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Status report on HEU/LEU transition of reactor fuel and target material of medical isotopes producing research reactors

1. Supplies of medical reactor isotopes

production methods
Currently more than 80% of the medical radioisotopes are produced by research reactors. The remaining isotopes are made by particle accelerators, mostly with circular accelerators (cyclotrons) and sometimes with linear accelerators (linacs), or by other methods.

technetium-99m (Tc-99m): workhorse of the medical use of radioisotopes
The most common radioisotope used in diagnosis is technetium-99m (in technical jargon: Tc-99m), accounting for at least 80% of all nuclear medicine procedures worldwide. The European Association of Nuclear Medicine (2008) mentions the figure of 90% of all diagnostic procedures in Europe.

production of reactor isotopes
For many years, at least until 2007, around 95% of the worldwide medical reactor-produced isotopes were made by five aged research reactors in Belgium, Canada, France, Netherlands and South-Africa . The Canadian NRU reactor and the Dutch HFR together supplied for about 80% in the worldwide demand of molybdeen-99 (Mo-99), of which 60% was delivered by the Canadian company MDS Nordion in Canada, and 20% by the US company Covidien (Mallinckrodt, Tyco) in the Netherlands. The other three reactors (20%) supplied Europe and parts of Asia and also served as back-ups when one of the large reactors broke down because of maintenance. This was especially the case from 2007, when these five reactors were frequently shut down for a longer period of time and the first of a series of shortages in the supply of isotopes started. All these reactors are 45 to 54 years old. The life span extension of the reactors cause - and will inevitably remain to cause – problems due to age. smaller reactors could increase their production capacity, such as the Maria research reactor in Poland, but none of these reactors has the capacity of the HFR or the NRU to take over the production rate of radioisotopes. Radioisotopes production with these wobbly nuclear reactors has been appeared very uncertain in the past years.

Currently, according to an update of the World Nuclear Association of October 2011, Of fission radioisotopes, 40% of Mo-99 (for Tc-99m) comes from MDS Nordion, 25% from Covidien, 17% from IRE and 10% from NTP. (By the way, for I-131, the second most used medical isotope, 75% is from IRE, 25% from NTP. Over 90% of the Mo-99 is made in five reactors: NRU in Canada (40%), HFR in Netherlands (30%), BR-2 in Belgium (9%), Osiris in France (5%), and Safari-1 in South Africa (10%). Canadian 2008 data gives 31% for NRU.

2. The main research reactors used by large and regional producers of medical isotopes, their type of fuel and target material

Large producers

1. MDS Nordion (Canada)

Reactor(s) / Location(s)	*reactor fuel(s) / target material(s)*
NRU / Chalk River, Canada	HEU / HEU

Canada will stop entirely with isotopes production based on nuclear reactors. National Research Universal (NRU) reactor will be in service until October 31, 2016. The license was recently extended to 2016, including the production for isotopes. It could be extended with a few years, but not for isotopes production. The new MAPLE reactors should be in service with HEU, but they never came into operation due to failures. A budget of $48m was allocated for investments in R&D of particle accelerator technology for isotopes production. The fuel and target material of NRU will not be converted from HEU to LEU, because the NRU is approaching its expiration date.

New developments
In September 2010 the Russian joint venture Isotop-NIIAR signed a framework agreement with MDS Nordion to explore commercial opportunities outside Russia, initially over ten years. [See under: 6. Russian suppliers of medical isotopes]

2. Covidien (United States)

Reactor(s) / location(s)	*reactor fuel(s) / target material(s)*
HFR / Petten, Netherlands	LEU / HEU
Maria/ Swierk, Poland	HEU / HEU

[HFR] NRG, the operator of HFR, has announced plans to construct the Pallas reactor, a new facility with Mo-99 production capabilities. Use of LEU targets are planned from 2020 when the Pallas reactor has to come into operation. [Note: Most literature mentions the year 2016 or 2018, however Ronald Schram from NRG, Petten, noticed on a symposium of engineers on June 24, 2011, that Pallas will come into operation in 2020, HvdK] Covidien has said it will first develop LEU production techniques for Pallas then investigate the use of those techniques for the conversion of targets at HFR if it is still operating. Covidien has not provided specifics on its LEU conversion research.

[Maria] In 2007, during a supply crisis in the molybdenum 99 market, Poland's MARIA reactor increased its HEU-based production of molybdenum 99 to fill the gap. Though the crisis has passed, the Polish reactor does not appear to have reduced its production. The irradiated HEU targets are sent to the facilities of Covidien in Petten, Holland. Poland is on track to convert reactor fuel to LEU in mid-2012. Though the reactor would not face technical obstacles to switch to LEU targets, it’s not clear when the conversion will take place. According to the HLG-MR interim report (OECD/NEA 2010) the reactor started producing Mo-99 for global distribution in February 2010. According to information from Covidien they also import irradiated HEU targets from the BR-2 reactor in Belgium and other European research reactors as well (Germany, France).

New developments

In January 2009 Babcock & Wilcox (B&W) announced an agreement with Covidien to produce Mo-99 sufficient for half of US demand, if a new process involving an innovative reactor and separation technology is successful. They plan to use Aqueous Homogeneous Reactor (AHR) technology with LEU in small 100-200 kW units where the fuel is mixed with the moderator and the U-235 forms both the fuel and the irradiation target. A single production facility could have four such reactors. B&W and Covidien expect a five-year lead time to first production.

3. Institut National des Radioéléments – IRE (Belgium)

Reactor(s) / location (s)	*reactor fuel(s) / target material(s)*
BR-2 / Mol, Belgium	HEU / HEU
Osiris / Saclay, France	LEU / HEU
Orphée / Saclay, France	HEU / HEU
FRM-2 / Munich, Germany	HEU / HEU
LVR-15 / Rez, Czech Republic	LEU / HEU

[BR-2] The BR-2 reactor is listed by the US General Accounting Office (July 2004) as one of the 31 reactors that “need HEU fuel to operate and conduct research until LEU fuel with the right performance characteristics is developed.” Meanwhile many tests have been done and in the past half year “the simulation of the a BR2 test was undertaken to support the safety analysis of the conversion of the BR2 research reactor to LEU fuel.”
IRE has previously stated that it is not pursuing conversion to LEU targets, nor has it discussed any research regarding LEU technologies, though the National Academy of Sciences believes conversion at Petten by Covidien would likely force IRE to convert. [Alex Fay, 2011]

[Osiris] The Osiris 70 MW reactor is due to shut down in 2015.

[Orphée or Orpheus] In 1998, Russia shipped 228 kg weapons grade HEU to France, and a second one of undisclosed size in 2001 that will fuel among others France’s Orphee reactor for the remainder of its life.

[FRM-2] In 2001, Russia shipped about 400 kg of weapons grade HEU to France to be fabricated into a 10-year supply of cores for Germany’s new FRM-2 reactor. The reactor is operated by Technical University in Munich since 2005.

In 2010 the Minister-President of Bavaria announced the extension of the conversion [HEU to LEU fuel – HvdK] deadline until at least 2018 due to the unavailability of high density fuel. At present, it is unclear whether the fuel will be available even by 2018. All other German research facilities using HEU have been converted to LEU or shut down. [NTI, July 22, 2011]

It is planned to start Mo-99 production from 2014 and is able to supply 50% of European needs when operating. [NRG, 2011]

[LVR-15] The LVR-15 reactor in Czech Republic started producing Mo-99 for global distribution in May 2010. Conversion to LEU targets is investigated.

4. NTP Radioisotopes, Necsa (South Africa)

Reactor(s) / location(s)	*reactor fuel / targets*
Safari I / Pelindaba	LEU / LEU

[Safari] After years of resistance South Africa has experienced a fast and successful transition from HEU to LEU with support of the Argonne National Lab in the US, within a few years. By which it demonstrates that it can be done very quickly – certainly within less than

five years. According to information from NECSA: “In 2006 the test irradiations of LEU fuel commenced and in September 2008, conversion from HEU to LEU started and completed 25 June 2009.”
During the 2009-10 supply crises, South Africa's (NECSA) Safari was able to supply 25% of the supply of Mo-99.

Regional producers

5. Australian Nuclear Science and Technology Organisation (ANSTO)

Reactor(s) / location(s)	*reactor fuel (s) / target material(s)*
OPAL / Lucas Heights, South Sydney	LEU / LEU

Australia has been expanding LEU-based medical isotope production after its new OPAL reactor came on line in 2007. Australia's Opal reactor has the capacity to produce half the world supply of it, but a much larger Mo-99 production facility would be required.

6. Argentina

Reactor(s) / location(s)	*reactor fuel (s) / target material(s)*
RA-3 / Ezeiza Atomic Center (Ezeiza -Buenos Aires)	LEU / LEU
RA-6 / Ezeiza Atomic Center (Ezeiza -Buenos Aires)	LEU / LEU

In 2002, Argentina completed conversion from HEU to LEU targets in the production of medical isotopes. Currently, Argentina is a global leader in high-density LEU fuel fabrication. LEU targets have been irradiated, disassembled, and processed in Australia, Argentina, and Indonesia. Argentina has been exporting isotopes produced using this technology for several years. The IAEA has been a major supporter of these activities. In 2010, the Agency launched an International Working Group to provide assistance in the conversion from HEU to LEU by Mo-99 producers. Additionally, research reactor coalitions have been created to pool regional efforts to produce non-HEU Mo-99.

Another LEU-based commercial scale facility has been constructed in Egypt. Several other states have set up or explored processes utilizing LEU targets in the production of Mo-99 for both domestic and export purposes. (Algeria, Indonesia)

7. Russian suppliers of medical isotopes

Reactor(s) / location(s) *reactor fuel (s) / target material(s)*

Karpov VVR-T / Obninsk	HEU / HEU
Research Institute of Atomic Reactors (RIAR or NIIAR) / Dimitrovgrad	
High-Flux Research Reactor SM	HEU / HEU
Pool-Type Reactor RBT-6	HEU / HEU
Pool-Type Reactor RBT-10	HEU / HEU

In 2011 99% of Russia’s demand for Mo-99 was met by production at Obninsk, just outside of Moscow, using one processing facility at the Karpov Institute of Physical Chemistry. The Karpov VVR-T research reactor uses HEU fuel and irradiates HEU targets produced at the institute. The Mo-99 produced is intended for domestic use only and therefore Russia has been considered a regional producer instead of a major producer.

In 2012 this situation will change. The Research Institute of Atomic Reactors (NIIAR or RIAR, with 3 reactors) and Trans-regional Izotop Association (VA Izotop) have established a joint venture, Isotop-NIIAR to produce Mo-99 at Dimitrovgrad from 2010. Phase 1 of the Mo-99 production line was commissioned in December 2010, reaching a capacity of 1700 TBq/yr in May 2011, and Phase 2 to take capacity to 4800 TBq/yr in 2012, according to Rosatom. VA Izotop is authorized since 2009 by Rosatom to control all isotope production and radiological devices in Russia. This JV is aiming to capture 26% of the world market for Mo-99 by 2012. In September 2010 JSC Izotop signed a framework agreement with MDS Nordion to explore commercial opportunities outside Russia on the basis of this Isotop-NIIAR JV, initially over ten years.

Regarding potential conversion from HEU to LEU, in August 2010 NIIAR Deputy Director Rostislav A. Kuznetsov told a conference that it is possible in Phase III of expansion. There is no further information about such potential. The existing literature indicates no technical obstacles to such conversion using LEU. In regard to economic obstacles, however, Russia’s first priority is expanding market share quickly rather than delaying expansion for conversion. After it establishes market share, it may be more willing to consider conversion to LEU. In regard to political obstacles for conversion from HEU to LEU, Russia’s past cooperation in other threat reduction initiatives, such as the Russian Research Reactor Fuel Return Program, suggests that they would not be opposed to converting if it is economically feasible. However, further research in this area would be useful to determine whether or not the Russian government and Rosatom would be willing to convert to LEU.

8. Japan

Japan has begun research on technology to use commercial nuclear power plants (NPPs) to manufacture medical isotopes. The project is aimed at producing Mo-99 by irradiating molybdenum with neutrons in boiling water reactors (BWRs). Japan has the second largest demand for Mo-99 following the US, and now depends entirely on imports. Hitachi-GE Nuclear Energy Ltd is conducting the research. [McCloskey Nuclear Business, January 2011]

US DoE's National Nuclear Security Agency [NNSA] is funding a project for GE [General Electric] Hitachi Nuclear Energy to build a reactor for this purpose. The goal of the project is to use a domestic nuclear power reactor to generate domestic medical isotopes. [..] The GE Hitachi project is one of four that are funded by a NNSA initiative that requires that 50 percent of the reactor-produced medical isotopes used in the US, should be created domestically by 2013.
http://www.healthimaging.com/index.php?option=com_articles&article=26770&publication=10&view=portals

9. China

Two research reactors, among which the HFETR at Chengdu used for isotopes production, have been converted to LEU fuel in 2007. No information about HEU / LEU target conversion.

10. Romania

The TRIGA reactor operated by the Institute for Nuclear Research in Pitesti, Romania has a potential to contribute to global Mo-99 supply chain. In the last years, the reactor was subjected to an ample upgrading program, its full HEU/LEU fuel conversion has been accomplished in 2006 and it is foreseen to be operated till 2030. HEU/LEU target conversion has been accomplished recently or will be done in 2012.

11. France

In France, Osiris will be shut down when the Jules Horowitz reactor (JHR) in Cadarache becomes operational. This is expected to be the case in 2014-2015. There should therefore be no discontinuity in irradiation facilities in France provided that the price asked for irradiating U targets in the JHR is commercially acceptable. The JHR will use LEU fuel and LEU targets. Planned capacity: 25% of European needs when operating, 50 % if needed.

12. Egypt

The ETRR-2 reactor uses LEU fuel and will use LEU targets for isotopes supplies to the domestic market in the nearby future.

13. United States

The US aims to production based on reactors with LEU (fuel and targets) and on particle accelerators.

NNSA's Global Threat Reduction Initiative (GTRI) is working to accelerate the development of LEU fission technology, neutron capture technology, and accelerator technology to produce Mo-99 in the United States. GTRI's four cooperative agreement partners are:

- B&W Technical Services Group to develop LEU Solution Reactor technology
- GE Hitachi Nuclear Energy to develop neutron capture technology
- NorthStar Medical Radioisotopes to develop accelerator technology
- Morgridge Institute for Research to develop accelerator technology with LEU fission

November 2011 factsheet: www.nnsa.energy.gov/mediaroom/factsheets/factsheet20100125

Also in the USA, the University of Missouri is reported to be planning to produce half of US requirements of Mo-99 at its research reactor using LEU targets by 2012.

Appendix
Current situation in Europe and the near future

The main problems connected to medical isotopes production based on HEU have been in Europe where some producers don't want to convert in the nearby future. There is no serious investment in other production methods than reactors. Other reactors are used to set off the shortages, among which the Polish HEU using Maria reactor.

Covidien and IRE are receiving support from the NNSA and are working in the direction of conversion. IRE estimates that full conversion could take 6-7 years if they began immediately. However, according to IRE, conversion is not yet economically viable due to other technical and economic obstacles. Belgium and the Netherlands have declared their support for conversion as part of the Nuclear Security Summit (NSS), but neither government has provided tangible support to the production companies.

The efforts of the US, Belgium, and Netherlands are particularly significant because, historically, the US and Europe have accounted for the large majority of Mo-99 demand. This demand has been met by a small number of suppliers: As of 2009, Nordion of Canada, Covidien of Netherlands, and IRE of Belgium provide nearly 90% of the demand.

Regional suppliers, including Comisión Nacional de Energía Atómica (CNEA) of Argentina, NTP of South Africa, and the Australian Nuclear Science and Technology Organisation (ANSTO) of Australia, produce Mo-99 on a smaller scale and, until very recently (in periods of shortages), have not been involved in the global supply network. Nordion, Covidien, and IRE all produce Mo-99 by the same general process: irradiation of HEU targets, dissolution of the irradiated targets, and purification of Mo-99 from the dissolved target.

Estimates of the costs associated with conversion to LEU targets suggest that conversion is viable with a minor increase in the price per dose of the radiopharmaceutical. One cost estimate for the conversion of Covidien's facilities at Petten is $10 million, a cost that could be offset by an increase in the price of the radiopharmaceutical of less than 1%. It should be noted, however, that the industry has stated that the National Academy of Sciences underestimated these conversion costs, as well as the regulatory hurdles incurred by conversion.

Additional estimates of the costs along the supply chain were made by the OECD High-level Working Group on Security of Supply of Medical Radioisotopes (HLG-MR) in its interim report. Based on these estimates, it was concluded that even substantial increases in reactor costs to the producers would not result in substantial increases in the patient cost of the radiopharmaceutical, although this report did not explicitly address the effects of conversion on costs along the supply chain.

Belgium and Netherlands, among other countries, are effectively subsidizing Mo-99 production and artificially reducing the reactor costs to Covidien and IRE. These subsidies are the reason that the Mo-99 market is currently deemed unhealthy and unsustainable. Upon publication of the final
HLG-MR report, these subsidies will be scaled back and reactor costs increased according to recommendations in the report. The market value of the reactor operations could be 5-7 times higher than current costs, according to Mr. Seeverens (NRG).