CORAR

The Council on Radionuclides and Radiopharmaceuticals, Inc.

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Via email March 22, 2016

Chairman Stephen G. Burns
U.S. Nuclear Regulatory Commission
Mail Stop O-16G4
Washington, DC 20555-0001

Re: Training & Experience for Authorized Users of Alpha and Beta Emitters Under 10 CFR 35.390

Dear Chairman Burns:

The members of the Council on Radionuclides and Radiopharmaceuticals, Inc. (CORAR) would like to follow-up the January 26th NRC meeting attended by both CORAR and Spectrum Pharmaceuticals where we discussed the training and experience requirements for Authorized Users (AUs) of Alpha and Beta Emitters Under 10 CFR 35.390. CORAR members include the manufacturers and distributors of both FDA approved Xofigo® (Radium Ra 223 dichloride) and Zevalin® (ibritumomab tiuxetan), as well as other therapeutic products that are still undergoing research and development.

Since our January meeting the Advisory Committee on the Medical Uses of Isotopes (ACMUI) adopted the Draft Report on Training & Experience for Authorized Users of Alpha and Beta Emitters Under 10 CFR 35.390 (Draft Report) submitted by the ACMUI Subcommittee on Training and Experience for Alpha and Beta Emitters (Subcommittee). By adopting the Draft Report, ACMUI accepted the Subcommittees' first recommendation that no modifications be made to the current 700-hour training and experience requirement for alpha- and beta- emitters. In addition, the Subcommittee recognized a need for a thorough review of the current training and experience requirements and recommended, "… that the ACMUI establish a standing subcommittee with a specific charge of periodically reviewing the T&E requirements currently

in effect and making recommendations for changes as warranted."

CORAR appreciates the evaluations by the ACMUI and NRC with regards to stakeholder requests to update the training and experience requirements, to ensure patient access and to support technological advances and changes in medical procedures. However, CORAR continues to believe that the current regulatory framework requiring 700-hours of training and experience to become an AU licensed to administer alpha- or beta- emitting radiopharmaceuticals is excessive. If steps are not taken the modify the training framework in the current rulemaking, we believe that patient access to important radiopharmaceutical drugs, such as Xofigo and Zevalin, will continue to be limited.

As an alternative to the current 700-hours, CORAR recently provided comments to the ACMUI recommending a specific scope of training requirements for Radioisotope Handling and Radiation Safety for physicians wishing to administer intravenous therapeutic radiopharmaceuticals containing alpha- or beta- emitting radioisotopes, which have been prepared by a licensed nuclear pharmacist in a state-licensed radiopharmacy and dispensed to physicians as patient-ready doses. In determining the appropriate amount of time (and scope of content) for Radioisotope Handling and Radiation Safety training that physicians, such as medical oncologists and hematologists, should receive to enable them to safely administer these types of therapeutic drugs, we provided the following factors for the ACMUI to consider:

- The limited role in handling these radiolabeled drugs (which would be dispensed and delivered to them in patient-ready doses from a licensed radiopharmacy);
- The radiological safety profiles of radiopharmaceuticals containing alpha- and beta-emitting isotopes;
- Physician's experience and training in handling toxic non-radioactive chemical therapies, e.g., cytotoxic chemotherapy agents.

CORAR continues to believe that the didactic training required to adequately prepare physicians to safely administer patient-ready doses of alpha- and beta- emitting drugs would entail about 70-80 hours of classroom and laboratory time. The ACMUI has received training statements from experts in radiation safety education which is consistent with this 70-80 hour recommendation. The Draft Report concluded that it has been "...nearly 15 years since the current requirements were established." The Draft Report continues by stating that, "Since that time new radiopharmaceuticals have been introduced and this is a trend that likely will continue. Appropriate T&E requirements for these agents need to be established."

It is encouraging that the Subcommittee recognized that an appropriate training and experience framework is necessary and needs to be established, ostensibly for patient-ready doses of alpha- and beta- emitters like Xofigo and Zevalin, both of which have been launched over the last 15 years. However, we believe that the ACMUI's decision to oppose reductions in the current training and experience framework and recommend a standing subcommittee to address appropriate requirements in the future does not meet the current need of patients.

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Specifically, by endorsing the recommendations in the Draft Report, we believe that ACMUI failed to:

1. Explain why 700 hours of Training and Experience is necessary for patient-ready doses of alpha- and beta- emitters;
2. Offer specific safety concerns that would preclude the ACMUI from recommending modifications to the Training and Experience requirements for patient-ready doses of alpha- and beta- emitters;
3. Acknowledge the significant stakeholder feedback that the ACMUI and NRC have already received on training and experience requirements for patient-ready doses of alpha- and beta- emitters;
4. Seriously consider Training and Experience expert statements to safely administer alpha- and beta- emitting radiopharmaceuticals. For example, Nicki Hilliard, Kara Weatherman, and Kristina Wittstrom provided a tailored 80-hour didactic program recommendation to modify the Training and Experience requirements for Authorized Users who administer patient-ready alpha- and beta- emitter doses. Their recommendations included 25 hours on Nuclear Physics & Instrumentation, 20 hours on Radiation Biology, 25 hours on Regulations and Radiation Protection, and 10 hours on Mathematics Pertaining to Use & Measurement of Radioactivity;
5. Recognize that patient access to alpha- and beta- emitters in the community and rural settings remains problematic. For example, Laura Weil, ACMUI Patient's Right Advocate stated in her dissent to the Draft Report that logistical barriers exist for patients who are limited to receiving therapy in the rural or community setting. In addition to Ms. Weil's comments, patient access concerns have been communicated through testimony and comments to the ACMUI and NRC staff by organizations such as Leukemia and Lymphoma Society, Lymphoma Research Foundation, Community Oncology Alliance, American Society of Hematology, and Florida Cancer Specialists;
6. To establish a specific recommendation for the number of T&E hours for Authorized Users of alpha- and beta- emitters that appropriately balances safety with reasonable patient access.

CORAR believes it is critical that the NRC address the appropriate level of training and experience requirements for Authorized Users of alpha- and beta-emitters in the current rulemaking on the ***Medical Use of Byproduct Material: Medical Event Definitions, Training and Experience***. Unfortunately, several ACMUI members have commented in public meetings that addressing the training requirements in the current rule making period would delay the release of the final rule. CORAR continues to believe that a delay would not be necessary, however, if the NRC decides to move forward with the ACMUI recommendation (and not modify the 700-hour training and experience requirements), we request that the Final Rule direct the NRC and ACMUI to expeditiously initiate separate rulemaking on training and experience requirements for alpha- and beta- emitters. Also, in the near term, CORAR requests that the NRC create an exemption pathway under 10 CFR 35.19 for practicing physicians to receive and administer patient-ready doses of alpha- and beta-emitters.

In closing, CORAR would like to again thank the ACMUI and NRC for considering our request to modify the excessive training and experience requirements for alpha- and beta-emitters, such as Xofigo and Zevalin. We look forward to continuing to engage with both the ACMUI and NRC to ensure that patients are safely treated with these important radiopharmaceutical drugs.

Sincerely,

Michael J. Guastella

Michael J. Guastella
Executive Director

cc: NRC Commissioner Jeff Baran
NRC Commissioner William C. Ostendorff
NRC Commissioner Kristine L. Svinicki

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