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Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Comment On: NRC-2018-0230-0162
Draft Approaches for Addressing Training and Experience Requirements for Radiopharmaceuticals Requiring a Written Directive

Document: NRC-2018-0230-DRAFT-0189
Comment on FR Doc # 2019-10760

Submitter Information

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Organization: Council on Radionuclides and Radiopharmaceuticals, Inc.

General Comment

See attached file(s)

Attachments

CORAR Add'l Comments to NRC-2018-0230 Final (6-28-19)

CORAR

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Executive Director

June 28, 2019

Office of Administration
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U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001
ATTN: Program Management, Announcements and Editing Staff

RE: DOCKET ID NRC–2018–0230, DRAFT APPROACHES FOR ADDRESSING TRAINING AND EXPERIENCE REQUIREMENTS FOR RADIOPHARMACEUTICALS REQUIRING A WRITTEN DIRECTIVE

The Council on Radionuclides and Radiopharmaceuticals, Inc. (CORAR) appreciates the opportunity to provide comments on the U.S. Nuclear Regulatory Commission (NRC) request for comment on the draft approaches that would potentially revise the training and experience requirements for radiopharmaceuticals requiring a written directive; Federal Register Vol. 84, No. 85; May 2, 2019. CORAR is an industry association of firms that manufacture diagnostic and therapeutic radiopharmaceuticals, radionuclides, and other radioactive products primarily used in medicine and research, and also includes firms that operate nuclear pharmacies that prepare and dispense radiopharmaceuticals in patient-ready doses for administration to patients in health care facilities.

On October 29, 2018 the U.S. Nuclear Regulatory Commission (NRC) requested comments on its training and experience (T&E) requirements. The feedback received from this prior request for comments provided a variety of options for NRC to consider and prompted the development of several draft approaches. This current comment period seeks additional feedback on the draft approaches. CORAR's comments are enclosed for your review and consideration.

As stated in previous CORAR comments dated January 24, 2019, CORAR believes that the current 700-hours alternate pathway (under 10 CFR 35.390) of training and experience to become a licensed AU to administer all radiopharmaceutical drugs is excessive with regard to the limited administration of alpha-, beta-, or beta-gamma- emitting radiotherapies (non-imaging radiotherapies). If steps are not taken to modify the training framework in the current rulemaking, we believe that patient access to important radiopharmaceutical drugs, such as Xofigo®, will continue to be limited.

Please do not hesitate to contact me at (202) 547-6582 if you have questions.

Sincerely,

Michael J. Guastella
Executive Director

MG:mdl, gps

Council on Radionuclides and Radiopharmaceuticals, Inc.

COMMENTS ON DRAFT APPROACHES FOR ADDRESSING TRAINING AND EXPERIENCE REQUIREMENTS FOR RADIOPHARMACEUTICALS REQUIRING A WRITTEN DIRECTIVE; DOCKET ID NRC-2018-0230 PUBLISHED IN FEDERAL REGISTER VOL. 84, NO. 85

Please find CORAR comments offered below on select T&E draft approaches described in the May 2, 2019 Federal register Notice:

Tailored Training & Experience Requirements

Limited AU for Unit-Dose, Patient Ready Radiopharmaceuticals

CORAR believes that the current 700 hour training and experience alternate pathway (under 10C FR 35.390) for physicians who wish to become limited Authorized Users (AUs) to safely administers patient-ready, non-imaging radiotherapy doses is not reasonable and is excessive.

CORAR proposed an alternate pathway under 10 CFR Part 35 Subpart E in previous comments dated January 24, 2019, outline provided again in our response to Question 13 below, to administer intravenous therapeutic radiopharmaceuticals containing non-imaging radiotherapies which are prepared by a licensed nuclear pharmacist in a state licensed radiopharmacy and dispensed to physicians as patient-ready doses or received directly from the manufacturer in a patient-ready dose container. **Please note that under this alternate pathway, the limited AU will not be mixing, radiolabeling, or preparing patient doses and is not conducting/interpreting imaging studies on the patient.**

CORAR's proposed alternative pathway appears to be a hybrid between draft approach III.B.1 and III.B.2. However, there is one significant difference. CORAR's recommended alternate pathway under 10 CFR Part 35 Subpart E would include 40-80 hours of didactic training, 10 hours of experiential training, and three (3) to five (5) patients treated under supervision to satisfy the requirements for a licensed physician to attain a proposed limited AU status. This contrasts with at least 400 total hours of T&E requirements included in draft approaches III.B.1 or III.B.2. CORAR believes that the 400 hours of total T&E requirements is excessive for a licensed physician (e.g. medical oncologist) interested in seeking limited AU status.

Question 5: Under what conditions should a radiopharmaceutical be considered patient-ready such that the T&E requirements could be tailored?

A patient-ready dose is an individual (single) dose that is prepared by a licensed nuclear pharmacist in a licensed nuclear pharmacy or received directly from the manufacturer in a patient-ready dose container. The patient-ready dose is dispensed for an individual patient pursuant to a prescription order.

Performance-Based

In addition to CORAR's proposed alternate pathway, CORAR considers the performance-based draft approaches as a viable T&E alternate pathway option for certain categories of radiopharmaceuticals. For example, under draft approach III C.2. a licensed physician could administer a non-imaging radiotherapy after the completion of competency based training or equivalent as determined by the site license condition and application. This would allow each licensee the opportunity to develop risk-informed policies and procedures based on non-imaging radiotherapy characteristics such as radiation emission profiles, amount of activity administered to the patient, route of administration, route of elimination from the patient, etc. Additionally, this would allow licensees to achieve compliance with 10 CFR Part 35.41 and 10 CFR Part 20. As with the draft approach discussed above under "Limited AU for Unit-Dose,

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Patient Ready Radiopharmaceuticals," CORAR believe that this approach would increase patient access to non-imaging radiotherapies without adversely affecting patient, provider, and public safety.

Question 6: How could a competency-based evaluation ensure appropriate training and experience for AUs administering radiopharmaceuticals?

The goal of the T&E Requirements under an alternate pathway is to provide licensed medical specialists (e.g., oncologist, hematology-oncologists, urologists) with competency in cognitive and psychomotor skills necessary to effectively and safely prescribe and administer specific non-imaging radiotherapies. Training should be contingent upon the non-imaging radiotherapy, its characteristics and its use. Specifically, low risk agents (e.g., patient-specific doses) should have reduced training requirements when compared to higher risk radiopharmaceuticals (e.g., those needing compounding, iodine-131 [I-131]).

Currently, regulators, medical specialty boards, or professional societies administer AU written or practical exams. In previous comments, CORAR has recommended that a reasonable demonstration of didactic knowledge be accomplished through examination. The hands-on laboratory training component of a program can be completed at a hospital nuclear medicine department, a radiopharmacy, or manufacturer provided location. The hands-on laboratory training must be completed under the supervision of a preceptor who has obtained AU status, is an authorized nuclear pharmacist, radiation safety officer, or health physicist. Each area of competency should follow the general progression:

- Explanation and demonstration of a skill to the student
- Preceptor assesses the student's level of competency

Question 7: How could physicians in small practices be credentialed (e.g. physicians not associated with hospitals or other large institutions and their credentialing boards)?

CORAR recommends that a reasonable demonstration of didactic knowledge be accomplished through examination which could be taken through an on-line AU Education program. The hands-on laboratory training component of a limited AU T&E program could be completed at a hospital nuclear medicine department, a radiopharmacy, or manufacturer provided location.

Additional Questions for Consideration

Question 10: What are the advantages and disadvantages of the draft approaches?

The advantages of a Limited AU for Unit-Dose, Patient Ready Radiopharmaceuticals and Performance Based draft approaches would provide hematologists, medical oncologists, and other specialists who sought to administer non-imaging radiotherapies the opportunity to complete requirements under an alternate pathway under 10 CFR Part 35 Subpart E. However, as mentioned above CORAR believes the 400 hours of total T&E requirements for draft approaches III.B.1 and III.B.2 is excessive and has outlined our recommended T&E requirements to attain limited AU status in question 13.

CORAR's recommended T&E program would obviate the need to achieve competency in the full range of nuclear medicine clinical activities (e.g., kit preparation, imaging techniques, camera Quality Control, image interpretation, etc.) that should not be required for licensed physicians who wish to become limited AUs to safely administer patient-ready doses of non-imaging radiotherapies to their patients. This position also comports with NRC's Medical Use Policy Statements which note that NRC can only intervene into the practice of medicine, if the practice presents a radiation risk to the public.

Question 11: Are there significant costs or benefits associated with any of the approaches?

CORAR believes that our proposed alternate pathway under 10 CFR Part 35 Subpart E would reduce the costs associated with time and expense for licensed physicians who wish to become credentialed while

increasing benefit to patients and potentially transferring the cost reduction to patients. For example, this would be a very important benefit for an oncologist who wishes to closely monitor a patient's response to a non-imaging radiotherapy treatment and quickly treat any complications. These clinical efforts might be delayed if the patient was required to travel for treatment to a distant healthcare facility and return home to receive ongoing care.

CORAR has not evaluated the cost associated with the remaining draft approaches, however, it seems likely that the performance based draft approaches (III.C.1 and III.C.2) could reduce costs, without risk to public safety, while increasing benefit to patients.

Question 12: Would any of the draft approaches impact patient access to radiopharmaceuticals or address stakeholder concerns of overly burdensome (regulatory) requirements?

Before the 2002 Medical Use of Byproduct Material final rule went into effect, hematologists, medical oncologists, and other specialists who sought to administer beta-emitting radiopharmaceuticals such as Zevalin® and Metastron® could become licensed to do so after completing 80 hours of classroom and laboratory training. Under the current framework, the NRC created a licensure pathway under which, with 700 hours of training and experience, physicians would be trained for the full range of activities in handling byproduct material including activities such as eluting molybdenum-99/technetium-99m generators, preparing and dispensing radioactive drugs, as well as administering a wide variety of radionuclides requiring written directives.

In addition, NRC stated in the 2002 final rule that physicians in training would attend to other "clinical matters" including the diagnostic use of the material under the supervision of an AU such as reviewing case histories or interpreting nuclear medicine scans. These diagnostic "clinical matters" also include supervising nuclear medicine technologists, learning about imaging equipment, understanding imaging Quality Assurance standards, and other important clinical skills necessary to ensure comprehensive high quality imaging in the nuclear medicine department. Even though these clinical matters are not specifically required by the NRC, this type of supervised work experience is counted toward the supervised work experience to obtain the required 700 hours. CORAR believes that the T&E requirements necessary to achieve competency in the full range of nuclear medicine clinical activities (e.g. kit preparation, imaging techniques, camera Quality Control, image interpretation, etc.) should not be required for licensed physicians who wish to become limited AUs to safely administer patient-ready doses of non-imaging radiotherapies to their patients. This position also comports with NRC's Medical Use Policy Statements which note that NRC can only intervene into the practice of medicine, if the practice presents a radiation risk to the public.

Another important point from the 2002 final rule is the fact that the NRC retained in its regulations a pathway under which, with 80 hours of training and experience, a "limited authorization" could be achieved for the oral administration of I-131 (67 CFR 20250; 10 CFR 35.392, 10 CFR 35.394). The NRC noted the impeccable safety record of the product, the low risk of therapeutic misadministration, and the burden placed on patients who might have to travel long distances to unfamiliar settings if their primary treating physician were unable to administer the treatment. In addition, NRC noted that any additional hours would be inconsistent with NRC Medical Policy to minimize intrusion into medical practice since additional hours were not justified by radiation risk.

It is important to note that in previous meetings of the Advisory Committee on the Medical Uses of Isotopes (ACMUI), the *Subcommittee on Training and Experience Requirements for All Modalities* had acknowledged that alpha- and beta- emitters also have an exceptional safety record. CORAR would like to point out that this safety record of handling and administration of alpha- and beta- radiotherapies includes those oncologists who became licensed AUs under the 80 hour alternate pathway. The overall safety record of oral I-131 administration and the non-imaging radiotherapies should support the request for an alternate T&E pathway for non-imaging radiotherapies, delivered to licensed healthcare sites as patient-ready doses prepared at a licensed radiopharmacy, and dispensed by a licensed nuclear

pharmacist, or received directly from the manufacturer in a patient-ready dose container, with no additional manipulations needed before patient administration.

With this said, CORAR believes that our proposed alternate pathway under 10 CFR Part 35 Subpart E for licensed physicians to be credentialed as limited AU's for receipt and administration of non-imaging radiotherapies dispensed as patient-ready doses would improve patient access to non-imaging radiotherapies and significantly reduce overly burdensome regulations.

Question 13: For the draft approaches that consider tailored hours of T&E, what are the appropriate number of hours and what radiation safety topics should comprise the limited T&E.

CORAR has proposed an alternate pathway under 10 CFR Part 35 Subpart E to administer intravenous non-imaging radiotherapies which have been prepared by a licensed nuclear pharmacist in a state licensed radiopharmacy and dispensed to physicians as patient-ready doses. The radiation safety topics include:

- Nuclear Physics & Instrumentation:
    i. Structure and Properties of Atoms
    ii. Radiation and Radioactive Decay
    iii. Production of Radionuclides
    iv. Interaction of Radiation with Matter
    v. Gas-Filled Detectors
    vi. Scintillation Counters
    vii. Personnel Monitoring Devices

- Radiation Biology:
    i. Physical Effects of Radiation
    ii. Chemical effects of Radiation
    iii. Cellular Effects of Radiation
    iv. Biological Effects of High Dose Radiation
    v. Biological Effects of Low Dose Radiation
    vi. Therapeutic Application of Particulate Radiation

- Regulations and Radiation Protection:
    i. Characteristics of Ionizing Radiation
    ii. Definitions of Radiation Measurement
    iii. Principles of Radiation Protection
    iv. Personnel Monitoring & Safety Precautions
    v. Regulatory Agencies
    vi. Documentation and Regulatory Reporting
    vii. Sealed Reference Sources
    viii. Area Monitoring
    ix. Waste Management & Disposal
    x. Packages containing Radioactivity

- Mathematics Pertaining to Use & Measurement of Radioactivity:
    i. Includes fundamental calculations: decay equation, half-value layers, exposure calculations, instrumentation needs.

Basic didactic instruction could be covered appropriately in 40 – 80 hours. The majority of T&E should be specific to patient safety – calculating dose, administration, post administration monitoring -- and to general radiation safety for patient, workers and public. Experiential training could be covered in 10 hours with three (3) to five (5) patients treated under supervision.

Question 14: Should the NRC consider inclusion of a formal radiation safety competency assessment for any of the draft approaches above? If so, who should establish and administer these assessments?

Please see our response to Question 6 above.

Question 15: How would the draft approaches impact the medical organizations that use the NRC's T&E requirements as a basis for establishing their training programs?

CORAR does not anticipate a negative impact to medical organizations that will potentially use limited NRC T&E requirements as a basis for establishing their training programs.

Question 16: Are there concerns regarding implementation and/or viability for any of the approaches described above?

CORAR has focused our comments on a proposed alternate pathway under 10 CFR Part 35 Subpart E that appears to be a hybrid between draft approaches III.B.1 and III.B.2. as well as the Performance Based draft approach, and has no concerns regarding implementation and/or viability.

Question 17: Are there any unintended consequences of the draft approaches?

With regard to the Unit-Dose, Patient Ready Radiopharmaceuticals and Performance Based draft approaches, CORAR anticipates no unintended consequences.

Question 18: Which of the draft approaches best positions the NRC to effectively regulate future radiopharmaceuticals?

It is important to note that in previous meetings of ACMUI, the *Subcommittee on Training and Experience Requirements for All Modalities* had acknowledged that alpha- and beta- emitters have an exceptional safety record. CORAR would like to point out that this safety record of handling and administration of alpha- and beta- radiotherapies includes those oncologists who became licensed AUs under the 80 hour alternate pathway.

CORAR believes that it is most likely that future non-imaging radiotherapies will be dispensed as patient-ready doses by licensed nuclear pharmacists from state licensed nuclear pharmacies or received directly from the manufacturer in a patient-ready dose container, pursuant to a prescription order, with no additional manipulations needed before patient administration. The overall safety record of non-imaging radiotherapies supports the request for an alternate T&E pathway for non-imaging radiotherapies, delivered to licensed healthcare sites as patient-ready doses.

With this said, in evaluating the draft approaches using a risk-informed approach, a 40 - 80 hour Unit-Dose, Patient Ready Radiopharmaceuticals T&E program or Performance Based alternate pathway T&E program would position the NRC to efficiently and effectively regulate future radiopharmaceuticals without adversely affecting public health and safety.

Question 19: Should the NRC continue to play a role in the review and approval of AUs?

NRC should continue to play a role in the review and approval of AUs based on a risk-informed approach. This justified NRC's decision in 2002 to retain the regulatory pathway under which, only 80 hours of T&E is required to attain limited AU status to administer oral sodium iodide-131. This same consideration by the NRC should support the creation of a limited AU pathway under 10 CFR Part 35 Subpart E for tailored T&E for specific non-imaging radiotherapies.