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

September 7, 2016

MEMORANDUM TO: Pat B. Zanzonico, Ph.D., Vice Chairman
Advisory Committee on the Medical Uses of Isotopes

FROM: Daniel S. Collins, Director */RA/*
Division of Material Safety, State, Tribal
and Rulemaking Programs
Office of Nuclear Material Safety
and Safeguards

SUBJECT: U.S. NUCLEAR REGULATORY COMMISSION ACTION IN RESPONSE TO THE AUGUST 10, 2016, TELECONFERENCE MEETING OF THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

Below are the recommendations from the August 10, 2016, teleconference meeting of the Advisory Committee on the Medical Uses of Isotopes (ACMUI). These recommendations reflect the ACMUI's comments on the draft "Germanium-68/Gallium-68 Generators Licensing Guidance." Following the list of recommendations is the U.S. Nuclear Regulatory Commission (NRC) staff response and/or position.

ITEM (1): The Committee agreed with the recommendation that the section entitled, "Licensing Guidance," be re-named, "Purpose," and re-located to the beginning of the Guidance (i.e., immediately following the Table of Contents). An explicit statement such as the following should be included, "This Guidance provides applicants with an acceptable means of satisfying the requirements for a license for the use of a column based Ge-68/Ga-68 generator for producing Ga-68 to be used in the preparation of Ga-68 radiopharmaceuticals."

The recommendation passed unanimously with nine favorable votes.

ITEM (2): The Committee agreed with the recommendation to provide clarification of what is regulated under Title 10 of the *Code of Federal Regulations* (10 CFR) 35.200 and 10 CFR 35.1000. The guidance should state that the regulation of Ga-68 radiopharmaceuticals under 10 CFR 35.200 applies to patient dosages obtained from appropriately trained authorized users or authorized nuclear pharmacists within a medical facility as well as from commercial nuclear pharmacies.

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Accordingly, the subcommittee recommended revisions of the passage in lines 73-84 on page 2 of the Licensing Guidance, including the section entitled, “Commercial Nuclear Pharmacy User under 10 CFR 30.33,” as follows:

Use of Ga-68 Radiopharmaceuticals

Please note that licensees that use unit dosages of Gallium-68 (Ga-68) radiopharmaceuticals for medical imaging and localization studies will be regulated under 10 CFR 35.200 and authorized users (AU) must comply with the requirements of 10 CFR 35.290. The licensee may use a Ga-68 radiopharmaceutical that is prepared from the elution of a Germanium-68 (Ge-68)/Ga-68 generator for medical use for imaging and localization studies that is either:

1) Obtained in a manner described in 10 CFR 35.200 (c) or (d);

2) Obtained from a manufacturer or preparer licensed under 10 CFR 32.72 or equivalent Agreement State requirements and has made commitments as described in this guidance; or,

3) Prepared by an authorized nuclear pharmacist (ANP); a physician who is an AU who meets the requirements of this license guidance and the requirements specified in 10 CFR 35.290, or 10 CFR 35.390 and 10 CFR 35.290(c)(1)(ii)(G); or an individual under the supervision, as specified in 10 CFR 35.27, of the ANP or the physician who is an AU and have made commitments as described in this guidance.

Licensees that use cyclotron-produced Ga-68 radiopharmaceuticals for medical imaging and localization studies will be regulated under 10 CFR 35.200 and AUs must meet 10 CFR 35.290.

The recommendation passed unanimously with nine favorable votes.

ITEM (3): The Committee agreed with the recommendation to modify the language in the “Use of Ge-68/Ga-68 Generators” Section to the following language:

Use of Ge-68/Ga-68 Generators

Recently, the Food and Drug Administration approved a Ga-68 radiopharmaceutical for diagnostic imaging of somatostatin

receptor-positive neuroendocrine tumors. Ga-68 is a positron emitter which allows Ga-68 radiopharmaceuticals to be imaged using positron emission tomography in a manner similar to fluorine-18 (F-18) radiopharmaceuticals. Ga-68 produced in a cyclotron, like F-18, may be used to produce Ga-68 radiopharmaceuticals for use under 10 CFR 35.200. However, unlike F-18, Ga-68 can also be produced from the elution of a Ge-68/Ga-68 generator to prepare Ga-68 radiopharmaceuticals. As such, the Ge-68/Ga-68 generator eluate generally cannot be used directly in patients for imaging, but only as a precursor for the preparation of Ga-68-labeled radiopharmaceuticals.

The recommendation passed unanimously with nine favorable votes.

ITEM (4): The Committee agreed with the recommendation to modify the language in the "Authorized Individuals" Section to the following language:

4) Meets the criteria under 10 CFR 35.290, "Training for imaging and localization studies;"

5) Has completed the following training in the use of a Ge-68/Ga-68 generator for producing Ga-68 radiopharmaceuticals for 35.200 use:

a. elution and quality control procedures needed to determine Ga-68 activity and Ge-68 breakthrough levels appropriate for the preparation of radiopharmaceuticals for imaging and localization studies;
b. measuring and testing the eluate for radionuclidic purity; and
c. safety procedures for the use of the Ge-68/Ga-68 generator.

ITEM (5): The Committee agreed with the recommendation to modify the language in the "Training for individuals other than AUs and ANPs" Section to the following language:

Training for individuals others than AUs and ANPs

The applicant shall commit to provide training in the licensee's procedures to all individuals involved in Ge-68/Ga-68 generator use for the production of Ga-68 radiopharmaceuticals for 35.200 use, commensurate with the individual's duties to be performed.

> This training must be provided to all individuals eluting the generator or preparing, or measuring the Ga-68 unit dose.

ITEM (6): The Committee agreed with the recommendation to modify the language in the "Radiation Protection Program Changes" Section to the following language:

> This guidance may be revised as additional experience is gained regarding the use of a Ge-68/Ga-68 generator for preparation of Ga-68 radiopharmaceuticals for 35.200 use. An applicant initially applying for authorization for use of Ge-68/Ga-68 generator under this 35.1000 use may request to incorporate into its license a change process similar to 10 CFR 35.26. Such a change process can allow some future changes without the need to amend the license to radiation safety programs provided that the change process requires the following conditions to be met for revisions to the radiation safety program:

The recommendation passed unanimously with nine favorable votes.

The ACMUI submitted their final report to the NRC staff on August 25, 2016. The NRC staff will consider the ACMUI's recommendations for possible changes to the "Germanium-68/Gallium-68 Generators Licensing Guidance." The NRC staff will issue the finalized licensing guidance once they have completed their analysis and evaluation of ACMUI recommendations and other recommendations from the NRC Regions and Agreement States. A formal memorandum will be transmitted to the ACMUI that will include specific responses to ACMUI's recommendations.

This training must be provided to all individuals eluting the generator or preparing, or measuring the Ga-68 unit dose.

ITEM (6): The Committee agreed with the recommendation to modify the language in the "Radiation Protection Program Changes" Section to the following language:

> This guidance may be revised as additional experience is gained regarding the use of a Ge-68/Ga-68 generator for preparation of Ga-68 radiopharmaceuticals for 35.200 use. An applicant initially applying for authorization for use of Ge-68/Ga-68 generator under this 35.1000 use may request to incorporate into its license a change process similar to 10 CFR 35.26. Such a change process can allow some future changes without the need to amend the license to radiation safety programs provided that the change process requires the following conditions to be met for revisions to the radiation safety program:

The recommendation passed unanimously with nine favorable votes.

The ACMUI submitted their final report to the NRC staff on August 25, 2016. The NRC staff will consider the ACMUI's recommendations for possible changes to the "Germanium-68/Gallium-68 Generators Licensing Guidance." The NRC staff will issue the finalized licensing guidance once they have completed their analysis and evaluation of ACMUI recommendations and other recommendations from the NRC Regions and Agreement States. A formal memorandum will be transmitted to the ACMUI that will include specific responses to ACMUI's recommendations.

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