CORAR

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Good morning. Chairman Manchin, Ranking member Barrasso and members of the committee. I am Michael Guastella, the Executive Director of the Council of Radiopharmaceuticals and Radiopharmaceuticals (CORAR). CORAR is an association of companies in the United States and Canada that manufacture and distribute radiopharmaceuticals, radioactive sources and medical isotopes marketed in the United States for therapeutic and diagnostic nuclear medical applications (referred to as nuclear medicine) and, in some cases, for industrial, environmental, and biomedical research and quality control.

Thank you for the opportunity to provide the committee with the perspective of medical and industrial isotope producers, processors, and distributors on the current supply of isotopes used by the industrial and medical communities.

At the outset let me provide the committee an overview on the use of isotopes and the current state of isotope supply for industrial and medical applications. In the mid-1990s the last US commercially-operated research reactor that produced fission based medical isotopes was closed and decommissioned leaving the US without a domestic source of essential medical isotopes.

Also, the US government closed the stable isotope production facility in Oak Ridge National Laboratory in the late 1990s, leaving the U.S. largely dependent on foreign sources of such isotopes which are often used as target material for the production of radioactive isotopes. Frankly few in the U.S. government focused on the loss of domestic production until 9-11 as in its immediate aftermath the supply of many radioisotopes coming from abroad was temporarily cut-off due to the cessation of flights into the U.S. The US Government recognized that essential medical procedures were being postponed with serious potential health consequences.

In the years following 9-11 your committee took up the concern over the lack of a domestic supply of medical isotopes, and in an effort to remove the use of Highly Enriched Uranium (HEU) in the production of medical isotopes, led the effort to enact the American Medical Isotope Production Act of 2012 (AMIPA). AMIPA has focused the Department of Energy on assisting in the development of a domestic medical isotope industry from non-HEU sources which led to a close relationship between several CORAR member companies and the Department of Energy as they strive to aid in the development of a domestic supply of medical isotopes and to meet the needs of our researchers and drug developers for the next generation of isotopes. These public-private relationships include several awards of Cooperative Agreements with Government cost-share by the National Nuclear Security Administration (NNSA).

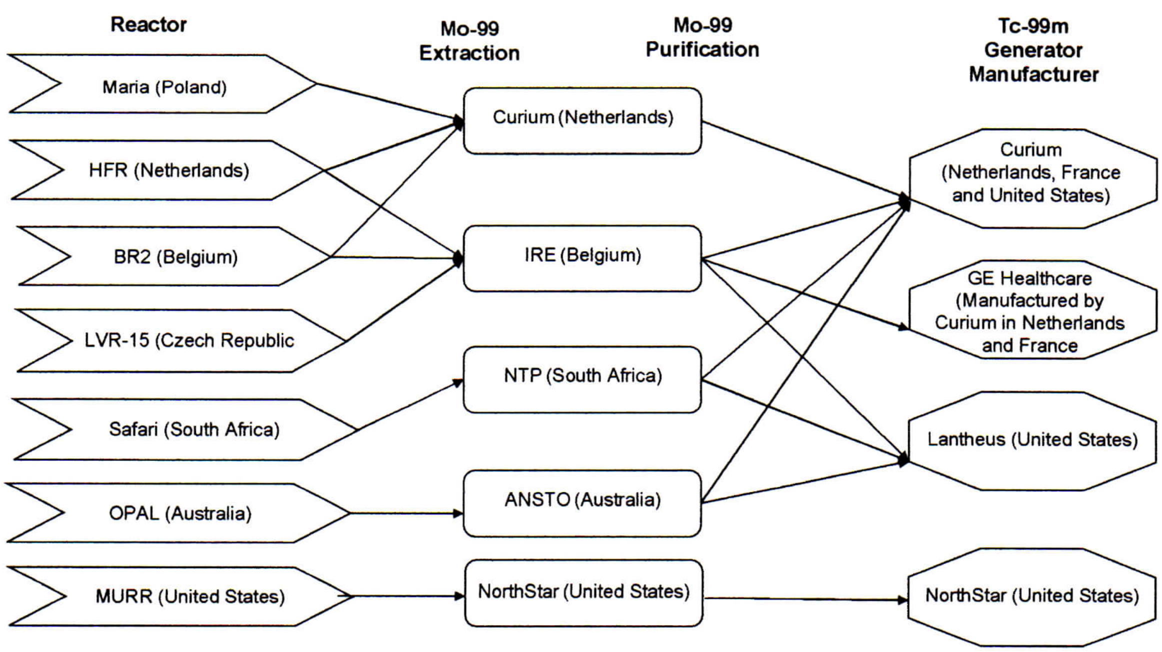
The Senate Energy Committee led on these issues, and I am proud to be here before you to say thank you for this committee's support for the medical and industrial isotope supply concerns and I want to recognize Past Chairman Bingaman and Ranking Member Lisa Murkowski for their leadership and efforts that resulted in the enactment of AMIPA.

Now let me update the committee on U.S. isotope supply opportunities and challenges.

Nuclear medicine involves the injection of radioactive materials (i.e. medical isotopes and radiopharmaceutical drugs) into a patient's body for diagnostic or therapeutic procedures. For example, Single-Photon Emission-Computed Tomography (SPECT) imaging cameras, capable of detecting and using the signals from the injected radiopharmaceutical, are used to create detailed images of patients' organs, arteries, or certain cells, as well as assessing organ function. Nuclear medicine is integral to the care of patients with cancer, heart disease and brain disorders and offers not only structural images, but allows physicians to see how the body is functioning and to measure its chemical and biological processes. There are currently twenty (20) million nuclear medicine procedures performed annually in the United States as reported by the Society of Nuclear Medicine and Molecular Imaging[1]. In 2017, there were approximately 2,900 hospitals in the United States that performed diagnostic nuclear medicine procedures to diagnose and treat several million Medicare beneficiaries[2].

For example, the most common medical isotope used in nuclear medicine procedures in the United States is technetium-99m (Tc-99m), with a half-life of six (6) hours. Technetium-99m is derived from molybdenum-99 (Mo-99), with a half-life of 66 hours. Technetium-99m based radiopharmaceuticals are used by nuclear medicine physicians and radiologists to diagnose diseases, such as heart disease and many forms of cancer, and inform treatment plans. Of the 20 million nuclear medicine procedures performed annually in the United States, an estimated 15 million of these procedures[3] utilize Tc-99m based radiopharmaceuticals. For example, over 1 million doses of Tc-99m sestamibi, needed to diagnose coronary artery disease, were dispensed to Medicare beneficiaries in CY 2017.[4]

Based on publicly available information, the majority of Mo-99 production is based overseas and handled by a series of long-established research reactors and processors in Europe, South Africa, and Australia – please see below:

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1 Society of Nuclear Medicine and Molecular Imaging, http://www.snmmi.org.
2 Centers for Medicare and Medicaid Services Claims Data.
3 US Department of Energy, https://www.energy.gov/nnsa/nnsa-s-molybdenum-99-program-establishing-reliable-supply-mo-99-produced-without-highly
4 *Id.* at 2.

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Six multi-purpose research reactors (excluding MURR[5]) and four Mo-99 processors (excluding NorthStar) supply greater than 95% of Mo-99 for patients in the United States[6].

Although we primarily discuss Tc-99m above, we note that U.S. patients rely on other medical isotopes that are also sourced from overseas, either as the sole source provider or the predominant provider. For example, Palladium-103 (Pd-103) is used to manufacture brachytherapy permanent implant seeds and a primary source of Pd-103 is Russia. These radioactive seeds are primarily used in early stage prostate cancer treatment. An estimated 174,650 men in the United States are diagnosed annually with prostate cancer[7] and approximately 60% of cases are diagnosed in men over 65. The average age of diagnosis is 66 and the disease rarely occurs before age 40. Restrictions on access to Pd-103 will impact the ability of oncologists to treat patients.

In addition, all of the Xenon-133 (Xe-133) is produced overseas and shipped to the United States for the diagnosis of lung disease. Also, foreign sourced Iodine-131 (I-131) used to treat thyroid disease is required to meet the domestic needs for this isotope

In order to function accurately, each nuclear medicine camera requires a calibrating device, known as a sealed source. Sealed sources are made from isotopes such as Gadolinium-153 (Gd-153), and Cobalt-57 (Co-57). Due to the relatively short half-life of these isotopes, hospitals need to replace sealed sources frequently and Russia is the sole source provider in the world of Gd-153 and the majority supplier of Co-57.

Stable isotopes play a particularly important role in the production of innovative new radiopharmaceutical therapies. These include Ytterbium-176 (Yb-176) for the production of non-carrier added Lutetium-177 (Lu-177 is a beta-emitter for therapeutic application) and Zinc-68 (Zn-68) for the production of copper-67 (Cu-67 is a beta-emitter for therapeutic application). Both Lu-177 and Cu-67 are being used to develop the next generation of targeted radiopharmaceutical therapies that will enhance the treatment of disease especially cancer. However, the stable isotopes needed to commercialize these targeted radiopharmaceutical therapies are either sole sourced or predominantly sourced from overseas.

Foreign supplied radioisotopes also play a crucial role in supporting US oil, gas and coal production – interruption of supply would quickly result in shortages and cause significant revenue losses to American energy sector producers. Radioisotopes such as Iridium-192 (Ir-192) and Selenium-75 (Se-75), when encapsulated in sources, assure operational safety in refineries and pipelines by carrying out "radiography" of metal structures to test for corrosion, leaks and cracks. The DOE Office of Science Isotope Program provides major amounts of Se-75 through production at the High Flux Isotope Reactor in Oak Ridge, Tennessee. However, the three largest suppliers in the world of these radiography sources procure Iridium-192 primarily from two powerful high-flux reactors in Russia.

Foreign produced Americium-241 (Am-241) is used to build neutron sources for Oil Well Logging applications and smoke detectors. Russia is the largest source for Am-241with very limited amounts produced domestically since the late 1970s. Russian reactors also provide Barium-133 (Ba-133), used in extraction and refining to separate oil, water and gas. Ba-133 has recently been produced at the High Flux Reactor in Oak Ridge, Tennessee using Russian sourced Barium-132 (Ba-132). Ba-132 is an enriched stable isotope and is only available from Russia.

Please note that Exhibit 1 includes a number of isotopes produced through a supply chain heavily reliant on overseas production[8].

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[5] University of Missouri Research Reactor

[6] National Academies of Sciences, Engineering, and Medicine Report on Molybdenum-99 for Medical Imaging; https://www.nap.edu/catalog/23563/molybdenum-99-for-medical-imaging

[7] Cancer.net; https://www.cancer.net/cancer-types/prostate-cancer/statistics

[8] Information available through selling entities public websites

Beyond support to domestic production of Mo-99 by NNSA, the DOE has also been a supportive and constructive partner through efforts of the Office of Science, Isotope Program to domestically produce both radioactive and stable isotopes that are needed because commercial production has not been established or is not sufficient to meet U.S. medical and industrial demands. The DOE Isotope Program accomplishes this through a network of production sites that utilize national laboratory resources such as the High Flux Isotope Reactor at Oak Ridge National Laboratory, the University of Missouri Research Reactor, and the Low Energy Accelerator Facility at Argonne National Laboratory to name a few. Exciting new DOE projects such as the Facility for Rare Isotope Beams at Michigan State University, and the U.S. Stable Isotope Production and Research Center (SIPRC), being built in Oak Ridge, Tennessee, are intended to expand the nation's capability to enrich stable isotopes for medical, industrial, research, and national security uses. The SIPRC will house two types of isotope separation equipment: Electromagnetic Isotope Separators (EMIS), and Gas Centrifuge Isotope Separators (GCIS).

DOE especially plays a critical role in producing and distributing isotopes needed in scientific research and for initial medical clinical development, as there are not sufficient commercial incentives for production of such isotopes. CORAR and its member companies believe that where commercially feasible, medical, and industrial radioisotopes should be produced by the private sector. Various companies are currently developing reactor and non-reactor capabilities to help scale up domestic production of essential, mature market medical radioisotopes such as Mo-99, I-131, and Xe-133. In addition, private sector projects are underway to increase domestic supply of Actinium-225 (Ac-225 is an alpha-emitter for therapeutic application), Lu-177, and Cu-67 for targeted radiotherapies through the use of particle accelerators and reactors. CORAR believes that when diverse commercial production sources can meet U.S. demand, the DOE Isotope Program should exit the market for such isotopes, consistent with the mission of the DOE Isotope Program.

CORAR is aware of additional opportunities being explored by industry stakeholders to augment domestic supply of essential medical and industrial isotopes such as the use of current nuclear power reactors as a neutron source for isotope production. Also, some have considered using advanced nuclear reactors in the future for isotope production.

CORAR wants to thank the committee for the opportunity to highlight these issues and would recommend that the committee continue to support the DOE's research, development, and production activities. Also, CORAR suggests that the committee support an increase in DOE's industry and government cooperation through a stakeholder and agency advisory committee to help define the nation's isotope needs and help identify opportunities to increase domestic isotope production.

I thank you for the opportunity to testify today, and I would be pleased to answer any questions.

Respectfully Submitted,

Michael J. Guastella

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## Exhibit 1

| Medical Isotopes | Stable | Isotope Details |
|---|---|---|
| Cobalt-56 (Co-56) | | Calibration standard |
| Cobalt-57 (Co-57) | | Medical Imaging |
| Cobalt-60 (Co-60) | | Cancer treatment and medical product sterilization |
| Cesium-137 (Cs-137) | | Cancer treatment, Thickness gauging, flow dectection |
| Cadmium-112 (Cd-112) | Stable | Target material for In-111 production |
| Erbium-168 (Er-168) | Stable | Production of Er-169 used for radiation synovectomy |
| *Gadolinium-153 (Gd-153)* | | *Medical Imaging Quality Control Source (SPECT)* |
| Germanium-68 (Ge-68) | | PET imaging, cancer treatments |
| Nickle-64 (Ni-64) | Stable | Target material for Copper-64 production which is used for cancer diagnosis |
| Palladium-103 (Pd-103) | | Treatment for Prostrate Cancer |
| *Rubidium-85 (Rb-85)* | | *Cancer treatment, target for Sr-82* |
| *Ruthenium-106 (Ru-106)* | | *Brachytherapy for treatment for ocular melanoma* |
| Thallium-203 (Tl-203) | Stable | Traget material for Thallium-201 production used in heart imaging. |
| Tin-112 (Sn-112) | Stable | Cancer diagnosis of brain , liver kidney tumors |
| *Molybdenum-98 (Mo-98)* | *Stable* | *Target material for Mo-99 production* |
| *Molybdenum-100 (Mo-100)* | *Stable* | *Target material for Mo-99 production* |
| Rhenium-185 (Re-185) | Stable | Production of Re-186 for cancer treatment |
| Samarium-152 (Sm-152) | Stable | Production of Sm-153 used in cancer treatment |
| Uranium-235 (U-235) | | Research reactor fuel and irradiation targets for Mo-99 production |
| Ytterbium-176 (Yb-176) | Stable | Production of non-carrier added Lutetium-177 for cancer treatment |
| Yttrium-88 (Y-88) | | Medical diagnostics, LED's |
| Xenon-124 (Xe-124) | Stable | Production of Iodine-123 and Iodine-125 radioisotopes for imaging and cancer treatment |
| Xenon-133 (Xe-133) | | Production of Xe-133 for evaluation of pulmonary function and lung imaging |
| Zinc-68 (Zn-68) | Stable | Target material for Ga-67 and Cu-67 production |

***Please note: highlighted italic isotopes are single sourced from Russia.***

| Industrial Isotopes | Stable | Isotope Details |
|---|---|---|
| Americium-241 (Am-241) | | Oil/Gas exploration |
| Barium-133 (Ba-133) | | Oil/Gas exploration |
| *Barium-132 (Ba-132)* | *Stable* | *Target Material to US DOE for Ba-133 production* |
| *Cadmium-109 (Cd-109)* | | *Metal analysis/lead in paint* |
| Cerium-139 (Ce-139) | | Used in Metal production |
| *Helium-3 (H-3)* | | *Oceanic transient tracer, fuel for nuclear fusion reactions* |
| Iridium-192 (Ir-192) Disks | | Industrial Radiography |
| *Krypton-85 (Kr-85)* | | *Radioactive tracer, Arc discharge lamps, exit signs* |
| Polonium-210 (Po-210) | | Static remover |
| Selenium-75 (Se-75) | | Industrial Radiography |
| Tellurium-122 (Te-122) | Stable | Target material for I-122 gamma imaging |
| Xenon-124 (Xe-124) | Stable | Instrumentation for radiation detection |

***Please note: highlighted italic isotopes are single sourced from overseas.***