Explaining the shortage of medical radioisotopes
by C. Westmacott

As part of its work to examine the problems and to suggest possible solutions for ensuring the long-term, reliable supply of molybdenum-99 (\(^{99}\text{Mo}\)) and technetium-99m (\(^{99m}\text{Tc}\)), the NEA undertook an economic study on the \(^{99}\text{Mo}\) supply chain. This article presents an overview of the findings from The Supply of Medical Radioisotopes: An Economic Study of the Molybdenum-99 Supply Chain.

The supply chain and historical implications

The supply chain consists of uranium target manufacturers, reactor operators who irradiate the targets to create \(^{99}\text{Mo}\) as part of the fission reaction, processors who extract the \(^{99}\text{Mo}\) from the irradiated targets and purify it to produce bulk \(^{99}\text{Mo}\), generator manufacturers who produce generators with the bulk \(^{99}\text{Mo}\), and radiopharmacies and hospital radiopharmacy departments who elute \(^{99m}\text{Tc}\) from the generator and couple it with “cold kits” to prepare radiopharmaceutical doses for nuclear medical imaging of patients (see Figure 1). Given the short half-lives of \(^{99}\text{Mo}\) (66 hours) and \(^{99m}\text{Tc}\) (6 hours), the logistical arrangements have to be quick and predictable, since the economics and medical utility of \(^{99}\text{Mo}/^{99m}\text{Tc}\) depend on minimising decay losses.

Historically, only five reactors have been producing 90-95% of global \(^{99}\text{Mo}\) supply, all of which are over 43 years old and subject to longer and more frequent planned and unplanned shutdowns. All the major producers irradiate targets using multipurpose research reactors, which were originally constructed and operated with 100% government funding, mainly for research and materials-testing purposes. When \(^{99}\text{Mo}\) production started, the reactors’ original capital costs had been paid or fully justified for other purposes. As a result, \(^{99}\text{Mo}\) was seen as a by-product that provided another mission for the reactor that could generate extra revenue to support research. This resulted in:

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

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*Mr. Chad Westmacott ([chad.westmacott@oecd.org](mailto:chad.westmacott@oecd.org)) works in the NEA Nuclear Development Division.*

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Figure 1: \(^{99}\text{Mo}\) supply chain

![Figure 1: \(^{99}\text{Mo}\) supply chain](image-url)
As a result, prices paid to the reactor operator were too low to sustainably support the portion of reactor operations attributable to $^{99}$Mo production, did not even cover short-run marginal costs in some cases, and did not provide enough financial incentive to support the replacement or refurbishment of ageing reactors.

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

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

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

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

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

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

**Governments are re-examining their subsidies**

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

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

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

The LUCM calculations indicated that significant price increases are necessary in the upstream supply chain in order for the latter to become economically sustainable. Reactor irradiation service prices would need to increase from EUR 45 per six-day curie (calculated from end of processing) to a range of approximately EUR 55 to 400. However, the analysis also finds that there is very little effect on the prices per patient dose. The reactor share in the final reimbursement rates would increase from approximately EUR 0.26 per procedure at pre-shortage prices to between EUR 0.33 and EUR 2.39 (see Table 1).

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

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

**Conversion to LEU would also have small effects on end users**

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

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

**Recommendations and options**

The study makes a number of recommendations and investigates options to assist decision-makers in restructuring the supply chain.

**Government role in supporting the industry**

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

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

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

**Paying for the full costs of 99Mo**

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

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

Under a social contract of increased commercial funding, more appropriate market prices will be required to cover full costs. Reactor operators will need to require a substantial increase in prices, with commercial-based pricing becoming the norm in industry contracts over time.
For reserve capacity, end users should demand reliable supply and be willing to support it through a “reliability premium”. This demand and remuneration should flow back through the supply chain, resulting in the upstream providing reserve capacity and being paid for it. However, it is possible that there may be a role for government intervention, requiring minimum levels of reserve capacity.

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

Changes must occur to secure long-term supply

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

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

For more information regarding NEA work on medical radioisotopes and to read the full economic study, please visit the NEA website: www.oecd-nea.org/med-radio/.

Reference