TRAINING AND EXPERIENCE REQUIREMENTS FOR UNSEALED BYPRODUCT MATERIAL: STAFF EVALUATION

In addition to gathering stakeholder feedback and coordinating with the Agreement States and the Advisory Committee on the Medical Uses of Isotopes (ACMUI), the staff evaluated the U.S. Nuclear Regulatory Commission's (NRC's) regulatory framework for training and experience (T&E) requirements more broadly to inform its consideration of the available options. The discussion below summarizes the staff's considerations.

The NRC's Medical Policy Statement

The Medical Policy Statement[1] says that the NRC will regulate the medical uses of radionuclides as necessary to provide for the radiation safety of workers and the general public; the NRC will not intrude into medical judgments affecting patients, except as necessary to provide for the radiation safety of workers and the general public; when justified by the risk to patients, the NRC will regulate the radiation safety of patients primarily to assure that the use of radionuclides is in accordance with the physician's directions; and, in developing a specific regulatory approach, will consider industry and professional standards that define acceptable approaches of achieving radiation safety.

The NRC staff, some members of the medical community, the Organization of Agreement States Executive Board, and some Agreement States have questioned whether the requirement that the NRC and Agreement States review and approve T&E for physicians to become authorized users (AUs)—thus acting as the final arbiters on whether a physician can prescribe radiopharmaceuticals—is aligned with the Medical Policy Statement. Some view this AU gatekeeper role and the prescriptive hourly and patient casework requirements in Title 10 of the *Code of Federal Regulations* (10 CFR) 35.390, "Training for Use of Unsealed Byproduct Material for Which a Written Directive Is Required," as encroaching on the practice of medicine, and public comments on the T&E evaluation often conflated AU status with a physician's medical competency. From the NRC's regulatory standpoint, the responsibilities of AUs involved in medical use include:[2] (1) radiation safety commensurate with use of byproduct material, (2) administration of a radiation dose or dosage and how it is prescribed, (3) direction of individuals under the AU's supervision in the preparation of byproduct material for medical use and in the medical use of byproduct material, and (4) preparation of written directive, if required. Revising the existing T&E regulatory framework to increase medical community involvement in setting T&E requirements and credentialing AUs would better align the T&E requirements with the Medical Policy Statement and the radiation safety-related responsibilities of AUs.

Patient Access to Radiopharmaceuticals

Despite the concerns about patient access raised by some pharmaceutical and medical stakeholders, the ACMUI[3] and the nuclear medicine and radiation oncology communities have

[1] "Medical Use of Byproduct Material; Policy Statement, Revision" (65 FR 47654; August 3, 2000).
[2] NUREG-1556, Volume 9, Revision 3, "Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses, Final Report," page 8-26, issued September 2019 (Agencywide Documents Access and Management System (ADAMS) Accession No. ML19256C219).
[3] "Advisory Committee on the Medical Uses of Isotopes (ACMUI) Training and Experience (T&E) for All Modalities Subcommittee Final Report," page 2, dated February 27, 2019 (ADAMS Accession No. ML19058A598), includes a table depicting the current and average numbers of resident physicians who are eligible to become AUs under 10 CFR 35.300 through the board certification and alternate pathways.

concluded that the number of existing AUs and medical residents eligible for medical specialty boards recognized by the NRC is sufficient to meet current and future demand for radiopharmaceuticals under 10 CFR 35.300, "Use of Unsealed Byproduct Material for Which a Written Directive Is Required."

The staff mapped the locations of medical licensees authorized to use 10 CFR 35.300 materials with at least one AU listed on the license who would be permitted to use any radiopharmaceutical, along with population density data obtained from the 2010 U.S. Census. The maps affirm that most 10 CFR 35.300 licensees are located in more populous areas; however, the need to travel for specialized health care is a fact of life in rural areas and is not limited to radiopharmaceutical procedures. The staff did not draw any conclusions about whether the number and location of licensees are sufficient to satisfy patient demand for radiopharmaceuticals, as such a determination would require detailed health care market data and analyses outside the NRC's purview. The NRC regulates medical uses of byproduct material to ensure the safety of workers and the general public, and, while the staff considered patient access concerns, the NRC cannot regulate T&E with a primary goal of increasing patient access to radiopharmaceuticals or improving the geographic distribution of AUs. The staff's evaluation of rulemaking options included consideration of whether the options would create new pathways for physicians to become AUs. However, staff notes that for reasons outside the NRC's purview, creation of new AU pathways would not guarantee increased AU availability in rural areas or increased overall patient access to radiopharmaceuticals. The staff discusses this mapping effort and provides licensee location maps in "Evaluation of 10 CFR 35.300 Medical Facility Locations" (ADAMS Accession No. ML19176A456).

Regulating for the Future of Radiopharmaceuticals

Radiopharmaceutical therapies are expected to increase from 13 percent of the global nuclear medicine market in 2017 to 60 percent of the market by 2030.[4] Emerging radiopharmaceutical therapies will likely become increasingly targeted to individual patients—considering patient anatomy, physiology, and genetic background to determine the most appropriate radiopharmaceutical and prescribed dose.[5] The staff envisions that some emerging targeted radionuclide therapy procedures will require more extensive treatment planning, dosimetry modeling, and evaluation of tumor response. Administration protocols for these emerging radiopharmaceuticals will inherently be more complex. Conversely, other radiopharmaceuticals may trend towards less complex administration protocols requiring little or no dose manipulation. The staff also anticipates that nonnuclear medicine and nonradiation oncology physicians (such as hematologists, medical oncologists, and urologists) will increasingly want to serve as both the referring and treating physicians for some therapies. Given that the expansion of the number and type of radiopharmaceuticals is just beginning, the staff believes that a less prescriptive, more performance-based approach, would provide the flexibility needed to accommodate future radiopharmaceuticals. While tailored requirements are possible in some cases, definitive, specific requirements for current radiopharmaceuticals would not best accommodate the vast number of emerging and future technologies.

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[4] MEDraysintell, "Nuclear Medicine World Market Report & Directory, Edition 2018"; see http://medraysintell.com/resources/Nuclear%20medicine%20Market%20Report%20and%20Directory%202018%20-%20Presentation.pdf.

[5] Society of Nuclear Medicine and Molecular Imaging, "Fact Sheet: Targeted Radionuclide Therapy and Prostate Cancer," available at http://www.snmmi.org/AboutSNMMI/Content.aspx?ItemNumber=12772.

Risk-Informing Training and Experience for Specific Radiopharmaceuticals

The staff determined that the T&E requirements in the alternate pathway may not be well-suited for certain radiopharmaceuticals. For example, 700 hours of T&E may not be necessary to ensure the safe use of a radiopharmaceutical that is provided to the physician in a unit-dose, patient-specific form and features an uncomplicated administration protocol, patient release without restrictions,[6] and sufficient operating history demonstrating safe use. Conversely, the existing knowledge topics and supervised work experience requirements may not encompass the safety-related characteristics of future radiopharmaceuticals, which may feature complex treatment procedures and higher administered doses. Tailoring T&E requirements for different categories of radiopharmaceuticals may not consider the unique aspects of radiopharmaceuticals within these categories that may indicate the need for additional T&E. Given these complexities, more involvement by the medical community in determining the appropriate training for the safe use of radiopharmaceuticals would be beneficial.

Review of Medical Events

The Idaho National Laboratory (INL) performed a study to determine whether there were trends in the number of medical events caused by inadequate training.[7] The review focused on reportable medical events that occurred in fiscal years 2017 and 2018 (86 events total). Of the 86 events, the description of only one event identified inadequate training as the cause, while in three others, inadequate training was inferred. The specific cause of inadequate training was difficult to establish from the reference documents because they typically indicate only that events result from human error and do not describe why the human error occurred. The INL and NRC staff determined that the available records and references did not contain enough detailed information to identify how many medical events are caused by inadequate training of medical staff, and the study was inconclusive in identifying any trends in medical events caused by inadequate training of medical staff.

Review of International Regulations

Training for the use of radiopharmaceuticals in many European and Asian countries is generally under the practice of nuclear medicine and diagnostic and therapeutic radiopharmaceuticals are primarily administered by nuclear medicine physician specialists. The international community generally does not regulate the type and amount of T&E for these physician specialists; rather, the international community requires that the physicians administering radiopharmaceuticals have the proper certification as nuclear medicine specialists as set forth by the medical community. “International Benchmarking” (ADAMS Accession No. ML19176A453) documents the staff’s independent research and outreach to several international regulators and one nuclear medicine society.

[6] The NRC’s patient release criteria are contained in 10 CFR 35.75, “Release of Individuals Containing Unsealed Byproduct Material or Implants Containing Byproduct Material.”

[7] INL/LTD-19-52843, “Nuclear Material Events Database—Review of Medical Events for Inadequate Training (Fiscal Year 2017–2018),” issued February 2019 (ADAMS Accession No. ML19065A234).

Summary

The staff finds that given the expected growth in the field of nuclear medicine and uncertainties in the safety-related characteristics of emerging and future radiopharmaceuticals, such as energy level, dose, half-lives, and administration protocol, a less prescriptive and more performance-based approach to regulating T&E would be beneficial because it could cover radiopharmaceuticals beyond those currently known or in use. In addition, increased involvement by the medical community in determining the appropriate safety criteria for radiopharmaceuticals and setting the associated T&E requirements could help accommodate the increasing interest of nonnuclear medicine and nonradiation oncology physicians in using radiopharmaceuticals. While the staff considered stakeholder concerns about patient access, the availability and geographic distribution of AUs did not drive the staff's evaluation of T&E.