Written Testimony

of

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on behalf of the

Lantheus Medical Imaging, Inc. (Lantheus) and
Council on Radionuclides and Radiopharmaceuticals (CORAR)

Before the United States House of Representatives
Committee on Energy and Commerce

Subcommittee on Energy and Environment

September 9, 2009

My name is Michael Duffy, and I am Vice President and General Counsel of Lantheus Medical Imaging, Inc. (Lantheus) and a member of the Board of Directors of the Council on Radionuclides and Radiopharmaceuticals (CORAR). I have been asked by Chairman Markey to testify on the American Medical Isotopes Production Act of 2009 (H.R. 3276) on behalf of both Lantheus and CORAR. More specifically, Chairman Markey has requested that my testimony focus on (i) H.R. 3276 itself, (ii) the impact that the molybdenum-99 (Mo-99) supply shortage is having on Lantheus, its customers and the rest of the medical isotopes industry, and (iii) the potential role of the private sector in establishing a robust domestic supply of Mo-99 and its important radioactive decay product technetium-99m (Tc-99m).

Tc-99m derived from Mo-99 is a critical medical isotope used in over 14 million nuclear medicine procedures in the U.S. each year. Performed with Tc-99m imaging agents (Tc-99m radiopharmaceuticals), these procedures are primarily diagnostic and most often relate to life-threatening conditions such as heart disease and cancer. Procedures using Tc-99m imaging agents can save lives, improve patient outcomes and reduce costs. Today, we face a global Mo-99 supply crisis – an aging supply infrastructure entirely located outside of the U.S. does not consistently produce enough Mo-99 to meet the Tc-99m needs of the nuclear medicine community and the patients they serve.

The written testimony will be divided into two parts. First, I will present Lantheus' views on the impact the global Mo-99 supply crisis and then describe a path forward to developing a robust domestic supply of Mo-99. I will conclude with a health care policy discussion that shows Tc-99m-based diagnostic medical imaging procedures improve patient outcomes and reduce costs. Second, I have attached a statement prepared by CORAR on the global Mo-99 supply crisis. This will include introductory comments, and a discussion of the legislation, including several concerns and suggestions.

I. Introduction

Lantheus endorses H.R. 3276. We strongly support the Committee's efforts to promote the production of Mo-99 in the United States for medical isotope applications.

Based in Billerica, Massachusetts, Lantheus has been a worldwide leader in diagnostic medical imaging for the past 50 years, first as New England Nuclear, then as part of DuPont, Bristol-Myers Squibb and now as a stand-alone company. Lantheus has over 600 employees worldwide, approximately 400 of whom work in Massachusetts. Lantheus is the home to leading diagnostic imaging brands, including, among others, Technelite® (Technetium Tc99m Generator). Lantheus sells Technelite® generators to customers located in the United States and around the world. Mo-99 is the key ingredient in the Technelite® generator. Mo-99 spontaneously decays into Tc-99m which is then eluted from the generator to radiolabel site-specific imaging agents. These radio labeled agents are then used in a variety of heart, brain, bone and other diagnostic imaging procedures.

II. Impact of the Mo-99 Crisis

The U.S. consumes approximately half of the Mo-99 produced in nuclear reactors around the world. In times when the major Mo-99-producing nuclear reactors are operational, we believe Lantheus is the largest producer of Tc-99m generators in the U.S. and the largest consumer of Mo-99 in the U.S. We rely for our Mo-99 supply on reactors in Canada, South Africa, Belgium and The Netherlands, and are working with Australia to receive initial commercial quantities from there. Most of these reactors (all located outside of the United States) are aging and are increasingly subject to unscheduled outages and shutdowns and time-consuming repairs, which limit the predictability of and accessibility to potentially millions of important medical diagnostic procedures for patients in the United States and throughout the world.

Chronic Crisis Made Acute

The Mo-99 supply crisis is a chronic crisis resulting from an aging supply infrastructure and a market failure to attract sufficient replacement capacity on a timely basis. Some projects – like the MAPLE reactors in Canada – were nearly completed until they ran into operational and regulatory challenges which have prevented any further development. Other projects such as the Jules Horowitz reactor in France and the proposed Pallas reactor in The Netherlands are in the early stages of development but will not be available to manufacture commercially meaningful quantities of Mo-99 for a number of years to come. Still other reactors around the world which have not historically manufactured commercially meaningful quantities of Mo-99 for the North American market may be able to do so in the nearer term, subject to operational, regulatory and, in certain circumstances, logistical challenges that must first be overcome. However, current and projected U.S. and international demand for Mo-99 for important diagnostic medical isotope procedures that impact patients lives outstrip the capability of the global

reactor community to reliably and consistently supply until significant new capacity becomes operational.

Historically, Lantheus has relied on the National Research Universal (NRU) reactor operated by Atomic Energy of Canada, Ltd (AECL) in Chalk River, Ontario for the majority of the Mo-99 used in the Technelite® generators. The National Academy of Sciences prophetically stated "The extended shutdown of NRU without a backup source of production would have dire consequences for Mo-99 supply worldwide." (NAS 2009 at 119). Unfortunately, on May 15, 2009, that prophesy came true when AECL announced an unscheduled shutdown of NRU because of the discovery of a heavy water leak. Subsequently, multiple points of corrosion were identified in the NRU reactor vessel. Current estimates by AECL state that NRU will become operational again in the first quarter of 2010.

Lantheus' Response to Crisis

Fortunately for Lantheus, its customers and the patients they serve in the nuclear medicine community, after the one month NRU outage in 2007 and under new management, Lantheus in 2008 implemented an aggressive Mo-99 supply chain diversification strategy. As a result of that strategy, Lantheus has entered into an agreement with NTP Radioisotopes (Pty) Ltd., a subsidiary of the Nuclear Energy Corporation of South Africa (NECSA) to manufacture and supply Lantheus with an on-going volume of Mo-99 from the Safari reactor located in South Africa. NTP has, in turn, partnered with Belgian radiochemical producer Institute for Radio Elements (IRE) to co-supply the Lantheus Mo-99 requirement and thereby maximize the reliability of on-going supplies of Mo-99 to Lantheus. IRE processes Mo-99 from the BR2 reactor in Belgium, the OSIRIS reactor in France and the High Flux Reactor (HFR) in The Netherlands. In addition, Lantheus has finalized an arrangement with the Australian Nuclear Science and Technology Organisation (ANSTO) to receive Mo-99 produced from LEU targets in ANSTO's new OPAL reactor. This latter supply arrangement positions Lantheus to be the first company to supply Tc-99m derived from LEU targets in the U.S. market. This overall supply chain diversification strategy has allowed Lantheus to be able to access all of the major medical isotope-producing reactors in the world.

Despite all of these new arrangements, however, in the face of the prolonged NRU shutdown, Lantheus is still not able to fully meet its weekly demand for Technelite® generators from its customers and the patients they serve. According to the National Academy of Sciences, NRU and its processing partner MDS Nordion provide "approximately 60% of the U.S. supply of Mo-99 and approximately 40% of world supply depending on global reactor production schedules." (NAS 2009 at 40) With NRU shut down for several more months, a number of the other global reactor groups have attempted to increase their volumes of Mo-99 produced. This surge capacity, however, has not been able to produce sufficient amounts to fully replace all of the missing supply capacity from NRU. In addition, HFR, the second largest Mo-99 producer in the world, was shut down for repairs this past winter for several months, this summer for one month and is expected to be shut down again in early 2010 for what some estimate to be up to 6

months. As a result, global availability of Mo-99 has fluctuated dramatically over the past several months resulting in the postponement and cancellation of important diagnostic imaging procedures that impact patients lives.

Faced with these supply challenges, Lantheus has been forced to allocate our Mo-99 supply and our Tc-99m generators so that we can serve as many customers and patients as possible. We have modified our production and distribution schedules to further assist our customers and their patients. Our manufacturing team is available on a 24/7 basis to ensure that Mo-99 we receive is utilized to the fullest extent possible. We are committed to serving the needs of patients and the nuclear medicine community by mitigating as much as we can the effect of the Mo-99 supply crisis on nuclear studies and patient care.

Buying Ice on a Warm Day

Even though Lantheus has been able to obtain substantial amounts of Mo-99 from supply sources outside North America, it is important to note that Mo-99 is a radioactive substance that continually decays from the time of its manufacture with a half-life of approximately 66 hours. Certain of the old hands at Lantheus describe the procurement of Mo-99 as "buying ice on a warm day". Given the travel logistics and transport time associated with overseas supply of Mo-99, approximately one-third of the Mo-99 manufactured outside of North America decays before it even reaches the Lantheus manufacturing facility where it is incorporated into the Technelite® generators. By comparison, given the relative proximity of the NRU reactor and MDS Nordion processing facility in Ontario, less than 5% of the Mo-99 decays in transit to the Lantheus manufacturing facility in Billerica, MA. As a result, because of travel logistics and transport time, substantially more Mo-99 is available from a North American supplier from the same quantity of targets and identical processes.

This latter point cannot be overstated – shorter transport time means less decay. Less decay means more efficient use of radioactive targets and facilities, less waste stream attributable to wasted Mo-99, and lower costs that have to be borne by the health care system for Mo-99 produced and never used. In addition, shorter domestic transport means increased reliability of supply because transport is conducted over domestic routes. As a result, Lantheus believes a robust U.S. supply of Mo-99 is important U.S. public policy for reasons of accessible and affordable health care, efficient waste stream management and nuclear non-proliferation.

Less Mo-99, Less Tc-99m, Fewer Tc-99m Studies

After the Mo-99 is incorporated into a Technelite® generator, the Mo-99 decays into its daughter isotope Tc-99m, the half life of which is approximately 6 hours. This relatively short half life of Tc-99m is one of the many attributes that make the Tc-99m-based tracers so attractive for cardiology and other applications. (Approximately 50% of Mo-99 is used for cardiology procedures – NAS 2009 at 75.) For example, an older generation cardiac tracer called Thallium-201 (which Lantheus also manufactures) emits photons of different energies than those emitted by Tc-99m, making imaging more

challenging, and has a half life more than ten times longer than Tc-99m-based cardiac tracers, resulting in higher radiation exposure to the patient and potentially to the health care professionals performing the diagnostic procedure.

At this point in time, Lantheus does not have firm numbers as to how constrained the global supply of Mo-99 has become because the absence of NRU and HFR has been, in the short term, partially mitigated by surge capacity from other Mo-99 manufacturers, most of which have similarly fragile reactor infrastructures. In addition, Lantheus does not have firm numbers which indicate the aggregate and per procedure diagnostic impact of the global Mo-99 crisis. Generally speaking, radiopharmacies and large health care institutions, the two principal customers of Tc-99m generators, are receiving substantially fewer generators than their historic demand. We understand that important diagnostic procedures often related to life-threatening conditions such as heart disease and cancer are being postponed or cancelled because of the decreased volume of Tc-99m generators available to the nuclear medicine community. And diagnostic modalities appear to be shifting – with the decreased availability of Tc-99m generators for Tc-99m-based cardiac tracers, there has been a substantial increase in the demand for and use of the older-generation Thallium tracers to perform cardiac nuclear exams. Although Thallium is a well-regarded and widely prescribed cardiac tracer, a Thallium patient does receive greater cumulative radiation exposure, and Thallium may provide the clinician less diagnostic certainty than Tc-99m-based cardiac tracers because of Thallium's less than optimal energy profile.

In addition to trying different radioisotopes, some clinicians may be foregoing nuclear medicine completely and opting instead to sending patients for cardiac catheterization, a more invasive, more expensive, higher risk, surgical procedure. According to Dr. Michael M. Graham, President of the Society of Nuclear Medicine (SNM), with the decreased availability of Tc-99m cardiac imaging agents "some people will be operated on that don't need to be, and vice versa" (Wald, Matthew, "Radioactive Drug for Tests is in Short Supply" The New York Times, July 24, 2009 at 1.)

Evidence of Impact

The SNM has recently conducted surveys to collect anecdotal information from health care professionals about the impact of the global Mo-99 shortage on their own practices. While these surveys are subject to a number of qualifications about survey design and statistical significance, they do provide some insight into the state of the crisis from within the nuclear medicine community. A recent survey (SNM, Isotope Shortage Survey Final Results, August 10, 2009) reports that 80% of the 710 respondents said their practice or facility was impacted by the current Mo-99 shortage. Of the participants, 81% reported postponing procedures, 47% cancelling procedures, 57% changing procedures, 60% changing the isotope used in a procedure, and 11% transferring a patient to another facility. Of those who changed an isotope in a procedure, 58% reported changing from a Tc-99m agent for cardiac imaging to Thallium.

In a much smaller survey of 97 radiopharmacists (SNM, Isotope Shortage Survey Final Results, August 10, 2009), 60% said their pharmacy was impacted by the current Mo-99 shortage. In response to the shortage, radiopharmacists reported doing one or more of the following: 76% rescheduled patient orders to another day or time, 65% cancelled orders, 82% changed the radiopharmaceutical used, 81% decreased dosage, 71% cancelled backup doses, 81% eliminated bulk orders, 71% changed delivery schedules, 68% eliminated standing orders, 59% shifted dosing times, 85% eluted older generators more often, 34% modified the preparation, 21% sent doses with later calibration times, 66% delayed and divided deliveries, and 64% eliminated all contingency doses. Of those who changed a radiopharmaceutical used, 82% reported changing from a Tc-99m agent for cardiac imaging to Thallium.

Subject to all of the necessary qualifications, the answers to these SNM surveys show a substantial adverse impact on the nuclear medicine community of the ongoing Mo-99 shortage. And from this it is reasonable to deduce that the adverse impact has resulted in greater diagnostic uncertainty for clinicians and adverse outcomes for patients.

III. Developing a Robust Domestic Supply

As a pioneer in the nuclear medicine community with a long history of innovation, Lantheus has developed and commercialized important, life-changing technologies, employing hundreds of workers in Massachusetts and throughout the U.S., and paying significant amounts of federal, state and local taxes as result of its entrepreneurial success. Lantheus believes that the private sector can and should have a major role in resolution of the on-going Mo-99 supply crisis. At the same time, Lantheus also believes there is a strong role for government in helping resolve this crisis – a role that government can and should exercise because of (i) the market failure to attract on a timely basis sufficient production capacity to replace the aging supply infrastructure, and (ii) important public policy supporting accessible and affordable health care, efficient waste stream management and nuclear non-proliferation.

Lantheus is pursuing a number of different alternatives in connection with the longer term global Mo-99 supply. Not only have we diversified our Mo-99 supply chain among the existing global reactor groups, but we are also investigating obtaining Mo-99 from reactors in countries that have not historically generated commercially meaningful quantities of medical isotopes. In addition, we are exploring a number of different U.S-based technologies and opportunities that could provide significant amounts of Mo-99 in the intermediate and longer term. Given the significant Mo-99 decay issues and logistics and transportation challenges associated with supply sourced outside of North America, U.S-based supply solutions are the most attractive longer term alternatives to Lantheus.

Each of these U.S.-based opportunities Lantheus is currently evaluating requires close cooperation between regulators and project sponsors in connection with design, construction, regulatory approval, implementation, operation, waste stream management and disposal, safety and security. These opportunities have different timelines, costs and project sponsors, and different financial resources available from the private sector. In

addition, given the direct and indirect government support of the Mo-99 reactors located outside of the U.S., some of these domestic projects may not be successful without a public-private partnership designed to level the playing field. Indeed, given the potential size of an investment in one or more new U.S. sources of Mo-99, the length of investment timelines, and the financing, construction, regulatory, operational, safety and market risks associated with some of these opportunities, U.S. government financial support in the form of outright grants or long term loans could potentially make the difference between whether an important new source of Mo-99 is viable or not. This is even before the public policy issues of accessible and affordable health care, efficient waste stream management and nuclear non-proliferation are considered.

As an entrepreneurial company, Lantheus recognizes that the Committee does not want the DOE to commit to support one or more projects if those projects themselves are not eventually self-sustaining. Lantheus believes that when making decisions on which projects to fund and in what amounts, the Committee and the DOE should consider, among other things, the following:

- the magnitude of technological risk associated with each proposed project
- timelines to completion
- execution risk
- the potential supply of Mo-99 the proposed project could provide
- waste stream generation and management
- the capability of a project to be self-sustaining when operational
- the aggregate cost of the proposed project to the U.S. taxpayer

Lantheus believes that the U.S. government financial support of multiple projects with appropriate investment risk profiles will be the best way to develop a robust domestic supply of Mo-99. The private sector will play a major role in the development of new technologies and this domestic supply – the strong support of the U.S. government, however, will also be necessary to overcome market failure and to advance important public policy goals.

IV. Health Care Policy – Improving Patient Outcomes and Reducing Costs

It is important to note that the medical imaging procedures that rely on Tc-99m-based imaging agents contribute to improved patient care as well as cost savings for the entire health care system. According to Einstein et al, "The powerful diagnostic and risk-stratification data provided by these [nuclear medicine] procedures play a central role in clinical cardiology and have contributed to the decrease in morbidity and mortality from coronary heart disease." (Einstein et al, *Circulation* 2007 at 1290)

Tc-99m-based imaging agents allow physicians to risk-stratify – with a proven and accurate non-invasive diagnostic modality, clinicians can determine whether a patient requires additional, more expensive and riskier invasive diagnosis or treatment. This leads to more appropriate treatments, better patient outcomes, less morbidity associated with inappropriate treatments and significant cost savings for the system.

As an example of this, between approximately 20 and 40% of patients that undergo a diagnostic cardiac catheterization – an invasive and costly procedure with significant morbidity and mortality risks – are found not to have significant coronary artery disease. In other words, hundreds of thousands of procedures are performed each year at an annual cost to the system of potentially billions of dollars, and no significant underlying disease is identified. A number of these cardiac catheterization procedures could be avoided if the patients had had a nuclear cardiology imaging study using a Tc-99m-based tracer. A nuclear imaging study is non-invasive and the radiation exposure to the patient is comparable to a cardiac catheterization (although the radiation exposure to health care professionals performing the procedures is substantially less for nuclear imaging). Moreover, a nuclear diagnostic study is between approximately 20 and 30% of the cost of a cardiac catheterization.

Thus, cardiac medical imaging procedures that rely on Tc-99m-based imaging agents can improve patient outcomes and reduce costs – particularly when performed in accordance the appropriateness criteria developed by the American College of Cardiology and the American Society of Nuclear Cardiology. Strategic investments to help develop a domestic supply of Mo-99 should pay large dividends – for both U.S. patients and U.S. taxpayers.

V. Conclusion

The Mo-99 supply crisis is chronic, resulting from an aging supply infrastructure and a market failure to attract sufficient replacement capacity. The crisis has become acute because of the ongoing shutdown of NRU and the on-going repairs of HFR. Lantheus has been able to diversify its global supply chain and now has access to all of the major medical isotope-producing reactors in the world. However, Lantheus is still not able to fully meet its weekly demand for Technelite® generators, and we have been forced to allocate our Mo-99 supply and Technelite® generators so that we can serve as many customers and patients as possible.

Because approximately one-third of the Mo-99 manufactured outside of North America decays before it even reaches the Lantheus generator manufacturing facility – "buying ice on a warm day" – Lantheus believes a robust U.S. supply of Mo-99 is important U.S. public policy for reasons of accessible and affordable health care, efficient waste stream management and nuclear non-proliferation.

In the face of the Mo-99 supply crisis, important diagnostic procedures often relating to life-threatening conditions such as heart disease and cancer are being postponed or cancelled because of the decreased volume of Tc-99m available to the nuclear medicine community. In addition, clinicians appear to be turning to older nuclear modalities with potentially less diagnostic certainty and more patient risk. Clinicians may also be foregoing nuclear medicine completely, opting for more invasive, more expensive, higher risk, surgical procedures. The nuclear medicine community seems widely affected by the

supply crisis and appears to be adopting a variety of strategies to try to conserve the Mo-99 which is available.

Lantheus believes that the private sector should have a major role in the resolution of Mo-99 supply crisis. However, Lantheus also believes that there is a strong role for the U.S. government to play in helping resolve the crisis. U.S. government financial support of multiple projects with appropriate investment risk profiles will be the best way to develop a robust domestic supply of Mo-99 – overcoming market failure and advancing important public policy goals.

As a matter of health care policy, medical imaging procedures that rely on Tc-99m based imaging agents can improve patient outcomes and reduce costs. Strategic investments to help develop a domestic supply of Mo-99 should pay large dividends – for both U.S. patients and U.S. taxpayers.