MeV per cavity at 100 mA. The high-power coupler and klystron designs were demonstrated in 2007. This linac has been undergoing systems integration tests since May 2008 and beam tests started in December 2008.

To first order, this design is directly scalable: 50 cavities driven by 50 klystrons (see Figure 2.3) provide 5 MW electron beam power. The cavities would be divided in ten cryostats with focusing elements between.

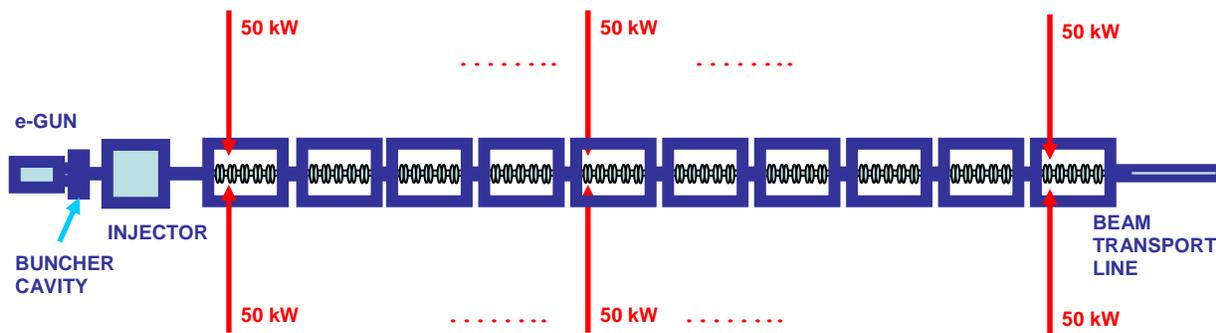


Figure 2.3. Schematic layout of a 5 MW electron linac based on 1.3 GHz SRF technology.

The input couplers, devices that are used to transfer the power from the microwave generators (e.g., klystron) to the cavities, and to a lesser extent the klystrons, form a bottle neck in the design. As microwave frequency increases the physical size of components decreases making

high power RF delivery more challenging. High power electron linac applications, such as Energy Recovery Linac prototypes at 1.3 GHz, presently under development around the world, drive the development of high-power couplers and CW klystrons for their injectors, so it is safe to assume that 100 kW couplers and 200 kW klystrons will be successfully tested and operated in the near future. Doubling the power handling would allow the number of high-power RF building blocks to be halved: 25 cavities and 200 kW beam power per cavity.

This linac-based approach to Mo-99 production offers great flexibility, scalability and modularity. A single 5 MW accelerator can be replaced by five 1 MW devices should this turn out to be the preferred option. These relatively compact accelerators can be distributed geographically, thereby minimizing the travel time to processing facilities. The simple layout and straightforward design concept results in ease in tunability and overall machine operation.

Converter and Target

Photo-fission is a mechanism that utilizes the excitation of the giant dipole resonance by a high-energy photon to induce breakup of a fissile nucleus such as U-238. The high-energy photons can be produced using bremsstrahlung or braking radiation, for example, from an electron beam. Bremsstrahlung is electromagnetic radiation produced when a charged particle is subjected to acceleration. For example, when an electron passes through matter it can be deflected by the charged nucleus of an atom. The resulting spectrum of radiation is continuous.

A schematic of the photo-fission process is shown in Figure 2.4. The intense electron beam impinges onto a converter material (Ta or Pb); the gamma rays created in the process then interact with a U-238 target.

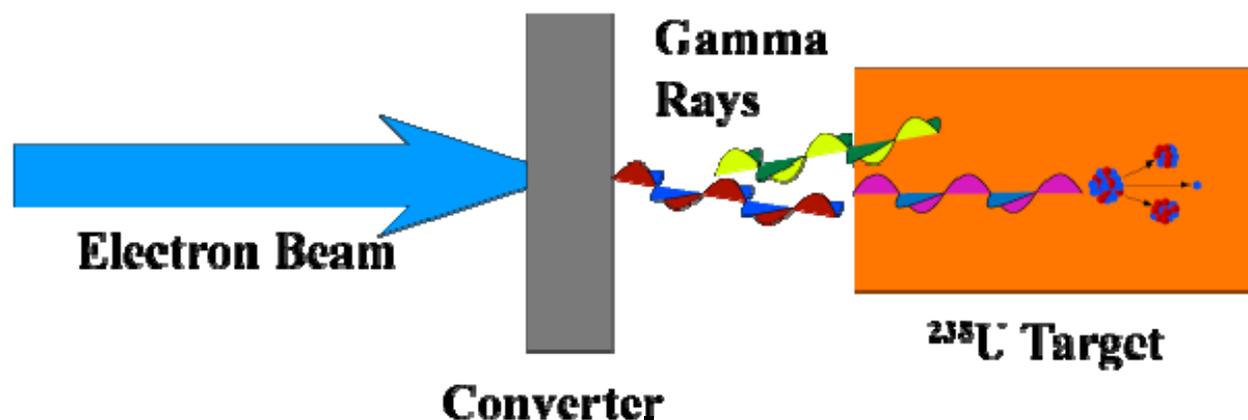


Figure 2.4. Schematic of the photo-fission setup.

The photo-fission threshold is around 6 MeV and the excitation of the giant dipole resonance (GDR) leads to large fission probability. The energy range of these GDR excitations is 10 to 20 MeV. For high-power electron beams, it is not practical to send the electrons directly into a thick uranium target. It is preferable to use a converter that produce photons by bremsstrahlung. The photon-energy distribution is a continuous spectra from zero up to the

maximum energy of the electron. The optimum energy for the electrons to produce photons for photo-fission is around 45 MeV. Figure 2.5 shows the bremsstrahlung spectrum for a 25 and 50 MeV electron beam and the giant dipole resonance (GDR) cross section for U-238. The photon intensity is proportional to the square of the charge of the nucleus.

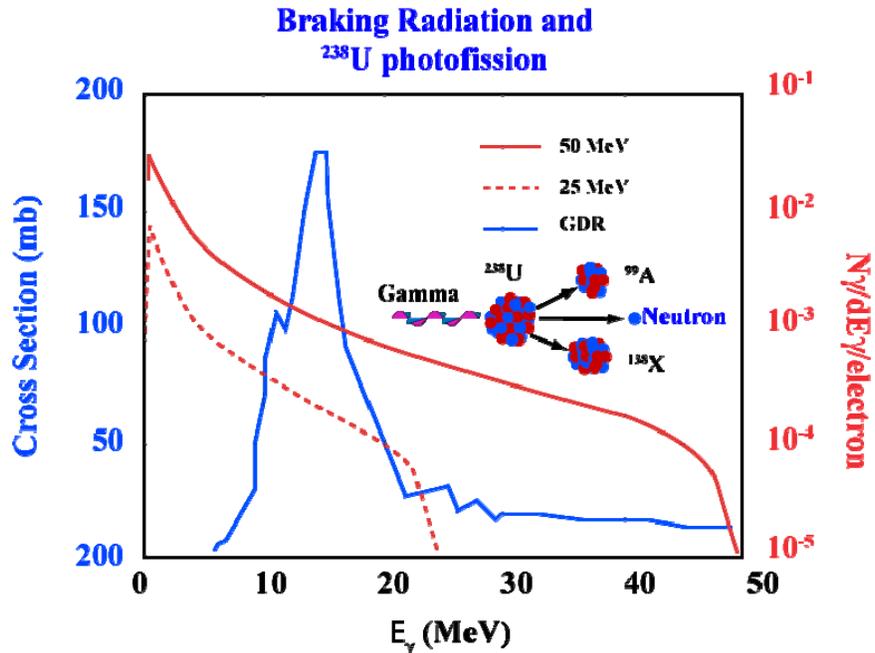


Figure 2.5. Plot of the braking radiation spectrum for a 25 and 50 MeV electron beam onto Pb convertor and the cross section for the GDR. These results come from simulations using the GEANT4 advanced physics package.

The high-power beam of electrons is converted into photons by the use of a convertor material, which has greater efficiency for large atomic number; when passing through this material, the electrons will slow down and radiate energy as photons via the bremsstrahlung process. The photons emerge with a broad spread in energy and direction from the convertor. The target of natural uranium is placed behind the convertor material in the path of the photons. The photons impinge on the target material and fission the uranium atoms. The geometry of the convertor and target can be optimized for highest efficiency capture of the photons and their fissions of the uranium nuclei. The target is also subject to certain design constraints to make it easy to cool during irradiation and to be mechanically and then chemically disassembled for the next steps of preparing Mo-99.

Extraction and Purification

The irradiated target will be mechanically extracted from the beam-line module. The target material will be transported to MDS Nordion's facilities in Kanata, Ontario, where it will undergo a modified chemical process to dissolve the target material and remove the majority of fission byproducts. For the purification phase, a modified chemistry will be developed to allow for final purification of the Mo-99 in order for it to meet the current product specifications.

Quality-control testing will also be modified in order to ensure that final product purity is met and confirmed.

Commercialization

The intention of this project proposal is to explore bringing ZEUM technology to market. Once the technology demonstration is complete, the technology will be viable for licensing to the private sector. That is, TRIUMF is not planning to be in the business of reliably producing commercial quantities of medical isotopes for Canada. Rather, TRIUMF will develop the technology and transfer it to the private sector.

Because the technology avoids the use of enriched uranium and has a substantially lower up-front capital cost, it is highly probable that private interests will seek to license the technology and become an independent supplier of Mo-99 to Canada—and even the world (several expressions of interest have been received). TRIUMF or one of its subsidiaries could serve as a technical resource or supplier of elements of the technology.

2.1.2 Partners and Collaborators

The work outlined in this proposal would be performed by TRIUMF and MDS Nordion (see Appendix E for supporting letters) with participation by Advanced Applied Physics Solutions, Inc., PAVAC Industries, Inc., and the Variable Energy Cyclotron Centre in Kolkata, India.

MDS Nordion is a global leader in providing medical isotopes for molecular and diagnostic imaging, radiotherapeutics, and sterilization technologies. The company is based in Ontario and has enjoyed supply agreements with both AECL and TRIUMF for selected isotopes. MDS Nordion exports its products to more than 50 countries.

MDS Nordion is the ideal partner in this project as it is a global supplier and performer of radiochemical purification and analysis; the requested work is consistent with activities it performs regularly. The company has the intellectual property, demonstrated business acumen, and proven track record to (a) assist in the design and engineering of the ZEUM target such that it is maximally compatible with the existing supply chain, (b) perform the radiochemical extraction and purification of the Mo-99 from the irradiated target, and (c) conduct the chemical analysis of the final product to verify equivalency and overall yield. A non-disclosure agreement is in place between TRIUMF and MDS Nordion for this work.

Advanced Applied Physics Solutions, Inc., (AAPS) is TRIUMF's commercial arm, formed with the receipt of a federal Centre of Excellence for Commercialization and Research (CECR) award in February 2008. AAPS worked with TRIUMF to organize the international Task Force which reviewed the ZEUM technology concept. AAPS would provide engineering consulting and project-management services to the proposed project on an as-needed basis.

PAVAC Industries, Inc., is a partner of TRIUMF in the commercialization of SRF technology. TRIUMF developed this technology in Canada and worked with PAVAC to develop an industrial basis for it; PAVAC is one of five private-sector-based groups in the world with SRF-cavity manufacturing capabilities. PAVAC has manufactured multiple SRF cavities for

TRIUMF's existing ISAC accelerator and is being qualified by U.S. laboratories to serve as a commercial supplier for these devices.

VECC is collaborating with TRIUMF on the development and assembly of several SRF cryomodules for use in a research accelerator designed to produce exotic isotopes for physics research.

2.2 Methodology and Risk Mitigation

This proposal seeks support for the proof-of-principle demonstration in the context of the larger commercialization effort for ZEUM technology. MDS Nordion and TRIUMF are a solid team covering the breadth of technical expertise from physics through chemistry to biology in this sector. Not only is there a strong market need for this type of technology, but there is a convergence of talents, resources, and opportunities that make developing and commercializing ZEUM technology especially timely. This section outlines the specific pathways envisioned for the technology demonstration.

2.2.1 Statement of Work

TRIUMF and Nordion are well-suited for the collaborative development of Mo-99 production by photo-fission in an expedited and phased approach. The proposed development program will be conducted in three stages: (1) the expedited development of key technology elements for the proposed equipment and systems, (2) proof-of-principle demonstration and product testing, and (3) construction of a pilot facility for commercial product demonstration. Figure 2.6 shows the staged approach to the development program.

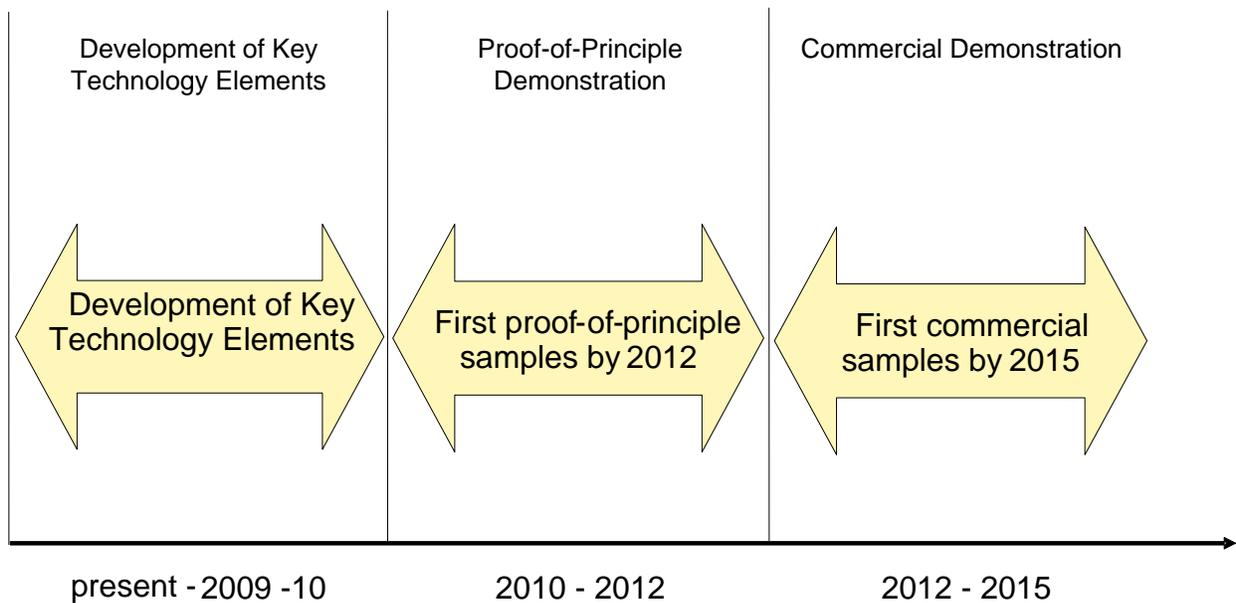


Figure 2.6. Timeline for project phases.

The sections below provide more details on the three development phases followed by a discussion of the technology elements. The technology demonstration is prepared in Phase I and then executed in Phase II; its results directly determine the parameters and viability of Phase III. The demonstration would take place primarily on the TRIUMF site to fully leverage existing and planned infrastructure. The chemical processing and analysis would be performed in MDS Nordion facilities in Kanata.

Phase I — Development of Key Technology Elements (2009-2010)

Phase I of the development program will be conducted during the remainder of 2009 and through 2010 and will include completion of the following work items and associated deliverables:

- Design of Mo-99 target & preliminary testing of target design;
- Preliminary assembly and beam testing of accelerator components at 35 kW;
- Define parameters for accelerator requirements;
- Define the extraction and purification processes to be used, drawing upon current processes employed in Canada by AECL and MDS Nordion;
- Develop estimate of the capital and operational costs for the accelerator required; and
- Develop estimate of the capital and operational costs for the processing facilities required.

Phase II — Proof-of-Principle Demonstration (2010-2012)

Phase II will be aimed at implementing the ZEUM technology elements developed in Phase I to generate proof-of-principle Mo-99 samples by 2012. As such this work will entail assembly of the proposed accelerator and processing facility systems and running these systems to generate, extract, and purify Mo-99 products for product-quality demonstrations. Phase II will include the following steps:

- Preparation of test site (TRIUMF’s Proton Hall), shielding, and safety systems;
- Fabricate and commission targets jointly with MDS Nordion;
- Assemble accelerator system and targets at TRIUMF and run system to generate product;
- Transfer “hot” target to extraction facility and perform bulk extraction steps;
- Transfer raw Mo-99 stock to purification process and purify to Mo-99 product; and
- Performance of various quality control tests to assess product quality and process performance.

These steps will be completed under the supervision of appropriate project leads—a TRIUMF expert will lead activities related to the accelerator and a Nordion expert will lead activities related to processing, extraction, and quality testing of the resulting Mo-99 products. The critical intellectual property of the ZEUM technology is in the convertor and target.

Phase II will also include an evaluation of the Health Canada and USFDA regulatory requirements for sale of this new source of Mo-99 product and inclusion of any quality tests required to meet these regulatory requirements. As a result of the Phase II work, the final parameters for the various systems and processes (accelerator, extraction, and purification) will be determined for the future commercial manufacturing facilities.

Phase III — Commercial Demonstration Facility (2012-2015)

During the period of 2012 to 2015, after completion of the Phase II development program, work will be conducted to demonstrate commercial manufacturing of Mo-99 using photo-fission. This Phase III work will include the formation of a joint venture to implement commercial demonstration facilities as required. A formal business plan will be developed in conjunction with capital partners. Appropriate regulatory and licensing approvals will be secured for the construction of a pilot plant to demonstrate commercial manufacturability. Whenever possible, existing elements of the supply chain will be leveraged and included in the overall plan.

The pilot plant will be designed, built, and commissioned as part of the Phase III work. The pilot plant will then be operated to demonstrate manufacturing and to generate Mo-99 product samples for final purification and quality testing. Commercial product samples will be used to perform the required regulatory submissions and to have the final product approved for sale by Nordion.

The goal is to complete Phase III and have commercial scale quantities (perhaps hundreds of Curies) of product available by 2015. The work in Phase III will allow for determination of the baseline parameters that will be required to scale-up the process for greater market penetration and increased product output.

Discussion of Key Technology Elements*Site*

The accelerator will be constructed and operated at TRIUMF in conjunction with several related but non-overlapping programs. Phase I would be developed inside the ISAC-II building at TRIUMF. The higher power Phase II test would be performed in the Proton Hall building at TRIUMF where shielding will be straightforward.

Local shielding surrounding the ZEUM target is required when the electron beam impinges the target. Radiation monitors, safety systems, and a detailed analysis of the potential radiation hazards will also be required. The accelerator will require liquid cryogenics to achieve and remain at its operating temperature below 4 K. To supply these in a reliable manner, a cryogenic plant will be required to cycle the cryogenics through the system.

The radiochemistry purification and analysis in Phase II will be performed by MDS Nordion, most likely in their Kanata, Ontario, facilities that are already configured for this type of work. The irradiated target would be transferred from TRIUMF to the MDS Nordion facilities using standard containers for the transport of radioactive material.

Accelerator

The accelerator for the technology demonstration will be constructed drawing on a collaboration with the Variable Energy Cyclotron Center (VECC) in Kolkata, India. The laboratory in Kolkata is a nuclear physics research center for the study of stable and radioactive ions. The ultimate goal of the collaboration is to design and build two 50 MeV electron linear accelerators (e-linac) at 10 mA—one each for TRIUMF and VECC. The accelerators are to be used as drivers to

produce radioactive ion beams through the photo-fission process to be used for scientific study. The first phase of this collaborative project, now underway, is to design and build the injector section of the e-linac at TRIUMF consisting of an electron gun, bunching section and an Injector Cryomodule (ICM). Two ICMs are to be produced, one for VECC and one for TRIUMF and each tested with beam by the end of 2011. The beam test is aimed to prove the capability of the ICM to accelerate a low intensity beam of electrons, 3 mA, up to 10 MeV.

The ICM consists of a large vacuum chamber that houses cryogenically cooled accelerating structures. The accelerating structures, called cavities, produce high amplitude microwave fields to accelerate the electrons. The cavities are made from highly refined niobium and when cooled to 2 K can maintain the high fields extremely efficiently. The cavity fabrication is a technically advanced process that TRIUMF has mastered and successfully transferred to PAVAC Industries of Richmond, B.C. The accelerating cavities for both the TRIUMF and VECC e-linacs will be produced in PAVAC. The cavities for each ICM will be processed at TRIUMF and assembled into a 'cavity string' before being installed in the vacuum chamber. A test area is being established at TRIUMF where both ICMs will be tested independently with beam to confirm their performance.

Although the ICMs are designed to accelerate beams from source energies, 100 keV, to a final energy of 10 MeV they can also be configured to accelerate beams in tandem with a higher final energy. The proof of principle test involves the installation of both ICMs in the TRIUMF Proton Hall in the final e-linac location along with the electron gun and bunching section of the e-linac (see Figure 2.7). When placed in tandem the two modules can produce from 25-30 MeV of electrons at 3-4 mA in order to generate the specified beam power of 100 kW. The two ICMs would be installed in early 2012 with a beam test by June 2012.

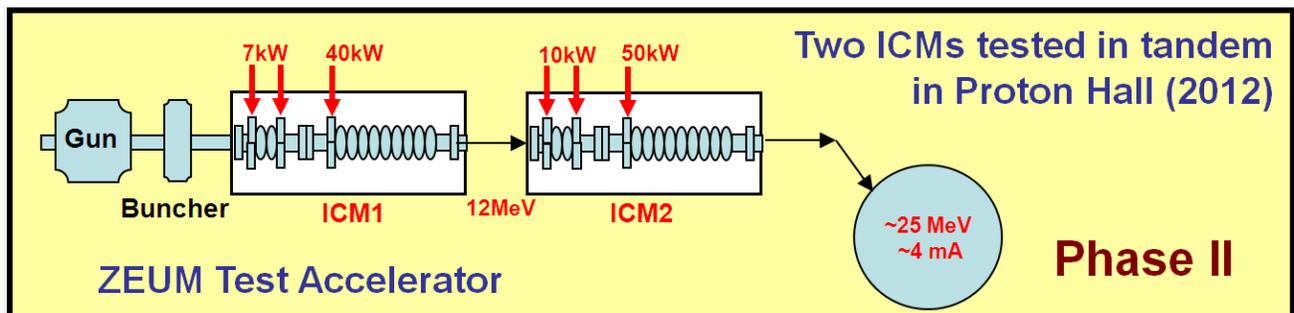


Figure 2.7. Deployment of ICMs for Phase II test.

The choice of 1.3GHz for this proof-of-principle test does not preclude the choice of an alternate frequency for the final installation. The test will give experience in accelerating high intensities of electrons with high microwave power delivered to a cryogenic load while utilizing e-linac technology. In addition the technology of solid niobium cavity production at 1.3GHz can be directly employed to produce cavities at lower frequencies if required.

Converter

The demonstration test will use a 100 kW beam and will use a converter material to generate the photons through bremsstrahlung of the incident electron beam. The MW-class converter and target design will commence once the 100 kW design program is underway. A design team will

be assembled with experts in extreme heat flow simulations and target cooling techniques as well as analysis chemistry. The research area of high power targets is of great interest to the international community in particle and nuclear physics and reactor communities. Collaborations will be established as needed.

The proof-of-principle test will use a 25 MeV, 4 mA beam of electrons. For such a machine combined with a 15 g/cm² of U-238, one can envisage producing 10 Ci of Mo-99 or 2.3 6-day Ci after 7 days of irradiation.

The convertor will be made of Tantalum (Ta) with variable thickness to minimize the power density (see Figure 2.8). Water flowing around the Ta and the U₃O₈ 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 cooling flow necessary is:

Power in Convertor (kW)	Flow (l/min)	Power in Target (kW)	Flow (l/min)
25	11.9	15	7.1

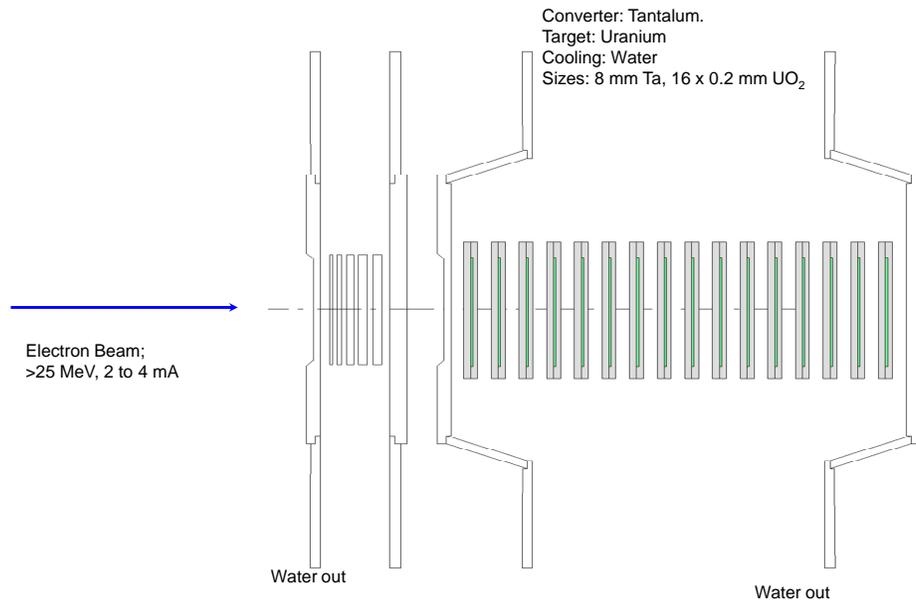


Figure 2.8. Cross-sectional view of proposed convertor and target system.

Target

The target will be made of U₃O₈ ceramic disc encased into a Zr alloy capsule. The U₃O₈ is the most common form of uranium material; it has an olive green colour and the main advantage is

that it is insoluble in water. The density is 8.3 g/cm^3 . For the test, a target geometry will be prepared that presents about 15 g/cm^2 to the incident beam.

According to GEANT4 simulations, a 50 kW, 25 MeV electron beam with a convertor and target size described above yields 4.4×10^{12} fissions per second (see Table 1). The half-life of Mo-99 is 2.7476 days, or 237392.64 s. The cumulative yield for Mo-99 represents 6% of the total fission products. Table 1 gives a summary for different e-linac options. Since the power source in this case is turned off after the irradiation, one can gain access to the uranium target immediately and start the processing at $t=0$. This mitigates some losses due to decay.

Table 1. Mo-99 production estimate for the test. The first column gives the electron beam energy, the second column the total beam power, the resulting electron current, the fourth column gives the target thickness, then the number of days for the irradiation, the amount of Mo-99 produced and the resulting activity.

Driver Energy (MeV)	Driver Power (kW)	e Cur. A	Target (g/cm ²)	Irrad. Time (days)	Mo-99 ($\times 10^{17}$)	Activity [t=0] (Ci)	Activity [t=6days] (Ci)
25	50	0.002	15.0	7	1.32	10.4	2.30
25	100	0.004	15.0	7	2.65	20.9	4.60
50	100	0.002	15.0	7	3.31	26.1	5.75
50	500	0.010	15.0	7	16.5	131	28.7
50	2500	0.050	35.0	7	82.7	653	144

Handling & Radio-Chemistry

Facilities will be set up for the target handling and dissolution of the photo-fission targets. Modified chemistry will be developed and cold experiments will be carried out to ensure experiments are successful. Regulatory review and assessment will be made to ensure proper authority to carry out experiments; this will include the preparation of a safety analysis report.

Irradiated targets will be shipped to the MDS Nordion facility in Kanata, in this location the targets will be received and inspected. Once received targets will be dissolved and initial purification steps will be carried out. The solution will then be characterized. After characterization the product will be further purified and then tested to ensure it meets specification.

Analysis will be carried out at each stage of the chemistry in order to note the types and level of impurities. The chemistry and impurity profile is expected to be similar to current methods of producing Mo-99 by nuclear fission of a U-235 target.

2.2.2 Milestones and Deliverables

Deliverables and project phasing are discussed above. The project plan is described in Table 2.

Table 2. Milestones and deliverables.

Activities	Start Date	Principal Milestones	Completion Date	Deliverables
Accelerator	2009	Cryomodule design complete	Jan 2010	Cryomodule design Injector Cryomodule (10 MeV, 3 mA; 30 kW) ZEUM Test Accelerator (25 MeV, 4 mA; 100 kW)
		Capture cavities complete	May 2010	
		Multi-cell complete	Jul 2010	
		ICM1 fabricated	Jul 2010	
		ICM1 assembled	Jan 2010	
		ICM1 test with beam	Jul 2011	
		ICM2 fabricated, assembled, Combine ICM1 & ICM2 for 100 kW beam test	Dec 2011 Jul 2012	
Target & Converter Design: 100 kW	2009	Form target engineering group	2013	Conceptual design for 100 kW target U-238 target & converter assembly
	Feb 2010	Design & develop converter, target, and assembly	Jan 2011	
	Jun 2011	Fabricate target assembly	Jan 2012	
Chemistry Purification & Analysis	Late 2010	Develop protocols with MDS Nordion or transferring and processing U-238 target	Late 2011	Safety analysis report Written procedure & protocols for chemistry phase of the test
Target & Converter Design: 1 MW	2011	Design & develop converter & target assembly	Late 2012	Conceptual for target & converter assembly that distributes MW beam power over multiple targets
Site preparation	Sep 2009	Prepare test stand for 35 kW beam test	Dec 2010	Test protocol and services in place
	Oct 2009	Prepare TRIUMF Proton Hall for 100 kW test (cryoplant, electrical infrastructure, local shielding)	Apr 2010	Safety analysis report
			Dec 2011	Test protocol and services in place
Demonstration Test	Mid 2010	Design & develop test protocols	Late 2010	Conceptual design review of demonstration test
	Jan 2012	Fabricate production target	Mar 2012	Dry run of irradiation, target transfer, handling, and chemical processing
	2012	Commission target assembly with 100 kW beam	2012	
	Sep 2012	Irradiate target & transfer to MDS Nordion	Sep 2012	
	Sep 2012	Mechanical, chemical purification and analysis	Oct 2012	Measurement of overall yield, purity, and efficiency
Business Case	2011	Identify capital and operational inputs	Late 2012	Proprietary business model and pricing structure for commercialization of
	Jun 2012	Develop business plan for	Sep 2012	

TRIUMF EOI for ZEUM Technology Demonstration

		commercial ZEUM production of Mo-99		ZEUM technology
Close-out	Late 2012	Prepare results for publication	2013	Peer-reviewed scientific journal publication
	2013	Identify private-sector partners and license technology	2015	Private venture to pilot commercial production

2.2.3 Financial Structure and Business Case

The ZEUM technology is attractive because it has the potential to be fully commercialized for operation in the private sector without the need for ongoing public funding.

Financial Structure

The financial structure for the ZEUM technology demonstration is built on the assumption of TRIUMF's continued operation. TRIUMF is Canada's national accelerator laboratory and has a broad program that includes particle and nuclear physics, molecular and materials science, and nuclear medicine (see Appendix A). As a laboratory supported by the Government of Canada in five-year funding cycles, TRIUMF could be closed if its budget request is declined. The viability of TRIUMF and thus the ZEUM project is contingent upon positive consideration of the funding request for TRIUMF's operating budget (*i.e.*, the Five-Year Plan 2010-2015). The requested level of support (to be part of Budget 2010) is \$305 million over 5 years.³

These requests are being routed through distinct, independent channels and it is not expected that they come under the purview of the Expert Panel. If, after 40 years of TRIUMF's successful operation, the federal government chooses to close TRIUMF, this proposal for demonstrating ZEUM technology becomes infeasible.

Within this context, the ZEUM technology demonstration is a new, defined-term project for TRIUMF which only requires incremental funding to cover additional labour, materials, and supplies to perform the work. The ZEUM technology demonstration takes advantage of several already scheduled efforts and temporarily redirects certain activities. For instance, the University of Victoria led a national \$52 million proposal to the Canada Foundation for Innovation for a superconducting electron linear accelerator at TRIUMF. The CFI proposal was approved in June 2009; pending the successful finalization of award documentation, the funds from the CFI will be combined with matching BC provincial monies and funds from TRIUMF's Five-Year Plan (via National Research Council) to secure part of TRIUMF's future program. Several deliverables covered under the CFI project (*e.g.*, 400 W, 4K cryoplant and electrical infrastructure) can be utilized in the short-term to perform the high-priority ZEUM technology demonstration.

³The total value of TRIUMF's Five-Year Plan is \$328 million; a successful proposal to CFI has covered some of these costs (\$23 million).

Table 3 provides an overview of the total project cost and the required incremental funding to complete the work.

Table 3. Total project cost.

<i>Item</i>	<i>Cost</i>
Site Infrastructure & Prep	
Site preparation (Proton Hall)	\$0.6 M
Electrical infrastructure	\$2.0 M
Local shielding	\$1.0 M
Cryogenic plant	\$4.0 M
Accelerator	
2 ICMs	\$3.2 M
100 kW RF power	\$1.0 M
Beam test	\$2.0 M
Manpower	\$1.6 M
Target	
Development & engineering	\$3.2 M
Fabrication	\$0.4 M
Radio-Chemistry and Processing	\$2.3 M
TOTAL	\$21.3 M

Drawing together existing resources, planned activities, and redirected efforts, the expected contributions and existing commitments are as follows.

Contributions & existing commitments

VECC, India	\$2.75 M
TRIUMF (NRC-\$1.6M, CFI-\$6.95M)	\$8.55 M
MDS Nordion	\$2.30 M
TOTAL	\$13.6 M

The gap is therefore \$7.7 million.

Business Case

ZEUM technology must be demonstrated in the laboratory prior to its commercialization. As outlined in this proposal, ZEUM technology will produce Mo-99 by irradiating U-238 targets. Calculation of expected yield shows that a two-week irradiation with 100 kW of beam power will yield 18 six-day Curies with an optimal target. In unit terms, calculations suggest that yields would be above 1 six-day Curie per gram of uranium per 100 kW of incident beam power. The technology demonstration test is required to fully and irrefutably establish the overall yield of the process.

A distinct advantage of this production technique is that the “chemistry” stage of the supply chain remains essentially unchanged in spite of this dramatic change in the “physics” of the production method. That is, the framework of business and regulatory activities that presently

take irradiated U-235 samples from NRU for extraction, purification, and distribution of Mo-99 throughout Canada and around the world would still apply. Alternative production methods that introduce new physics and new chemistry would not easily take advantage of the existing, highly successful supply chain.

This proposal does not include the design and development of Canadian domestic capacity for the production of Technetium-99m (Tc-99m) generators using the Mo-99 product. For Canada to have true independence from the globally integrated supply chain, domestic capability for producing the Tc-99m generators is required. ZEUM technology does not explicitly address this issue although TRIUMF has discussed it with MDS Nordion. ZEUM could easily be integrated into such a solution.

Although the projected Mo-99 yield is perhaps a hundred times lower per unit of target mass (at 100 kW) than the yield by neutrons from a nuclear reactor, it can still be commercially viable. TRIUMF proposes the use of MW-class beams which bring in an immediate order of magnitude. Recall also that the nuclear reactor business case is aimed at supplying isotopes sufficient for global demand. The accelerator-driven photo-fission solution provides quantities of Mo-99 that are regionally sized and whose production yields can be tuned precisely.

In the long-term, the commercial pricing of Mo-99 from ZEUM technology has a highly probable chance of being competitive. As the nuclear-reactor scheme for producing Mo-99 must move from HEU to LEU targets, an inefficiency factor of 5-10 will be absorbed into the industry. The dominant cost in pricing ZEUM products will be the operating costs which are primarily the electrical power required to drive the accelerator beams.

The proposed technology demonstration will establish the detailed business case and allow quantitative comparison to present market conditions.

2.2.4 Expectations of Government

Expectations of government are minimal in the proposed model for ZEUM technology development and deployment. The public sector is requested to support the technology demonstration at which point the risks and costs can be transferred to the private sector. The long-term business model is designed to eliminate public subsidies in the medical-isotope supply chain and as the market pricing for critical isotopes re-equilibrates, cost recovery plus profit for Mo-99 produced by ZEUM will be priced competitively.

The expectations of government for ZEUM success are:

- Public funding for ZEUM technology demonstration (as requested in this proposal); and
- Favourable and expeditious regulatory environment for the development of alternative supply lines of critical medical isotopes (in terms of CNSC and Health Canada approvals as well as business environments or tax incentives to attract private capital).

2.2.5 Risks and Risk Mitigation

The ZEUM technology demonstration is budgeted at less than \$10 million. It offers a robust and scalable solution that is complementary to existing production methods for Mo-99. The project has some technical risk but offers substantial reward. The project has been designed as a technology demonstration so that no long-term capital costs are sunk and no long-term operational commitments are entrenched if the technology fails to meet calculated expectations. If the technology is established, the commercialization risk will be largely borne by the private sector. We assert, therefore, that the overall risk is low.

We discuss several categories of risk here.

Accelerator

While MW-class electron SRF accelerators are state-of-the-art machines, they are technically feasible with present day technology. Recent interest in energy recovery linacs (ERLs) drives worldwide development and optimization of MW-class electron linacs to be used as ERL injectors. For example, in addition to the Cornell 0.5 MW Injector Linac discussed above, Brookhaven National Laboratory (BNL) is constructing a 20 MeV R&D Energy Recovery Linac facility based on SRF 5-cell cavities operating at 704 MHz, and designed to accelerate up to 0.5 A of average current. A single 1 MW CW klystron will power the 2.5 MeV SRF injector cavity. The 500 kW input couplers for this injector are presently under construction and will be tested in a conditioning box at BNL in 2009. The 5-cell SRF linac cavity has been successfully tested in the vertical test facility at Jefferson Laboratory demonstrating a quality factor in excess of 10^{10} at an accelerating gradient of 10 MV/m fully compatible with the specifications presented here. Finally, a >1.3 MW SRF electron linac based on 1.5 GHz is in operation as a Free Electron Laser driver at Jefferson Lab, in energy recovery mode. The 7-10 MeV injector has been operated up to nearly 10 mA of average current.

Operational reliability of accelerators is sometimes cited as a category of risk. A tuned, single-purpose machine such as proposed for commercial production would have reliability exceeding 90% on its own. Paired with a second machine, the overall performance would be quite stable at 99% reliability that at least one machine is running.

In conclusion, construction and operation of a 100 kW electron accelerator has minimal risk. A higher-power device, operating at 0.5-2.0 MW, faces engineering challenges but is within reach as demonstrated by other present-day examples.

Convertor and Target

The largest risk in the ZEUM technology is the technical challenge of engineering the photo-convertor and target to maximally dissipate excess heat while optimally presenting the uranium to the incident beam power for maximum photo-fission yield of Mo-99. As noted above, a number of research laboratories around the world are already engaged in serious MW-class target development programs. At TRIUMF, 100 kW on target is within reach assuming the addition of technical and engineering expertise and advanced modeling and testing tools (as indicated above). Scaling up to multi-MW targets is the key issue; analyzing this situation will be a key outcome of the proposed work. We estimate that the convertor and target assembly holds the largest technical risk.

Business Case

Establishing the ZEUM business case is the subject of the proposed work, including navigation of the appropriate regulatory approvals. However, the proposed work would not be valuable if there were not strong indications that the business case would turn out to be quite viable. In confidential discussions with business experts such as MDS Nordion and AECL, it seems quite likely that if ZEUM technology performs as well in the laboratory as it does on paper, the business case will be compelling. To be conservative, we assign the business case a level of moderate risk.

Risk Mitigation

Two core strategies will be employed to mitigate these risks.

- Where relevant and appropriate given intellectual-property considerations, TRIUMF will seek collaborations with other efforts around the world that are pursuing high-power targets. TRIUMF is a world leader in this area. Likewise, preliminary testing of prototype technology elements will be performed in partner laboratories around the world.
- As described above, the project is staged by design. The completion of Phase I will inform Phase II and the technology demonstration of Phase II will determine whether Phase III will take place in the private sector.

In parallel with this one-time technology demonstration, TRIUMF will be completing construction of a full e-linac accelerator and the ARIEL underground beam tunnel and target-hall facility. These facilities will be completed by the end of 2013 and would become available for 300 kW studies of Mo-99 production (in competition with other TRIUMF programs). The primary purpose of this facility is basic research in nuclear physics, materials science, and nuclear medicine; it will provide, however, an ideal environment for developing advanced studies of high-power convertors and uranium targets for photo-fission.

2.2.6 Regulatory Issues

There are important considerations for proposing a new source of Mo-99, independent of the specific technical details. Both Health Canada and the US Food and Drug Administration would need to be involved. Because the present system of Mo-99 recovery and refinement is optimized for the present nuclear-reactor producers, any perturbations introduced to accommodate additional production facilities will need careful consideration and involvement of the drug regulators.

The proposed means for the production of Mo-99 uses a different target material than the present-day thermal neutron fission process, U-238 versus U-235, respectively. Although the fission yield from both processes are nearly identical in terms of elemental and isotopic distribution, the regulatory bodies will require proof that the Mo-99 available for preparing the Mo-99/Tc-99m generators meet or exceed the existing specifications for purity and specific activity. The proposed technology demonstration is designed to provide that proof.

Because the distribution of elements is almost identical in both processes, the validation of the chemical process should be fairly straightforward. One caveat is the contamination level from the production of Pu-239 from the neutron capture on U-238 and the subsequent decay of U-239 to Pu-239. The chemistry for removing Pu-239 has been worked out for LEU targets where the abundance of U-238 is >80%. The U-238 targets for photo-fission will probably be larger but the thermal neutron flux will be lower and therefore the Pu-239 production quite negligible.

The proof-of-principle demonstration will be conducted within the operating licenses of TRIUMF and MDS Nordion. The proposed project will address licensing and regulatory issues for commercial-scale supply chain for accelerator-produced Mo-99 as part of designing the business model. Both the irradiation facility (accelerator and target) and the processing facility (radio-chemical extraction and purification) would fall under the guidelines of the Canada Nuclear Safety Act. Considerations around how to combine the new supply of Mo-99 with the existing regulatory framework (e.g., drug master file) and distribution network would also be examined.

Using Nordion's proprietary purification processes, existing Ottawa based facilities and medically approved Mo-99, ZEUM technology can more easily achieve regulatory approval. By pooling at Nordion with other approved sources of Mo-99 from existing reactors, access to the supply chain can be achieved without an independent drug regulatory approval process that would take years to complete.

For products such as Mo-99, government regulatory bodies have ruled that active pharmaceutical drug ingredients (APIs) are themselves drugs. The regulatory approval of isotopes for use in humans depends in part on the nature and quantity of impurities found in the product and in part on the results of human clinical trials. Impurities in this case would be the presence of other radioactive isotopes that could have unfavourable biodistribution, higher energy, or much greater half-lives than are desirable for the intended purpose. Changes to either the products or the process must meet equivalency requirements (see GMP regulations, § CFR 210 & 211). Partnering with Nordion will bring Mo-99 from ZEUM technology to market sooner because the licensing strategy will be based on amending existing regulatory dossiers to allow pooling of photo-fission based Mo-99 with existing approved supplies.

In addition to the medical regulatory approvals necessary for the final Mo-99 product, the proposed production facilities will need a nuclear operating license. The design, construction and operation of a facility utilizing ZEUM technology will be subject to the scrutiny of the Canadian Nuclear Safety Commission (CNSC) and their counterparts in other foreign jurisdictions where such facilities might be built. The development, design and commissioning of a Class I-B facility in Canada is highly regulated. The licensing of facilities constructed under this project will involve almost continuous communication between the CNSC and Nordion/TRIUMF on all technical aspects relating to nuclear safety requirements as well as estimating possible levels of waste or environmental emissions. The licensing requirements will need to be addressed throughout the development and refinement of the technology. This will be done in consultation with the CNSC to ensure that all uncertainties relating to nuclear licensing issues are investigated and work is performed to resolve them.

TRIUMF and MDS Nordion are already both holders of Class I-B nuclear operating licenses and therefore are well positioned to understand the perspectives of the CNSC and apply sufficient resources to collaborate and comply with them.

2.3 Impact and Expected Outcomes

This proposal moves ZEUM technology to the commercialization stage with the following outcomes:

- Design and engineering specifications for a pilot commercial plant are defined;
- Production of Mo-99 using ZEUM technology is demonstrated to meet regulatory standards for pooling with existing supplies for commercial use;
- Proof-of-principle demonstration and analytical results are submitted for publication in a peer-reviewed scientific journal; and
- The ZEUM technology is ready for licensing.

The impact of developing and commercializing ZEUM technology is simple: the security of Canada's supply of critical medical isotopes, especially Mo-99, would be dramatically enhanced. With a few MW-class accelerators, ZEUM technology would diversify the "portfolio" of Mo-99 suppliers and ensure that the overall supply chain is reliable for Canada. This proposal seeks to validate the technology and position commercial deployment on the timescale of relicensing the NRU reactor in Chalk River (2015-2016).

Several megawatt-class accelerators will generate sufficient supplies of Mo-99 for Canada's domestic needs; a facility with one accelerator would cost about \$50 million. Electrical power operating costs would dominate the long-term pricing of the product in a full cost-recovery model (although a wind farm could provide the necessary ~100 MW). Private-sector interests may choose to invest in expanded production capacity in order to export and sell isotopes around the world. Accelerator-based Mo-99 production systems will be globally attractive both in terms of technology purchase and in terms of diversifying the supply chain; that is, international radiopharmaceutical manufacturers and distributors would preferentially add Mo-99 product from ZEUM sources to add robustness to their product lines. Deployment of ZEUM technology is completely compatible with the development of a new domestic research-reactor supplier of medical isotopes as ZEUM facilities could easily compensate for the ups and downs of that primary supply.

ZEUM technology combines Canada's historical strengths in accelerators, nuclear science and technology, and nuclear medicine. Canada's reputation as a destination of choice for talented researchers and technologists would be enhanced.

There are multiple routes to strengthening the global supply chain for Mo-99. Other countries around the world are pursuing new research reactors, conversion to LEU targets, or other novel

accelerator-based schemes. Three considerations will shape the future of this market and the future of Canada's role in it:

1. The first technology shown to be commercially viable and scalable will quickly overtake most other contenders;
2. A technology that eliminates dependence on highly enriched uranium, avoids government subsidy, and can be transferred entirely to the private sector will serve Canada best; and
3. If Canada develops this technology, not only will its significant presence in the world market be assured, but Canada will have easy access to a secure and robust supply of medical isotopes.

2.4 Conclusion

To enhance the security of Canada's supply of critical medical isotopes, the portfolio of producers must be diversified. Developed in Canada, Zero-Enriched Uranium Molybdenum-99 (ZEUM) technology offers one option. Employing accelerators rather than nuclear reactors and using natural rather than weapons-grade uranium, ZEUM can be used to supplement or wholly supply Canada's domestic needs for isotopes. ZEUM technology integrates easily with the present-day supply chain in terms of business, product handling and regulation, and distribution.

This project proposes to demonstrate ZEUM technology in the laboratory to clear the way for private-sector deployment. The demonstration will take advantage of existing plans and activities at TRIUMF for using high-power beams to produce isotopes using a process known as photo-fission. A sample target will be irradiated at TRIUMF in 2012 and contributing partner MDS Nordion will perform chemical purification and analysis to benchmark the overall yield and efficiency of Mo-99 production. The proposed demonstration will validate analytical predictions; the integration of the accelerator, target, and chemistry systems; and the business and technology case for private-sector deployment.

This proposal requests \$7.7 million. The outcome of this project will be technology ready for licensing, a business plan studying private-sector deployment of ZEUM, and published, peer-reviewed scientific results.

Appendix A: Background on TRIUMF

TRIUMF is Canada's national laboratory for particle and nuclear physics. It is owned and operated as a joint venture by a consortium of Canadian universities via a contribution through the National Research Council Canada with building capital funds provided by the Government of British Columbia. Its mission is:

- To make discoveries that address the most compelling questions in particle physics, nuclear physics, nuclear medicine, and materials science;
- To act as Canada's steward for the advancement of particle accelerators and detection technologies; and
- To transfer knowledge, train highly skilled personnel, and commercialize research for the economic, social, environmental, and health benefit of all Canadians.

TRIUMF was opened forty years ago by Simon Fraser University, the University of British Columbia (UBC), and the University of Victoria to meet research needs that no single university could provide. The University of Alberta joined the TRIUMF consortium almost immediately. There are currently eleven full members and four associate members from across Canada in the consortium that governs TRIUMF.

Since its inception as a local university facility, TRIUMF has evolved into an internationally renowned laboratory while strengthening ties to the research programs of the Canadian universities. The science program has expanded from nuclear physics to include particle physics, molecular and materials science, and nuclear medicine. TRIUMF provides research infrastructure and tools that are too large and complex for a single university to build, operate, or maintain. There are over 350 scientists, engineers, and staff performing research on the TRIUMF site. It attracts over 500 national and international researchers every year and provides advanced research facilities and opportunities to 150 students and post-doctoral fellows each year.

TRIUMF's operations are primarily supported by five-year contributions from the Government of Canada, enhanced by research grants and awards from NSERC, CFI, CIHR, and other agencies. The present cycle of funding completes in 2010. Working together with the scientific community and its patrons, TRIUMF has proposed a new five-year plan for 2010-2015. The new plan requests an enhanced level of investment of \$328 million over the five-year period coupled with a capital infrastructure project of \$60.7 million.

TRIUMF's new vision brings together university, industrial, and international partners in three priority areas with the promise of true competitive advantage. For the next decade, TRIUMF is focusing on the development and deployment of two platform technologies: radiochemistry & bio-markers for nuclear medicine and superconducting radio-frequency cavities (SRF) for next-generation accelerators. Nuclear medicine is undergoing a revolution and has great potential for dramatically improving health care for all Canadians while trimming costs. Using nuclear medicine, doctors are able to image detailed disease metabolism within the body, before, during,

and after treatment, dramatically improving success rates. SRF technology has widespread applications, ranging from next-generation accelerators for research in materials, nuclear and particle physics, production of medical isotopes, and environmental remediation through “scrubbing” of flue gases. TRIUMF has partnered with PAVAC Industries, Inc., in Richmond to develop the first “Made in Canada” SRF device—one of only 5 teams in the world with this capability.

TRIUMF is also one of Canada’s centres of excellence in nuclear medicine. For instance, a TRIUMF scientist is co-chair of the Canadian Medical Imaging Network which is supported by GE Healthcare. TRIUMF partners with the Pacific Parkinson’s Research Centre and the BC Cancer Agency to research, develop, and supply medical isotopes (and advanced PET-imaging technologies). The primary isotopes used in these programs are the PET isotopes Fluorine-18 and Carbon-11.

Because of TRIUMF’s technical skills and abilities, MDS Nordion has a manufacturing plant in Vancouver that produces and sells a variety of medical isotopes to the world. This partnership is more than 30 years old. The current isotopes commercially produced include:

- Iodine-123, used in medical imaging of the thyroid, brain, heart, neuroblastoma
- Thallium-201, used in medical imaging of the heart
- Gallium-67, used in medical imaging of soft tissue, abscesses, lymphoma)
- Indium-111, used in medical imaging of tumours
- Palladium-103, used in preparing therapeutical “seeds” (prostate cancer)
- Strontium-82, used in generators for Rubidium-82 and in medical imaging of the heart (PET)
- Copper-64, used in medical imaging for hypoxia; labeled antibodies, proteins (PET)
- Germanium-68, used in generators for Gallium-68; medical imaging (PET) (in progress)

The fastest-growing part of TRIUMF’s Five-Year Plan is in nuclear medicine and includes developing next-generation cyclotrons to dramatically expand the production of PET isotopes around the world and developing new PET isotopes in combination with novel radiochemistries for new types of disease diagnosis and treatment.

The future of nuclear medicine is in PET isotopes. They offer superior “chemistry” meaning that they can be combined with more sophisticated biomolecules to selectively target, identify, or destroy specific aspects of neurological disease and cancer. The intrinsic precision and resolution of PET isotopes is also superior to that of SPECT isotopes. The main barriers for PET imaging technology to overcome are the initial capital cost of the imaging cameras and a distribution model built around regional cyclotron accelerator networks rather than international centres of production.

Appendix B: Medical Isotopes

The medical revolution, sometimes called the personalized medicine revolution, is driven by advances in two areas: genomics and molecular imaging. The study of genomics allows us to understand the basic blueprints and program of the human body, both for its optimal operation and its predisposition to disease states. Molecular imaging, on the other hand, is the study of what is occurring at the level of molecules in the body—the very chemistry, biology, and even physics of life.

Nuclear medicine provides one of the primary modalities of molecular imaging. Nuclear medicine combines compounds with specific or selective biological activity with radioactive labels such that the location of the compounds can be “traced” inside the body. The radioactive labels are called medical isotopes (see Figure B.1 for examples).

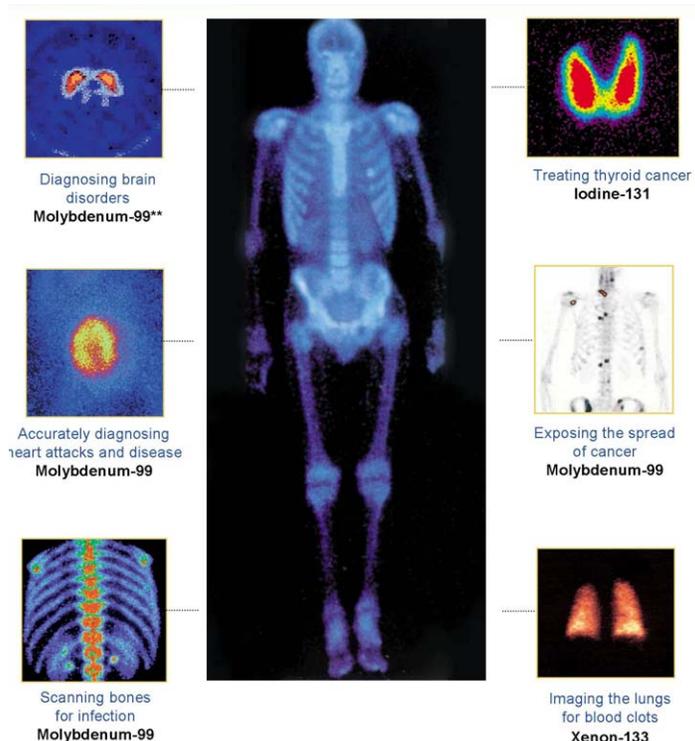


Figure B.1. Examples of medical isotopes used in medical-imaging procedures.

The most widely used medical isotope is Molybdenum-99, used in more than 30 million medical procedures around the world each year.

Molybdenum-99 (Mo-99) does not occur in nature. It is a man-made radioactive isotope of the chemical element Molybdenum used to produce Technetium-99m, the radio-pharmaceutical most used in nuclear medicine, in particular during studies carried out *in vivo*. Mo-99 has a half-life of 66 hours, and must therefore be consumed as soon as possible following production. It

cannot be stored, shipped great distances, or sold from inventory without unacceptably large losses.

Most medical isotopes, including Mo-99, are produced from high-powered research reactors owned by governments or academic institutions. For example, in Canada the National Research Universal (NRU) is a unique 140 MW (megawatt) reactor currently owned and operated by Atomic Energy of Canada Limited (AECL) in Chalk River, Ontario, and is used to produce medical isotopes processed, marketed, and sold by MDS Nordion. This reactor, in addition to its national research mandate, irradiates isotope targets quickly, resulting in a high yield of isotopes of the variety required by Nordion.

Currently, Nordion produces Mo-99 and Xe-133 from the fission of highly enriched uranium targets (HEU) irradiated in the NRU. The isotopes are initially processed at Chalk River to extract, by way of chemical processes, the crude Mo-99 from uranium and other actinides thereby rendering the isotopes suitable for shipment to Nordion's production facilities in Ottawa. The current process uses a variety of acids and other chemicals that result in category 4 liquid waste (highly radioactive liquid waste that has a half-life in excess of 500 years)

Further chemical purification steps are applied to the extracted isotopes at Nordion's facilities in Ottawa to remove impurities and produce a medically acceptable product, licensed for human usage. Jointly, these processes involve highly specialized equipment and proprietary technology to isolate the medical fraction from the fission mix of hundreds of isotopes generated during the irradiation of Mo-99 targets in the NRU reactor.

In recent years the aging nuclear infrastructure in Canada and other countries has resulted in a consolidation of the global production capacity of medical isotopes in research reactors. Presently only four suppliers remain capable of producing regulatory approved, medical grade Mo-99. In addition, federal governments particularly in North America have moved to limit the availability of HEU to commercial and academic institutions in a drive towards elimination of HEU availability outside of military applications. The result is that most of the world's research nuclear reactors have converted from HEU to Low Enriched Uranium (LEU) fuels thus greatly reducing the amount of HEU in commercial circulation. A small remaining requirement still exists for medical HEU used in targets needed for the manufacture of Mo-99, I-131 and Xe-133. Sustained efforts have been underway for years attempting to find technically feasible and economically viable methods to utilize LEU targets at commercial scales sufficient to meet the global demand for Mo-99 and other medically necessary isotopes.

Appendix C: Choice of Accelerating Frequencies

The 704 MHz option can be configured as follows: a thermionic injector can be used to supply 100 mA average current at a bunch repetition rate of 704 MHz and charge per bunch of 140 pC. The gun is followed by a buncher cavity and an injector cryomodule, consisting of a capture cavity and a multi-cell accelerating cavity each cryogenically cooled. The main accelerator (see Figure C.1) consists of a single cryomodule housing five 5-cell cavities, each providing an energy gain of approximately 10 MeV. For 100 mA of average current, the required RF power per cavity is 1 MW, supplied by a 1 MW klystron via two 500 kW input couplers. The wall-plug to beam efficiency for this design concept has been estimated to be in excess of 40%, dominated by the klystron efficiency at 60%. The total wall plug power consumption is about 12 MW, assuming an operating temperature of 2 K for the accelerator. Since the boiling temperature of liquid helium is 4 K at atmospheric pressure, 2 K operation assumes sub-atmospheric pumping and although employed at many installations increases the technical complexity. The ohmic losses at cryogenic temperatures are strongly frequency and temperature dependent making the frequency choice of 704 MHz interesting since in principle 4 K cryogenic operation may be considered while for higher frequencies, the use of lower temperature (2 K) may be more efficient. For an industrial-scale application, such as the production of Mo-99, this option should be explored.

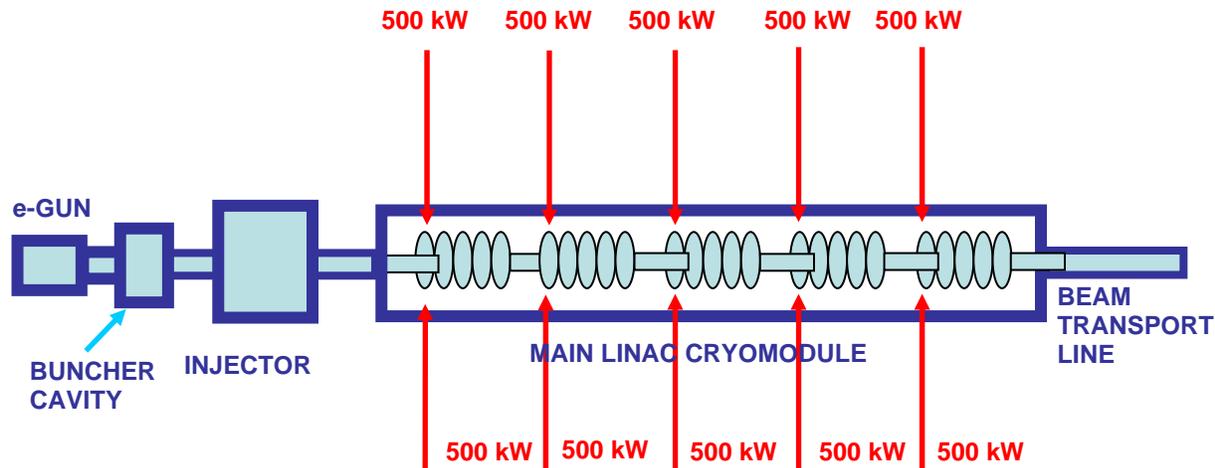


Figure C.1. Schematic layout of 5 MW electron linac based on 704 MHz SRF technology.

A 5 MW photo-fission driver is certainly feasible based on available technology. The frequency choice of 704 MHz has several advantages over that of 1.3 GHz:

- This frequency lies in the television broadcast and the klystron design is less specialized than at 1.3 GHz;

- The structures have larger apertures which is beneficial to beam quality preservation and halo losses;
- Input RF couplers can operate at significantly greater power levels than at higher frequencies, resulting in simpler designs (fewer components, therefore lower capital costs and higher reliability); and
- Cryoplant operation at 4 K (rather than 2 K) is a possibility that needs to be studied.

Appendix D: Estimated Yields

This appendix excerpts the discussion of estimated yields from the Making Medical Isotopes report which was internationally reviewed before publication by TRIUMF. This material comes from Chapter 3.

The photo-fission process is similar to the photo-neutron process. Fission of natural uranium is produced via the reaction $^{238}\text{U}(\gamma, f)$ where one of the common fission products is Mo-99.

The cross section for photo-fission of U-238 is about the same as it is for the photo-neutron process using Mo-100, and it is about 60 to 70 percent of the photo-fission cross section for a HEU target (see Figure D.1). Therefore, this small advantage in cross section does not justify the extra challenges of using enriched uranium.

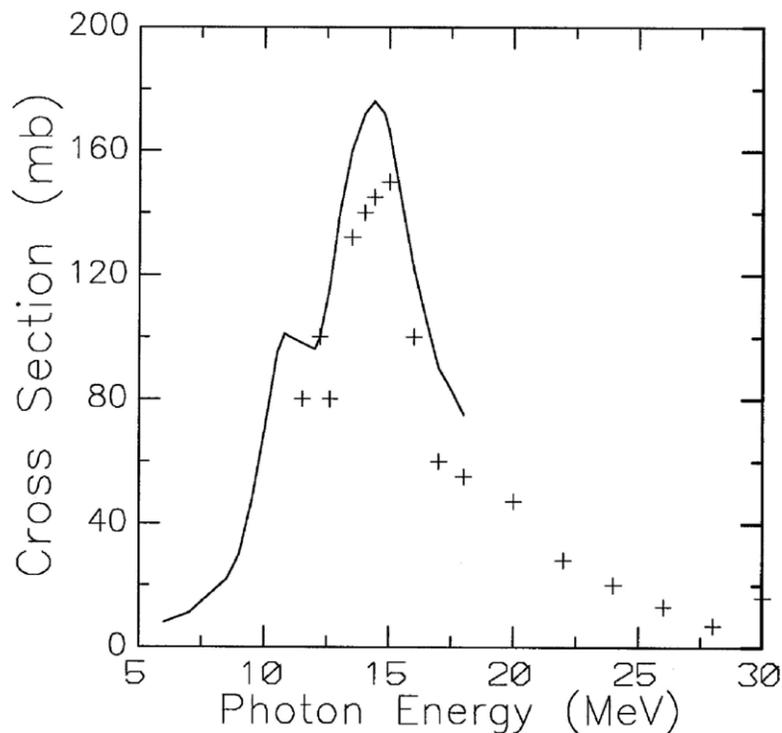


Figure D.1. Experimentally measured cross-sections for photo-fission of U-238 for photon energies up to 30 MeV. The solid-line is a fit to data and the plus signs are data from another laboratory.

Some assumptions about the target are necessary to compute the Mo-99 yield. Conservative estimates are provided here (for instance, more advanced geometries or scanning of the beam

across a matrix of targets would allow higher beam powers to be used for the same target mass and lower power densities).

The radiation length of uranium is about 0.33 cm, so a two-radiation length target is about 0.66 cm thick and a thick target is about 2 cm thick. The fission yield per 100 kW of electron beam power has been calculated using analytical procedures⁴ and in detail using Monte Carlo techniques.⁵ Depending on the details of the target and convertor designs, it is reasonable to expect fission yields of about 5×10^{11} f/s/kW of electron-beam power for a thick target and electron energies of greater than about 30 MeV. A thick target can be used because the cost of the target material is not a significant cost of the process. The fission yield is 5×10^{11} f/s/kW x 100 kW = 5×10^{13} f/s in that target volume. Realistic yields might be somewhat lower (tens of percent).

Six percent of the fission yield will be Mo-99. At saturation (equilibrium), about 14 days of irradiation, there will be $0.06 \times 5 \times 10^{13}$ Bq of Mo-99 produced by a 100 kW electron beam. This is equal to $3 \times 10^{12} / 3.7 \times 10^{10} = 81$ Ci.

This would produce about $81 \times 0.22 = 18$ six-day curies in a two-week irradiation. A one-week irradiation will produce about 83% of saturated yield or 15 six-day curies per week. Some present-day reactors choose the shorter irradiation period for economic reasons.

Producing 500 six-day curies requires about $500/15 = 33 \times 100$ kW of electron beam power, or just over 3 MW.

Both photo-neutron reactions on a separated-isotope target of Mo-100 and neutron-fission of HEU or LEU targets require expensive target material that represents a significant fraction of the cost of the end product. The irradiation is generally extended to between three and five half-lives to obtain the highest yield from the expensive target material. The natural uranium used for a photo-fission target is much less expensive than the separated-isotope targets and would not be a significant fraction of the isotope cost. Therefore, it is not an unreasonable approach to use shorter irradiations to obtain a higher amount of total isotope production. Irradiation to one half-life (2.75 days) of Mo-99 yields 50% of the saturation yield but will produce five separate irradiations in a two-week period (2.5 x saturation yield) or 22.5 six-day curies per week. The down side of this approach is that reduced irradiation cycle might significantly affect present hospital and radiopharmacy routines.

This approach reduces the size of the accelerator to about 2.2 MW, with a modest increase in waste handling. 2.2 MW is a reasonable scale for a single electron linear accelerator (linac). However, another solution might be to build several 1.1 MW photo-fission accelerators that provide backup to each other. Targeting issues at about 1 MW become more easily managed.

Potential Advantages and Disadvantages of This Approach

⁴A Radioactive Ion Beam Facility Using Photo-fission, William T. Diamond, Nucl. Inst. And Meth. In Physics Research A, 432 (1999) 471.

⁵Monte Carlo Calculations done by Dr. J.R. Beene, Director, Holifield Laboratory, Oak Ridge National Laboratory, USA, *Used with permission.*

The main advantages of this approach are:

- Would use natural uranium targets which have lower cost, no criticality issues, and would reduce security required for waste-storage site.
- Could use existing processing techniques, although the volume of the dissolved uranium solution used for Mo-99 recovery could be larger than present (depending on the target designs). Once recovered, the Mo-99 refinement and purification steps should be identical.
- Could continue to use existing generator technologies.
- Higher predictability of schedule, cost and licensing than for a reactor. The main facility costs and licensing issues should be reasonably low in risk.

The significant disadvantages of this approach are:

- Could result in higher waste volume than HEU reactor target technology because of low concentration of the product per gram of target material used (depending on the target design). The specific activity of the actual Mo-99 product should be similar to the value obtained from neutron-fission of HEU, but the total target volume may be significantly higher because of thermal or mechanical issues associated with handling beam power.
- Higher operating and capital costs for the accelerator than the photo-neutron process because of higher beam-power requirements.
- The facility would likely be a Class I-B facility similar to existing hot-cell facilities used in Mo-99 recovery and refinement.

After considering the three accelerator-based methods listed above, the Task Force examined the photo-fission option more carefully. It was judged that much of this technology was readily available and could be deployed in a straightforward fashion.

The possibility of using an accelerator—as opposed to a reactor—to generate high intensities of thermal-energy neutrons (neutrons of energy ~0.02 eV, relevant for stimulating fission) was not seriously considered by the Task Force primarily because of the projected costs. The U.S. Spallation Neutron Source and the Japan Proton Accelerator Research Complex will be capable of producing approximate time-averaged neutron intensities of perhaps 10^{16-18} neutrons/sec. These machines use high-intensity proton beams of a few GeV to strike liquid-metal targets capable of handling megawatts of beam power. However, each project exceeded US\$1 billion in construction and took more than a decade to design and build. Other schemes for producing intense beams of low-energy neutrons are possible but have not been as rigorously developed by the research community.

A qualitative comparison of neutron and photo-fission is presented here.

Neutron-fission

One gram of U-235 in the rough thermal-neutron flux of a nuclear reactor of 3×10^{14} n/cm²/s produces:

$$Y = N \times \sigma \times \phi$$

Where N = number of target atoms in one gram = $1/235 \times 6 \times 10^{23} = 2.6 \times 10^{21}$; $\sigma = 600$ barns = $600 \times 10^{-24} \text{ cm}^2$ and $\phi = 3 \times 10^{14} \text{ n/s/cm}^2$. Hence, $Y = 4.6 \times 10^{14} \text{ f/s/g}$

One watt of fission energy is produced by $3.1 \times 10^{10} \text{ f/s}$ so this would correspond to $4.6 \times 10^{14}/3.1 \times 10^{10} =$ nearly 15 kW/g of U-235. In the neutron-fission technique, the actual target contains a large fraction of aluminum to handle the extreme power density.

About 6% of the fission yield is Mo-99 or about 2.8×10^{13} atoms of Mo-99/s/g of U-235. If the target is left in the reactor for about five half-lives, it will reach secular equilibrium with a rate of decay equal to the rate of production, *i.e.*, $Y = 2.8 \times 10^{13}$ decays per second or Bq. This is equivalent to $2.8 \times 10^{13}/3.7 \times 10^{10} \text{ Bq/Ci}$ or 760 Ci/g of separated HEU. This would be reduced to $93\% \times 760 = 700 \text{ Ci/g}$ of target material for a HEU target at 93% enrichment.

This is equivalent to $700 \times 0.22 = 150$ six-day curies per gram of HEU. This is at the very high end of production and a yield of about 50% to 70% is more typical. Using a yield of 100 six-day curies per gram of HEU leads to only 5 grams of HEU in the waste stream to make 500 six-day curies.

Photo-fission

An analysis comparable to the one above is presented here for comparison for an estimate of power per gram of target. One can calculate the yield using the same basic formula that was used for neutron fission but using some estimates of useful photon flux and an average cross section.

$$Y = N \times \sigma \times \phi$$

Where N = numbers of target atoms in one gram = $1/238 \times 6 \times 10^{23} = 2.5 \times 10^{21}$; $\sigma = 0.2$ barns = $2 \times 10^{-25} \text{ cm}^2$. An estimate of the photon flux is needed.

About 50% of the energy of a 50 MeV electron beam will be converted into bremsstrahlung with an energy spectrum from near zero up to 50 MeV. Perhaps 45% of that spectrum will overlap the giant dipole resonance of the uranium nucleus between about 10 and 20 MeV. Assuming that the 45% overlap is all at 15 MeV, then the total number of photons per mA of beam current (assuming 50 kW of beam power) is given by:

$$50 \text{ kW} \times 0.5 \times 0.45 = 11.25 \text{ kW of photons of 15 MeV}$$

$$11.25 \text{ kW} = 11.25 \text{ kJ/s} = 7 \times 10^{16} \text{ MeV/s}$$

$$7 \times 10^{16} \text{ MeV/s}/(15 \text{ MeV per photon}) = 4.7 \times 10^{15} \text{ 15-MeV photons per second}$$

and $Y = 2.4 \times 10^{12} \text{ f/s/g}$. Recall that the neutron fission rate was $4.6 \times 10^{14} \text{ f/s}$ per gram of U-235 in a typical reactor flux. The photo-fission rate per gram of U-238 in a modest 50 kW beam is lower by about a factor of 200. This estimate employs a conservative, unoptimized target design.

Using a 6% production of Mo-99 produces 1.44×10^{11} atoms of Mo-99 at saturation or 3.9 production curies per gram of uranium or 0.86 six-day curies per gram.

One watt of fission energy is produced by 3.1×10^{10} f/s which corresponds to $2.4 \times 10^{12}/3.1 \times 10^{10} = 78\text{W/g}$ of U-235. Creating 150 six-day curies (equivalent to estimates for one gram of HEU material via neutron fission) would need 200 grams of photo-fission target material at the high power density. However, there would be 11.25 kW of photons on that same gram of material. This power density is rather high and stretches present-day experience; there is room for substantial improvement in the photo-fission target design.

Survey of Yield Projections

The cumulative yields of Mo-99 from photo-fission of U-238 are about the same as those from thermal neutron fission of U-235 when considered on a “per fission” basis. Reported $^{235}\text{U}(n_{\text{thermal}}, F)$ yields are of the order of 6%.^{6,7,8} Cumulative ^{99}Mo yields from $^{238}\text{U}(\gamma, F)$ have been reported by several studies with some comparisons to $^{235}\text{U}(n_{\text{thermal}}, F)$.^{9,10}

Schmitt and Sugarman measured $^{\text{natural}}\text{U}(\gamma, F)$ mass yield curves with 48 MeV photons and determined peak and trough fission product distributions at 7, 10, 16, 21, 48, 100 and 300 MeV photon energies.¹¹ They normalize their measured yields to a 6.6% cumulative yield of Mo-99 at all photon energies and compare to a 6.8% yield from $^{235}\text{U}(n_{\text{thermal}}, F)$. The authors state, “The observed photo-fission yield curves are interpreted as a superposition of two components, a low energy (double- humped) curve and a high energy single-humped curve, produced by the absorption of high-energy photons.” Since Mo-99 falls at the peak of the lower mass double-humped curve, increasing photon energy has little effect on its cumulative yield. Photo-fission mass yield curves for natural uranium at 7-300 MeV photon energies are compared to the yield curve from $^{235}\text{U}(n_{\text{thermal}}, F)$ in Figure 2 of Schmitt and Sugarman.

In their study of independent fission yields from U-238 photo-fission with ≤ 23 MeV bremsstrahlung, Cuninghame *et al.* normalized production of Br, Nb, Cs and La nuclides to an assumed ^{99}Mo yield of 5.30% compared to 6.06% for $^{235}\text{U}(n_{\text{thermal}}, F)$.

Richter and Corell compared the fission mass yield curves from $^{\text{natural}}\text{U}(\gamma, F)$ ($\gamma \leq 16$ MeV) with those from $^{235}\text{U}(n_{\text{thermal}}, F)$. While no numerical comparison of cumulative Mo-99 yields is given, a graphical comparison of yield curves (Figure 1 of Richter and Corell) shows essentially equal yields at $A=99$. The reported Mo-99 cumulative yields were 4.94% for $\gamma \leq 10$ MeV and $(6.06 \pm 0.16)\%$ for $\gamma \leq 16$ MeV.

⁶A. Turkevich and J.B. Niday, Phys. Rev. 84(1) (1951) 52

⁷R.A. Schmitt and N. Sugarman, Phys. Rev. 95(5) (1954) 1260

⁸J.G. Cuninghame, M.P. Edwards, G.P. Kitt and K.H. Lokan, Nucl. Phys. 44 (1963) 588

⁹H.G. Richter and C.D. Corell, Phys. Rev. 95(6) (1954) 1550

¹⁰J.L. Meason and P.K. Kuroda, Phys. Rev. 142(3) (1966) 691; H. Thierens, D. De Frenne, E. Jacobs, A. De Clerq, P. D’hondt and A.J. Deruytter, Phys. Rev. C 14(3) (1976) 1058; E. Jacobs, H. Thierens, D. De Frenne, A. De Clerq, P. D’hondt and A.J. Deruytter, Phys. Rev. C 19(2) (1979) 422

¹¹See Schmitt and Sugarman.

A $(5.6 \pm 1.0)\%$ ^{99}Mo cumulative yield was reported for $^{238}\text{U}(\gamma, F)$ ($\gamma \leq 17.5$ MeV) by Meason and Kuroda.

The above values are summarized in Table C.1 along with total cumulative $A=99$ mass chain yields. While the independent fission yield of Mo-99 may be small, the cumulative yield is enhanced by feeding the relatively long-lived Mo-99 from short-lived $A=99$ progenitors produced in higher quantities. This is clearly demonstrated by comparing cumulative Mo-99 yields with $A=99$ yields.

Product	$^{235}\text{U}(n_{\text{th}}, F)$ Yield	$^{238}\text{U}(\gamma, F)$ Yield	E_{γ} (MeV)	Ref.
Mo-99	6.2			Turkevich & Niday
Mo-99	6.8	6.6	7-300	Schmitt & Sugarman
Mo-99	6.06	5.30	≤ 23	Cuninghame & Edwards
Mo-99		4.94	≤ 10	Richter & Corell
Mo-99		6.06 ± 0.16	≤ 16	Richter & Corell
Mo-99		5.6 ± 1.0	≤ 17.5	Meason & Kuroda
$A = 99$		6.48 ± 0.28	≤ 25	Thierens <i>et al.</i>
$A = 99$		6.76 ± 0.28	≤ 12	Jacobs <i>et al.</i>
$A = 99$		6.13 ± 0.26	≤ 15	Jacobs <i>et al.</i>
$A = 99$		6.17 ± 0.26	≤ 20	Jacobs <i>et al.</i>
$A = 99$		6.09 ± 0.25	≤ 30	Jacobs <i>et al.</i>
$A = 99$		5.90 ± 0.25	≤ 70	Jacobs <i>et al.</i>

Table D.1. Comparison of reported Mo-99 cumulative yields in terms of percentage of total fission yield.

Appendix E: Letters of Support

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www.mdsnordion.com



July 24, 2009

Dr. Timothy I. Meyer
Head, Strategic Planning and Communications
TRIUMF
4004 Wesbrook Mall
Vancouver, BC V6T 2A3
Canada

Dear Dr. Meyer,

MDS Nordion is a global leader in providing medical isotopes for molecular and diagnostic imaging, radiotherapeutics and sterilization technologies. As part of MDS Inc., one of the world's foremost global life sciences companies, MDS Nordion exports its products to more than 50 countries. Every day, MDS Nordion's products and services are used in hospitals and clinics, by large medical supply companies, biotechnology and pharmaceutical companies, and by food processors and manufacturers.

MDS Nordion has an exclusive (but presently disputed) long term contractual relationship with Atomic Energy of Canada Limited ("AECL") for the supply of isotopes. MDS has an on-going dispute with AECL and the Government of Canada regarding the contract and related matters.

Subject to MDS Nordion's legal rights, remedies and obligations, and if a transaction can be designed that respects MDS Nordion's rights and obligations, which we believe is achievable, MDS Nordion is pleased to provide a positive response to your request for our development collaboration on photo fission technology to produce medical isotopes from your proposal. MDS Nordion can provide radiochemistry expertise to develop and process samples to evaluate their compliance to commercial specifications.

Recognizing MDS Nordion's world wide expertise and reputation, we believe it is the ideal partner for the development of medical isotope production technologies for the Canadian market.

If you have any questions, please do not hesitate to call me.

Yours very truly,

A handwritten signature in black ink, appearing to read "Steve West", written over a horizontal line.

Steve West
President

AAPS
Advanced Applied
Physics Solutions



ETPP
Exploitation des Techniques
de Pointe en Physique

21 July, 2009

Dr. Nigel Lockyer,
Director,
TRIUMF,
4004, Wesbrook Mall,
Vancouver, B.C.
V6T 2A3

Dear Dr. Lockyer:

In June 2009 the Government of Canada, under Natural Resources Canada (NRCan), established an Expert Review Panel on Medical Isotope Production to report on "new options for secure medium to long-term supply of medical isotopes for the Canadian health care system, specifically, Tc-99m and its generators". This Expert Panel has duly requested that interested parties submit Expressions of Interest for innovative methods of producing medical isotopes, notably Tc-99m and its generators.

On October 19 and 20, 2008 TRIUMF and its commercial arm, AAPS, jointly sponsored a Workshop at TRIUMF that brought together experts on medical isotope production. Central to the discussion of the Workshop was the TRIUMF proposal to produce Mo-99 using an e-linac accelerator and a photo fission converter. This creative approach would avoid the use of HEU and could supply the entire Canadian market with Mo-99.

AAPS fully supports this TRIUMF proposal for Mo-99 production using photo fission, and believes that this approach could solve the supply problems that currently exist in Canada and internationally. AAPS is committed to collaborate with TRIUMF on this exciting and challenging project, recognizing that the initial phase will involve some advanced research and development that will be focused within TRIUMF's mandate and expertise. The ultimate commercial development will evolve from TRIUMF through AAPS, and may ultimately incorporate a process that AAPS is developing for increasing specific activity, as part of an integrated system.

Sincerely,

Philip L. Gardner
President and CEO,
AAPS,
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Vancouver, B.C.
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