UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

March 27, 2018

MEMORANDUM TO: Christopher J. Palestro, M.D., Chairman
Advisory Committee on the Medical Uses of Isotopes

FROM: Kevin Williams, Acting Director ***/RA/***
Division of Materials Safety, Security, State and Tribal Programs
Office of Nuclear Material Safety and Safeguards

SUBJECT: U.S NUCLEAR REGULATORY COMMISSION ACTION IN RESPONSE TO THE FEBRUARY 15, 2018, TELECONFERENCE MEETING OF THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

Below are the recommendations from the February 15, 2018, teleconference meeting of the Advisory Committee on the Medical Uses of Isotopes (ACMUI). Following the recommendations is the U.S. Nuclear Regulatory Commission (NRC) staff response and/or position.

Recommendations 1-7 listed below, are related to the ACMUI Nursing Mothers' Guidelines Subcommittee Report.

ITEM (1): For technetium-99m (^{99m}Tc)-labeled radiopharmaceuticals, rather than a radiopharmaceutical-specific interruption period, a single interruption period of 24-hours is recommended. Although this time interval may be longer than absolutely necessary for some ^{99m}Tc-labeled radiopharmaceuticals, it is compliant with the 100-mrem dose limit and simplifies the guidance, thereby avoiding confusion and reducing the likelihood of error.

ITEM (2): For flourine-18(^{18}F)-fludeoxyglucose[1], all other ^{18}F-labeled and all gallium-68 (^{68}Ga)-labeled radiopharmaceuticals, a 12-hour interruption period is recommended. This conservative recommendation is cautious and simplifies safety instructions for patients and medical professionals. A 12-hour interruption period is recommended for ^{68}Ga for the following reasons: (a) a physical half-life comparable to that of ^{18}F, (b) the propensity of free radiogallium to accumulate in breast milk, and (c) the lack of relevant data on ^{68}Ga-labeled agents in nursing mothers.

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[1] Fludeoxyglucose is commonly referred to as FDG.

ITEM (3): For very-short-lived positron-emitting radionuclides used in imaging, carbon-11 (^{11}C) (physical half-life: 20.4 min), nitrogen-13 (^{13}N) (9.97 min), oxygen-15 (^{15}O) (2.04 min), and generator-produced rubidium-82 (^{82}Rb) (1.27 min), no interruption in breast-feeding is recommended, since there is no significant activity remaining in the mother after the procedure is completed.

ITEM (4): For iodine-123 (^{123}I) in the form of sodium-iodide (NaI) (^{123}I-NaI), an interruption period of 7 days is recommended. This is in marked contrast to the past, where complete cessation of breast-feeding for the current child was recommended. This older, more stringent ^{123}I-NaI recommendation was largely based on contamination (up to 2.5 percent of the total activity) with long-lived iodine-125 (^{125}I) (physical half-life: 60 days) that occurred with older methods of ^{123}I production. Such contamination of ^{123}I with ^{125}I no longer occurs. Therefore, the restrictions on breast-feeding following ^{123}I-NaI administration to the nursing mother may be justifiably relaxed to an interruption period of 7 days.

ITEM (5): For gallium-67 (^{67}Ga)-gallium-citrate, an interruption period of 28 days is recommended, which is consistent with the most conservative recommendations for ^{67}Ga in the literature. For indium-111 (^{111}In)-labeled white cells an interruption period of 7 days and for thallium-201 (^{201}Tl-chloride) an interruption period of 14 days are recommended. These recommendations mirror that of the NRC in the Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses, NUREG-1556, Volume 9, Revision 2, Appendix U, 2008.

ITEM (6): For zirconium-89 (^{89}Zr), a 28-day (i.e., 4-week) interruption period was set equal to the maximum recommended interruption period for ^{67}Ga. The rationale for this recommendation are the comparable physical half-lives of ^{89}Zr (3.27 days) and ^{67}Ga (3.26 days). Both ^{89}Zr and ^{67}Ga are radiometals and may share some common chemical properties, and lastly, there is a lack of relevant data on ^{89}Zr-labeled agents in nursing mothers.

For lutetium-177 (^{177}Lu), based on the foregoing ^{89}Zr rationale and a longer physical half-life (6.65 days), an interruption period of 35 days (i.e., 5 weeks) is recommended for ^{177}Lu-labeled radiopharmaceuticals used diagnostically. For ^{177}Lu-labeled radiopharmaceuticals used therapeutically, much higher activities are administered, and thus, permanent cessation of breast-feeding for the current child is recommended.

ITEM (7): For radium-223 (^{223}Ra) and all other alpha particle-emitting radionuclides, permanent discontinuation of breast-feeding for the current child is recommended. Alpha particles are densely ionizing, have high-linear energy transfer radiations that potentially incur far more significant biological effects than beta-particles, and are of particular concern in the young child in whom rapid growth and development are occurring. In the absence of relevant data and out of an abundance of caution, permanent

discontinuation of breast-feeding for the current child is therefore recommended.

These recommendations and the ACMUI subcommittee report were passed unanimously by the full ACMUI with 9 favorable votes. The NRC staff will review and evaluate the report for possible revisions to Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials."

Recommendations 8-11 listed below, are related to the ACMUI Physical Presence Requirements for the Leksell Gamma Knife® Icon™ Subcommittee Report.

ITEM (8): The authorized user (AU) and authorized medical physicist (AMP) should be physically present during the initiation of all treatments involving the Icon™ unit.

ITEM (9): The current physical presence requirements for the AU can be modified by allowing the AU to be close enough to the console to respond quickly to any issue that arises, which is defined as within a two minute walking distance to the Icon™ console area, **and** immediately available to come to the treatment room. An AMP needs to be physically present during the entire treatment.

In addition to the AU and AMP, as a matter of good practice, we recommend that appropriately trained nursing or auxiliary staff be present during Icon™ treatment to respond to any immediate medical needs. It will be the responsibility of the AU to determine the necessary training and experience required of the nursing staff, who will be present throughout the procedure.

ITEM (10): If there is an interruption of treatment secondary to medical or mechanical issues, the AU must return to the Gamma Knife® Icon™ console to evaluate the patient and/or to review any mechanical issues. The AU must be present to ensure that the correct site is being treated during re-initiation of treatment.

ITEM (11): At the conclusion of treatment, the AU must be present at the Icon™ console to discuss any treatment or patient issues with the patient, physicist, and nurse.

These recommendations and the ACMUI subcommittee report were passed unanimously by the full ACMUI with 9 favorable votes. The report was provided to the joint Physical Presence Requirements for the Leksell Gamma Knife® Perfexion™ and Leksell Gamma Knife® Icon™ NRC and Agreement State Working Group as part of its evaluation to determine if changes are warranted to the licensing guidance.

SUBJECT: NRC ACTION IN RESPONSE TO THE FEBRUARY 15, 2018 TELECONFERENCE MEETING OF THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES DATE: March 27, 2018

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