EUROPE

# MOLYBDENUM SUPPLY REVIEW

IBA MOLECULAR

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## INTRODUCTION

Dear Nuclear Medicine professional,

Since summer 2008, our community has become aware of the fragility of the supply chain of Tc99m generators. While it is clear now that no short term solution will allow us to avoid supply disruption over the next 2 years, our teams remain committed to minimize the impact of this crisis on Nuclear Medicine departments.

In the last year, IBA has reorganized its generators supply processes in order to ensure a fair and minimal level of supply to its customers in disrupted times. We are also actively putting in place now production capability to provide you with alternative non-technetium products during the most severe shortage periods foreseen for next year. Finally, our Group is finalizing a 60 Mio Euros investment plan that is making our central radiopharmaceutical facility the most advanced in the world, in line with the strictest safety and quality standards.

As part of our ongoing support, we are pleased to provide you with this Molybdenum supply review. This monthly newsletter is keeping you up to date with the latest Molybdenum supply developments by consolidating the major news and scientific articles published recently. The first edition also includes a selection of the essential information published through 2009.

Our team remains at your disposal for further information.

## ESSENTIAL NEWS PUBLISHED IN 2009

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### INDUSTRIALS

**Important gathering in the background of an AIPES Reactor & Isotope working group**

**March 06, 2009, AIPES**

On the 6th of March 2009, the world's main producers of medical radioisotopes together with the reactor operators were gathered in the background of an AIPES Reactor & Isotope working group

**French nuclear reactor maker offers Canada help**

**May 25, 2009**

French nuclear reactor maker AREVA NP offered to help Canada solve its medical isotope shortage Monday while opposition politicians, returning from a week in their ridings, will get their first chance in the House of Commons to grill the government on the failed Chalk River, Ont., nuclear reactor that produces more than half of the world's medical isotopes.

**Another isotope distributor [GE Healthcare] hikes its prices**

**June 03, 2009, Canadian Press.**

GE Healthcare has increased the price of its isotope generators used in diagnostic imaging amid an isotope shortage caused by the temporary shutdown of a Canadian nuclear reactor. The company said the price increase, which might not be the last, was necessary to offset the higher rates charged by its supplier

**Ottawa Hospital running out of isotopes**

**June 06, 2009, Ottawa Sun**

Doug Abrams, president of the Canadian Society of Nuclear Medicine, said the shortage will ease as the Petten reactor in the Netherlands revs up production by 50%. Isotope supplier Covidien is charging roughly 50% above previous prices, said Dr. Christopher O'Brien, president of the Ontario Association of Nuclear Medicine.

### Facing Mo-99 shortage, nuclear medicine economizes

**June 11, 2009, AuntMinnie**

The two main suppliers of technetium generators in the U.S., Lantheus and Covidien, have scrambled to deal with the crisis, which is extreme enough that the firms have agreed to cooperate to meet customer demand.
Sodium fluoride PET scans could be alternatives to SPECT studies with Tc-99m and thallium for cardiac studies. Another option is reducing the average technetium dosage of 25 to 30 mCi.
It is important to find a way to produce Mo-99 in the U.S : two plans, at least, are under way with the University of Missouri Research Reactor (MURR) in Columbia and Babcock & Wilcox (B&W) of Lynchburg, VA.
“This whole shortage is going to be a problem for quite a long time, but nuclear medicine will be open for business,”

### South Africa isotope reactor ramps up Mo-99 production

**June 25, 2009, Health Imaging**

The Safari-1 reactor at the Pelindaba nuclear facility in South Africa has geared up production of molybdenum-99 (Mo-99) in response to the global shortage of medical isotopes, which has disrupted and halted treatments for cancer patients.

## EXPERTS OPINIONS

### Expert advocates for medical isotope production in U.K.

**March 20, 2009, Health Imaging**

Alan Perkins, a medical physicist from the University of Nottingham in England, has warned that the government of the United Kingdom should start producing medical isotopes or «face a dangerous shortage that threatens to compromise patient healthcare.»

### Nuclear experts tackle isotope shortages, fuel risks at UN meeting

**March 27, 2009, Health Imaging**

Operators of the 250 global nuclear reactors, which are used for scientific testing and the production of medical isotopes, met this week in Vienna, Austria, to tackle isotope shortages and fuel risks at a meeting supported by the United Nations (UN), according to the International Atomic Energy Agency (IAEA).
Another issue discussed was the shortage of the isotope technetium-99m which is used for medical treatment and for which 95 percent of the world’s needs are supplied by only five research reactors, all of them over 40 years old, the agency report.

## USERS

### SNM poll: Isotope shortage affecting users, procedures

**June 15, 2009, AuntMinnie**

A poll of SNM members has confirmed the severity of the global molybdenum-99 shortage, as 90% say the lack of medical isotopes has impacted their practice or facility. Two-thirds of the responses noted they do not have access to a technetium generator source beyond their current supplier. In addition, approximately 26% are operating at less than 50% of their capacity because of the isotope shortage, 36% are operating at 52% to 75% of capacity, and 38% are running at 76% to 100% procedure capacity.

### Medical isotope shortage threatens treatments

**August 14, 2009, USA Today**

The Canadian nuclear reactor in Chalk River is offline until the beginning of 2010. The Dutch reactor is down for maintenance for several weeks, then will be offline for up to six months next year.
Nuclear medicine physicians and pharmacists say they can handle 75 percent of the caseload with as little as half pre-shortage isotope amounts by scheduling patients when isotopes are more available and scanning them longer using smaller amounts of the isotope. The cost will rise for a technetium-99 study from $20 to $40.

### Isotope bill could rise to $250,000 this year

**August 27, 2009, SNM SmartBrief**

Hospitals in Canada’s Regional Health Authority B are anticipating the actual cost of medical isotopes for the year to significantly exceed the projected cost. The increase in costs is being attributed to isotope suppliers’ price hikes since the start of the month as a result of the global isotope shortage

### SNM: Nuclear medicine tests being postponed

**September 09, 2009, AuntMinnie**

In the SNM survey, 75% of nuclear medicine physicians said they are rescheduling patient tests by at least one day, and in more than one-third of these cases, nuclear studies have been delayed by more than a month.

### Nuclear imagers adjust to practice without Mo-99 during lengthy shortage

**September 14, 2009, Diagnostic Imaging**

Despite the shortage, about 40% of respondents said they have been able to fill more than half of client prescriptions for Tc-99m during the shortage. Only 6% said they were able to fill less than 25% of prescriptions.

### Commentary: supplies of molybdenum-99--need for sustainable strategies and enhanced international cooperation.

**Ramamoorthy N.**

**Nucl Med Commun. 2009 Dec;30(12):899-905.**

The field of functional diagnostic imaging has been dominated by nuclear medicine procedures thanks to the excellent features of 99mTc – nuclear and chemical characteristics, as well as inexpensive and abundant availability [1–3]. The latter attribute – 'ease of availability' – has been in question as never before since the fall of 2007 because of serious disruptions in supplies of the precursor nuclide, molybdenum-99 (99Mo), which has stretched until February 2009. The vulnerability of irradiation services from the five old research reactors (RR) used for 99Mo production, compounded by certain other (unrelated) incidents, has led to approximately 20–70% cancellations or delays in patient services depending on the week and location of nuclear medicine centre [4,5]. The issues to be addressed in seeking sustainable solutions will, however, need to go far beyond the reactors. It is true that the current problems are related mainly to the reliance on five old reactors for irradiation of enriched uranium-235 targets for the production of fission-based 99Mo, but there are other important issues that should not be overlooked. These include, inter alia, the complex and demanding technological issues in fission molybdenum production combined with the scale of operations for acceptable business/economic reasons, a multicomponent complex chain of supply logistics, conflicts of commercial interests among the limited number of current major producers some of them implicitly conveying discouraging signals to new entrants, and the important and inevitable concerns with regard to the continuing use of highly enriched uranium (HEU) targets for fission-based 99Mo production [6]. It is imperative to consider all the above aspects in evolving holistic and long-lasting approaches to ensure reliable and secure supplies of 99Mo for the immediate future and for longterm requirements.

### The medical isotope crisis

**European Nuclear Society News, Issue No. 26 Autumn (November 2009)**

Last year saw a major worldwide crisis in the availability of medical radioisotopes. More specifically in the production of Mo-99/Tc-99m generators for diagnostic nuclear medicine. We will shortly analyse the causes of the shortage and point to necessary long-term measures to avoid future crisis.

When highly enriched U targets are irradiated in a high-flux reactor, a number of fission products are created, among which Mo-99 with a half-life of 66h. Radioactive decay of Mo-99 produces Tc-99m, a pure gamma emitter (140 keV) with a half-life of 6h. By separating Mo-99 out of the U targets, Mo-99/Tc-99m generators ('cows') are produced and shipped to hospitals worldwide. Some other production schemes exist, but their yield is much lower and the activity produced is too small to be of importance on the world market.

Tc-99m is used in about 80% of all diagnostic nuclear imaging procedures, corresponding to about 30 million examinations yearly worldwide, among which several million in Europe alones.

Interesting chapter about cost analysis of Mo-99/Tc-99m generators: "assembling the generators and selling them does not seem to be a very lucrative business".

### Molybdenum supplies and nuclear medicine services.

**Perkins AC, Vivian G.**

**Nucl Med Commun. 2009 Sep;30(9):657-9.**

All who train in the basic science of nuclear medicine learn of the merits of technetium-99m (99mTc) and its ideal characteristics for radionuclide imaging. The attributes of 99mTc are commonly listed as: a short physical half life, monoenergetic 140 keV gamma emission, no particulate radiation, a daughter product of the longer lived parent molybdenum-99, cheap and readily available. Not any more! After recent events, the textbooks will need revision. Molybdenum is about to become much more expensive and its routine availability can no longer be taken for granted.

Globally, nuclear medicine investigations are the second most common diagnostic imaging procedure after X-ray computer tomography. Over 28 million procedures are carried out each year using 99mTc. The majority of the procedures are for cardiac and bone imaging. Eighty percent of the clinical nuclear medicine workload is dependent upon the routine availability of molybdenum-99 for the production of 99mTc radiopharmaceuticals. To meet this demand the Association of Imaging Producers and Equipment Suppliers has estimated that of the order of 400TBq of molybdenum-99 is delivered to radiopharmacy units on a weekly basis. Until recently very few end users have given much thought to the manufacturing and supply chain ahead of their weekly generator delivery.

### (99)Mo supply--the times they are a-changing.

**Lewis DM.**

**Eur J Nucl Med Mol Imaging. 2009 Sep;36(9):1371-4.**

Recently there has been a phenomenal growth in clinical PET using 18FDG as well as a resurgence of interest in imaging with 123I. However, 99mTc still remains the most popular radionuclide; approximately 80% of all the world's nuclear medicine procedures are carried out using 99mTc. The supply of its parent radionuclide (99Mo) relies on access to nuclear research reactors and nuclear fission radiochemical processing. During the last 18 months, there have been supply problems with both the reactors and radiochemistry operations; therefore, it is timely to re-visit this issue and examine the options that exist for 99Mo supply in Europe.

In a 1995 editorial in this journal on the availability of suitable reactors [1], I wrote that "the situation in North America was dire" and "whereas Europe was blessed with several good isotope-producing reactors, the situation in Europe was far from secure". It is with regret that I can only report that the situation has deteriorated considerably since that time.

## LATEST NEWS

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### Chalk River repairs have $70-million price tag: AECL
**October 19, 2009, Google alert**
Atomic Energy of Canada Ltd. has put a $70-million price tag on repairing its downed Chalk River reactor.

### Isotope producers cooperate to avoid shortage
**November 05, 2009, SNM SmartBrief**
European Reactor Operators Coordinate to Optimize Mo-99 Production in 2010. The AIPES (European Industrial Association for Nuclear Medicine) has announced that due to the continued shutdown of the NRU (Chalk River, Canada) reactor, and the planned shutdown of the HFR (Petten, The Netherlands) reactor in 2010, the BR2 (Mol, Belgium) reactor has agreed to add an additional irradiation cycle. In addition, the planned shutdown of the OSIRIS (Saclay, France) reactor will now be postponed by approximately 2 months. This coordination has reduced the amount of time when a further reduction of Mo-99 production capacity would have occurred.

### Nuclear Research and Consultancy Group starts process for new reactor
**November 20, 2009, AuntMinnie**
Dutch radiopharmaceutical producer Nuclear Research and Consultancy Group (NRG) has begun the regulatory approval process to build a nuclear reactor to replace its High Flux Reactor (HFR) in Petten, Netherlands. The goal is to have Pallas operating in 2016, pending funding and regulatory approvals.

### NRG endorses Petten site for reactor
**December 08, 2009, AuntMinnie**
The Dutch Nuclear Research and Consultancy Group said it is considering Petten, Netherlands, as the location for the proposed research reactor Pallas. NRG said that compared to the Zeeland province, the other site in consideration, Petten already has the nuclear infrastructure needed for the operation of Pallas. A final decision on the site of the new reactor is expected by spring next year.

### Best option to restore isotope supply is new reactor: Panel
**December 03, 2009, Vancouver Sun**
The best, but most expensive way, to secure a stable supply of medical isotopes is to build a new multi-use nuclear reactor, an expert panel appointed by the federal government concludes in its report released Thursday. The report estimates the cost of building a new reactor at between $500 million and $1.2 billion, depending on its features. Operating the reactor would cost $35 million to $70 million a year. The expert panel did not appear keen on re-igniting the MAPLE project, saying «the ongoing economics for this project remain questionable.»

### Panel wasted time on useless isotopes report: expert
**December 06, 2009, Toronto Sun**
“The report is comprehensive but doesn’t bring anything new to the table. Everything we knew already,” said Jean-Luc Urbain, president of the Canadian Society of Nuclear Medicine.

## LINKS

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IBA Molecular.

Society of Nuclear Medicine.

European Association Of Nuclear Medicine.

Sociedad Espanola de Medicina Nuclear.

Société Française de Médecine Nucléaire.

Société Belge de Médecine Nucléaire.

Nederlandse Vereniging voor Nucleaire geneeskunde.

Associa Italiana di Medicina Nucleare ed Imaging Moleculare.

British Nuclear Medicine Society.

Deutsche Gesellschaft für Nuklearmedizin e.V.

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