Annex A. Broader responses to the 2009/10 Mo-99/Tc-99m shortage

Canada

The Ad Hoc Group used a SWOT (i.e. strengths, weaknesses, opportunities and threats) framework to guide a broader set of recommendations, which are summarised as:[1]

1. "Ensure efficient and effective communication with the medical community and the public.
2. In decision-making, ensure a balance between the health and safety of the public and the health outcomes of individual patients.
3. Assure appropriate physician participation and input into the decision-making process.
4. Minimise the potential for future interruptions in the supply of medically necessary materials and equipment.
5. Mitigate the consequences of unpredicted disruptions.
6. Enhance the capability of suppliers and end users to respond to interruptions in supply.
7. Establish a clear and appropriate alignment of authority and accountability for the management of medical radioisotopes."

The following is a summary of the strategies presented at the Federal/Provincial/Territorial workshop hosted by Health Canada.

Communications

- A list of key personal were identified- e.g. NM Physicians, Senior NM Technologist, and Radiopharmacy, middle and senior health care sector mangers and key government contacts.
- E-mail communications trees were established.
- Ad hoc teleconferences were held as the crisis evolved.

Efficient Rationing

- Use of more than one Mo-99 generator vendor (there were two major vendors at the time) increased the probability of getting some activity in a given week.
- Maximise use of available activity (i.e. reduce waste due to decay) via:
    - Enhancing volumes when "fresh" generators arrived.
    - Extended weekday shifts (i.e. work into the evening).
    - Weekend shifts.
- Enhanced physician protocolling of requisitions to ensure that patients were prioritised by clinical need titrated against Tc-99m availability taking into account the utility of alternate diagnostic imaging options. Studies which had immediate impact on medical management, and for which NM was the ideal choice, were preferentially selected. An example would be pre-surgery sentinel lymph

node studies for breast cancer patients or gated cardiac studies (MUGA) prior to cancer chemotherapy.

- Sharing available activity between sites allowed for priority to be given to higher risk acute patients versus elective studies.
- Stratify response to the local, regional or provincial levels depending on the level of shortages.
- Prioritising NM studies to be done at tertiary care sites reduced loss of activity due to multisite distribution and decay during transportation.
- Co-ordination with other imaging modalities (e.g. US, CT and MRI) to ensure enhanced capacity to accommodate increased demand (e.g. CT pulmonary angiograms versus NM VQ scan to rule out pulmonary embolism).

Thinking outside the box

- Manitoba (MB) was the only Canadian Province to seek alternate Mo-99 generator sources outside of the normal commercial supply chain. Mo-99 generators were sourced from Argentina and, from a regulatory point of view, this was made possible due to the ability of the Winnipeg central radiopharmacy to conduct all required quality assurance testing and prove the product met the United States Pharmacopeia standards for Mo-99 / Tc-99m. This strategy considerably ameliorated the impact of isotope shortages in MB.

Regulatory

- Health Canada streamlined emergency access and approval for products not yet licensed in Canada (e.g. ^{18}F as NaF, for bone scans).
- Health Canada also made the drug Special Access Program (SAP) more efficient for “orphaned” radiopharmaceuticals. These radiopharmaceuticals, such as mebrofenin (used for liver imaging) and DMSA (used for kidney imaging) have relatively small markets in Canada and supply chains are not as stable as other NM radiopharmaceutical kits. At the time an SAP application was required for each patient which did not allow for efficient scheduling and batching of product/activity. A request was made for a generic “future use” SAP and this was generally well received by the regulator.
- The Government of Canada ensured co-operation that would allow the planning of preventive maintenance closures of major ^{99}Mo sources/reactors to prevent avoidable shortages in global supply.

Key challenges

- Short shelf life depending on the produced radiopharmaceutical.
- Transportation challenges (e.g. ground, air and ferry transport), especially during inclement weather.
- Uncertainty regarding the length of the NRU outage.
- Complicated, and at times limited, timely communication between various jurisdictions during the medical isotope shortage crisis.

Europe

European NM providers were faced with a 20% – 40% reduction in the delivery of NM studies. This was due to the simultaneous unexpected shutdown of the NRU combined with a planned shutdown of the HFR

in Petten.[2] One of the lessons learnt from this medical isotope crisis was to globally co-ordinate planned preventive maintenance time to minimise the effects on supply.

As an outcome the European Commission and stakeholders established on 29 June 2012 a **European Observatory on the Supply of Medical Radioisotopes**, aimed at bringing together all relevant information to the decision makers in the EU institutions and national governments in order to assist them in defining strategies and policies for their implementation.[3]

The European Observatory general strategic objectives are:[3]

- "to support secure Mo-99/Tc-99m supply for the medium and long term, across the EU taking into account the worldwide need and supply,
- to ensure that the Mo-99/Tc-99m supply issue is given high political visibility in international and national institutions, organisations and bodies,
- to encourage the creation of a sustainable economic structure of the Mo-99/Tc-99m supply chain through supporting the implementation of the full-cost recovery methodology developed by OECD/NEA High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR),
- to establish periodic reviews of the Mo-99/Tc-99m supply chain and capacities, with all stakeholders across the EU, taking into account the worldwide needs and supply capacities, and to forecast future needs."

Nuclear Medicine Europe (NMEu) through their Security of Supply Working Group have partnered with the European Commission and regularly monitor the planning and availability of irradiation and processing capacity and work to mitigate risks such as the recent temporary supply interruptions at the NTP Radioisotopes (South Africa) production facility.

Global

In 2009, the OECD Nuclear Energy Agency (NEA) established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR). The OECD/NEA Steering Committee for Nuclear Energy subsequently confirmed its support for the policy approach suggested by the HLG-MR, which is based on the following six principles: [4]

Principle 1: All 99mTc supply chain participants should implement full-cost recovery, including costs related to capital replacement.

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

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

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

These changes should occur expeditiously, recognising however that time will be required to allow for the market to adjust to the new pricing paradigm.

Principle 4: Given their political commitments to non-proliferation and nuclear security, governments should provide support, as appropriate, to reactors and processors to facilitate the conversion of their facilities to

low enriched uranium or to transition away from the use of highly enriched uranium, wherever technically and economically feasible.

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

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

The OECD/NEA Steering Committee for Nuclear Energy called on governments and industry to work together to implement these principles in a timely and effective manner, recognising the need for an internationally consistent approach to ensure the long-term secure supply of medical radioisotopes.

Eleven countries (Australia, Belgium, Canada, France, Germany, Japan, the Republic of Korea, the Netherlands, Poland, the Russian Federation, South Africa, Spain, the United Kingdom and the United States of America) signed a Joint Declaration on the Security of Supply of Medical Radioisotopes "which seeks to ensure the security of supply of the most widely used medical radioisotope, molybdenum-99 (^{99}Mo)."[5]

"WE COMMIT, with the aim of jointly promoting an internationally consistent approach to ensuring the long-term secure supply of medical radioisotopes, to implement the HLG-MR principles in a timely and effective manner, and to:

- Take co-ordinated steps, within our countries' powers, to ensure that ^{99}Mo or ^{99m}Tc producers and, where applicable, generator manufacturers in our countries implement a verifiable process for introducing full-cost recovery at all facilities that are part of the global supply chain for ^{99m}Tc;
- Encourage the necessary actions undertaken by ^{99}Mo processing facilities or ^{99m}Tc producers in our countries to ensure availability of reserve capacity capable of replacing the largest supplier of irradiated targets in their respective supply chain;
- Take the necessary actions to facilitate the availability of ^{99m}Tc, produced on an economically sustainable basis, as outlined in the HLG-MR principles;
- Encourage all countries involved in any aspect of the ^{99m}Tc supply chain, and that are not party to the present Joint Declaration, to take the same approach in a co-ordinated manner;
- Take the necessary actions described above by the end of December 2014 or as soon as technically and contractually feasible thereafter, aware of the need for early action to avoid potential shortages of medical radioisotopes that could arise from 2016;"

To report on an annual basis to the OECD Nuclear Energy Agency (NEA) on the progress made at the national level and support an annual review of the progress made at the international level, both in light of this Joint Declaration."[5]

The NEA has formed the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) which is referenced in the third bullet above. The HLG-MR has the main objective "…to strengthen the reliability of ^{99}Mo and ^{99m}Tc supply in the short, medium and long term…" and has broad representation from producing and end-user countries and agencies such as the European Commission (Euratom Supply Agency) and the International Atomic Energy Agency (IAEA).[5]