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January 13, 2009

Re: Comments on Nuclear Science Advisory Committee Isotopes Subcommittee Report, "The Nation's Needs for Isotopes: Present and Future"

Dear Prof. Aprahamian and Dr. Geesaman:

The American Association of Physicists in Medicine (AAPM)[1] is pleased to have the opportunity to provide input to the Isotopes Subcommittee of the Nuclear Science Advisory Committee (NSAC). AAPM remains concerned about the availability of isotopes to diagnose and treat disease, especially cancer, as well as to ensure their availability for research. AAPM commends the Subcommittee for providing this forum to address these important issues.

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[1] The AAPM's mission is to advance the practice of physics in medicine and biology by encouraging innovative research and development, disseminating scientific and technical information, fostering the education and professional development of medical physicists, and promoting the highest quality medical services for patients. Medical physicists contribute to the effectiveness of radiological imaging procedures by assuring radiation safety and helping to develop improved imaging techniques (e.g., mammography CT, MR, ultrasound). They contribute to development of therapeutic techniques (e.g., prostate implants, stereotactic radiosurgery), collaborate with radiation oncologists to design treatment plans, and monitor equipment and procedures to insure that cancer patients receive the prescribed dose of radiation to the correct location. Medical physicists are responsible for ensuring that imaging and treatment facilities meet the rules and regulations of the U.S. Nuclear Regulatory Commission (NRC) and various State regulatory agencies. AAPM represents over 6,700 medical physicists.

AAPM is pleased to see the creation of the new Office of Nuclear Physics within the Department of Energy's Office of Science. We hope that this organizational restructuring and creation of an office, whose goal is to "create an optimized and prioritized program for the development and production of key isotopes for use in research, medicine, industry and national security," is successful and facilitates addressing our issues of concern.

AAPM is particularly concerned that patient care not be adversely impacted by shortages of critical isotopes used in molecular imaging, targeted therapies and brachytherapy applications. Recent delays in availability of isotopes demonstrate the fragility of the existing production streams for these isotopes. As we indicated in our September 25, 2008, letter to the Nuclear Regulatory Commission (NRC), "[M]edical isotopes are used to diagnose potentially life-threatening conditions such as heart disease and to treat serious diseases such as cancer. Establishing a reliable supply of medical isotopes is an important issue for patients worldwide. Canada's National Research Universal (NRU) reactor is one of only five[2] reactors in the world with the capacity to produce isotopes for commercial use. NRU supplies isotopes to MDS Nordion, who in turn processes them into medical isotopes that are then distributed to radiopharmaceutical companies worldwide, including licensees in the United States. Continuity of medical isotope supply is critical, so the proposed conversion to low enriched uranium (LEU) has to be technically and economically feasible to ensure medical isotope supply for patient care is not jeopardized or interrupted. To date, there is no demonstrated, qualified, large-scale commercial process for production of medical isotopes from LEU targets. It is important to note that Canada has already taken significant steps to use LEU. The NRU reactor has been converted to LEU fuel and irradiates HEU targets." AAPM believes that a U.S. solution to isotope production should be established and that efforts to establish domestic U.S. production capacity are critical.

AAPM agrees with the assessment found in the executive summary of the "Workshop on The Nations Needs for Isotopes: Present and Future". The working group for Radioisotopes for Applications cited the dependence on foreign sources for key medical isotopes, such as Molybdenum-99 (^{99}Mo) jeopardizes the ability of the United States to provide lifesaving medical tests to its citizens. In 2008, a failure at the 50 year old Chalk River reactor in Canada resulted in a serious and prolonged shortage of ^{99}Mo in the United States. Technetium-99m (^{99m}Tc), the daughter product of ^{99}Mo, is used for the majority of nuclear medicine diagnostic procedures. The disruption in supply of ^{99}Mo resulted in the delay of important medical testing for many citizens of the United States. AAPM strongly encourages the NSAC to support the effort of facilities such as the University of Missouri to add a ^{99}Mo production facility to their existing reactor. If this facility is added, the University of Missouri states that they can meet 50% of the U.S. needs for ^{99}Mo. This would be the sole U.S. producer. Additional information regarding this effort can be found at: http://www.columbiatribune.com/2008/Dec/20081226News008.asp. Additional isotopes used in medicine currently can be found in Attachment 1.

Critical isotopes used in radiation therapy currently include Iridium-192, Indium-111, Yttrium-90, Iodine-125 and Palladium-103. While all modalities used to treat cancer are important, brachytherapy is a proven treatment that saves lives and preserves the quality of life by

[2] The other four reactors are located in South Africa, Belgium, France and the Netherlands.

delivering radiation doses more precisely to certain tumor sites, while minimizing dose to healthy tissue. In addition, iodine isotopes are critical for thyroid therapies. AAPM notes that in molecular imaging and targeted therapies, the total activities of the desired isotopes for this young field are not large, but the scarcity of novel radionuclides results in extremely high costs, which have both slowed medical research and negatively impacted routine medical uses. Furthermore, Tritium (^{3}H), Phosphorus-32, Sulfur-35 and Carbon-14 are vital to research and should all be included on the list of priorities.

The working group on Radioisotopes for Applications also cited Cesium-137 (^{137}Cs) as an important isotope with critical supply issues that should be addressed by government. AAPM is in total agreement with this concern and availability of ^{137}Cs, including Cesium Chloride (CsCl), for use in the irradiation of blood and for research. AAPM and others provided extensive comments to the NRC at their recent roundtable on this subject. We recommend that the Subcommittee review the NRC report from this roundtable at http://www.nrc.gov/reading-rm/doc-collections/news/2008/08-223.html, as it represents a significant analysis of ^{137}Cs use and supply issues reflecting broad input from stakeholders.

AAPM strongly recommends coordination between all federal agencies that support the use of isotopes in medical applications and research (e.g., Food and Drug Administration, Department of Energy, National Science foundation and the National Institutes of Health) and those involved in regulating the use of isotopes (NRC and the Agreement States) to ensure a comprehensive and effective U.S. solution to this critical problem.

Thank you for providing the AAPM an opportunity to provide input for consideration in developing a long-term effective strategy for ensuring that the US remains an integral entity in producing and supplying isotopes., U.S.-based production is crucial to ensure the continued availability of critical isotopes for the diagnosis and treatment of disease, as well as for research and national security programs. For correspondence or to arrange further discussion, please contact Lynne Fairobent, AAPM's Manager of Legislative and Regulatory Affairs at 301-209-3364 or via email at: lynne@aapm.org.

Sincerely,

Maryellen L. Giger, Ph.D.
President

Douglas E. Pfeiffer, MS, DABR
Chair
AAPM's Government and Regulatory
Affairs Committee

1 Attachment

Attachment 1
Isotopes Used in Medicine
Taken from: http://www.radiochemistry.org/nuclearmedicine/radioisotopes/ex_iso_medicine.htm

Reactor Radioisotopes (half-life indicated)

- Molybdenum-99 (66 h): Used as the 'parent' in a generator to produce technetium-99m.
- Technetium-99m (6 h): Used in to image the skeleton and heart muscle in particular, but also for brain, thyroid, lungs (perfusion and ventilation), liver, spleen, kidney (structure and filtration rate), gall bladder, bone marrow, salivary and lacrimal glands, heart blood pool, infection and numerous specialized medical studies.
- Bismuth-213 (46 min): Used for Targeted Alpha Therapy (TAT).
- Chromium-51 (28 d): Used to label red blood cells and quantify gastro- intestinal protein loss.
- Cobalt-60 (10.5 mth): Formerly used for external beam radiotherapy.
- Copper-64 (13 h): Used to study genetic diseases affecting copper metabolism, such as Wilson's and Menke's diseases.
- Dysprosium-165 (2 h): Used as an aggregated hydroxide for synovectomy treatment of arthritis.
- Erbium-169 (9.4 d): Use for relieving arthritis pain in synovial joints.
- Holmium-166 (26 h): Being developed for diagnosis and treatment of liver tumors.
- Iodine-125 (60 d): Used in cancer brachytherapy (prostate and brain), also diagnostically to evaluate the filtration rate of kidneys and to diagnose deep vein thrombosis in the leg. It is also widely used in radioimmuno-assays to show the presence of hormones in tiny quantities.
- Iodine-131 (8 d): Widely used in treating thyroid cancer and in imaging the thyroid; also in diagnosis of abnormal liver function, renal (kidney) blood flow and urinary tract obstruction. A strong gamma emitter, but used for beta therapy.
- Iridium-192 (74 d): Supplied in wire form for use as an internal radiotherapy source for cancer treatment (used then removed).
- Iron-59 (46 d): Used in studies of iron metabolism in the spleen.
- Lutetium-177 (6.7 d): Lu-177 is increasingly important as it emits just enough gamma for imaging while the beta radiation does the therapy on small (e.g., endocrine) tumors. Its half-life is long enough to allow sophisticated preparation for use.
- Palladium-103 (17 d): Used to make brachytherapy permanent implant seeds for early stage prostate cancer.
- Phosphorus-32 (14 d): Used in the treatment of polycythemia vera (excess red blood cells). Beta emitter.
- Potassium-42 (12 h): Used for the determination of exchangeable potassium in coronary blood flow.
- Rhenium-186 (3.8 d): Used for pain relief in bone cancer. Beta emitter with weak gamma for imaging.
- Rhenium-188 (17 h): Used to beta irradiate coronary arteries from an angioplasty balloon.

- Samarium-153 (47 h): ^{153}Sm is very effective in relieving the pain of secondary cancers lodged in the bone, sold as Quadramet. Also very effective for prostate and breast cancer. Beta emitter.
- Selenium-75 (120 d): Used in the form of seleno-methionine to study the production of digestive enzymes.
- Sodium-24 (15 h): For studies of electrolytes within the body.
- Strontium-89 (50 d): Very effective in reducing the pain of prostate and bone cancer. Beta emitter.
- Xenon-133 (5 d): Used for pulmonary (lung) ventilation studies.
- Ytterbium-169 (32 d): Used for cerebrospinal fluid studies in the brain.
- Yttrium-90 (64 h): Used for cancer brachytherapy and as silicate colloid for the relieving the pain of arthritis in larger synovial joints. Pure beta emitter.
- Radioisotopes of cesium, gold and ruthenium are also used in brachytherapy.

Cyclotron Radioisotopes

- Carbon-11, Nitrogen-13, Oxygen-15, and Fluorine-18: These are positron emitters used in PET for studying brain physiology and pathology, in particular for localizing epileptic focus, and in dementia, psychiatry and neuropharmacology studies. They also have a significant role in cardiology. ^{18}F in FDG has become very important in detection of cancers and the monitoring of progress in their treatment, using PET.
- Cobalt-57 (272 d): Used as a marker to estimate organ size and for in-vitro diagnostic kits.
- Gallium-67 (78 h): Used for tumor imaging and localization of inflammatory lesions (infections).
- Indium-111 (2.8 d): Used for special diagnostic studies (e.g., brain studies, infection and colon transit studies).
- Iodine-123 (13 h): Increasingly used for diagnosis of thyroid function, it is a gamma emitter without the beta radiation of ^{131}I.
- Krypton-81m (13 sec) from Rubidium-81 (4.6 h): ^{81m}Kr gas can yield functional images of pulmonary ventilation, (e.g., in asthmatic patients, and for the early diagnosis of lung diseases and function).
- Rubidium-82 (65 h): Convenient PET agent in myocardial perfusion imaging.
- Strontium-92 (25 d): Used as the 'parent' in a generator to produce ^{82}Rb.
- Thallium-201 (73 h): Used for diagnosis of coronary artery disease other heart conditions such as heart muscle death and for location of low-grade lymphomas.
- Germanium-68/Gallium-68[1]

[1] Added to list, not from original link: http://www.radiochemistry.org/nuclearmedicine/radioisotopes/ex_iso_medicine.htm.