ALL AGREEMENT STATE RADIATION CONTROL PROGRAM DIRECTORS

OPPORTUNITY TO COMMENT ON DRAFT U.S. NUCLEAR REGULATORY COMMISSION’S STAFF EVALUATION OF TRAINING AND EXPERIENCE REQUIREMENTS FOR ADMINISTERING RADIOPHARMACEUTICALS (RCPD-18-003)

Purpose: To provide Agreement States the opportunity to comment on the draft U.S. Nuclear Regulatory Commission’s (NRC) staff evaluation of training and experience (T&E) requirements for administering radiopharmaceuticals.

Background: The evaluation was conducted in response to Staff Requirements Memorandum (SRM)-M170817, “Staff Requirements - Affirmation Session, 10:30 A.M., Thursday, August 17, 2017, Commissioners’ Conference Room, One White Flint North, Rockville, Maryland (Open to Public Attendance),” dated August 17, 2017 (Agencywide Documents Access and Management System (ADAMS) Accession No. ML17229B283). The staff’s evaluation specifically focused on Title 10 of the Code of Federal Regulations (10 CFR) Part 35, “Medical Use of Byproduct Material,” Subpart E, “Unsealed Byproduct Material - Written Directive Required.” In the SRM, the Commission directed the NRC staff to evaluate: (1) whether it makes sense to establish tailored T&E requirements for different categories of radiopharmaceuticals, (2) how those categories should be determined (such as by risks posed by groups of radionuclides or by delivery method), (3) what the appropriate T&E requirements would be for each category, and (4) whether those requirements should be based on hours of T&E or focused more on competency.

The T&E requirements in 10 CFR 35.390 provide three ways that a physician can be authorized to administer unsealed byproduct material (or radiopharmaceuticals) requiring a written directive. A physician can: (1) be certified by a medical specialty board, whose certification process is recognized by the NRC or an Agreement State; (2) satisfy the T&E requirements via an alternate pathway; or (3) be previously identified as an Authorized User (AU) on an NRC or Agreement State license or permit. The alternate pathway consists of completing a structured educational program and supervised work experience totaling 700 hours, including a minimum of 200 hours of classroom and laboratory training. A preceptor must attest that the physician has satisfactorily completed the T&E requirements and has demonstrated the ability to function independently as an AU for the medical uses authorized under 10 CFR 35.300. Preceptor attestation is not required if the physician is certified by a medical specialty board or has been previously identified as an AU for that specific medical use on an NRC or Agreement State license or permit.

Since the last revision of the T&E requirements in 2005 (70 FR 16336), stakeholders have raised concerns about the effects of T&E requirements in 10 CFR 35.390 on patient access to certain therapeutic radiopharmaceuticals. Specifically, stakeholders attest that the 700-hour requirement is overly burdensome for physicians who wish to use radiopharmaceuticals but are not certified by a medical specialty board whose certification process is recognized by the NRC or an Agreement State or have been previously as an AU on an NRC or Agreement State license or permit.
Stakeholders have expressed concerns that the extensive requirements have resulted in a shortage of AUs.

In 2016, the ACMUI formed a subcommittee to periodically review the T&E requirements for all medical modalities (unsealed and sealed byproduct material) in 10 CFR 35.100, 35.200, 35.300, 35.400, 35.500, 35.600, and 35.1000, beginning with review of 10 CFR 35.300, and make recommendations for changes as needed. This subcommittee was formed as a result of: (1) continued concerns raised by stakeholders, (2) development of new radiopharmaceuticals since the T&E requirements went into effect in 2002 (67 FR 20249), and (3) a shift of educational paradigm from hours and experience to one that is more competency-based. The subcommittee provided the NRC staff with its draft interim report (ADAMS Accession No. ML18051A725), dated February 19, 2018, and, in a public teleconference on March 1, 2018, discussed the report with the full committee. In the report, the subcommittee expressed concerns about the decreased number of nuclear medicine physicians, noting that this may be a problem in the future. Therefore, the subcommittee recommended the creation of new alternative approach for AUs under 10 CFR 35.390.

The NRC staff has completed its initial outreach to a small, but representative, stakeholders in order to determine if it’s feasible to tailor the T&E requirements for different categories of radiopharmaceuticals. These stakeholders included medical organizations such as the American Society for Radiation Oncology, the American Board of Nuclear Medicine, and the Council on Radionuclides and Radiopharmaceuticals, Inc. The NRC staff also reached out to five medical licensees, selected to represent a variety of sizes of medical facilities in different areas of the country. The NRC staff also sought input from the Commonwealth of Virginia to gain another regulator’s perspective, as well as a number of Army and Navy medical centers, to solicit feedback from Federal organizations that are subject to the T&E requirements. These stakeholders provided valuable input for the staff to consider as we develop our outreach plans going forward. The NRC staff is not recommending any changes to the T&E requirements at this time and plans to conduct extensive stakeholder outreach before any changes would be proposed to the Commission. This outreach will include, but is not limited to, medical professional societies, such as the Society of Nuclear Medicine and Molecular Imaging, medical specialty boards, universities with nuclear medicine programs, medical licensees, and Agreement States.

Discussion: Enclosed for your review and comment are the draft results and conclusion of the NRC staff’s evaluation that the NRC staff is planning to submit to the Commission. In addition to comments on the staff’s initial evaluation, comments of an editorial nature will be considered; however, the draft text will undergo additional technical editing and formatting by the NRC prior to publication.
Please provide any comments to the point of contact listed below. We would appreciate receiving your comments within 30 days of this letter. This comment period was coordinated with the Organization of Agreement States. If you have any questions regarding this correspondence, please contact me at 301-415-3340 or the individual named below:

POINT OF CONTACT: Irene Wu
TELEPHONE: (301) 415-1951
E-MAIL: Irene.Wu@nrc.gov

Andrea L. Kock, Acting Director
Division of Materials Safety, Security, State and Tribal Programs
Office of Nuclear Material Safety and Safeguards

Enclosure:
Draft U.S. Nuclear Regulatory Commission
Staff Evaluation of Training and Experience Requirements for Administering Radiopharmaceuticals

This information request has been approved by OMB 3150-0029 expiration 1/31/2019. The estimated burden per response to comply with this voluntary collection is approximately 3 hours. Send comments regarding the burden estimate to the Information Services Branch, U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by e-mail to infocollects.resource@nrc.gov, and to the Desk Officer, Office of Information and Regulatory Affairs, NEOB-10202 (3150-0029), Office of Management and Budget, Washington, DC 20503. If a means used to impose an information collection does not display a currently valid OMB control number, the NRC may not conduct or sponsor, and a person is not required to respond to, the information collection.
DISCUSSION:

To conduct the evaluation directed by the Commission in Staff Requirements Memorandum (SRM)-M170817, the U.S. Nuclear Regulatory Commission (NRC) staff first determined the knowledge topics that should be covered in the T&E requirements and then conducted outreach with various medical stakeholders. In developing the list of knowledge topics, the NRC staff used as a starting point the specific areas listed in Title 10 of the Code of Federal Regulations (10 CFR) 35.390 (radiation physics and instrumentation, radiation protection, mathematics pertaining to the use and measurement of radioactivity, chemistry of byproduct material for medical use, and radiation biology) and considered additional topics that may be needed to address the depth of knowledge that Authorized Users (AU) need to possess to safely administer radiopharmaceuticals. The NRC staff then developed a questionnaire covering four main areas: (1) the fundamental knowledge necessary for administering any radiopharmaceutical under 10 CFR 35.390, (2) the additional specific knowledge necessary for administering specific types of radiopharmaceuticals under 10 CFR 35.390, (3) how best to acquire this knowledge, and (4) how this knowledge and ability to function independently should best be evaluated. The NRC staff sent the questionnaire to a limited number of external stakeholders in the medical community (Agencywide Documents Access and Management System (ADAMS) Accession No. ML18108A266). The NRC staff received responses from three Federal medical stakeholders, as well as six non-Federal medical stakeholders including three medical licensees, one Agreement State, a professional society, and a trade organization. The comments are summarized below and can be found in ADAMS Accession No. ML18130A786.

**Fundamental and Specific Knowledge**

In general, the stakeholders responded that the list of topics included in the questionnaire were appropriate and that the majority of the topics are covered in sufficient depth during a physician’s residency program. Several stakeholders stated that the detailed list of topics should not be incorporated into the T&E regulations and instead should be provided in guidance documents.

**Means of Acquiring Knowledge**

For this question, the responses by stakeholders were more varied. Some stakeholders indicated that this knowledge would mostly be acquired in a physician’s residency or fellowship program or through a combination of didactic training and hands-on experience, and ultimately, no change to the T&E regulations is needed. Two stakeholders indicated that the regulators (the NRC and Agreement States) should not focus on how to best acquire the knowledge; rather, they should focus on whether or not physicians possess that knowledge. Two stakeholders suggested that the alternate pathway that exists in current requirements should be eliminated and that the NRC should require board certification as the only method of gaining appropriate T&E. However, one stakeholder stated that the alternate pathway should be maintained to provide flexibility due to the length of the board certification process. One stakeholder indicated that the requirement of supervised clinical experience with at least three administrations of each type of therapy is reasonable. Another stakeholder indicated that the current number of cases (three) required for iodine-131 is too few.
Evaluation of Knowledge and Abilities

The responses to the question about how knowledge and abilities should be evaluated also varied. Some stakeholders suggested that the medical specialty boards create and administer an examination to test competency; specifically, one of those stakeholders suggested the American Board of Nuclear Medicine. One stakeholder stated that the alternate pathway with preceptor attestation that exists in current requirements should be maintained. While most of the stakeholders expressed that a written examination was an appropriate method to determine if the physician has demonstrated the ability to function independently as an AU, one stakeholder did not support a practical examination because these examinations are difficult to standardize on a national basis, and one stakeholder was not sure if a written examination was a reliable evaluation by itself. Another stakeholder suggested that the professional medical societies may be able to administer an examination as a method to evaluate knowledge and abilities, and another stakeholder suggested that the NRC could administer such an examination. The overarching comment made by most of the respondents was that the NRC should collaborate with knowledgeable external entities to determine how the knowledge and ability to function independently should best be evaluated.

The NRC staff also received additional comments on whether and how the T&E requirements for administration of radiopharmaceuticals can be categorized. One stakeholder suggested creating an alternative means by which a limited AU status could be obtained for specific radiopharmaceuticals. Similarly, another stakeholder suggested that training should be contingent upon the characteristics and use of the radiopharmaceutical and balancing safety and risk to patients, workers, and the public. Specifically, this stakeholder suggested that radiopharmaceuticals that are lower risk should have reduced training requirements as compared to radiopharmaceuticals that are higher risk. Another suggestion was to create a specific provision for administering intravenous therapeutic radiopharmaceuticals containing alpha and beta emitting radioisotopes that have been prepared by a licensed nuclear pharmacist in a state-licensed radiopharmacy and dispensed to physicians as patient-ready doses.

In addition to the categories suggested by the Commission (risks posed by groups of radionuclides and delivery method), the NRC staff evaluated two additional categories: type of emission (alpha, beta, gamma, and low energy photon) and preparation method (single-unit, multiple dose). The NRC staff also considered combinations of these categories. The NRC staff evaluated radiopharmaceuticals that are currently available and those known to be under development within the scope of 10 CFR Part 35 Subpart E, and determined that several of these radiopharmaceuticals possess unique characteristics and/or would fall under multiple categories. For example, lutetium-177 dotatate, which was approved by the U.S. Food and Drug Administration in January 2018, is a single-dose radiopharmaceutical used primarily for its beta emission, is delivered parenterally, and has some unique radiation properties that require specific knowledge. Its properties include a high-energy gamma emission in addition to the beta emission, a unique administration process that requires administration of a dose-blocking agent to prevent overexposure to the kidneys, and the potential for the presence of a long-lived radionuclide impurity. These properties present complexities in developing categories and demonstrate the unique risks that need to be considered in establishing categories.

In addition to the comments received from external stakeholders, the NRC staff considered how the NRC administers the reactor operator licensing program as a benchmark for the appropriate T&E process for radiopharmaceuticals. Specifically, the NRC staff considered the relevant
requirements and guidance, how operator license examinations are developed and administered, and how the NRC qualifies examiners. It was noted that the operator licensing program was developed with substantial input from the regulated community, including the Institute of Nuclear Power Organization and Nuclear Energy Institute. The NRC staff also considered the resources it takes to implement the NRC’s operator licensing program in assessing the potential for a similar program to approve AUs.

As a benchmark for the appropriate content and number of hours of classroom training for authorization to administer radiopharmaceuticals, the NRC staff also explored the agency’s process for determining the length of courses with similar content and the instructional material covered in such courses. Through those discussions, the NRC staff estimated that it would take approximately 90 to 300 hours of classroom training to cover the topics in the list of fundamental knowledge and skills developed by the NRC staff, and endorsed by the stakeholders that the NRC staff engaged. Based on the NRC staff’s evaluation of the current T&E requirements and in combination with the responses received on the questionnaire, the NRC staff determined that the number of didactic training hours under the alternate pathway in current requirements (i.e., 200) is likely reasonable for the fundamental knowledge that an AU would need to administer any radiopharmaceutical.

The NRC staff evaluated several different approaches to demonstrate the knowledge and abilities to function independently. One option is to require a written examination to demonstrate competency combined with preceptor attestation for clinical experience, in lieu of didactic training. This examination could be developed by medical specialty boards, professional medical societies, or other experienced training professionals, then reviewed and approved by the NRC. This approach is analogous to the NRC’s approach to training and qualification requirements for reactor operator licensing. Another option is to require a written examination developed and administered by the NRC. This option was not supported by the several stakeholders that the NRC staff has engaged to date and would require additional resources for the NRC to create the infrastructure, processes, and procedures to write and administer the examinations. Additionally, the NRC staff notes that there is a lack of clinical expertise within the NRC to implement this option. The NRC staff also discussed the option of the medical industry developing new medical specialty boards for the NRC to consider for recognition and certification under 10 CFR Part 35, similar to the current NRC medical specialty board approval process. The NRC staff also considered the possibility of a hybrid approach where the number of didactic training hours could be reduced when combined with a competency demonstration (i.e., an examination and demonstration of clinical experience).

In summary, based on the information considered to date, the NRC staff has concluded that it may be feasible to establish tailored experience requirements for the limited administration of certain categories of radiopharmaceuticals (i.e., a limited AU status). These tailored requirements would be less extensive than the current T&E requirements for all radiopharmaceuticals. In establishing these categories, care will need to be taken to ensure that the unique risks of various radiopharmaceuticals can be considered and the categories established are distinct enough that radiopharmaceuticals do not fall into more than one category. Several options for developing categories of radiopharmaceuticals are feasible, and the NRC staff intends to further engage a wider range of stakeholders to develop a preferred option. In considering the appropriate T&E requirements and approach, the NRC staff has identified an initial list of knowledge topics that were mostly supported by the stakeholders engaged to date. Based on the NRC staff’s initial outreach, it appears that a competency-based approach to the T&E requirements in 10 CFR 35.390 may be feasible.
The NRC staff plans to conduct further outreach with the medical community, focused on how to tailor the T&E requirements to establish a limited AU status, the specific T&E requirements that should apply, and how the T&E requirements should be met (e.g., hours of training, demonstration of competency). That outreach, at a minimum, will include a Federal Register notice with specific questions, several public meetings or webinars, and presentations to professional medical societies. These outreach activities will be conducted in accordance with budgeted resources and agency priorities. If, based on this feedback, the NRC staff proposes to revise the T&E requirements in 10 CFR Part 35 Subpart E, the NRC staff will provide a rulemaking plan to the Commission.

CONCLUSION:

The NRC staff concludes that it may be feasible to establish tailored T&E requirements for categories of radiopharmaceuticals under 10 CFR Part 35 Subpart E and create a means of approving the limited administration of certain radiopharmaceuticals (i.e., limited AU status). This approach would require less extensive T&E requirements than the current T&E requirements for all radiopharmaceuticals. In addition, there are feasible options for creating a competency-based approach to demonstrate acceptable T&E. The NRC staff plans to conduct more extensive outreach with the medical community to identify the best approach for demonstrating an AU's knowledge and skills. These outreach activities will be conducted in accordance with budgeted resources and agency priorities. The NRC staff will continue to engage the ACMUI and will keep the Commission informed of its outreach efforts through the semiannual updates directed by SRM-M170817. The NRC will raise any policy issues to the Commission, and will provide a rulemaking plan if the NRC staff determines it is appropriate to propose changes to the current T&E requirements.