Maria Research Reactor Announcement

Q. What is this announcement?
A. Covidien and Poland’s Institute for Atomic Energy (IAE POLATOM) are announcing an agreement that will provide an additional resource for the critical medical isotope, now in short supply, used in 80 percent of the world’s 35 million nuclear medicine diagnostic procedures. The agreement will add IAE POLATOM’s Maria Research Reactor (Maria) to the global supply chain for molybdenum 99 (Mo 99) from which the medical isotope technetium 99m (Tc 99m) is derived. More than a million additional patients are expected to benefit from this additional supply in just the first six months.

Q. Why is this agreement important?
A. The agreement brings the first new reactor into the worldwide supply chain in more than a decade to help meet the demand for medical isotopes at a time when shutdowns of two major medical isotope reactors have led to critical shortages.

Q. How soon will this new supply result in additional Tc 99m for nuclear medicine diagnostic and functional studies?
A. Recent tests completed at Covidien’s Mo 99 processing facility in Petten suggest Tc 99m derived from Mo 99 produced in Poland could be commercially available to meet European demand within 30 days. Approval from the U.S. Food and Drug Administration is pending for use in the United States, and from Health Canada for use in Canada. Until approval is received in the U.S. and Canada, Covidien’s overall available Mo 99 will be equitably distributed globally—shifting supply from current sources when needed so all regions may share the benefit of this new reactor source—as we have done throughout this situation.

Q. How long have Covidien and IAE POLATOM been working on this agreement?
A. More than six months.

Q. How much experience does IAE POLATOM have with medical isotope production?
A. The Radioisotope Centre POLATOM was created in 1990 and has more than a decade of experience in the production of a wide array of medical isotopes.

Q. How does Maria compare to the other major medical isotope reactors in the global supply chain related to age?
A. Maria is located approximately 30 km southeast of Warsaw, and first operated from 1975 until 1985, when it was taken offline for a complete redesign. It resumed normal operations in 1993. Maria is considered to be a relatively new reactor compared with the other five aging reactors that supply most of the world’s medical isotopes.
Q. Was it difficult to bring IAE POLTATOM and Maria into the worldwide supply chain of medical isotopes?
A. Completing this agreement required significant technical engagement, investment and cooperation between Covidien and IAE POLATOM. It also required the acquisition of more than 20 licenses and permits from multiple regulatory agencies in five European nations. Both Covidien and IAE POLATOM applaud all who were involved for their prompt assistance to bring this critical supply of medical isotopes to patients in need as quickly as possible.

Q. Will the additional Mo 99 from Maria completely offset the combined shutdowns of the HFR and NRU reactor?
A. No. Adding Maria to Covidien’s global supply chain is expected to help Covidien to meet the needs of more than one million additional patients in just the first six months after the reactor begins supplying Mo 99. Our efforts also continue toward maximizing Mo 99 supply arrangements with all viable sources. The combined use of Mo 99 from the Maria, BR2, OSIRIS and Safari reactors improves the outlook for the coming months, but we estimate intermittent ability to fully meet existing customer orders mixed with some periods of more serious shortages for Tc 99m generators. This variability will be due to already scheduled brief maintenance shutdowns of the remaining Mo 99 reactors, including Maria.

However, the supply produced by Maria will be especially helpful to ease certain periods of extreme isotope shortage we anticipate when some of the other operating reactors are unavailable, improving availability to patients.

Q. Will the access to Maria for irradiation of targets to produce molybdenum 99 be restricted to Covidien?
A. Covidien has invested in Maria with infrastructure improvements and equipment necessary to enable it to irradiate targets for the production of molybdenum 99. We have exclusive rights to the irradiation capacity made possible through this investment for the term of our agreement. Covidien also has preferential rights to any additional irradiation capacity IAE POLATOM may offer during the term. At this time, the Mo 99 supplied by Maria will only be utilized by Covidien at our processing facility in the Netherlands.

Q. Will Maria remain a supply option for Covidien in the future, or is it only a short term back-up supply?
A. Maria will continue to be an option for Mo 99 supply for Covidien in the future.

Reactor Shutdowns

Q. Do you believe the Canadian NRU reactor will truly return to service?
A. AECL, operator of the National Research Universal (NRU) reactor, states the repairs are currently expected to be complete in April, 20101.
Q. What is Chalk River and who operates the facility?
A. The NRU reactor is a Canadian nuclear-research facility located near Chalk River, Ontario, and sometimes referred to simply as “Chalk River” or “CRL”. The facility is operated by Atomic Energy of Canada Limited (AECL).

Q. Why is the planned 2010 shutdown at the HFR necessary?
A. The High Flux Reactor (HFR) in the Netherlands is scheduled to go offline beginning February 19, and expected to be shut down for 22 to 26 weeks for extensive planned maintenance work by government directive. In 2009, the Dutch government granted permission for HFR to continue operation (inclusive of periodic maintenance) only until March 1, 2010. Covidien will continue bolstering our arrangements with the remaining online reactors in the coming months to obtain the maximum Mo 99 available, doing everything possible to minimize patient impact during this shutdown.

In an effort to maximize patient access to Tc 99m, the five major Mo 99 reactors share maintenance schedules and coordinate scheduling required maintenance and refueling, and also processing of other targets to meet contractual obligations. The 2010 HFR shutdown has been scheduled for months. Regulatory obligations demand these maintenance schedules occur as scheduled without deviation—even in situations where global supply would be further challenged.

Maria adds a sixth supply source to the global supply chain, and more than a million additional patients are expected to benefit from this new resource in just the first six months.

Q. What is the expected lifespan of the HFR in Petten once the 2010 repairs are complete?
A. According to NRG, the operational life span of the HFR extends until after 2015. NRG is working on the design and construction of a new nuclear reactor, Pallas, which is targeted to replace HFR.

Q. Does Covidien own the HFR in Petten?
A. No, the HFR is owned by the Joint Research Center (JRC) of the European Union and operated by the Nuclear Research and consultancy Group (NRG). Covidien has targets that are irradiated at the HFR to produce Mo 99.

Covidien does own two manufacturing sites across the street from the HFR; one processes irradiated uranium targets to produce Mo 99, and the second processes the Mo 99 into Tc 99m generators that are distributed in Europe, the Middle East and Africa, as well as areas in the Asia-Pacific region.

Q. Is this the first time there has been a Mo 99 shortage?
A. No. During the past four years, different reactors have been offline unexpectedly for extended periods of time, creating Mo 99 shortages. Routine maintenance shutdowns, however, are coordinated well in advance and generally do not create shortages.
Additional Major Medical Isotope Reactors

Q. What was Covidien’s role in the additional June, 2010, cycle added by the BR2 reactor in Belgium?
A. Covidien was actively engaged with the Belgian Nuclear Research Centre SCK-CEN Board of Directors during its decision making process and is providing significant funding to support the added BR2 cycle.

Q. What access will Covidien have to the additional Mo 99 supply from BR2 in June, 2010?
A. Covidien will receive a significant portion of the Mo 99 produced by BR2 in June, helping tremendously to offset the lack of supply from the HFR during that time.

Q. Are there other initiatives between Covidien and the BR2 reactor?
A. Yes. Covidien has secured an additional target position in the BR2 reactor that will increase output throughout the period that HFR is offline in 2010, allowing additional generator production to improve patient access to Tc 99m for critical procedures.

Q. Will Covidien have access to Mo 99 produced by the OSIRIS reactor in France during the HFR shutdown?
A. Yes, as a result of our long-standing arrangement with the IRE Mo 99 processing facility, we will receive Mo 99 produced by the OSIRIS reactor when needed to supplement other suppliers.

Q. Recently there was an announcement related to the Australian reactor supplying Mo 99 to the U.S. What is the status on that becoming a reality?
A. The Australian Nuclear Science and Technology Organization (ANSTO) operates the Opal reactor in Australia. Per information posted on the ANSTO web site from October 2009, they are not yet exporting Mo 99 into the global supply chain.

Q. What can be done to alter reactor schedules for planned maintenance?
A. Planned maintenance and irradiation schedules follow strict timelines. Regulatory obligations demand these maintenance and operation schedules are adhered to without deviation—even in situations where global supply would be further challenged.

Role of Covidien and the Nuclear Medicine Industry

Q. What is Covidien doing to help customers and patients through the global Mo 99 shortage?
A. Covidien has led the industry in direct and frequent communication with nuclear medicine providers about the supply challenge. These efforts include:
• Providing detailed monthly calendars projecting the availability of Tc 99m generators on a daily basis,
• Published these calendars and supply updates on a public website: www.covidien.com/Mo99supply
• Encouraged clinicians to more efficiently schedule procedures and order Tc 99m-based products to maximize the number of doses available to the greatest number of patients
Q. In addition to the agreement with IAE POLATOM for Mo 99 from Maria, what else is Covidien doing to address the short and long term supply issues affecting the availability of medical isotopes?
A. There are a host of measures Covidien has taken to lead the industry in addressing the supply issues affecting the availability of medical isotopes, including:
- Actively supporting additional Mo 99 production cycles and an increase in the number of targets at Belgium’s BR2 reactor during the shutdown of the HFR in Petten
- Increasing the production of potential alternative, clinically appropriate medical isotopes such as thallium Tl 201
- Expressing public support for the Dutch government’s efforts to develop the new Pallas reactor in the Netherlands
- Supporting H.R. 3276, the American Medical Isotopes Production Act of 2009 (AMIPA), which was introduced by Congressmen Markey and Upton. The Act promotes U.S. production of Mo 99 for medical isotope manufacturing, while also phasing out the export of highly enriched uranium for the medical isotope production. The bill has obtained broad support and has been passed by the U.S. House of Representatives. It is currently awaiting action by the U.S. Senate.

Q. How does Covidien provide supply projections to the industry?
A. Covidien routinely updates supply projections by producing calendars that detail anticipated Covidien Mo 99/ Tc 99m generator production in three-month increments. Daily projections are based on current information and subject to change. These calendars are sent to customers in letter form, and posted to the [www.covidien.com/Mo99supply](http://www.covidien.com/Mo99supply).

This same information is shared with professional associations and government agencies such as the U.S. Food and Drug Administration and Health Canada to broaden the reach of information. Our goal is to help clinicians plan as efficiently as possible to provide maximum access to those patients most critically in need of this vital isotope.

Q. How can individual clinicians in the U.S. positively impact this situation?
A. It is very important to maximize the availability of technetium 99m (Tc 99m) for patients by using as much as possible in procedures rather than allowing it to decay on the shelf. Covidien encourages clinicians to adjust their ordering practices from their local radiopharmacy to a more “just in time” approach. To illustrate the benefits to Tc 99m conservation, consider how ordering habits can affect supply:
- A department orders a 30mCi dose of Tc 99m calibrated for use at 2:00 p.m.
- The order requests a delivery on the first morning run at 6:00 a.m., requiring 75mCi of Tc 99m to meet the 30mCi dose requirement.
- Conversely, if the same order was placed for delivery at noon—ample time to meet the procedural need at 2:00 p.m.—only 38mCi of Tc 99m would be needed to meet the 30mCi target.
- This is a Tc 99m savings of 37mCi—enough activity for one bone or cardiac imaging dose, and up to five or six doses for certain other nuclear studies. That’s ONE MORE PATIENT—maybe more—who can benefit from a nuclear medicine procedure.
This more thoughtful ordering approach has resulted in **hundreds of additional patient doses daily.** Similar efforts are encouraged industry wide. We appreciate the nuclear medicine community's willingness to carefully schedule patients, providing greater access to those most critically in need of this vital isotope. We are still boosting production of thallium Tl 201 injection for those procedures where it can be a clinically appropriate substitute.

**Q. How can individual clinicians in Europe, Canada, Latin America and Asia/Pacific positively impact this situation?**

A. In a collaborative effort to maximize patient access to critical nuclear medicine procedures, we encourage physicians to plan for the most efficient use of Tc 99m. These efforts are encouraged industry wide. We appreciate the nuclear medicine community's willingness to carefully schedule patients, providing greater access to those most critically in need of this vital isotope. We continue to boost production of alternative isotopes such as thallium Tl 201 and other products for those procedures where either can be a clinically appropriate substitute.

**Q. Are there alternatives to using Tc 99m for patient procedures?**

A. Clinicians may consider using other isotopes such as thallium TI 201 (Tl 201) when clinically appropriate. Covidien has significantly boosted production of Tl 201 globally to help meet increased demand. In addition, krypton Kr81m is available from Covidien in Europe, and may also be considered as an alternative when medically correct.

**Q. Does Covidien have plans to raise generator pricing in the near term?**

A. At any given time, Tc 99m generator pricing reflects the need to invest in stabilizing the supply chain over the long term as well as to cover operating costs. Recent events, including the NRU and HFR shutdowns, have led to industry-wide increases to Mo 99 costs. As these costs impact our operations and ability to invest in the business, we will evaluate the impact regionally in the months ahead.

**Future Mo 99 Supply**

**Q. Can you provide details about the proposed Pallas reactor in the Netherlands?**

A. The Dutch government recently announced it supports construction of a new nuclear reactor for medical isotopes to replace the current HFR in Petten. The Nuclear Research and Consultancy Group (NRG), which operates the reactor in Petten, has plans to build a new modern reactor in the Netherlands that will be called 'Pallas'.

**Q. What is Covidien's position related to the proposed Pallas reactor?**

A. We support replacement of the HFR with a new Pallas reactor based on LEU technology. Covidien is a member of the steering committee for the project and readily provides our expertise as needed. We are focused on maximizing patient access to important medical isotopes, and applaud the Dutch Cabinet’s decision to develop plans that help ensure long-term reliable and continuous supply of Mo 99.
Q. What is low enriched uranium (LEU) conversion and why should the industry look to convert?

A. LEU conversion refers to transitioning from utilizing highly-enriched uranium (HEU) targets. Currently, with the exception of the newer Maria, much of the global Mo 99 production depends on aging HEU reactors with inconsistent reliability, contributing to isotope shortages and impacting patient care. (Maria also utilizes HEU targets.)

LEU has the potential of addressing global security initiatives aimed at limiting possible diversion of HEU for nuclear terrorism. HEU is a weapons grade material; LEU is not.

Q. What is the Covidien-Babcock & Wilcox (B&W) partnership?

A. In January, 2009, Covidien formed a game-changing partnership with Babcock & Wilcox Technical Services Group, Inc. (B&W). Covidien and B&W are collaborating to develop solution-based reactor technology for medical isotope production. The agreement combines Covidien expertise in radiopharmaceutical production and global regulatory approvals with B&W’s patented liquid phase nuclear technology. B&W was recently awarded funding from the U.S. Department of Energy’s National Nuclear Security Administration (NNSA) for this initiative.

Q. What can you tell me about the American Medical Isotopes Production Act of 2009 (AMIPA) or Markey bill in the U.S Congress?

A. The American Medical Isotopes Production Act (AMIPA) (H.R. 3276) is a bi-partisan bill introduced in July 2009 by Congressmen Edward Markey (D-MA) and Fred Upton (R-MI). The Act promotes U.S. production of Mo 99 for medical isotope manufacturing, while also phasing out export of HEU for medical isotope production. The bill has been approved by the House of Representatives and is moving through the Senate review process. Covidien and many others in the U.S. support AMIPA, including the Council on Radionuclides and Radiopharmaceuticals (CORAR), the Society for Nuclear Medicine, the American College of Cardiology, and the Nonproliferation Policy Education Center. To learn more, you may read the full bill at: http://thomas.loc.gov/cgi-bin/query/z?c111:H.R.3276:

Additional Information

Q. How can I learn more about the Mo 99 supply situation?

A. To learn more about the current Mo 99 supply situation, please visit our website at www.covidien.com/Mo99supply. You may also visit these sites for regular updates:

- Society of Nuclear Medicine http://www.snm.org/
- FDA Drug Shortage http://www.fda.gov/cder/drug/shortages/
- Association of Imaging Producers and Equipment Suppliers (European Industrial Association for Nuclear Medicine and Molecular Healthcare) http://www.aipes-eeig.org/index.php?id=7
- Canadian Association of Nuclear Medicine http://www.canm-acmn.ca/
1. NRU Status Report #42 - “AECL provides update on NRU activities” (last accessed 2/15/10)
   http://www.aecl.ca/NewsRoom/Community_Bulletins/100210.htm
   Updates are posted to the AECL site each Wednesday, where you may check back for status reports.
2. Repair of cooling water pipework High Flux Reactor will commence on 19 February 2010 (accessed 12/15/09)
4. Government supports construction of new nuclear reactor for medical isotopes” (last accessed 2/15/10)
   http://international.vrom.nl/pagina.html?id=44577