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SOLVING THE MEDICAL ISOTOPE CRISIS

HEARING

BEFORE THE

SUBCOMMITTEE ON ENERGY AND ENVIRONMENT

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

ONE HUNDRED ELEVENTH CONGRESS

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SOLVING THE MEDICAL ISOTOPE CRISIS

WEDNESDAY, SEPTEMBER 9, 2009

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON ENERGY AND ENVIRONMENT,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 2:09 p.m., in Room 2322, Rayburn House Office Building, Hon. Edward J. Markey [chairman of the subcommittee] presiding.

Present: Representatives Markey, Barrow, Upton, Shimkus, and Scalise.

Staff Present: Jeff Baran, Counsel; Matt Weiner, Special Assistant; and Peter Ketcham-Colwill, Special Assistant.

OPENING STATEMENT OF HON. EDWARD J. MARKEY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF MASSACHUSETTS

Mr. MARKEY. Welcome ladies and gentlemen to the Subcommittee on Energy and the Environment and our very important hearing.

Every day in the United States, thousands of people go to the hospital to be treated for life-threatening illnesses such as heart disease and cancer. But right now, due to the breakdown of a nuclear reactor in Canada, many of these critical procedures are being delayed and compromised.

The United States is facing a crisis in nuclear medicine. We face a severe shortage of a crucial radioactive isotope which is required for nearly 50,000 medical procedures every day, usually to produce a detailed image such as a cancer or a bone scan. The shortage of this isotope, which usually costs only $10 of a multi-thousand dollar procedure, is threatening the health care of millions of Americans. Worst of all, the United States does not currently produce any of the isotope domestically. Instead, we are entirely dependent on a handful of foreign nuclear reactors, most of which are several decades old, some of which are literally falling apart and which rely upon weapon usable highly enriched uranium for their operation.

In May, the 51-year-old Canadian NRU reactor broke down. It is not yet clear whether the reactor will ever operate again. In mid July, the 47-year-old HFR reactor in the Netherlands was taken off-line for maintenance for 1 month. Together, these two reactors usually produce our entire isotope supply. While the United States was able to secure a small supply during this time from other reactors, Americans health care suffered as a result. A recent survey

of the nuclear medicine community provided sobering results. Eighty percent said their practice was impacted by the shortage. Eighty percent said they have postponed procedures. Forty-seven percent said they have cancelled procedures, and 57 percent said they had substituted alternative procedures. Unfortunately, in most cases the alternative procedures are more invasive, less effective, more costly, and pose greater radiation risk to both patients and technicians.

We don't need alternatives. We need the state of the art to be fully available again. Medical care in this country for cancer, heart disease, bone scans simply cannot be held hostage to the maintenance schedules of a 50-year-old reactor in Europe. It is absolutely vital that we act to bring a robust domestic supply of these critical medical isotopes online as soon as possible.

In order to address the crisis in nuclear medicine, I have introduced, along with my good friend, colleague and partner, Fred Upton, H.R. 3276, the American Medical Isotopes Production Act of 2009. The bill will provide the Department of Energy new authorities and resources to assist the private sector in establishing as rapidly as possible a robust medical isotope production capacity here in the United States. In addition, the bill will end the export of bomb-usable highly enriched uranium for medical isotope production in 7 to 10 years, as recommended in a recent National Academy of Sciences report that also said there was no reason that these isotopes couldn't be made using low enriched uranium. In fact, both Argentina and Australia have started producing medical isotopes with low enriched uranium. Highly enriched uranium is nuclear bomb material, and the national security of the United States demands that we never export it again.

The Markey-Upton bill is a bipartisan bill. It has been endorsed by the Society for Nuclear Medicine, the American College of Radiology, the American Society for Radiation Oncology, the American College of Cardiology, the American Society of Nuclear Cardiology, the American Association of Physicists in Medicine, the Health Physics Society, the Council on Radionuclides, a list of companies as well plus the Nuclear Threat Initiative, the Union of Concerned Scientists and Physicians For Social Responsibility.

I would like to ask for unanimous consent that the letters of endorsement from these organizations be entered into the record. I also would like to ask unanimous consent that members will have 5 legislative days to revise and extend their remarks and to insert extraneous material in the record.

Today's hearing will allow the subcommittee to explore this important issue and to hear the panel's views on H.R. 3276. I hope that we can all work together to address this crucial problem facing American hospitals and patients.

Now I would like to turn and recognize my good friend, the gentleman from Michigan, Mr. Upton for his opening statement.

Mr. UPTON. Thank you, Mr. Chairman. I am going to ask unanimous consent that my full statement be made part of the record.

And trying to shorten up some of the time as we are expecting votes soon, let me just make a couple of comments. We are really at a crisis. As you indicated, 16 million medical procedures in the U.S. that rely on the import of Moly-99. That's 50,000 a day. It is

clear that our Nation must produce these lifesaving isotopes domestically to ensure that the public health is protected. And when I learned of this situation when you and I talked about it in July before the August break, I was delighted to partner with you to introduce legislation that I hope can move quickly.

There are a good number of organizations that are onboard. I would like to think that this hearing will catapult us into getting a bill to the House very soon. And at this point, I yield back the balance of my time.

[The prepared statement of Mr. Upton follows:]

September 9, 2009
Statement of Congressman Fred Upton
Ranking Member
Subcommittee on Energy and Environment
Legislative Hearing on
"Solving the Medical Isotopes Crisis"

Thank you Chairman Markey for calling this hearing today, on a bi-partisan bill that addresses a looming crisis in nuclear medicine by ensuring that a robust and reliable supply of the most critical medical isotopes are produced in the United States.

Every year, 16 million medical procedures in the United States rely on the import of Moly-99. That's 50,000 per day. We import 100% of our supply of this critical isotope. The Canadian reactor that, for decades, has been the source of over 60% of our Moly-99 is now off-line – and may never restart. Without a proper supply of this critical isotope, tens of thousands of patients a day will be affected. And they will be affected in a major way. Among other uses, these isotopes are used in procedures for the detection and staging of cancer and the detection of heart disease.

Typically, when we talk about nuclear in this committee it is relating to generating clean, zero emission power. But with our hearing today, we see that the benefits of

nuclear are many, from providing the catalyst for clean power to life saving medicine. Problems abroad have exposed troublesome flaws here at home in nuclear medicine – it is clear that our nation must produce these life saving isotopes domestically to ensure the public health is protected.

I hope this legislation that we are examining today will just be a first step to ensure there will be a stable supply of Molly-99. My desire is to have it produced here at home.

The *American medical Isotopes Production Act* is a testament to bipartisan cooperation. This legislation has been endorsed by countless organizations, such as:

- The Society for Nuclear Medicine
- The American Association of Physicists in Medicine
- The American College of Radiology
- The American College of Cardiology
- University of Missouri

I look forward to hearing from our witnesses today and making any necessary changes to this legislation as it moves though the process.

I yield back.

Mr. MARKEY. Thank you. The Chair recognizes the gentleman from Illinois.

Mr. SHIMKUS. I will waive.

Mr. MARKEY. The Chair recognizes the gentleman from Louisiana.

Mr. SCALISE. I will waive.

Mr. MARKEY. That is great. We will recognize our very distinguished panel. Our first witness is Dr. Parrish Staples, director of the Office of European and African Threat Reduction at the National Nuclear Security Administration of the Department of Energy. Dr. Staples has played a leading role within the Department of Energy to help solve the medical isotopes crisis. In addition, his office is responsible for implementing the Department of Energy's efforts to reduce the use of highly enriched uranium around the world including in the production of medical isotopes.

STATEMENTS OF PARRISH STAPLES, DIRECTOR, EUROPEAN AND AFRICAN THREAT REDUCTION, OFFICE OF GLOBAL THREAT REDUCTION, NATIONAL NUCLEAR SECURITY ADMINISTRATION, UNITED STATES DEPARTMENT OF ENERGY; STEVEN LARSON, M.D., CHIEF, NUCLEAR MEDICINE SERVICE, DEPARTMENT OF RADIOLOGY, MEMORIAL SLOAN-KETTERING CANCER CENTER, VICE-CHAIRMAN, COMMITTEE ON MEDICAL ISOTOPE PRODUCTION WITHOUT HIGHLY ENRICHED URANIUM, NATIONAL ACADEMY OF SCIENCES; AND MICHAEL DUFFY, VICE PRESIDENT AND GENERAL COUNSEL, LANTHEUR MEDICAL IMAGING, MEMBER OF THE BOARD, COUNCIL ON RADIONUCLIDES AND RADIOPHARMACEUTICALS

Mr. MARKEY. We welcome you, Dr. Staples. Whenever you're ready please, again.

STATEMENT OF PARRISH STAPLES

Dr. STAPLES. Thank you, Chairman Markey, Ranking Member Upton, and the subcommittee members. Thank you for the opportunity to testify on the National Nuclear Security Administration's Global Threat Reduction Initiative's role in minimizing, and to the extent possible, eliminating the use of highly enriched uranium in civilian nuclear applications including in the production medical radioisotopes. As part of my testimony, I will briefly describe recent efforts to mitigate the impact of the current and anticipated shortages of the medical isotope moly-99 and discuss in more detail our efforts to accelerate the establishment of a domestic commercial supply of moly-99 that does not use highly enriched uranium.

Finally, I will highlight how the proposed American Medical Isotopes Production Act of 2009 can greatly help to advance our progress on the dual U.S. policy priorities to, one, establish a secure supply of this critical medical isotope for U.S. citizens, and two, to minimize the civilian use of proliferation-sensitive highly enriched uranium around the globe.

First, section 2 of the American Medical Isotope Production Act of 2009 very appropriately and succinctly covers the history, the use of moly-99, the decay product technecium-99 nine, the issues

surrounding the current medical isotope production industry, the current acute shortage of moly-99 within the medical community, and the critical importance that this isotope provides to the health care of Americans on a daily basis. And most importantly, it also covers the state of the art technology regarding conversion to low enriched uranium.

Very important to us, on January 14, 2009, the National Academy published a report confirming that the production of moly-99 without the use of highly enriched uranium is both technically and economically feasible. In addition to the National Academy's determination that there are no technical reasons that adequate quantities of medical isotope cannot be produced without the use of HEU, the National Academy also stated that the single greatest threat to the supply reliability is the approaching obsolescence of the aging reactors that current large-scale producers utilize to irradiate HEU targets to obtain moly-99. The findings of this report unambiguously support the consistency of HEU minimization policies with the full-scale production of medical isotopes while highlighting the fragile nature of the current supply chain due to the age of the foreign moly-99 production facilities.

Now, with our mission to reduce and eliminate the use of HEU in civilian applications NNSA has been working for many years to convert research reactors from the use of HEU to LEU fuel. We agree with the language in the proposed legislation which makes clear that the U.S. should accelerate its effort to convert HEU research reactors worldwide from the use of HEU. In fact, this acceleration is already underway at NNSA.

We and the Global Threat Reduction Initiative have significantly accelerated our efforts over the past several years and to date have converted 57 highly enriched uranium fuel research reactors globally from the use of HEU to LEU fuels. Through GTRI efforts, another seven HEU research reactors have been verified to shut down prior to their conversion. These activities have resulted in more than 320 kilograms of HEU no longer being used annually for reactor operations.

In addition, NNSA has also been working with both existing and potential moly-99 producers for several years to convert or develop their moly-99 production processes to utilize non-HEU-based technologies. NNSA provides technical expertise on a nonproprietary basis to all existing and potential producers to assist in converting and developing their moly-99 production processes in accordance with the U.S. HEU minimization policy. Through these efforts NNSA has established longstanding relationships with current and future moly-99 suppliers and we are uniquely suited to accelerate efforts to establish a reliable domestic supply without the use of HEU. Due to the current lack of global production capacity of moly-99 by industry, we are actively engaging in discussions with all current and possible producers to best determine how to rapidly transform the industry into a diverse, stable, commercial supply network that will not use HEU for production of this vital medical isotope.

Given the market dynamics with the current supply shortage, we fully expect that the 7-year timeframe referenced in the American Medical Isotopes Production Act of 2009 is more than adequate to

ensure that a sufficient supply of non-HEU moly-99 can be available to the medical community. Further we believe that the development of new producers or the conversion of existing producers to low enriched uranium can be accomplished with no impact upon the current supply availability. In fact, through the current acute supply shortage of this critical medical isotope and the associated market dynamics with the focus of the American Medical Isotopes Production Act of 2009 on this issue, we believe that we can ensure the successful development of a diverse, reliable supply of moly-99 to the medical community that will also help to accomplish an important and longstanding nuclear nonproliferation mission.

Now, the United States has approached the moly-99 supply problem by——

Mr. MARKEY. If you could summarize please, Dr. Staples.

Dr. STAPLES. I would just go to my closing paragraph then. The American Medical Isotope Production Act of 2009 is crucial of ensuring the success of our efforts to accelerate development of a domestic supply of moly-99 nine without the use of HEU. This legislation will accelerate greatly and enhance the development of reliable supply of this isotope for the use in the U.S. medical community and further support U.S. objectives to reduce the use of proliferation-sensitive HEU in civilian applications.

I thank the subcommittee and Chairman Markey, in particular, for your continued leadership on such a crucial nuclear energy and civil nuclear application issue, and we stand ready to answer questions.

Mr. MARKEY. Thank you, sir.

[The prepared statement of Dr. Staples follows:]

Testimony before the House Energy and Environment Subcommittee
of the Energy and Commerce Committee

Dr. Parrish Staples
Director, Office of European and African Threat Reduction
Global Threat Reduction Initiative
National Nuclear Security Administration
U.S. Department of Energy

Wednesday, September 9, 2009

Chairman Markey, Ranking Member Upton, and Subcommittee Members, thank you for the opportunity to testify on the National Nuclear Security Administration's (NNSA) Global Threat Reduction Initiative (GTRI) role in minimizing and, to the extent possible, eliminating the use of highly enriched uranium (HEU) in civilian nuclear applications, including in the production of medical radioisotopes. As part of my testimony, I will briefly describe recent efforts to mitigate the impact of the current and anticipated shortages of the medical isotope molybdenum-99 (Mo-99) and discuss in more detail NNSA's efforts to accelerate the establishment of a domestic commercial supply of Mo-99 that does not use HEU. Finally, I will highlight how the proposed *American Medical Isotopes Production Act of 2009* can greatly help to advance progress on the dual U.S. policy priorities to: 1) establish a secure supply of this critical medical isotope for U.S. citizens, and 2) minimize the civilian use of proliferation-sensitive HEU around the globe.

Mo-99 is the parent isotope of Tc-99m, which is used in approximately 50,000 diagnostic medical isotope procedures performed everyday in the United States. With half-lives of only 66 hours and 6.7 hours respectively, the supply of Mo-99 and Tc-99m

cannot be stockpiled. Currently, there are no facilities within the United States that are dedicated to the production of Mo-99 for medical uses. Instead, the United States must import 100% of the domestic Mo-99 supply from foreign production facilities that use HEU in their production processes, leaving the United States dependent upon the continued operation of foreign facilities in order to obtain the Mo-99 needed to perform millions of essential medical procedures annually. In recent years, unexpected shutdowns of the primary producers have crippled the global Mo-99 supply chain, largely due to unforeseen required maintenance necessary to keep these aging facilities operational. Most recently, the primary foreign producer, which supplies approximately 60% of the U.S. supply, shut down for an extended period on May 14, 2009. Further exacerbating this situation, the remaining foreign producers that supply the U.S. market are also projecting supply reliability issues due to required maintenance shutdowns of their own facilities for the foreseeable future. The necessity of this key medical isotope for the healthcare of Americans, coupled with the deteriorating facilities of existing global suppliers, clearly highlights the need for commercial Mo-99 producers to develop new production capabilities. This incipient supply shortage is unfortunate, and requires action to expand and ensure adequate Mo-99 production capabilities worldwide. However, such actions can and should be undertaken in support of U.S. efforts to minimize the global use of civilian HEU. The United States must now move expeditiously to ensure that a robust and reliable supply of Mo-99 can be produced for the U.S. market without the use of HEU.

Historically, Mo-99 production processes have utilized the same HEU that can be used to produce nuclear weapons and nuclear explosive devices. Underscoring the global recognition of the grave threats posed by excess nuclear materials and the possible acquisition of such materials by terrorists or rogue states, new technical advances in Mo-99 production processes—just as in other civilian applications—are demonstrating that HEU is no longer required.

On January 14, 2009, the National Academies published a report confirming that the production of Mo-99 without the use of HEU is both *technically* and *economically* feasible. In addition to the National Academies' determination that there are "no technical reasons that adequate quantities [of medical isotopes] cannot be produced" without the use of HEU, the National Academies also stated that "...the greatest single threat to supply reliability is the approaching obsolescence of the aging reactors that current large-scale producers utilize to irradiate HEU targets to obtain Mo-99." The findings of this report unambiguously support the consistency of HEU minimization policies with the full-scale production of medical isotopes, while highlighting the fragile nature of the current supply chain due to the age of the foreign Mo-99 production facilities.

With our mission to reduce and eliminate the use of HEU in civilian applications, NNSA has been working for many years to convert research reactors from the use of HEU to LEU fuel. We agree with the language in the proposed legislation which makes clear that the U.S. should accelerate its efforts to convert HEU research reactors

worldwide from the use of HEU. This acceleration is already under way at NNSA. GTRI has significantly accelerated efforts over the past several years and, to date, has converted 57 HEU research reactors globally from the use of HEU to LEU fuels. Through GTRI efforts, another 7 HEU research reactors have been verified as shutdown prior to conversion. These activities have resulted in more than 320 kilograms of HEU no longer being used annually for HEU reactor operations.

In addition, NNSA also has been working with both existing and potential Mo-99 producers for several years to convert or develop their Mo-99 production process to utilize non-HEU based technologies. NNSA provides technical expertise, on a non-proprietary basis, to all existing and potential producers to assist in converting and developing their Mo-99 production processes in accordance with the U.S. HEU minimization policy. Through these efforts, NNSA has established long-standing relationships with current and future Mo-99 suppliers and is uniquely suited to accelerate efforts to establish a reliable domestic supply without the use of HEU.

The United States has approached the Mo-99 supply problem by focusing on near-term efforts to mitigate shortage problems, and long-term efforts to develop new future supply sources. The U.S. Department of Energy, including NNSA, the Office of Nuclear Energy, and the Office of Science, along with other Federal agencies and programs, was directed by the White House to investigate options to produce Mo-99 in the short-term to supplement the available supply while new longer-term production capabilities are developed. An Inter-agency Working Group led by Office of Science and

Technology Policy in the Executive Office of the President has been established and has identified several options that could result in stabilizing a reduced supply of Mo-99 in 2010 for use by the medical community until a permanent non-HEU supply infrastructure is established for domestic production capabilities.

For our part, NNSA is currently developing projects to accelerate the establishment of domestic commercial sources of Mo-99 without the use of HEU. NNSA is working on several Cooperative Agreements to potential commercial Mo-99 producers, whose projects are in the most advanced stages of development, accelerating their efforts to begin producing Mo-99 in quantities adequate to the U.S. medical community's demand by the end of 2013. These commercial producers each use a different non-HEU technology, in support of our strategy to diversify the supply chain and move away from reliance on a sole technology and a limited number of facilities, such as used by today's foreign producers. We intend to spend approximately $30 million annually to establish a non-HEU domestic Mo-99 production process and funding for this effort would come from within the Global Threat Reduction Initiative budget.

The *American Medical Isotopes Production Act of 2009* is crucial to ensuring the success of these efforts to accelerate development of a domestic supply of Mo-99 without the use of HEU. This legislation will accelerate greatly the development of a reliable supply of this isotope for use in the U.S. medical community, and further support U.S. objectives to reduce the use of proliferation-sensitive HEU in civilian applications. I thank the Subcommittee and Chairman Markey, in particular, for your continued

leadership on such crucial nuclear energy and civil nuclear application issues, and stand ready to answer any questions.

Mr. MARKEY. Our second witness is Dr. Steven Larson the Chair of the Nuclear Medicine Service, Department of Radiology at the Memorial Sloan-Kettering Cancer Institute. Whenever you are ready, please begin.

STATEMENT OF STEVEN LARSON, M.D.

Dr. LARSON. Good afternoon, chairman and members of the committee. My name is Steven Larson, and I am chief of nuclear medicine, as you have heard at Memorial Sloan-Kettering Cancer Institute in New York. I also served as vice chair of the National Research Council's Committee on medical isotope production without highly enriched uranium. I was asked to testify today regarding the report from the study, but first I want to offer some personal observations as a practicing nuclear medicine physician.

I am the director of a large nuclear medicine clinic at Memorial Sloan-Kettering Cancer Center. For most of the summer like other nuclear medicine clinics in the northeast, we have seen a reduction of 20 to 25 percent in the optimum amount of technetium for clinical use. Now, technetium 99m, as you have heard, is by far the most common clinical isotope and a bellwether for nuclear medicine isotope supplied health care. This reduction supply has negatively impacted our ability to efficiently deliver nuclear medicine-based care to patients.

Furthermore, medical isotope providers are telling us to expect continued shortages of technetium 99m during 2009 and beyond, and they are warning about the possibility of even deeper reductions in technetium 99m availability. Clearly we are in the need of a more reliable supply of medical isotope for American health care.

Let me turn to the National Research Council's study on medical isotope production without highly enriched uranium. The mandate for this study came from section 630 of the Energy Policy Act of 2005. Our study was completed in late 2008, and the final report was issued in January, 2009. It focused primarily on the use of HEU for the production of medical isotope molybdenum 99.

Briefly, some key findings. Adequate quantities of medical isotopes to meet U.S. demands could be produced without HEU. A report found that an anticipated average cost increase to convert to the production of medical isotopes without the use of HEU would likely be less than 10 percent for most current large-scale producers. Reliability of medical isotope supply is a significant problem now and likely to be a problem for the foreseeable future with demand close to total capacity for production and with little margin for additional production capacity in the event of an interruption of supply.

On the other hand demand for nuclear medicine services are stable with likely growth rates of utilization of 3 to 5 percent per year.

Several steps could be taken by the U.S. Government and others to improve the feasibility of eliminating the use of HEU for medical isotope production. I note that H.R. 3276 legislatively enshrines several of these steps. It authorizes the Department of Energy to provide technical assistance to producers who wish to convert to production without HEU. It provides financial assistance to develop a domestic isotope production capacity, and it provides for a 7-year phaseout period for HEU exports for medical isotope production.

When I began work on this study I was skeptical about the economic feasibility of conversion to LEU-based medical isotope production and the potential impact that that might have on conversion or supply reliability. But based on the information I received during this National Research Council study, I now believe that if medical isotope producers have the will to convert that, they can do so without undue costs. My opinion is based on the observations we made during the site visits to the medical isotope production facilities in Argentina and Australia and discussion with technical experts about conversion. Under modest circumstances and without elaborate additional infrastructure, Argentina was able to convert to LEU-based production in less than 2 years and for less than a million dollars in supplies and facilities modification.

The Argentina process is now being implemented in Australia and the Australian company, ANSTO, hopes to begin exporting small quantities of molybdenum 99 to the United States in the near future.

This concludes my oral testimony to the committee and I would be pleased to answer any questions.

Mr. MARKEY. Thank you so much, Dr. Larson.

[The prepared statement of Dr. Larson follows:]

Testimony of

Steven M. Larson, M.D.

Donna and Benjamin M. Rosen Chair

Chief of Nuclear Medicine Service

Department of Radiology

Memorial Sloan Kettering Cancer Center

Professor of Radiology

Weill Cornell Medical Center

New York, New York 10021

and

Vice-chair, Committee on Medical Isotope Production

without Highly Enriched Uranium

National Research Council of the the National Academies

Washington, DC

House of Representatives Committee on Energy and Commerce

Subcommittee on Energy and the Environment

Hearing on H.R. 3276, the American Medical Isotopes Production Act of 2009

September 9, 2009

Steven M. Larson, M. D., Testimony on H.R. 3276, the American Medical Isotopes Production Act of 2009

Good morning, Mr. Chairman and members of the Committee. My name is Steven M. Larson and I am the Donna and Benjamin M. Rosen Chair and Chief of Nuclear Medicine Service of the Department of Radiology at Memorial Sloan Kettering Cancer Center, New York, New York. I also served as vice chair of the National Research Council's (NRC's)[1] Committee on "Medical Isotope Production without Highly Enriched Uranium." I was asked to testify today regarding the findings and recommendations of this report.

First, if I may, I wish to offer some personal observations, as a practicing nuclear medicine physician with long experience, regarding the timeliness and importance of H.R. 3276 to the field of nuclear medicine and its importance to medical care. I am the director of a large nuclear medicine clinic at Memorial Sloan-Kettering Cancer Center in New York City. We have one of the larger clinical practices in the United States, and typically we see between 110 to 120 patients per day, of which two thirds require diagnostic procedures that utilize technetium 99m when this isotope is available. However, the recent and unplanned shutdown of the NRU reactor at Chalk River in Canada has disrupted supplies of this important isotope to our clinic and to other hospitals in the northeastern United States. For most of the summer, our clinic has seen a reduction of between 20% and 25% in the amount of technetium 99m available for clinical use. Furthermore, medical isotope providers are telling us to expect continued shortages of technetium 99m during 2009 and beyond, and they are warning about the possibility of even deeper reductions in technetium 99m availability on the near horizon,

[1] The National Research Council is the operating arm of the National Academy of Sciences, National Academy of Engineering, and the Institute of Medicine of the National Academies, chartered by Congress in 1863 to advise the government on matters of science and technology.

since continued U.S. supply is dependent on old Canadian and European reactors whose operational life expectancies are unpredictable.

We accommodated to this new reality by reducing the dose for bone scans, delaying patient care, particularly for ventilation and perfusion scans, and switching to other less optimal isotopes such as thallium 201. In addition, we have also begun to perform more procedures using rubidium 82 and a PET/CT scanner, even though the economics are not as favorable in our setting.

At present, we have the acute exacerbation of a chronic problem with technetium 99m supplies that is the result of an unhealthy dependency on reactors in other countries whose operational life expectancy is unpredictable. To make matters worse, continued operation of these reactors depends on the willingness of foreign governments in Canada, Europe, and South Africa to provide subsidies and in some cases modify their reactor operations to continue medical isotope production for the needs of our citizens

In my personal opinion, technetium 99m will continue to be the workhorse radiopharmaceutical for patient care in the United States for the foreseeable future, especially for cardiac and oncology applications. I personally support the objectives of the proposed legislation, H.R. 3276. The development of a reliable domestic supply of technetium 99m is good public policy.

Let me now turn to the key relevant findings and recommendations from the NRC report "Medical Isotope Production without Highly Enriched Uranium." The mandate for this report came from Section 630 of the Energy Policy Act of 2005. The Secretary of Energy was directed to contract with the National Academies for a study on the

elimination of highly enriched uranium (HEU[2]) from reactor fuel, reactor targets, and the production of medical isotopes. The study request arose because of a conflict between the Energy Policy Act of 1992, which created increasing pressure to phase out U.S. exports of HEU for medical isotope production, and the Energy Policy Act of 2005, which sought to increase the reliability of medical isotope supply by lifting the requirements of the 1992 Act for HEU exports to Canada, the Netherlands, Belgium, France, and Germany for medical isotope production. The balance between the dual objectives of securing HEU and providing a reliable supply of medical isotopes drove much of the discussion and work of the NRC committee. H.R. 3672 appears to be inspired by similar concerns.

Our study was completed in late 2008 and the final report was issued in January 2009. It focuses primarily on the use of HEU for the production of the medical isotope molybdenum 99, because its decay product, technetium 99m, is by far the most common clinical isotope and a bellwether for nuclear medicine isotope supply to healthcare. Our report concluded that the production of sufficient quantities of molybdenum 99 would ensure that other reactor-produced medical isotopes would also be available in sufficient quantities to meet healthcare needs.

The study had five specific charges, which I have paraphrased here:

1. Determine feasibility of procuring supplies of medical isotopes from commercial sources that do not use HEU.

[2] HEU is defined as uranium enriched in the isotope uranium 235 to levels greater than or equal to 20%. The United States supplies most of the HEU that is used to produce medical isotopes.

2. Determine current and projected demand and availability of medical isotopes in regular and current domestic use.
3. Determine progress being made by the Department of Energy and others to eliminate all use of HEU in reactor fuel, reactor targets, and medical isotope production.
4. Determine the potential cost differential in medical isotope production in the reactors and target processing facilities if the products were derived from the production systems that do not involve fuels and targets with HEU.
5. Identify additional steps that could be taken by DOE and medical isotope producers to improve feasibility of conversion of HEU based to LEU based processes.

Let me briefly summarize the key relevant findings and recommendations from the report.

With regard to charge 1, the committee found that at the present time there were not sufficient quantities of medical isotopes produced without HEU to meet U.S. domestic needs, but that the committee saw no technical reason that adequate quantities could not be produced. In fact, Argentina and Australia are now producing medical isotopes without HEU.

With regard to charge 2, the current U.S. demand for molybdenum 99 is about 5000-7000 6-day curies per week. Demand for nuclear medicine services is stable, with a likely growth rate in utilization of 3-5% per year. Technetium 99m is crucial to the nation's health care in oncology, cardiology, and neurology. Reliability of supply is a

significant problem now and likely to be a problem for the foreseeable future. Total capacity for production is very near current use, and there is little margin for additional production capacity in the event of an interruption of supply. The NRC report noted that "because current supplies of Mo-99 are produced in reactors built largely at government expense, private companies that can provide new domestic supplies of [molybdenum 99] might not choose to compete without government assistance."

With regard to charge 3, the U.S. Department of Energy (DOE) is leading the Global Threat Reduction Initiative (GTRI), which is working to convert reactor fuel and targets from HEU to low enriched uranium (LEU[3]). The report found that DOE is making considerable progress in converting reactor fuel and targets. However, much work remains to convert reactor targets for molybdenum 99 production from HEU to LEU. This is not a criticism of DOE, but rather the result of the reluctance of private-sector producers to convert. LEU targets are being used today to produce molybdenum 99 in Argentina and Australia. There is no technical reason that LEU targets could not be used by other producers.

With regard to charge 4, the report found that the anticipated average cost increase to convert to the production of medical isotopes without the use of HEU would likely be less than 10 percent for most current large-scale producers. This finding was based on a present value cost analysis at three steps in the molybdenum 99/technetium 99m supply chain: production of molybdenum 99, production of technetium generators, and

[3] LEU is uranium enriched in the isotope uranium 235 to less than 20 percent.

delivery of technetium 99m doses. This is probably the most controversial finding in the report. I will say more about this later in my testimony.

With regard to charge 5, the report identifies additional steps that could be taken by DOE and others to improve the feasibility of conversion of medical isotope production. These include the following:

- Producers should commit to conversion and announce a best-effort schedule for eliminating HEU-based production.
- DOE should make the considerable technical expertise of the national laboratory system available to assist producers with conversion-related research and development.
- The Department of State should intensify the diplomatic pressure on countries that still use HEU to induce them to convert. In particular, those countries that are partners in the GTRI have made a commitment to the minimization of HEU and should be encouraged to live up to their commitments.
- The Food and Drug Administration (FDA) should work with industry and technical experts to ensure that there is a common understanding of likely FDA requirements for obtaining regulatory approvals for the use of LEU produced Mo99 in radiopharmaceuticals.
- The U.S. Congress should provide clear and consistent policy directions concerning conversion to LEU-based molybdenum 99 production, consider a gradual phaseout of HEU exports for medical isotope production, and consider

incentives to motivate conversion and the development of domestic sources of molybdenum 99 production.

H.R. 3276 legislatively enshrines some of these steps: It authorizes DOE to provide technical assistance to producers who wish to convert, it provides financial assistance to develop a domestic production capacity, and it provides for a seven-year phase-out period for HEU exports.

As I mentioned before, the report's conversion cost analysis has proven to be controversial with some stakeholders. I can say that when I began work on the NRC study I too was skeptical about the feasibility of conversion to LEU-based medical isotope production and the potential impact of conversion on supply reliability. Based on the information I received during this NRC study I now believe that if the medical isotope producers have the will to convert they can do so without undo costs. I am not an economist or an expert accountant; instead, my opinion is based on the observations we made during site visits to medical isotope production facilities in Argentina and Australia and discussion with technical experts about conversion.

Under modest circumstances, and without elaborate additional infrastructure, Argentina was able to convert from HEU-based production to LEU-based production in less than two years and for less than a million dollars for supplies and facilities modification. The Argentina production process is now being implemented in Australia, and the Australian company ANSTO hopes to begin exporting small quantities of molybdenum 99 to the United States in the near future.

I was also initially concerned about the flexibility that FDA would have with respect to regulatory requirements for conversion. However, this concern was allayed when FDA regulators fast-tracked approval of the molybdenum 99 produced from Australia and South Africa for use in the United States. It is clear that FDA is prepared to act quickly when it receives high-quality applications from producers.

This concludes my testimony to the committee. I would be pleased to answer any questions.

Mr. MARKEY. And our final witness is Michael Duffy, vice president and general counsel of Lantheus Medical Imaging, one of only two U.S. manufacturers of these type of generators. Welcome, sir.

STATEMENT OF MICHAEL DUFFY

Mr. DUFFY. Good afternoon, Mr. Chairman, Mr. Upton, members of the committee, staff. I am here today to testify on behalf of the bill on behalf of both Lantheus and CORAR, the Council on Radionuclides and Radiopharmaceuticals. Lantheus endorses H.R. 3276. We strongly support the committee's efforts to promote the protection of moly in the United States for medical isotope applications. We have been a worldwide leader in diagnostic medical imaging for the past 50 years. Lantheus is the home to leading diagnostic imaging brands, including the Technelite generator which I have for those who want to take a look, and this is what actually causes the—the radioactive salient is put through here. It comes out here and is mixed with a powder and becomes the injection which is injected into the patient.

So what's so important about these imaging agents, these radionuclides? They allow a clinician to have a functional view of an organ like the heart more than just a mere anatomical image. Instead, a picture from the outside looking in, they allow the physician to see what is inside projecting out, for example, blood flow, heart function, tissue health. These are extremely helpful and important in the diagnosis and treatment of disease. The moly supply crisis is a chronic crisis resulting from an aging supply infrastructure and a market failure to attract sufficient replacement capacity. As Chairman Markey said, the crisis has become acute because of the ongoing shutdown in Canada at the NRU reactor and the ongoing repairs in the Netherlands at the HFR reactor. Although Lantheus has had access to moly supply from the major moly-producing reactors around the world, because of this crisis, we have not been fully able to meet our customers' needs and we are having to ration the generators on a weekly basis.

Approximately a third of the moly manufactured outside of North America decays before it reaches our manufacturing facility in Massachusetts. Some of the old hands at Lantheus refer to this as buying ice on a warm day. Lantheus believes that a robust U.S. Supply of moly is an important U.S. policy for reasons of accessible and affordable health care, efficient waste management, and nuclear nonproliferation.

As a result of the moly supply crisis, important diagnostic procedures are being postponed or cancelled. Clinicians are turning to older nuclear isotopes with potentially less diagnostic certainty and more patient risk. Clinicians may even be foregoing nuclear medicine entirely, opting instead for more invasive, more expensive, higher risk surgical procedures. Lantheus believes that the private sector should have a major role in the resolution of this issue. However, we also believe there is a strong role for government to play. The U.S. Government's financial support of multiple projects with appropriate investment risk profiles will be the best way to develop a robust domestic supply of moly. And as a matter of health care policy, medical imaging procedures that rely on moly-derived imaging agents can improve patient outcomes and reduce costs. Stra-

tegic investments to help develop a domestic supply of moly should pay large dividends for both U.S. patients and U.S. taxpayers.

Wearing my CORAR hat now, CORAR supports H.R. 3276 and increasing capacity for medical isotopes in the United States. CORAR has two concerns about the bill. First, how do we ensure a full supply of moly if we get to the 7- to 10-year period and we don't yet have sufficient commercial quantities of domestically-produced LEU available? Second, CORAR would like the bill to contain specific language that would direct the Nuclear Regulatory Commission to allow the new aqueous homogenous reactors which have been recently proposed to be properly licensed as research reactors. CORAR believes the bill provides good support to bring new and alternative supplies to moly online quickly and believes it is prudent to back several alternative technologies and multiple reactor sites in order to avoid a repeat of the current availability in capacity issues.

In sum, as H.R. 3276 moves forward, both Lantheus and CORAR hope to continue to work with the committee and staff to ensure both a swift and long-term solution to the moly crisis.

Thank you for the consideration of our perspectives. We look forward to working with you moving forward and I would be glad to answer any questions.

[The prepared statement of Mr. Duffy follows:]

Written Testimony

of

Michael P. Duffy

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.

Written Testimony

of

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

The United States today confronts a crisis regarding medical radioisotopes, which thousands of American patients rely on every day for diagnosis, treatment planning and treatment. While there is an immediate need to meet current Mo-99 demand with diminished supply, the future of nuclear medicine requires increased Mo-99 manufacturing capacity to ensure a long term and reliable supply of Mo-99 and Tc-99m. CORAR supports H.R. 3276 because it is an important step towards a stable source of these medical radionuclides for our patients and will contribute to enhancing supply well into the future.

CORAR is comprised of companies which produce products utilizing many different radionuclides. CORAR members include the major manufacturers and distributors of radiopharmaceuticals, radioactive sources, and research radionuclides used in the U.S. for diagnostic and therapeutic medical applications and for industrial, environmental and biomedical research and quality control. Several of CORAR's members are the primary processors of Mo-99, or are manufacturers of Tc-99m generators which use Mo-99. It is important to point out that the entities that actually own the reactors that produce the current global supply of Mo-99 are owned by various governments in North America, Europe, and South Africa. None of the reactors are owned by any CORAR members.

Mo-99 and Tc-99m play an important role in healthcare. The use of medical radionuclides is very important today – these compounds help provide early detection and treatment of diseases which can reduce health care costs and improve quality of life. There are more than 100 different nuclear medicine procedures in use today, of which more than 16 million nuclear medicine procedures performed each year in the U.S. Of these, 41,000 use Tc-99m each day. Roughly 95% of the medical radionuclides used in nuclear medicine are produced using HEU targets in nuclear reactors. The majority of nuclear medicine procedures are for diagnostic imaging, but there are also many therapeutic nuclear medicine treatments including Non-Hodgkin's Lymphoma, Liver Cancer, and Thyroid Cancer and for bone pain palliation related to Prostate Cancer.

I. Introduction

Production of Mo-99 and other medical radionuclide production from the fission of U-235 dates back to the early 1970s. At that time the production of Mo-99 and other medical radionuclides was developed around the use of High Enriched Uranium (HEU) targets. The use of HEU material in reactor targets was, and continues to be, a cost-effective method for large scale, commercial production of Mo-99 with a secure and manageable waste disposal path. Prior to the 1970s there was a relatively small quantity of Mo-99 used in medical applications, so the majority of Mo-99 and other medical radionuclides were produced utilizing neutron activation of natural and enriched stable isotopes.

Over the last few decades more than 90% of the Mo-99, (Iodine) I-131, (Iodine) I-125 and (Xenon) Xe-133 that was used in the U.S. came primarily from just two government owned reactors. Those two reactors are the NRU reactor operated by AECL in Chalk River, Ontario, Canada and the HFR reactor operated by NRG on behalf of the European Union in Petten, The Netherlands. Until recently, these two reactors had been extremely reliable. However, NRU and HFR were commissioned in 1957 and 1961, respectively, and proved extremely reliable until recently. However, the age of these reactors has led to age-related operating problems. NRU has been shut down since May while repairs are being made to the reactor vessel and is not expected to be back on-line until early 2010. HFR was recently shut down for a month for routine maintenance and is scheduled to be shut down again in early 2010 for several months while repairs are made to its reactor vessel. These planned and unplanned shutdowns have created the current shortage of Mo-99. Both of these reactors operate with Low Enriched Uranium (LEU) fuel and HEU targets.

Currently, many efforts are underway to alleviate the Mo-99 shortage, which can reach crisis proportions when both reactors are out of service. These efforts are coming from governments, industry, and professional societies around the world. CORAR believes that the primary focus of this new legislation should be to address the need for a longer term and sustainable solution to this problem. It should also provide a framework so that similar crises can be avoided in the future. CORAR has identified six needs that any long term solution should address or solve, including:

- Appropriate site security
- Reactor and isotope processing in proximity to each other
- Disposal path for the processing radioactive by-products must be defined and approved
- The manufacturing and processing sites should have good access to a well developed transportation network
- The reactor operation must use both LEU fuel and targets
- Knowledgeable and empathetic regulatory environment

II. Premature Prohibition of HEU Exportation

Enriched uranium is used for medical radionuclide production in both the reactor fuel and the fissionable targets. CORAR supports the conversion of HEU targets to LEU targets. This is evident by the conversion of reactor fuel from HEU to LEU that has taken place in the last several years. All of the major radionuclide-producing reactors use HEU targets for the production of Mo-99, I-131, I-125 and Xe-133. The production of Mo-99 from HEU targets has been used for large scale production for over 35 years. Production techniques and regulatory filings with the U.S. Food & Drug Administration (FDA) were based on these HEU target production techniques. Changes in the production methodology and target material to other than HEU must be reviewed and approved by the FDA. CORAR shares in the goals of the Committee to remove the use of HEU targets from medical radionuclide production. However, the conversion must be accomplished in a manner which does not interrupt the supply of medical radionuclides and radiopharmaceuticals to patients, nor put an undue cost burden on patients. Meeting patient's needs is a paramount concern to CORAR member companies.

The development of new LEU target designs to use in existing reactors is a very complex task. In order for a new target to be developed several factors need to be considered, including:

- Technical development of LEU targets that will work in existing reactors
- LEU target capacity that will be capable of producing commercial quantities
- LEU target qualification that will meet heat transfer requirements
- New radiochemistry to process new LEU targets
- Assessment of impact of new radiochemistry on radioactive waste generated
- Assessment of environmental impact of new radiochemistry techniques
- Drug Master Files for new target and radiochemistry
- Evaluation of the regulatory requirements for new target and radiochemistry

This process is currently underway, and it is anticipated these efforts will yield effective and productive targets. However, CORAR anticipates that we are a significant number of years away from fulfilling all these requirements necessary to implement a new LEU target that is capable of producing commercial quantities of Mo-99 and other medical radionuclides. Although there have been some successes using LEU targets in other reactors, these have been on a very small scale.

Section 4 of H.R. 3276 addresses the export of HEU. CORAR believes the seven year sunset provision with a possible extension in this section is an aggressive timeline for transitioning the current medical isotope production process. H.R. 3276 requires a prohibition of HEU exports from the U.S. after 7 years. CORAR is concerned that the actual time necessary to complete this conversion or build a new LEU facility to add capacity may be longer than 7 years and that an early termination of HEU exports could further jeopardize the supply of Mo-99 and other isotopes to patients in the U.S. CORAR fully appreciates the importance of the sunset provision and the ongoing DOE reports in providing Congress and the Administration a hard deadline and sufficient notice of any

unforeseen obstacles to meeting the medical isotope needs of the U.S. patients. CORAR and its member companies will endeavor to meet this aggressive schedule and asks that the Committee retain its focus and support for our patients and the U.S. medical community until the medical isotope shortage is resolved.

III. Increasing Medical Radionuclide Capacity

Current shortages of Mo-99 have demonstrated the fragile supply of medical radionuclides in the U.S. and worldwide and have illustrated the need for increased capacity. CORAR supports the project funding provisions and related criteria in the bill. Included among the projects that can be considered by the DOE for funding are:

Babcock & Wilcox/Covidien AHRs

Babcock & Wilcox and Covidien are planning to build Aqueous Homogeneous Reactors (AHRs) for the production of Mo-99. These reactors are being built in the U.S. and will utilize LEU fuel. In this particular design, the fuel itself acts as the target, so there is no need for a separate target. Their target is to have the capability of producing half of the U.S. reactor produced medical radionuclide needs. However, this effort could use some assistance from this legislation and the NRC. These reactors do not meet the definition of a research reactor under the language in Section 104 of the Atomic Energy Act (AEA), due to their production focus and lack of research being conducted. At the time the AEA was written, the use of this type of reactor for the production of medical isotopes was not envisioned. This type of reactor also does not have the inherent risk or security concerns of large commercial nuclear power reactors which are licensed under Section 103 of the AEA. Consequently, this type of reactor falls into a licensing gap for the Nuclear Regulatory Commission. CORAR would like to see H.R. 3276 either revise Section 104 of the AEA to recognize this type of reactor for the production of medical isotopes or direct the NRC to permit the licensing of these reactors under Section 104 of the AEA. If assistance of this type could be included in the legislation, it would help expedite the licensing of these AHR reactors and bring this new source of Mo-99 to market more quickly.

Missouri University Research Reactor

The Missouri University Research Reactor (MURR) has plans to produce Mo-99 at their reactor in Columbia, MO. MURR already produces several medical radionuclides used by CORAR member companies, so they are familiar with being a supplier of these products. CORAR understand from MURR that, if they are successful with their plans, they would be capable of producing roughly half of the U.S. Mo-99 needs. MURR has not yet publicly announced whether it has one or more commercial partners to assist it in the development of a possible Mo-99 production capability.

National Lab Green Field Reactor

A potential long-term solution to increasing the capacity of medical radionuclides is to design and construct a purpose-built reactor. The ideal site would address the six needs outlined above in the Introduction. Potentially all of these needs could be met if a purpose-built reactor were designed and constructed at an existing National Lab. A National Lab already has good security and an established waste disposal path. The design would need to include both the reactor and processing facilities and would need to operate using LEU fuel and targets.

Other Efforts

There are several other new technologies under development and other existing reactor scenarios that also deserve further consideration. These include the fuel pin reactor design at Sandia National Lab; the photo-fission and photo-neutron processes being examined by TRIUMF/MDS Nordion; use of the existing reactor at the University of California-Davis; and use of the ACRR reactor at Sandia National Lab. In light of the recent Mo-99 supply problems, CORAR believes it is prudent to back several alternative technologies and multiple reactor sites in order to avoid a repeat of the current availability and capacity issues.

IV. Other Important Medical Radionuclides

There are other medical radionuclides which are very important to nuclear medicine. Many of these radionuclides are used in therapeutic procedures for the treatment of cancer and other illnesses. Although their number of procedures do not come close to the annual usage of Tc-99m, they are also very important. These radionuclides can be produced in a fission reaction such as Mo-99, or they can be produced through neutron activation. The same reactors that produce Mo-99 also produce these other radionuclides including I-131, I-125, Xe-133. These radionuclides are used in diagnostic and therapeutic procedures and are being examined for use in exciting new products for nuclear medicine. It is important to remember these other radionuclides play an important role in the practice of nuclear medicine and should be included in the overall approach to assuring a reliable supply for critical medical radioisotopes.

V. Legislative Comments

As the Committee considers H.R. 3276, CORAR would like to identify several additions that would be important to achieve the needs of the US patients, including the following:

- The AMIPA legislation acknowledges that a "critical shortage of molybdenum-99, patient care in the United States is suffering. Medical procedures requiring

technetium-99m are being rationed or delayed, and alternative treatments which are less effective, more costly, and may result in increased radiation doses to patients are being substituted in lieu of technetium-99m." The bill also notes that isotopes are critical to the health care of Americans, and the continued availability of these isotopes, in a reliable and affordable manner, is in the interest of the United States."

Several agencies and offices within the Executive Branch play a key role in this area. For instance, as you know, the U.S. Department of Health and Human Services (HHS) is the lead Cabinet agency overseeing the health care policy and regulating pharmaceuticals and medical technology. In addition, the Office of Science and Technology Policy provides a coordinating function and provides important advice to the President, and of course the Department of Energy plays a central role in the efforts to regulate, maintain and expand the production of isotopes. It is important that these federal agencies meet regularly and coordinate their efforts. We are heartened that they are meeting now and encourage the Administration and Congress to seek methods for continuing this important interagency coordination. For example, the legislation could require that HHS, NRC and DOE develop a working group to oversee the development of the short and long term Mo-99 supply solutions.

- Provide NRC additional authority on siting, permitting, construction and waste disposal to facilitate a domestic medical isotope production facility. One example is the need to provide NRC the authority to permit and license a reactor like the B&W/Covidien proposal.

- Require FDA to consider Drug Master Files and Supplemental New Drug Applications for alternative Mo-99 suppliers on a priority basis.

VI. Conclusion

The current worldwide shortage of Mo-99 has illustrated the fragility of supply and the need for additional medical radionuclide production. CORAR is supportive of H.R. 3276 and increasing the capacity for medical radionuclides in the U.S. CORAR is concerned that the supply of necessary HEU for the current production of Mo-99 and other radionuclides may be cut off prematurely and believes a mechanism is necessary to allow for the export of HEU until adequate new LEU-produced Mo-99 capacity is on-line. In addition, CORAR would like H.R. 3276 to contain specific language that will direct NRC to allow the new AHR reactor technology to be properly licensed as research reactors under Section 104 of the AEA.

CORAR also believes the expenditure of money to investigate new and alternative supplies of radionuclides will bring new suppliers on-line more quickly. CORAR positively notes that the legislation does not limit the number of projects eligible for funding support provided the projects meet the legislation's criteria related to ability to

meet the legislation's deadlines, capacity to fulfill domestic Mo-99 demand and cost. CORAR believes it is prudent to back several alternative technologies and multiple reactor sites in order to avoid a repeat of the current availability and capacity issues.

As H.R. 3276 moves forward, CORAR hopes to continue to work with the Committee and staff to ensure both a swift and long term solution to the medical isotope crisis. Thank you for the consideration of our perspective. CORAR looks forward to working with you toward the enactment of this legislation.

Mr. MARKEY. They have called four roll calls on the House floor. There are 10 minutes left to go before we have to go to that roll call. Let me recognize the gentleman from Michigan, Mr. Upton.

Mr. UPTON. Thanks.

I have one very quick question, and that is the bill as you know has a 7- to 10-year timeframe. Do you think that is long enough? Is that the right amount of time or should we look at extending that? Go ahead, Mr. Duffy, Dr. Larson too.

Mr. DUFFY. The National Academies had a point of view on that, and I welcome Dr. Larson's views on that. The concern that industry has about the timeframe is one of technology and one of regulation. On the technology side can we design targets appropriately which generate commercially sustainable amounts of molybdenum and can we do this in a way that is going to pass muster with the EPA, the Nuclear Regulatory Commission, the FDA and all the other State and Federal regulatory authorities? Industry embraces the proposal, is going to work hard to try to implement it, but CORAR, in particular, is concerned that for reasons beyond its control the period may not be sufficient.

Mr. UPTON. Dr. Larson.

Dr. LARSON. The main report felt that after careful deliberation that it would be feasible to bring this conversion in a 7-year timeframe; however, it does depend on the actual type of conversion that was required. If one was talking about a complete refilled new facility, it may, in fact, take a bit longer. So we can—my feeling is that the 7 years is probably enough especially with the 3-year window that is offered. The committee does have expertise to bring to bear upon this, and if you wish, we can certainly review this issue and give you a more full description of it since it is such a key.

Mr. UPTON. That would be great. If you would like to do that that would be great. I will yield back.

Mr. MARKEY. Let me just ask one question, Dr. Larson. The National Academy of Sciences report recommended that Congress set a deadline to end the export of HEU for medical isotope. The report concluded that a 7- to 10-year phaseout period would likely allow enough time for all current HEU-based producers to convert to low enriched uranium. How did you arrive at that conclusion of 7 to 10 years?

Dr. LARSON. I think the conclusion was based on interviews, discussions, field trips, and reviews of time of development of new facilities. We had the opportunity to visit, for example, Australia and to observe their process and plan for this. But since this is such a key point, we certainly would be glad to provide some more detailed background on how this was arrived at.

Mr. MARKEY. Thank you, sir. The gentleman from Georgia.

Mr. BARROW. No questions.

Mr. MARKEY. Thank you.

Dr. Staples, I am going to ask you what I think is the single most important question and that is how long will it take for the U.S. industry with the help of the Department of Energy to establish a robust domestic supply without the use of HEU?

Dr. STAPLES. Thank you. We believe that to develop a robust supply without the use of HEU would take on the order of 5 years with

the type of attention focus that this bill could bring to the industry and the issue given the acute shortage of this isotope we are currently experiencing. As a clarification, we are not just talking about conversion of existing facilities. We are talking about looking at a diverse reliable supply network that would be implemented using non-HEU, not just LEU fission target-based technologies.

Mr. MARKEY. Dr. Staples, is DOE working with the foreign medical isotope producers to help them convert from HEU to LEU?

Dr. STAPLES. In fact, yes, we are. Given the recent supply shortage, we have engaged in at least informal discussions with all current producers regarding options and process and procedure for the conversion——

Mr. MARKEY. Have they asked for your help in conversions?

Dr. STAPLES. Yes. They have solicited our help and assistance in conversions.

Mr. MARKEY. Have they made those requests recently?

Dr. STAPLES. As recently as last week, yes sir.

Mr. MARKEY. Great. Does there seem to be a renewed interest in converting from HEU to LEU at this time?

Dr. STAPLES. Absolutely. Again, I think primarily driven by the shortage of supply in the current industry.

Mr. MARKEY. Would phaseout of export of HEU for medical isotope production in 7 to 10 years given the handful of foreign producers present a window of opportunity for their operations?

Dr. STAPLES. If I understand, we believe that the 7-year timeframe would give more than a sufficient timeframe for these facilities to work on conversion and for the development of a diverse domestic supply of moly 99 not using enriched uranium.

Mr. MARKEY. Does 7 to 10 years give the foreign producers adequate time to convert to LEU?

Dr. STAPLES. Yes.

Mr. MARKEY. The bill authorizes $163 million over 5 years for DOD to help establish a domestic supply. Is that the right of amount of money and is that the right amount of time?

Dr. STAPLES. Yes. We believe that is consistent with a program plan that we have in place where we would intend this year to place up to $10 million on programs to support the development of commercial industry and $30 million in each of the respective outyears to support the developments of domestic and/or commercial supply of isotope.

Mr. MARKEY. I have a group of other written questions here, and I am going to submit to you each for your response to the committee. We apologize to you. There is a whole series of roll calls which are House floor. We apologize to you for that, and with the thanks of the subcommittee and apologies because of the truncated form of the hearing, this hearing is adjourned. Thank you.

[Whereupon, at 2:42 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Statement for the record

I thank Chairman Markey for calling this hearing on alleviating the medical isotope shortage. Medical isotopes are a vital component of thousands of medical procedures every day in this country, and the current shortage is threatening the health of thousands of Americans. I find it very concerning that we have allowed such a vital part of our medical system to become dependent on increasingly unreliable foreign sources, and I support the efforts of Chairman Markey and Mr. Upton to develop a safe, reliable, domestic supply of medical isotopes.

HR 3276: The American Medical Isotope Production Act of 2009 provides funding to evaluate and support projects to produce medical isotopes without the use of highly enriched uranium (HEU), which can be used to make nuclear weapons, and bans the export of HEU for use in medical isotope production after 7 years. I support both of these goals. However, I am concerned about a provision in section 3 of the bill that would allow HEU-fueled reactors to qualify for these funds. The United States already has several reactors that have been converted from HEU to low enriched uranium (LEU) fuel, thanks to the dedicated work of people at DOE. Many of these reactors could be used to produce medical isotopes without the use of HEU. LEU fueled reactors using LEU targets are currently the most technologically and commercially viable way of producing medical isotopes without HEU. One such reactor is in my state of Washington, a research reactor operated by Washington State University (WSU). In response to the National Academies report on producing medical isotopes without HEU, WSU developed a plan for producing medical isotopes in the university's LEU reactor. I ask that the attached letter from Washington State University, outlining their capabilities and plans for producing medical isotopes without HEU, be included in the record.

I believe we should take advantage of our existing non-HEU capabilities to the fullest extent possible before subjecting ourselves to the proliferation risk inherent in the use of HEU. I hope that Chairman Markey and Mr. Upton will be willing to work with me to address these concerns.

Again, I recognize the severity of the current crisis before us, and I support the effort to develop a safe, reliable, domestic source of medical isotopes as quickly as possible.

Statement by the Honorable Joe Barton

September 9, 2009

Thank you Mr. Chairman for holding this hearing.

Today's hearing will consider the American Medical Isotope Production Act of 2009, which is designed to address the supply reliability of critical medical isotopes in the United States. These isotopes are critical for medical imaging and other procedures and I look forward to working with Chairman Markey and Ranking Member Upton on this bill as we begin the legislative process.

The bill's goal is developing a domestic capacity to produce the medical isotope molybdenum-99 (Mo-99). I believe, however, that the proposed 7-10 year timeline for bringing these facilities online may not be realistic, given the significant challenges that building these facilities encompasses, such as technology availability, facility siting, regulatory approvals and waste management, to name a few. We should take steps to ensure that this effort will be successful and that we are not setting a schedule that cannot be met.

The bill also seeks to mandate the use of new technologies that have yet to be demonstrated on a large, commercial scale. Given the urgent need for a reliable domestic supply of Mo-99, I believe we should provide greater flexibility to use already-proven

technologies, both domestically and abroad, if necessary to meet the demand for isotopes required by the medical community, including for diagnosis and treatment of critically ill patients.

On another front, one way to advance our non-proliferation goals is to encourage foreign producers to switch from the use of highly enriched uranium to low-enriched uranium in medical isotope production. However, I question whether it makes sense for the bill to ban on all U.S. exports of highly enriched uranium for medical isotope production after 7 years, with only a one-time 3 year extension if needed to meet U.S. needs. I wonder if the challenges associated with bringing a commercially-viable, low-enriched uranium alternative to market are simply too daunting to be achieved before that deadline.. Perhaps we should consider including a safety valve to prevent this ban from inadvertently causing critical supply shortages not only in the U.S., but globally, as well.

Finally, I believe we should consider whether the export ban will actually promote non-proliferation objectives. Because of the costs and the barriers to converting the production process, it may not be economical or practical for foreign producers to switch their aging reactors and facilities, and they may decide to seek highly enriched uranium from other countries where oversight is not as stringent. Although the export ban is intended to promote non-proliferation by reducing international commerce in highly enriched uranium, it may have the perverse effect of expanding it.

These are serious matters for our country. I look forward to examining these issues, to today's testimony and to working with my colleagues on this important bipartisan proposed legislation.

The Honorable Ed Markey
Chairman
House Energy and Commerce Committee,
Subcommittee on Energy and Environment
2106 Rayburn House Office Building
Washington, DC 200515

The Honorable Fred Upton
Ranking Member
House Energy and Commerce Committee,
Subcommittee on Energy and Environment
2183 Rayburn House Office Building
Washington, DC 200515

RE: H.R. 3276, The American Medical Isotopes Production Act of 2009

Dear Chairman Markey and Ranking Member Upton,

The United States is facing a severe shortage of an important medical isotope that is used to diagnose 50,000 patients a day. The lives of Americans are at risk and the United States is entirely dependent on unreliable foreign sources for this important medical isotope. The University of Missouri Research Reactor requests your support for this bill as it attempts to create a domestic source of this medical isotope to ensure the best health care for our citizens.

My initial response to the current medical crisis is simple and direct: "The University of Missouri Research Reactor can help. We were a major supplier of Mo-99 in the past, and we can be again in the future." Getting there is not so simple, nor is it direct. Times have changed, new production technologies, new requirements by the end users, and new regulations require new facilities. These changes affect most aspects of Mo-99 production, from the initial target material through every step of production, testing, packaging and shipping. We will soon be submitting an application to the Department of Energy for a cooperative agreement to support the design and construction of a Mo-99 manufacturing facility at the research reactor in Columbia Missouri..

This letter provides background on the University of Missouri Research Reactor Center - we call her the MURR - and gives context for the level of confidence we have that the University of Missouri can make a significant contribution to a near-future domestic supply of Mo-99 for medical use. Today MURR is the nucleus of an organic network of multi-disciplinary programs that span and impact the nation and the world. The reactor itself had its first start-up on October 13, 1966, and since that day it has been in safe and reliable operation, expanding and adapting its capabilities. The reactor maintains an average 150+ hours per week operating schedule with a full-time staff of more than 150 researchers and skilled operators and technicians.

The MURR Center is the realization of a vision that was first conceived in 1955, brought to mind as a way to support the national "Atoms for Peace" initiative that President Eisenhower had so boldly announced to the world in December 1953. In early 1959, University President Ellis declared that "New vistas of a nuclear age have touched every field of science, from agriculture to medicine, from geology to zoology, and from engineering to veterinary science, in addition to the important discoveries being made in chemistry and physics. All those fields are a part of the University of Missouri's educational responsibilities to our youth and to all our citizens. We have to move forward with the nuclear age, lest we fall hopelessly behind." Specific areas identified for study at that time included cancer research and treatment of malignant diseases, radiobiology,

genetic effects of radiation, metabolism in plants and animals, tracer studies in drugs, industrial materials, food preservation, solid state physics, nuclear power plants and reactor operation.

What does this mean? It means that long-term, time-intensive studies involving very basic physics can be carried out to advance mankind's understanding of matter and energy. It means that semester after semester faculty and new and returning students have a reliable working lab for their various research projects. It means that we can deliver continuously, on a weekly—if not daily—basis, needed products and services such as medical isotopes for patient and research use, analytical services for federal, non-profit and industrial entities, as well as enhanced materials for various industries.

In the field of medical applications and radiopharmaceutical development, the MURR Center has made a notable impact. The University of Missouri has the distinction of having developed and commercialized three radiopharmaceuticals. Working with industrial partners, MURR Center researchers and their collaborators developed, patented and commercialized with FDA approval:

- **Ceretec™**, the first radiopharmaceutical to image the brain effectively. It is used to diagnose and assess stroke victims and also to identify sites of infection and inflammation in the intestinal system. Ceretec™ is one of the many radiopharmaceuticals that uses Tc-99m derived from Mo-99.
- **TheraSphere®**, approved for the treatment of liver cancer and being investigated for treatment of breast and other cancers
- **Quadramet®**, a therapeutic radiopharmaceutical designed to relieve the pain associated with metastatic bone cancer

MURR produced Mo-99 into the early 1980s, until technological advancements allowed the medical industry to shift to a commercial reactor method—fission product Mo-99—that produced a higher specific activity (higher ratio) of Mo-99. However, by 1990 US commercial reactors had ceased production of Mo-99 altogether, leaving the nation completely dependent upon foreign suppliers for what is without question a key medical radioisotope.

Today, it is estimated that 50,000 patients are diagnosed each day in the United States with the aid of technetium-99m (Tc-99m) imaging agents derived from molybdenum-99 (Mo-99). Tc-99m is used to evaluate how well the blood flows through the heart during physical stress and at rest. Tc-99m helps physicians detect coronary artery disease, identify and visualize sites of infection and cancer in various organs, develop therapeutic strategies for their patients as well as monitor the progress of their treatment. It forms the basis for 85% of all the nuclear medicine imaging procedures performed in the US and elsewhere, with more than 30 Tc-99m-based radiopharmaceuticals used to image and perform functional studies of the brain, heart, thyroid, lungs, liver, gallbladder, kidneys, skeleton, blood and tumors.

Using US 2000 Census figures for Missouri, in just under 160 days, the entire Missouri citizenry could have had a Tc-99m-based diagnostic procedure. That is, as long as the parent radioisotope Mo-99 is made available in this country.

Tc-99m does not occur naturally, nor does Mo-99. Mo-99 is a byproduct of nuclear fission. Tc-99m is a decay product, or daughter, of Mo-99. Because Tc-99m has a half-life of just over 6

hours, it must be produced at or near the site where it will be administered. Within 24 hours of its being generated, less than 7% of the Tc-99m remains. Mo-99 too has a short half-life—about 66 hours—so it cannot be stored in a warehouse or pharmacy for more than a week and still be useful. It must be produced on a regular, weekly basis. Yet during that week's time, just a few micrograms of Mo-99 shipped to a hospital or nuclear pharmacy in a special generator can yield enough Tc-99m to diagnose up to 10,000 patients.

The Global Situation

There are less than a handful of major commercial reactors currently producing Mo-99 for the global market, none of them in the United States. Since November 2007 there have been serious disruptions in the availability of the radioisotope at two of these reactors because of unplanned and extended shutdowns for maintenance—first Canada's National Research Universal (NRU) reactor at Chalk River, Ontario, and then the High Flux Reactor (HFR) in Petten, the Netherlands.

MURR Center Capability

MURR, the largest university-operated research reactor in the United States, is already a major, reliable producer of medical, research and industrial isotopes. The reactor itself is compact in design, renewable and versatile. MURR's reliability—historically running for more than 90 percent of all available hours—is unique among similar reactors and a key factor in ensuring the nation's supply of medical isotopes. Isotopes produced for medical applications must be produced in accordance with FDA current Good Manufacturing Practices (cGMP), and a major expansion at MURR has included investments in infrastructure and implementing quality programs required for cGMP processing. The University of Missouri has a firm commitment to renew and relicense MURR, investing several million dollars in infrastructure upgrades and enhancements. We submitted a renewal license application in 2006 for an additional 20 years of operation and the relicensing process is underway with a clear path to approval.

Even before these Mo-99 supply shortages, the MURR Center had begun working with MU faculty and the US Department of Energy to address three key issues of Mo-99/Tc-99m production:

- *the short (66-hour half-life) of Mo-99, necessitating continuous weekly availability.* MURR has a history of safe, reliable, routine operation as well as investments in facility and program enhancements to support a global community.
- *desire to move away from high enriched uranium (HEU).* Producing Mo-99 from low enriched uranium (LEU) requires developing new technology and methodologies, which have been underway at MURR for three years.
- *reliance on one North American Mo-99 supplier, the Canadian NRU reactor and a European back-up supplier, HFR.* Even if these reactors continue to produce Mo-99, a security event that closes US borders to the shipment of radioactive materials would have devastating consequences for the health care of our citizens. Proof of concept and feasibility studies conducted indicate that MURR can produce enough Mo-99 to meet half of the national demand.

Having commercial-scale Mo-99 processing capabilities for the production of Tc-99m will ensure a significant domestic supply for patient use, clinical trials and new R&D applications of

a proven radioisotope. Time is of essence as the foreign sources are becoming less reliable by the day. We ask members of this Subcommittee to support HR 3276. We ask you to encourage the regulatory agencies, the Nuclear Regulatory Commission and the Food and Drug Administration, to take steps to expedite the licensing of both the facilities and the Mo-99 /Tc-99m product through waivers and exceptions to the extent possible. Specific to the Nuclear Regulatory Commission, we ask the facility to be constructed at the MURR for dissolving Mo-99 targets be classified as a 'utilization facility' for the purpose of licensing. We also ask you to direct the Department of Energy to ensure reliable and regular disposal for any waste generated in the production of Mo-99. Finally, we ask for your support as we embark upon the design and construction of a Mo-99 manufacturing facility at MURR.

H.R. 3276 will aid in the development of domestic sources of this important medical radioisotope. The MURR Center at the University of Missouri is capable and well positioned to become a large-scale, domestic source for this key radioisotope. We look forward to serving our great nation by ensuring a reliable supply this critical medical radioisotope. We thank you for your consideration.

Sincerely,

Ralph A. Butler, P.E.
Director, MU Research Reactor Center
University of Missouri

WASHINGTON STATE UNIVERSITY

Vice President for Research and
Dean of the Graduate School

The Honorable Jay Inslee
403 Cannon House Office Building
Washington, DC 20515-4701

September 9, 2009

Dear Representative Inslee:

Washington State University (WSU), in response to the National Academies report *"Medical Isotope Production without Highly Enriched Uranium (HEU)"*, can commit to the domestic-commercial production of Mo-99, for the U.S. market, using Low Enriched Uranium (LEU) targets and fuel by December, 2013. WSU's approach is to undertake parallel Commercial Scale Demonstration and Infrastructure Development Plans. The initial phase of the Commercial Scale Demonstration, collectively called the "Conversion Phase" includes (1) target design, (2) irradiation of targets, and (3) processing of the irradiated targets on a pilot scale. The following Commercial Scale Demonstration will ensure that the process, from irradiating targets to the chemical separation of Mo-99, satisfies necessary standards of quality, purity and reliability. The Infrastructure Development Plan calls for construction of necessary facilities to perform both target irradiation and the Mo-99 extraction process at the WSU facility.

The US DOE has been directed to facilitate a safe, reliable Mo99 supply by 2013. WSU believes that, with its partners, it can help meet that goal. WSU's reactor is currently fueled by LEU and is well situated to ground a Mo99 production site in Eastern Washington. **Please note that WSU's existing facilities, research expertise, and work plan can meet the timeline set by the United States Congress without the need to provide exemptions to HEU fueled reactors.**

WSU Reactor Capabilities: The WSU reactor was licensed for the new LEU fuel on September 29, 2008. WSU also has an associated license amendment that increases the level of LEU inventory ensuring more than a one-year supply for Mo99 production. The WSU reactor is unique in its design and geometry, permitting a high rate of Mo-99 production and allowing the irradiation of targets directly in the reactor. Placing the LEU targets directly within the reactor core maximizes the production rate due to high power densities at the in-core irradiation positions. The reactor's capacity is sufficiently large to accommodate four, eight or even 12 LEU targets that can generate up to 30 kW per target. Another important strength is the WSU reactor facilities large capacity pool which offers sufficient space to safely handle irradiated targets. The WSU reactor's personnel have demonstrated their expertise and capacity to supplement its research mission with commercial operations, successfully and safely operating 24/7 on multiple projects.

Target Design: WSU expects to complete necessary design and demonstration of target fabrication within 12 to 18 months, *i.e.*, after September 30, 2010 or possibly until February 2011. Target design characteristics will be based upon reactor behavior studies. Pacific Northwest National Laboratories (PNNL) will work with WSU in the specific design of target

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geometry and composition with a goal of designing targets that can operate at the maximum possible power (to maximize Mo-99 production rate) while maintaining adequate cooling. WSU is confident in its ability to undertake target fabrication with PNNL in a timely and effective fashion. WSU strongly believes this will be a key aspect to a secure Mo-99 supply in a manner that satisfies Congressional and NNSA goals.

Target Irradiation: The Infrastructure Development Plan includes the construction of a new utilization facility (*i.e.*, one or more rooms to process irradiated LEU targets). This eventual co-location of target irradiation and the Mo-99 extraction process will alleviate complex security implications and costs associated with shipping irradiated targets. During the Conversion Phase, WSU proposes transporting test-case irradiated LEU targets to the licensed PNNL for processing while it designs and constructs its own on-site post-irradiation processing.

Commercialization: In anticipation of the transition from demonstration to commercial production, WSU has engaged a commercial supplier of Tc-99m generators, Lantheus Medical Imaging, in conversations expressed interest in access to a stable, diversified supply of Mo-99. We are confident that given the continued supply constraints and the impending discontinuation of Canadian medical isotope production, commercial vendors of Mo-99 will be forthcoming. It is our intent to continually engage vendors to ensure our processes will produce a product suitable for use in medical imaging applications.

Based upon a market value of $225 per 6-day curie and conservative internal assumptions regarding costs for material, personnel, processing and waste management assumptions, we anticipate an annual net income of roughly $30 million at production a level of 3000 6-day curies per week.

On a longer term, our market development plan is to leverage the research infrastructure of both existing and future facilities to develop methods for isolation and use of other medical isotopes. While roughly 80 percent of all medical imaging procedures utilize Tc-99m, there are a range of other isotopes that have utility in diagnostic applications. Moreover, there are existing collaborative efforts between organic chemists, radiochemists and the veterinary hospital at WSU aimed at the development of novel radiolabling methods. WSU is strategically positioned for success in this area and will utilize operating revenue from Mo-99 production to provide funds to support innovative research, graduate student training and further develop our institutional commitment to the nuclear sciences. We intend to build a program that complements the needs of our commercial partners thereby providing a bank of developing technology for commercial exploitation.

WSU Partners & Key Personnel: WSU is well aware of the importance and complexity of the various licensing requirements and approvals necessary to begin successful Mo99 production. To address these issues with integrity and quality, WSU has established ties with highly qualified professional service organizations to assist throughout the design, conversion, demonstration and the commercial approach to market. These organizations will serve a critical role in working with

DOE, FDA, NRC and WDOH to secure the necessary licensing, permitting and regulatory approvals to insure a successful path to market. The university is currently working with a team lead by Robert Trout at Merrick and Company regarding facility design and construction. Merrick has significant experience in the design and development of post-irradiation processing facilities containing similar chemical processing technologies. Leading our licensing efforts will be Elise Zoli[1] and Robert Fitzgerald[2] at Goodwin Procter. WSU will coordinate efforts between the legal team at Goodwin Procter, and the design and construction team at Merrick to streamline the necessary permitting. Mark Heller[3] at Goodwin Procter will work with the university to submit the necessary information to the FDA to be made available in a Drug Master File (DMF), to be available as a source of information for technetium-99 (Tc-99m) generator producers seeking to supplement their New Drug application or submit a Change Being Effected notification in conjunction with their marketing of the radio labeled compound derived from Mo-99 produced in WSU's Conversion Phase.

Sincerely,

Howard D. Grimes, Ph.D.
Vice President for Research
Dean of the Graduate School

[1] Biographical sketch: http://www.goodwinprocter.com/People/Zoli%20-%20Elise.aspx
[2] Biographical sketch: http://www.goodwinprocter.com/People/Fitzgerald%20-%20Robert.aspx
[3] Biographical sketch: http://www.goodwinprocter.com/People/Heller%20-%20Mark.aspx

September 24, 2009

Dr. Parrish Staples
Director of European and African Threat Reduction
National Nuclear Security Administration
U.S. Department of Energy
1000 Independence Avenue, SW
Washington, DC 20585

Dear Dr. Staples:

Thank you for appearing before the Subcommittee on Energy and Environment on September 9, 2009, at the hearing entitled "Solving the Medical Isotope Crisis".

Pursuant to the Committee's Rules, attached are written questions for the record directed to you from certain Members of the Committee. In preparing your answers, please address your response to the Member who submitted the questions and include the text of the question with your response, using separate pages for responses to each Member.

Please provide your responses by October 5, 2009 to Earley Green, Chief Clerk, in Room 2125 of the Rayburn House Office Building and via e-mail to Earley.Green@mail.house.gov. Please contact Earley Green or Jennifer Berenholz at (202) 225-2927 if you have any questions.

Sincerely,

Henry A. Waxman
Chairman

Attachment

QUESTIONS FROM REPRESENTATIVE INSLEE

Q1. What is involved in converting a reactor from HEU to LEU fuel? What is the typical timeline for such a conversion? What kinds of technological risks affect this timeline? How much reactor and/or Mo-99 production downtime would be required to make this conversion?

A1. The process to convert a reactor from HEU to LEU fuel follows a few generalized steps. First, feasibility models are calculated to demonstrate the viability of conversion, and to verify that commercially available fuel can be used safely in the reactor without disruption to the basic parameters required to achieve the facility's mission. Next, a detailed analysis and safety report is prepared in order to obtain regulatory approval. Finally, new LEU fuel is manufactured for the reactor for LEU-based operation upon its license conditions. The typical timeline for this process varies widely, but is generally not less than two years and in some cases can take as long as five years. The schedule is impacted primarily by political motivation which influences the availability of resources to accomplish the conversion. Typically, the actual conversion process is accomplished during a normal shutdown period for maintenance or during refueling operations, in either case the physical process rarely takes longer than one month.

QUESTIONS FROM REPRESENTATIVE INSLEE

Q2. In your opinion, would it be preferable to produce medical isotopes from an existing LEU-fueled source rather than an HEU-fueled source that would need to be converted at a later date?

A2. In my opinion, the prime indicator of a facility's suitability for isotope production is the consistency of its operation. In addition, a generally accepted threshold for true commercial-scale production of medical isotopes is to utilize reactors with at least 10MW capacity simply due to total production capacity. The current global producers use reactors that range from 20 to 135 MW.[1]

Due to the different nature of reactor fuel operations and medical isotope production, the issues of fuel and targets are not directly related. It is not simply fuel enrichment which determines whether an HEU or LEU fueled facility is necessarily technically better for isotope production. The specific design and size of the facility for isotope production or other R&D projects is more important than fuel enrichment for medical isotope production. Isotope production is better suited to a facility specifically designed for large scale production, not necessarily whether the facility operates on HEU or LEU.

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[1] National Academies (2009). *Medical Isotope Production without Highly Enriched Uranium.* Washington, D.C., 39.

QUESTIONS FROM REPRESENTATIVE INSLEE

Q3. Please give a brief overview of the technology options available for producing medical isotopes without HEU, and the current status of each from a technical and commercial feasibility standpoint.

A3. The basic strategy of the NNSA program is to accelerate the demonstration of each of the following possible production methodologies to support the development of a diverse and reliable domestic supply to avoid any single point of failure. The goal of the program is to support the transition to commercial production as rapidly as possible where economic forces will dictate the future market for medical isotopes.

The following technology options are available for producing medical isotopes without the use of HEU. The evaluation of the commercial feasibility for each will be the result of many decisions taken by the commercial industry and cannot be easily summarized or predicted:

1. Fission (Targets) – Use of LEU targets: The irradiation of targets with a neutron source to produce Mo-99 is a demonstrated technology currently used by the industry (most current production being done with HEU targets). The overall process (target preparation, irradiation, and dissolution) is nearly identical to that of using HEU targets and may therefore offer the easiest transition for HEU-based producers and the easiest adaptation and support from the existing current commercial expertise. Production rates for a given facility are expected to be among the highest of the different technologies being considered. Development

of the processing facilities to dissolve the targets and extract Mo-99 needs to take place to support eventual production, however some LEU production facilities are already in existence, such as in Australia, Argentina and others, as listed in the National Academies report.[2] In addition, fission-based technology can use existing Tc-99m generators, which will expedite the delivery of Mo-99 to the market. However, among the technologies considered, fission-based production generates the most radiological waste. Depending on the categorization of this waste, there will be a need for addressing disposition of wastes from isotope production processes.

2. Fission (Solution reactors) – Use of homogeneous LEU solution reactors: Solution reactor technology has been demonstrated and there is experience in operating homogeneous solution reactors. Production rates for this technology are also expected to be among the highest of the different technologies being considered. Additional R&D on fuel solution chemistry during operation and the recovery of Mo-99 from the irradiated fuel solution is required. Also, this production process does generate radiological waste, although total amounts are less than the fission target technology. Nevertheless, as with the fission target technology, there will be a need for addressing waste disposition depending on the waste categorization.

3. Non-fission based accelerator technologies – This proposed technology is based on exposing Mo-100 targets to high energy gamma rays to induce a

[2] National Academies, 38.

reaction that produces Mo-99. The major components of this option are based on proven technologies. Once the technology is demonstrated in a complete process, it offers the possibility of relatively simple operation, both from the standpoint of operations of the accelerator as well as regarding the target processing facility because of the reduced radiological environment due to the absence of fission products. This non-fission based technology has the benefits of resulting in minimal radiological waste with an expected disposal path readily available. R&D is needed in the Mo-100 target designs and to the overall proof of concept. The lower specific activity of the Mo-99 (vice fission-based processes) resulting from this process prevents current FDA approved generators from being suitable for use, requiring the development of another generator design.

4. Activation technology – This process is based on neutron capture in targets of Mo-98. This is a well known technology and is historically how Mo-99 was supplied to the medical community when the industry was first being developed. It is based on utilizing Mo-98 targets and a source of neutrons, which are captured in the target and result in the production of Mo-99. As with the accelerator-based technology, this technology has the benefit of resulting in a minimal amount of waste but also results in lower specific activity of the Mo-99 than fission-based processes. Since current FDA approved generators in the nuclear pharmacies cannot use the Mo-99 generated from this process, another design would need to be developed.

QUESTIONS FROM REPRESENTATIVE BARTON

Q1. During your testimony, you stated in response to a question about how long it would take to establish a "robust domestic supply" of molybdenum-99 (Mo-99) without the use of highly enriched uranium (HEU), that "we believe…it would take on the order of 5 years." (Tr. 24:491-499). What is DOE's basis for this 5-year estimate?

A1. Several factors inform our estimate of a timeframe of five years to reach a robust domestic supply. NNSA already is working with potential producers on several established technologies to produce Mo-99, and each has its own timeframe to expected production.

The National Academies study *Medical Isotope Production without Highly Enriched Uranium* estimates that the greenfield construction of a new processing facility for LEU targets to take between four to six years. The National Academies study also indicates that it would take approximately five years to construct a new LEU solution reactor.[3] Of the four technologies identified in the answer to Question 3, the two fission-based technologies are expected to take the longest time. With funds to accelerate the private development of the two fission-based technologies, we hope to reduce those estimates significantly. Moreover, under NNSA's cooperative agreements, both potential producers for the fission-based projects agree to the objective to produce at least 3,000 six-day curies by December 31, 2013, which is less than five years.

[3] National Academies, 113.

The remaining two technologies are not expected to require as much time as the fission-based technologies to develop a commercial supply. We estimate the neutron activation technology will begin producing a small amount of Mo-99 for the domestic market in approximately two years, and achieving large-scale production by December 31, 2013. Similarly, the project to develop the accelerator technology is expected to begin production within a two to three year timeframe and is also expected to achieve full-scale production by the end of 2013. By developing four technologies in parallel, should unforeseen technical challenges arise with any of the projects, the remaining projects would continue development to meet a significant portion of U.S. demand.[4]

NNSA's estimate of five years to create a robust domestic supply is derived from the study of the National Academies and the estimates from NNSA's potential partners. Based on the best information available to NNSA, five years is a reasonable estimate to create a robust domestic supply of Mo-99.

[4] In other words, even if the probability of the successful implementation of each individual project is only 50% (a conservative estimate), the remaining projects would still have high likelihood of produceing 100% of domestic demand for Mo-99 by December 31, 2013.

QUESTIONS FROM REPRESENTATIVE BARTON

Q2. How long does DOE estimate it will take domestic producers to develop or obtain the technology necessary for commercial Mo-99 production facilities in the U.S. using low-enriched uranium (LEU) targets?

A2. NNSA is currently partnering with potential commercial producers to accelerate the establishment of domestic commercial sources of Mo-99 without the use of HEU. NNSA is currently working on cooperative agreements with potential commercial Mo-99 producers whose projects are in the most advanced stages of development.

NNSA anticipates that a group of domestic commercial producers will be able to produce *over* 100% of domestic needs of Mo-99 within the next five years, thus providing a continuous, reliable and sufficient supply during periods of individual facility maintenance or shutdown. Each potential commercial producer under NNSA's cooperative agreements uses a different non-HEU technology. This strategy aims to diversify the supply chain and move away from reliance on a sole technology and a limited number of facilities, as is presently the case with today's foreign producers.

NNSA anticipates that a portion of the U.S. medical community's demand for Mo-99 can be reached using an LEU target technology production process in 2013.

QUESTIONS FROM REPRESENTATIVE BARTON

Q3. What environmental reviews are likely to be required for commercial Mo-99 production facilities in the U.S. and how long does DOE estimate that it would take to complete those necessary environmental reviews?

A3. In order to remain in compliance with the National Environmental Policy Act (NEPA) requirements, NNSA will prepare, at minimum, a programmatic environmental assessment (EA) for its role in accelerating the establishment of a domestic commercial source of Mo-99 without the use of HEU. A programmatic EA is expected to take a minimum of six months to complete. The results of this programmatic EA may be either a Finding of No Significant Impact (FONSI) signifying that NNSA's NEPA Process has been completed, or a determination that the preparation of an Environmental Impact Statement (EIS) is necessary. The timeframe for a DOE EIS is expected to take at least eighteen months to complete. This is in addition to the NRC NEPA process, which currently would not begin until applications are submitted by potential private-sector producers.

QUESTIONS FROM REPRESENTATIVE BARTON

Q4. What regulatory approvals would likely be required for the construction and operation of commercial Mo-99 production facilities in the U.S., and how long does DOE estimate it would take for domestic producers to obtain all such necessary regulatory approvals?

The facilities for future Mo-99 production are currently in development stages only, and in some cases a location has not yet been chosen. This means that depending on the technology, NRC along with individual states would regulate construction and operation of those facilities. DOE cannot answer with certainty how long this would take, as the processes do not belong to DOE.

QUESTIONS FROM REPRESENTATIVE BARTON

Q5. The proposed legislation, H.R. 3276, has provisions that would require DOE to lease LEU to producers and then take back that waste pursuant to a lease/take-back program.

a. How would DOE anticipate administering that program?

b. How would DOE anticipate managing and disposing of the waste generated by the production process?

A5. DOE cannot at this time anticipate how a uranium lease/take-back program for the production of Mo-99 would be administered. If directed to do so, DOE would develop an approach that considers the goal of developing a sustainable commercial enterprise with thorough diligence to responsible and safe materials management. DOE recognizes the importance of meeting these program objectives.

QUESTIONS FROM REPRESENTATIVE BARTON

Q6. With regard to the potential conversion by foreign producers from the use of HEU to LEU for Mo-99 production, have any of the major foreign producers of Mo-99 provided assurances to DOE that they will convert to the use of LEU processes for mo-99 production?

A6. DOE has been in discussions with all foreign producers regarding converting Mo-99 production processes to use LEU. All have indicated at least some willingness to consider conversion to use LEU. Some, however, are in the process of already developing and demonstrating the technology to do so now and could be providing significant quantities of LEU based Mo-99 to the U.S. as rapidly as 18 months.

Q6a. Have the foreign producers of Mo-99 provided DOE with any estimated timeframes for converting to the use of LEU processes?

A6a. Some foreign Mo-99 producers have provided DOE with estimated timeframes to convert to LEU. These timeframes range from 18 months to 12 years, depending on the facility.

Q6b. Have the foreign governments where the foreign Mo-99 producers are located provided DOE with any assurances that they are willing to convert to the use of LEU processes for Mo-99 production?

A6b. Yes, South Africa has provided assurances on plans to convert its Mo-99 production process to LEU targets within approximately 18 months. However, the governments of other major foreign producers have not given assurances, having categorized medical isotope production as a commercial activity and limiting statements to indicate that they would support conversion when

technology is available, or only after commercial, large-scale LEU-based production has been demonstrated.

QUESTIONS FROM REPRESENTATIVE BARTON

Q7. Can foreign producers of Mo-99 currently obtain HEU from non-U.S. sources for medical isotope production?

A7. Yes, of all of the foreign producers can obtain HEU from sources other than the United States. Currently, only Canada receives regular supplies of HEU from the United States for Mo-99 production.

QUESTIONS FROM REPRESENTATIVE BARTON

Q8. If the U.S. bans HEU exports for medical isotope production in the 7-10 year timeframe envisioned under H.R. 3276, does DOE expect that foreign producers of Mo-99 would still be able to obtain HEU from other non-U.S. sources?

A8. Yes

QUESTIONS FROM REPRESENTATIVE BARTON

Q9a. Does DOE believe it is likely that 7 years will be enough time to develop a large-scale, commercial Mo-99 production capacity in the U.S., without the use of HEU targets, that would be sufficient to meet U.S. demand, or is it more likely that additional time will be required?

A9a. As stated previously, NNSA believes that the U.S. will have a large-scale domestic commercial Mo-99 production capability without the use of HEU targets within five years. This assertion is based on the schedules that have been laid out from the potential domestic Mo-99 producers. Given the technical demonstration and regulatory approvals needed for producing Mo-99 for the U.S. medical community, NNSA is concentrating its resources to support the schedule in its effort to accelerate the establishment of a domestic commercial source of this critical medical isotope.

In addition, it is possible that foreign producers could convert their existing production processes to LEU targets within this timeframe. Coupling the expected production capacity from these converted facilities with that from new non-HEU based production, U.S. demand for Mo-99 is expected to be available in adequate quantities from non-HEU suppliers in five years.

Q9b. Does DOE believe it is likely that foreign producers of Mo-99 to convert to the use of LEU technologies within 7 years, or is it more likely that additional time will be required?

A9b. NNSA believes that if the producers want to convert, resources are identified, and appropriate decisions in those countries are made to facilitate such conversion, seven years should be sufficient for conversion to LEU for all current producers.

This belief is based principally upon technical considerations for the timeframe for conversion of other existing facilities, or the construction of new facilities that have taken place or are underway.

Currently for example, both IRE and Covidien irradiate most of their HEU targets in the HFR reactor in the Netherlands. Current plans to replace the HFR with the PALLAS reactor in 2016, which is expected to only accept LEU targets, are leading both IRE and Covidien to develop LEU target processing for use within the seven year time frame.

NTP Radioisotopes in South Africa has also committed to converting its production processes to use LEU targets within approximately 18 months. The SAFARI reactor has recently completed the conversion to LEU fuel and is developing technology to convert to LEU targets as rapidly as possible. If NTP Radioisotopes is successful in achieving its goal, South Africa would be the world's first large-scale "all-LEU" source of Mo-99. Other nations have also developed "all-LEU" Mo-99 production, such as Argentina and Australia, to supply their own domestic needs.

Canada's MDS Nordion and AECL have made no commitment to convert to LEU, and problems related to the NRU shutdown make such a commitment in the current environment very unlikely. If NRU does come back into operation as scheduled by the end of the first calendar quarter of 2010, seven years would be sufficient to convert to LEU. However, the current operating license for the NRU

will expire in 2011. A renewal would allow it to operate for an additional five years.

QUESTIONS FROM REPRESENTATIVE SHIMKUS

Q1. Given the time it will take to scale up domestic production of MO-99 without HEU, what are the contingency plans to deal with the possibility of an acute shortage of MO-99 in near-term if the repairs to Canada's NRU reactor are not completed before all or part of the planned extended outage of the Netherlands' Petten reactor in 2010?

A1. The U.S. government coordinates through an interagency working group on international and domestic efforts to address the international shortage of Mo-99. To support international efforts, the U.S. Departments of Energy and Health and Human Services represent the U.S. government in the Organisation for Economic Co-operation and Development – Nuclear Energy Agency's High Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR). The HLG-MR focuses on global supply coordination and contingencies for short-term production by fostering information sharing among current Mo-99 producers on reactor operating schedules and quantities produced. The current producers are significantly increasing production capacity and optimizing their operations schedule to minimize the impact of the potential failure of either the NRU or HFR reactors to resume operations.

In response to the shutdown of the NRU reactor in Canada, a U.S. interagency working group, in cooperation with counterparts of the Canadian Government, investigated options for creating a backup supply of Mo-99 in North America for the expected shortages in 2010. The group submitted the identified alternatives to

the Office of Science and Technology Policy of the Executive Office of the President, which are currently under review.

House Committee on Energy and Commerce
Subcommittee on Energy and Environment
Hearing on Solving the Medical isotope Crisis
September 9, 2009

Questions for the Record for Steven Larson, Memorial Sloan-Kettering Cancer Center

Questions from Representative Markey

1. **The National Academy of Sciences report "Medical Isotope Production Without Highly Enriched Uranium," for which you were Vice-Chairman, concluded that "a 7-10 year phase-out period would likely allow enough time for all current HEU-based producers to convert" to low enriched uranium for the production of medical isotopes. Please provide the Subcommittee additional details concerning the process by which the Committee concluded that 7-10 years was adequate for existing molybdenum-99 producers to convert from the use of highly enriched uranium to low enriched uranium.**

The Committee's conclusion that a 7-10 year phase-out period would be adequate for current producers to convert to low enriched uranium (LEU) was based on the Committee's expert judgment. The Committee is comprised of members who have broad experience with reactor and target development, nuclear and medical isotope process development, and radioactive waste management. The Committee's judgment was informed by briefings from, discussions with, and facility visits to three of the four[1] major HEU-based producers (MDS Nordion/AECL in Canada, IRE in Belgium, and Mallinckrodt in the Netherlands); two LEU-based producers (CNEA in Argentina and ANSTO in Australia); one reactor fuel and target manufacturer (CERCA in France); and meetings with other experts involved in LEU target and process design.

The Committee's judgment was developed from the following line of reasoning:

i. The Committee determined that LEU targets and processes that could support the large-scale production of molybdenum-99 have already been developed and demonstrated, and that there are no technical barriers to their use by current HEU-based producers. This determination is based on the Committee's observation that LEU targets are now being used to produce molybdenum-99 in Argentina and Australia. The Argentine producer CNEA converted from HEU to LEU targets to produce molybdenum-99 in 2002; conversion took about 1 year. The Australian producer ANSTO adopted Argentina's LEU target technology in 2007 and just recently obtained regulatory approval for commercial production of molybdenum-99—about 3 years after implementing the Argentine production process. Although these organizations produce molybdenum-99 primarily for domestic and regional needs, the Committee could identify no technical barriers to scaling-up production using LEU targets.

[1] The fourth major producer, Nuclear Technology Products in South Africa, did not cooperate in our study.

ii. HEU-based producers might have to undertake some process research and development (R&D) work to implement an LEU-based molybdenum-99 production process, but much of this work could be carried out relatively quickly and at low cost using well-established process development and testing procedures. Full-scale testing of the LEU-based process would only be required once this R&D work was completed. Because the technology is already available and only needs to be adapted to each producer's facilities, the process R&D work could likely be carried out in 3 years or less, based on the time required to implement new LEU-based processes at CNEA and ANSTO. Based on its discussions with current and potential future producers, the Committee estimated that an additional 1-2 years could be required for process commissioning, staff training, and licensing approvals for reactor operations. However, some of the staff training and licensing approvals could be carried out in parallel with the process R&D work, which could reduce the overall time required for conversion.

iii. The Committee determined that MDS Nordion/AECL, IRE, and Mallinckrodt could likely convert to LEU-based production using their existing hot cell facilities. Because no new hot cell construction would be required, the time needed for conversion would be greatly reduced. These producers would likely need to replace some of the processing equipment in their facilities to enable LEU-based production, but most of this equipment is available off the shelf or can be fabricated quickly and at relatively low cost. There appears to be sufficient hot cell space at all of these producers' facilities to support the parallel production of HEU- and LEU-based molybdenum-99 for some interim period until the LEU-based process can be fully implemented.

iv. Once a new LEU-based process is implemented, U.S. Food and Drug Administration (FDA) regulatory approvals would be required to produce molybdenum-99 for medical use. Based on conflicting input from industry and the FDA, the Committee estimated that regulatory approvals could take between 4 and 18 months. Additional evidence to support the Committee's lower estimate has come to light since its report was published: In July 2009, the FDA granted approval to Lantheus Medical Imaging to use LEU-based molybdenum-99 imported from Australia. According to a Lantheus press release,[2] the approval process occurred within a one-week timeframe of the company's submission of a supplemental new drug application.

In sum, the total time required for conversion would be up to 3 years for process development, 1-2 years for process commissioning and staff training, and up to 18 months for regulatory approvals. This provides a conversion time of about 7 years. To be conservative, the Committee added an additional 3 years of schedule contingency in the event that producers needed additional time to address unanticipated technical or regulatory issues that arose during the conversion process. Thus, the total time needed to phase-out the use of HEU for medical isotope production was judged by the Committee to be 7-10 years.

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[2] http://www.lantheus.com/News-Press-2009-0709.html.

Based on the evidence presented to the Committee, I personally believe that current producers could convert to LEU-based production, either through conversion of their current facilities or by development of new molybdenum-99 production sources, in less than 7-10 years if they have the will to do so. However, during the course of its study, the Committee did not see any evidence that producers were carrying out the necessary R&D work to support conversion of their own facilities.

The shutdown of the NRU Reactor in Canada has created a huge molybdenum-99 supply gap that appears to have accelerated efforts by current and potential new producers to bring new supplies of molybdenum-99 to market. In my personal opinion, this supply gap could serve to hasten the conversion to LEU-based production in much less than 7-10 years, especially if the U.S. government sends clear signals to producers that it intends to phase out the use of HEU for medical isotope production.

2. **Why did the two newest molybdenum-99 production reactors in Argentina and Australia decide not to use highly enriched uranium?**

The Committee was told by a representative of the Argentine producer CNEA that it converted to LEU-based production to support global nonproliferation efforts and to eliminate the need to import HEU from the United States, because such imports might be restricted in the future. The Australian producer ANSTO has always used LEU targets to produce molybdenum-99. Prior to 2007, ANSTO used 1.8–2.2 percent LEU targets in its production process. It converted to the Argentine process, which uses 19.75 percent LEU targets, to increase the efficiency of molybdenum-99 production. This conversion occurred when Australia shut down its HEU-fueled isotope production reactor (HIFAR) to build a new LEU-fueled reactor (OPAL).

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