The U.S. Nuclear Regulatory Commission Staff Responses to the Advisory Committee on the Medical Uses of Isotopes Comments on the Draft Part 35 Proposed Rule

Introduction

The proposed rule would amend the regulations related to the medical use of byproduct material. First, this rule proposes amendments to the reporting and notification requirements for a medical event (ME) for permanent implant brachytherapy. Second, the rule proposes changes to the training and experience (T&E) requirements for authorized users (AUs), medical physicists, Radiation Safety Officers (RSOs), and nuclear pharmacists; changes to the requirements for measuring molybdenum contaminations and reporting of failed technetium and rubidium generators, and changes that would allow Associate Radiation Safety Officers (ARSOs) to be named on a medical license, as well as other clarifying and conforming amendments. Third, the U.S Nuclear Regulatory Commission (NRC) is considering a request filed in a petition for rulemaking (PRM) (PRM-35-20) to "grandfather" certain board-certified individuals.

Background

On December 21, 2012, the NRC staff provided the preliminary draft proposed rule to the ACMUI for its review and comments for a 90-day review. The Advisory Committee on the Medical Uses of Isotopes (ACMUI) discussed the draft proposed rule at two publicly held teleconferences on March 5 and March 12, 2013 (conference transcripts are available in ADAMS at ML13087A474 and ML13087A477, respectively), and provided a final report to the NRC on April 9, 2013 (ADAMS ML13071A690).

In accordance with the Office of Federal and State Materials and Environmental Management Programs procedures, the ACMUI comments and recommendations were considered in developing the proposed rulemaking.

The ACMUI provided its comments and recommendations under three separate sections:

1. General Comments
2. Specific Comments---Significant, and
3. Specific Comments---Minor

All of ACMUI's recommendations were incorporated into the proposed rulemaking except for the following items. In addition, although some of the recommendations were not directly incorporated into the proposed rule, they were addressed in another manner, as is explained below:

1. General Comments

Item 1. Medical event definitions for permanent implant brachytherapy.

ACMUI item a.

Issue: The ACMUI provided the background related to the ME definition and described the inadequacy of the current dose-based definition when applied to permanent implant brachytherapy. In summary, the ACMUI recommended that licensees be allowed to use total

source strength as a substitute for total dose for determining MEs for permanent implant brachytherapy until the Part 35 rulemaking is complete.

Staff response - The staff agrees with the ACMUI recommendation to allow licensees the use of total source strength as a substitute for total dose for determining MEs for permanent implant brachytherapy until the Part 35 rulemaking is complete. In this regard, in a Staff Requirements Memo dated, May 21, 2013, the Commission has approved the staff's proposed interim enforcement policy as described in SECY-13-0044, "Interim Enforcement Policy for Permanent Implant Brachytherapy Medical Event Reporting." On July 9, 2013, the NRC issued the interim enforcement policy for permanent implant brachytherapy ME reporting.

ACMUI item c.

Issue: The ACMUI expressed concern that the proposed ME definitions may discourage practitioners from utilizing this therapy. It recommended that NRC solicit information from its stakeholders on whether the proposed ME definitions for permanent implant brachytherapy will discourage licensees from using this therapy option or will otherwise adversely impact clinical practice.

Staff Response - Although the ACMUI's specific recommendation to solicit information on this subject was not incorporated into the *Federal Register* notice (FRN), we believe we addressed the intent of the ACMUI comment in our general solicitation of information related to the economic impact of the proposed rule. Additionally, the staff has prepared a regulatory analysis which will be available for public comment when the proposed rule is published.

ACMUI item d.

Issue: The ACMUI recommended that MEs related to permanent implant brachytherapy be designated as Compatibility Category B for the Agreement States. The ACMUI was concerned with the proposed designation as Compatibility Category C which would allow the Agreement States to retain the dose-based criteria for determining a ME for permanent implant brachytherapy. In summary, the ACMUI asserted that a Compatibility Category C would continue to result in clinically insignificant occurrences being identified as MEs by Agreement States and thereby perpetuate the confusion associated with the current dose-based criteria. Also, the ACMUI stated that the most important component of the rationale for conversion from dose-based to activity-based criteria is the failure of dose-based criteria to sensitively and to only specifically capture clinically significant MEs in permanent implant brachytherapy.

Staff response - The issue of the Compatibility Category for MEs is discussed in detail in the draft FRN. Currently, MEs are designated as Compatibility Category C. The Standing Committee on Compatibility (SCC) reviewed the proposed rule and strongly supported retaining Compatibility Category C designation for § 35.3045, the section that contains the criteria for determining if a ME has occurred. As noted in the discussion in the proposed draft FRN, with a Compatibility Category C designation, Agreement States would have the flexibility to require both the dose-based criteria and source strength-based criteria as long as the Agreement States' reports to NRC related to MEs are based on the requirements in § 35.3045.

The SCC stated that many Agreement States have additional state requirements and laws to gather information on MEs. A Compatibility Category B requirement would prohibit the Agreement States from gathering additional information, such as diagnostic reports, shorter reporting times, or lower dose limits for reporting. After reviewing the issue, the SCC determined that identical reporting requirements were not necessary for the national program on a transboundary basis. The SCC concluded that a change to a Compatibility B would not acknowledge the inherent state function to protect public health and safety of its citizens which forms the basis of the Section 274b amendment to the Atomic Energy Act of 1959.

Although the staff is proposing to retain the proposed Compatibility for MEs at Compatibility Category C, the NRC is seeking specific comments on the Compatibility Category in the draft FRN.

Item 2. Training and experience requirements for authorized users, medical physicists, Radiation Safety Officers, and nuclear pharmacists.

ACMUI item b.

Issue: The ACMUI recommended removing the work experience requirement on eluting generators for AUs who would not be responsible for proper operation and testing of generators. It asserted that the vast majority of AUs are not responsible for a generator system because they obtain unit dosages or bulk radionuclides from a commercial radiopharmacy. The ACMUI suggested that licensees approved to use generator systems could show specific training on the requirement now listed under § 35.290 (c)(1)(ii)(G) for those individuals (AUs and others) who are responsible for proper operation and test of the generator as part of their license conditions.

Staff response - The suggested change to remove the training requirement for AUs to have work experience in eluting generators is outside the scope of the proposed rulemaking. The staff agrees that a large number of licensees obtain unit dosages or bulk radionuclides from a commercial radiopharmacy. However, AUs at remote locations and large licenses still are involved in the elution of generators.

ACMUI item d.

Issue: The ACMUI recommended that the work experience for parenteral administrations under § 35.390 (b)(1)(ii)(G) and § 35.396 **not** be separated between administration of a beta/ gamma-emitting radiopharmaceutical and an alpha-emitting radiopharmaceutical as proposed. The ACMUI asserted that there is no fundamental difference in the clinical applications and radiation safety precautions among these radiations. Therefore, the T&E a physician receives to perform parenteral administration of a radiopharmaceutical, including the three cases of work experience, is sufficient in demonstrating the physician's competency to function as an AU for both the beta-/gamma-emitting and the alpha-emitting radiopharmaceuticals.

Staff response - The staff has determined that there are fundamental differences between the clinical use and the radiation safety of the two groups identified in proposed § 35.390(b)(1)(G)(3) or (4). The radiation detection equipment used to monitor and detect photons, electrons, and beta particles can be very different from that used to monitor and detect

alpha particles, and calibration procedures for measuring activities of beta emitters and alpha emitters are more complicated than for photon emitters. Further, the relationship between activity and radiation dose delivered to the patient for alpha emitters is not the same as that for low-energy photons, beta particles and electron emitters.

The staff recognizes that medical use licensees have radiation safety T&E, medical use experience, and ready access to low-energy photon and beta-emitting radionuclides. However, radioactive drugs primarily used for their alpha radiation characteristics are new to most medical use licensees (the first alpha-emitting radiopharmaceutical was approved by Food and Drug Administration (FDA) in May 2013). The staff determined that there are important radiation safety considerations associated with alpha-emitting radiopharmaceuticals. They include patient radiation safety (e.g., administrative controls to prevent an ME), steps to ensure the proper dosage is delivered (e.g., quality control procedures on instruments used to determine the activity of dosages, calculating, measuring, and safely preparing dosages), and radiation safety (e.g., ordering, receiving, performing radiation surveys, containing spills safely and proper decontamination procedures). Therefore, the staff has determined that an AU should have experience with alpha-emitting radiopharmaceuticals in addition to the experience the AU may have with the low-energy photon-and beta-emitting radionuclides.

Issue: The ACMUI asserted that the separation of beta-/gamma-emitting from alpha-emitting radiopharmaceuticals would expend licensee and regulatory staff resources in the prescriptive bookkeeping needed to track all the separate work experiences for the AUs.

Staff response - The staff has determined that this requirement would not be a burden on licensees. The proposed requirements will ensure that AU's have the proper radiation safety training in the use of alpha emitters. Licensees only need to document the physician's T&E using the broad categories listed in § 35.390(b)(1)(G) and need not document each individual radionuclide used in a category.

Issue: The ACMUI asserted that the proposed rule does not address how AUs currently approved under § 35.390 and § 35.396 for parenteral administration alpha-emitting radiopharmaceuticals will be grandfathered to allow them to continue to use them and to act as supervising AUs for § 35.390 (b)(1)(ii)(G).

Staff response - NRC will allow those AUs currently approved for parenteral administration of alpha-emitting radiopharmaceuticals to continue the medical use of those materials when the final rule goes into effect.

Item 3. Extending grandfathering to certain certified individuals (Ritenour petition).

ACMUI items a and c.

Issue: The ACMUI recommended that all individuals who were able to meet the requirements of the previous Subpart J for an AU, RSO, authorized medical physicist (AMP), or authorized nuclear pharmacist (ANP) before that subpart was eliminated on October 24, 2005, should be grandfathered, thus relieving them of meeting the current training and experience requirements. The ACMUI asserted that the date of recognition by the NRC of a certifying board should not impact individuals seeking to be named on a license via the certification pathway because once

a board has been recognized by the NRC, the date of recognition is irrelevant, and this should be stated in the proposed rule.

Staff response - The date of the individual's board certification is relevant. Boards that were recognized by the NRC or Agreement State on or prior to October 24, 2005 (listed in the now removed Subpart J), met different T&E requirements than boards whose processes have been recognized by the NRC or Agreement States after October 24, 2005.

Further, the staff determined that the ACMUI recommendation that all individuals who were able to meet the requirements of the previous Subpart J should be grandfathered would go beyond the intent of the resolution of the Ritenour petition, which requested recognition of individuals who were certified by boards listed under former Subpart J to perform AMP and RSO duties on or prior to October 24, 2005, but were not named on a license. The NRC, in resolving the Ritenour petition, determined that other medical professionals may have also been adversely affected when Subpart J expired. The intent of the resolution was to include all these individuals and grandfather them for the modalities they practiced on or prior to October 24, 2005. Grandfathering individuals who met the Subpart J requirements but were not board certified would also negate the new T&E requirements that became effective on October 25, 2005.

ACMUI item b.

Issue: Some of the terminology NRC has historically used and now uses in the proposed rule is somewhat confusing. For clarification of meaning, it is suggested that the terms "type of use," "modality," and "category" be explicitly defined in Section 35.2 (Definitions), so that the regulatory meaning of these three terms is clearly understood.

Staff response - The term "type of use" is already defined in Part 35.2. The terms "category" and "modality" were reviewed and determined to be defined by common use (i.e., what is found in a dictionary).

Item 4. Measuring molybdenum contamination for each elution and reporting of failed breakthrough tests.

ACMUI item a.

Issue: The ACMUI noted that only two generator systems are specified in the current and proposed rule, molybdenum-99 (Mo-99)/technetium-99m (Tc-99m) and strontium-82 (Sr-82)/rubidium-82 (Rb-82) generators, and questioned whether other generator systems should be included or whether the proposed rule should be generalized to all medical generator systems.

Staff response - Currently there are no other generator systems that are available for general medical use. Any new generator system that becomes available would need to be evaluated by the NRC before developing any requirements and would be authorized under § 35.1000. Additionally, expanding the regulations from the specific requirements for Mo-99/Tc-99m and Sr-82/Rb-82 generators to apply to generators generally is beyond the scope of this rulemaking.

Issue: The ACMUI recommended that the NRC adopt the FDA-approved package insert for breakthrough limits for radioisotope generators. The ACMUI noted that current FDA labeling is more restrictive than the current NRC rule for Mo-99/Tc-99m generators, (i.e., it requires testing of each elution) and that the proposed rule will match the FDA labeling requirements. The ACMUI asserted that the NRC's breakthrough limits for Sr-82 and Sr-85 are less restrictive than the package inserts and are not being revised. Additionally, the ACMUI asserted that the NRC would be able to inspect for compliance against the applicable FDA breakthrough testing requirements for all generators and thus would not have to await revision of its rules for testing requirements for newly introduced generators.

Staff response - The ACMUI recommendation that the NRC adopt the FDA-approved package insert for breakthrough limits for radioisotope generators was not accepted because revising the regulations to require licensees to follow the FDA-accepted package inserts with regard to testing eluates would reverse the NRC's December 2, 1994, rulemaking (59 FR 61781) that removed the requirements to follow the FDA package inserts for preparation of radiopharmaceuticals from NRCs regulations. The 1994 rulemaking was in response to a petition for rulemaking by the American College of Nuclear Physicians, the Society of Nuclear Medicine, and medical and pharmacy stakeholders. The petition asserted that the NRC was interfering with the practice of medicine and pharmacy by requiring licensees to follow the FDA package inserts. NRC granted the petition, and the ACMUI has not provided a sufficient basis to revisit this determination.

Furthermore, the NRC cannot inspect a licensee for compliance with FDA regulations. Licensees would not have to wait for the NRC to revise its regulations to establish licensing requirements for new generators as the NRC has a mechanism under § 35.1000 for authorizing new products in a timely manner.

Finally, the staff has determined the NRC's current breakthrough limits for both Tc-99m and Rb-82 radioisotope generators are safe. Also, the current FDA label breakthrough limits for Sr-82 and Sr-85 generators are at the lower limits of current standard dose calibrator measurement capabilities.

ACMUI item b.

Issue: The proposed rule would require a licensee to report to both the NRC and the manufacturer or distributor when a generator has failed a breakthrough test. The manufacturer or distributor would also be required to notify the NRC when it received a reported failure from a licensee. Commenters at the public workshops in 2011 stated that this reporting should not be required because the manufacturers are required to report failed generators to the FDA.

The ACMUI did not support this requirement for dual reporting and found that the rationale stated in the FRN (i.e., that the FDA may not investigate each reported incident), may take time in investigating reported failures, and that some incidents of failed generators may not be reported to the FDA because certain manufacturers are not in the United States and generators are distributed by vendors who are not required to report to the FDA somewhat specious. The ACMUI asserted that the licensee should only report to the manufacturer/distributor and not to the NRC when a generator fails. The ACMUI explained that FDA has a process for receiving

reports and investigating product failure and that the Memorandum of Understanding (MOU) between FDA and the NRC would allow the NRC to get this information.

Staff response - The staff agrees with the ACMUI that the FDA authority in relationship to foreign manufacturers or distributors of generators was incorrect and has revised the FRN for the proposed rule.

However, the staff determined that licensees should report to both the NRC and the manufacturer or distributor when a generator fails a breakthrough test because the information that would be reported by medical use licensees to the NRC is different than the information that would be reported to the manufacturers or distributors. For example, reports from a medical use licensee to the NRC would have information on patient exposures, probable cause and assessment of failure in the licensee's equipment, and procedures or training that contributed to the excessive readings if an error occurred in the licensee's breakthrough determination. The licensee would only report information related to the generator failure to the manufacturer or distributor. Also, the corrective actions reported to the NRC by the licensee and the manufacturer or distributor would be different for each. The licensees' corrective actions would focus on procedures while the manufacturers or distributors' corrective actions would focus on manufacturing processes. Breakthrough tests exceeding the regulatory standard could be due to many different issues including from problems with the generator elution procedures, as a result of transportation, or problems with the manufacturer's production of the generator. The two separate reporting requirements would provide the NRC with the necessary information to determine the scope of the issue and the appropriate actions applicable to each entity.

Although both NRC/Agreement States and FDA have regulatory authority over the radioactive drug manufacturers, their regulatory responsibilities are different. The NRC regulates both the end user and the radioactive drug manufacturer whereas FDA regulates only the product and drug manufacturer. The NRC/FDA MOU was initiated to provide a mechanism for sharing information that is of mutual regulatory interest to both agencies. The NRC believes that it is important for medical use licensees and commercial nuclear pharmacies that elute generators; (i.e., the end users) as well as manufacturers or distributors, to report breakthrough failures to NRC as quickly as possible. If the generator breakthrough values exceed the regulatory limits, the problem could be with the procedures of the generator elution site, a result of transportation, or with the manufacturer's production of the generator. The NRC believes that 24-hour notification will assist in quickly differentiating generator elution licensee problems from those of the manufacturer. Requiring end user reporting also provides the NRC with a confirmation of whether patients were administered radiopharmaceuticals with excessive breakthrough. The generator manufacturer/distributor report to the NRC of breakthrough within 24 hours would assist the NRC and the Agreement States in identifying the scope of the problem and the regulatory efforts needed to address it.

ACMUI item c.

Issue: The ACMUI asserted that with respect to the Sr-82/Rb-82 generator breakthrough issue, the proposed rule does not actually address the underlying cause of recent reported instances of excess radiostrontium breakthrough at two medical facilities which appeared to be the apparent failure of licensees to perform daily breakthrough testing.

Staff response - The staff agrees with the ACMUI that appropriate testing may have detected the occurrences of breakthrough at these sites. However, under current regulations, there is no requirement for the licensee to report the breakthrough failure. Had this information been reported in a timely fashion to the regulators, appropriate steps could have been taken to look at the quality of the licensee's generator testing program as well as the manufacturer's production processes. The new reporting requirements in the proposed rule are intended to correct this situation.

Issue: The ACMUI asserted that current training requirements in § 35.290 are only specific to Mo-99/Tc-99m generators; training requirements have not kept pace with new and different generators.

Staff response - The staff determined that the T&E requirements in § 35.290 apply to all generators. For any new and significantly different generators, T&E would be addressed under the provisions of § 35.1000.

ACMUI item d.

Issue: The ACMUI recommended that the NRC solicit comments in the FRN as to whether the proposed notification requirements would discourage licensees from using generators and would also have adverse economic impact on venders of generator systems.

Staff response: Although the ACMUI's specific recommendation to solicit information on this subject was not incorporated into the FRN, we believe we addressed the intent of the ACMUI comment in our general solicitation of information related to the economic impact of the proposed rule. Additionally, the staff has prepared a regulatory analysis which will be available for public comment when the proposed rule is published.

Item 5. Allowing Associate Radiation Safety Officers to be named on a medical license.

ACMUI item a.

The ACMUI recommended that the addition of ARSOs and Temporary RSOs be included in the broad scope exemptions under § 35.15 in the same manner as AUs, ANPs, and AMPs (i.e., allow broad scope medical licensees to review an individual's T&E and authorize the individual to work under the license).

Staff response - Unlike ANPs, AMPs, and AUs, who are not specifically listed on the broad scope medical use license, RSOs are listed on a broad scope medical use license, and the NRC specifically reviews the T&E of each individual before he/she is listed as an RSO on every medical use license including a broad scope medical license. This review is important because the RSO is responsible for implementing the radiation safety program for the licensee. An ARSO will have similar duties working under the RSO, and like the RSO, would be listed specifically on the license. Because of this, the staff has determined that the NRC needs to review the T&E of each individual before he/she is listed as an ARSO. The NRC does not exempt the medical broad scope licensee in § 35.15 from notifying NRC when it appoints a

temporary RSO because the NRC needs to know when an RSO leaves any medical use licensee and the licensee has to name a temporary RSO.

For these reasons, the provisions in § 35.15 for a temporary RSO is unchanged from the current regulations that allow a licensee to permit a qualified individual to serve as the RSO for up to 60 days each year. Additionally, changes to the temporary RSO provision are beyond the scope of this rulemaking.

ACMUI item b.

Issue: The ACMUI asked whether an individual who does not have board certification is named as an authorized individual, that individual would need a preceptor signature for any additional future training and recommended that, if so, the proposed rule include an example of how this would be done.

Staff response - Under the proposed rule, RSOs, ARSOs, or other authorized individuals who are not board certified would need to obtain a written attestation. The associated guidance will clarify that all individuals coming through the alternate pathway will need a preceptor statement for the additional training.

Item 6. "Plain language" requirements.

The ACMUI noted that although overall the proposed rule was well-written and well-organized, it could be shortened, and improved, by eliminating redundancies and consolidating related sections, eliminating identical or nearly identical passages appearing multiple times throughout the draft rule. A further improvement would be the inclusion of a detailed "executive summary" style section summarizing, perhaps in a "bullet" format, the key changes introduced in the draft rule. This would be in place of the current one-paragraph Summary.

Staff response - Although the staff has added an executive summary summarizing the key changes in the draft rule, the staff must follow the format required by the *Federal Register* and NRC administrative requirements in laying out the proposed rule. Therefore, the staff has retained the one-paragraph summary.

Item 7. Additional general comments.

The ACMUI noted that licensees will need to easily access Sealed Source and Device Registry (SSDR) documents and asked whether the NRC could provide access to copies of these registrations.

Staff response – Since the events of September 11, 2001, public access to the SSDR registry has no longer been provided for security reasons. The Agreement States have access to the registry via a password protected portal. Any licensee with a legitimate reason to have access to an SSDR document may request it from its regulatory authority or the manufacturer of the sealed source or device.

2. Specific Comments – Significant (pages 8 through 10 of the ACMUI's report)

The ACMUI recommended that individuals grandfathered under the provisions of the Ritenour petition be recognized for the modalities covered by their board certification and not for the modalities that they practiced as of October 24, 2005.

Staff response - This issue is related to the ACMUI's recommendation in Item 3 a and c above. The staff disagrees with the change for several reasons. First, all of the individuals grandfathered under the provisions of § 35.57 in the current regulation and the proposed rule are only recognized for the modalities that they practiced as of October 24, 2005. Second, if the NRC were to recognize individuals based on the modalities covered by their board certification, then recognition could be for a modality for which the individual may not have had the T&E, (such as an AU authorized for use of a gamma stereotactic unit prior to October 24, 2005, and who now wants to use a high-dose afterloader unit). Finally, the resolution to the Ritenour petition was based on recognizing individuals for the modalities that they practiced as of October 24, 2005, not for the modalities covered by their board certifications, so that this change would go beyond the intent of the Ritenour Petition.

The ACMUI suggested changing the phrase, "The maximum absorbed dose to any 5 contiguous cubic centimeters…," to "The minimum absorbed dose to the maximally exposed 5 contiguous cubic centimeters…"

Staff response - The staff reviewed the referenced language and did not agree with the suggested change because adding the word "minimum" caused confusion about the intended meaning. However, based on the review of the language, the staff revised the draft proposed rule for clarity. It now reads "the absorbed dose to the maximally exposed 5 contiguous cubic centimeters of normal tissue located within the treatment site."

The ACMUI questioned the proposed requirement to have all individuals who would operate remote afterloader units, teletherapy units, and gamma stereotactic radiosurgery units receive vendor operational and safety training prior to the first use for patient treatment of a new unit or an existing unit with a manufacturer upgrade that affects the operation and safety of the unit. The ACMUI asked how this requirement would impact licensees, if there will be enough trainers for the number of unit operators, and if computer-based training will be acceptable.

Staff response –The current regulations already require individuals who operate remote afterloader units, teletherapy units, and gamma stereotactic radiosurgery units to receive the training initially and annual refresher training. The proposed change would add a training requirement for when a new unit is installed or for when there is a manufacturer upgrade to an existing unit that affects the operation and safety of the unit to ensure the continued safe use of the device. The staff believes that vendors are already providing this training to ensure their devices will be used safety and there is little additional impact.

The ACMUI suggested restructuring of § 35.15 related to the ACMUI suggestion that changes be made to § 35.13 related to broad scope licensees being allowed to name their own ARSOs and temporary RSOs in Item 5(a) above.

Staff response – Because the staff did not accept the ACMUI recommendation in Item 5(a), the suggested restructuring of § 35.15 is not needed.

3. Specific Comments - Minor

The staff reviewed each suggested change in this section and incorporated as appropriate. Because the suggested changes in this section were minor, the staff has not included a list of items not accepted. The grammatical suggestions that met the requirements set forth by the Plain Writing Act, the Office of the Federal Register, and the Office of Administration (i.e., format, amendatory language, and the requirements set forth in the NRC Editorial Style Guide (NUREG-1379, Revision 2)) were accepted.