Enclosure 5

The U.S. Nuclear Regulatory Commission Staff Responses to the Advisory Committee on the Medical Uses of Isotopes' Final Comments on Part 35 Draft Final Rule – Medical Use of Byproduct Material – Medical Event Definitions, Training and Experience, and Clarifying Amendments

Background

In accordance with NMSS Policy & Procedure 2-5, "NMSS Procedure for Interfacing with the Advisory Committee on the Medical Uses of Isotopes [ACMUI] during Development of Major Medical Issues," the NRC staff consults with the ACMUI when NRC is revising its medical use regulations. Accordingly, on October 6, 2015, the NRC staff provided the preliminary draft final rule (Agencywide Documents Access and Management System (ADAMS) ML15278A469) to the ACMUI for a 90-day review. The ACMUI discussed the draft final rule at a publicly held teleconference on January 6, 2016 (ADAMS Accession No. ML16074A271), and provided a final report to the NRC on that same day (ADAMS Accession No. ML16007A771).

The ACMUI provided 13 recommendations for the NRC staff on the draft final rule. Six of the 13 recommendations endorsed items in the draft final rule, and therefore no change to the draft final rule is needed for these items. The NRC is accepting two recommendations in full from the ACMUI and is accepting one recommendation in part. The NRC is not accepting four recommendations from the ACMUI. Specific responses to each ACMUI recommendation are provided below. Please note that the recommendations were provided in bullet format and will be referred to below as "recommendation X" in numerical order by grouping of "endorse," "accept," "accept in part," and "not accept."

The ACMUI also provided general comments that served as the basis for its recommendations, specific comments, and editorial comments. These general, specific, and editorial comments are not part of the ACMUI's official recommendations. Therefore, the NRC staff took these comments into consideration, but did not provide specific responses to them.

ACMUI Recommendations That Endorse Specific Items in the Draft Final Rule

Recommendation 1: The ACMUI endorses that component of the current proposed rule re-defining medical events in permanent implant brachytherapy in terms of activity (i.e., source strength) rather than radiation dose.

> Issue: In the proposed rule, § 35.41(b)(6)(ii) and (iii) included a requirement for licensees to determine absorbed dose to the maximally exposed 5 contiguous cubic centimeters of normal tissue located both outside and within the treatment site. Based on public comments, the NRC staff removed these two provisions in the draft final rule.
>
> Staff response: The ACMUI endorses this change. No response is necessary.

Recommendation 2: The ACMUI endorses, with reservations, designating the current proposed rule re-defining medical events in permanent implant brachytherapy as Compatibility Category C, with activity-based medical event metrics defined as an essential program element.

Issue: At issue is the compatibility category designation for § 35.3045, "Report and notification of a medical event." In the proposed rule, the compatibility category for this section was designated as a Category B. In the proposed rule FRN, the Commission requested specific comments on whether the compatibility category should be a Category B or a Category C. The NRC received numerous comments on this issue. The Agreement States and the Organization of Agreement States supported a Category C designation while the medical community supported a Category B designation. These comments are addressed in the Comment Resolution section of the Statement of Considerations for the final rule. In the draft final rule, § 35.3045 is designated as Category C.

In its report on the draft final rule, the ACMUI expresses concern that designating medical events in permanent implant brachytherapy as Compatibility Category C would allow Agreement States to retain the dose-based criteria for a definition of a medical event. Therefore, the ACMUI explains, it originally recommended that the draft rule re-defining medical events in permanent implant brachytherapy be designated as Compatibility Category B.

The ACMUI stated that "[t]he reasons for conversion from dose-based to activity based criteria are: (1) the failure of dose-based criteria to sensitively and specifically capture clinically significant misadministrations in permanent implant brachytherapy, and (2) the practical difficulties in implementing and regulating dose-based criteria." The ACMUI went on to say that "[r]etaining the dose-based criteria would still result in *clinically insignificant* occurrences being identified as MEs [medical events] and thereby perpetuate the confusion associated with such criteria" (emphasis in original). The ACMUI included a detailed discussion of its views under the General Comments section, item 1.e. The ACMUI stated that the NRC's argument that medical events do not have significant "transboundary" health and safety implications was persuasive. However, the ACMUI noted that "a single 'national' definition of a medical event serves to minimize the risk of such an event through the standardization of all processes involved in the procedure… [e]mbedding safe and consistent procedures into the workflow of an authorized user and his/her department and team is perhaps the most important consideration in minimizing medical events, and it is not uncommon for AUs [authorized users] to practice in multiple jurisdictions."

The ACMUI strongly advised that "Agreement States *not* also adopt dose-based criteria for medical events" (emphasis in original). The ACMUI indicated that if such problematic multiplicity of criteria in different jurisdictions were to occur, the ACMUI's recommendation would have to be reconsidered.

Staff Response: The ACMUI endorses this change, with reservations. No response is necessary.

Recommendation 5: The ACMUI endorses the elimination of the preceptor-statement requirement for Board-certified individuals for an individual seeking regulatory authorization as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist;

and

Recommendation 6: With respect to the amended requirements for preceptor attestation for an individual seeking regulatory authorization as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist through the alternate pathway, the Sub-Committee endorses changing the language for the preceptor attestation *from*

> the individual "…has achieved a level of competency to function independently…" for the authorization *to*
>
> the individual can "…independently fulfill the radiation safety-related duties…" associated with the authorization being requested.

Issue: The current regulations provide three pathways for individuals to satisfy training and experience requirements to be approved as a radiation safety officer (RSO), authorized medical physicist (AMP), authorized nuclear pharmacist (ANP), or an authorized user (AU). These pathways are: 1) approval of an individual who is certified by a specialty board whose certification process has been recognized by the NRC or an Agreement State (certification pathway); 2) approval based on an evaluation of an individual's training and experience (alternate pathway); or 3) identification of an individual's approval on an existing NRC or Agreement State license or permit. Under the current certification and alternate pathways in the regulations, an individual seeking authorization for medical use of byproduct material must obtain a written attestation signed by a preceptor who has the same authorization. The attestation must state that the individual has satisfactorily completed the necessary training and experience requirements and has achieved a level of competency sufficient to function independently in the position for which authorization is sought.
The final rule will amend the training and experience requirements in multiple sections to eliminate the attestation requirement for individuals seeking authorization under the board-certification pathway. For individuals seeking authorization under the alternate pathway, the final rule will require the preceptor to attest that the individual "has demonstrated the ability to function independently" to fulfill the radiation safety-related duties required by the license.

Staff Response: The ACMUI endorses these changes. No response is necessary.

Recommendation 9: The ACMUI endorses allowing Associate Radiation Safety Officers (ARSO) to be named on a medical license.

Issue: Section 35.24(b) requires a licensee's management to appoint an RSO, who, in writing, agrees to be responsible for implementing the radiation protection program. The

current regulations do not allow for more than one permanent RSO to be named on a license. The ACMUI has expressed concerns to the NRC staff that the regulations have contributed to a shortage of available RSOs to serve as preceptors. The ACMUI indicated that by not allowing another RSO to be named on the license, a situation has been created in which an individual who is qualified and performing the same duties as an RSO cannot be recognized or listed as an RSO. The ACMUI noted that if an individual has been working as a contractor RSO at several hospitals or other licensed locations, that individual is unable to have actual day-to-day oversight at the various facilities.

The draft final rule amends the regulations to allow a licensee to appoint a qualified individual with expertise in certain uses of byproduct material to serve as an Associate Radiation Safety Officer (ARSO). The individual will be required to complete the same training and experience requirements as the named RSO for the individual's assigned sections of the radiation safety program.

This will increase the number of individuals who will be available to serve as preceptors for individuals seeking to be appointed as RSOs or ARSOs. Additionally, the ARSO could more easily become an RSO on other licenses for the types of uses for which the ARSO is qualified.

Staff Response: The ACMUI endorses this change. No response is necessary.

Recommendation 12: The ACMUI endorses the elimination of the requirement to submit copies of NRC Form 313, Application for Material License, or a letter containing information required by NRC Form 313 when applying for a license, an amendment, or a renewal.

Issue: Section 35.12(b)(1) includes a requirement for applicants to submit an original and one copy of Form 313, "Application for Materials License." Section 35.12(c)(1) includes a requirement for licensees submitting license amendments or renewals to submit an original and one copy of Form 313 or a letter containing equivalent information as required in Form 313. The final rule will remove the requirement to provide one copy of Form 313 or a letter.

Staff Response: The ACMUI endorses this change. No response is necessary.

ACMUI Recommendations NRC Staff is Accepting

Recommendation 3: The ACMUI recommends changing the language for a "wrong-location" medical event in permanent implant brachytherapy *from* the current proposed language,

> "Sealed source(s) implanted directly into a location where the radiation from the source(s) will not contribute dose to the treatment site, as defined in the written directive,"
>
> *to*

"Sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive."

Issue: The ACMUI has concerns with the meaning and implementation of the "wrong-location" criterion for a medical event in § 35.3045, "Report and notification of a medical event," subparagraph (a)(2)(iii)(C). The ACMUI has concerns with the portion of the criterion that provides "…radiation from the sources(s) will not contribute dose to the treatment site…." The ACMUI indicated that all sources would deliver some non-zero dose to a tumor elsewhere in the body. An AU may purposely implant seeds adjacent to (i.e., outside of) what might be considered the nominal treatment site. The ACMUI stated that regulators could misinterpret this as a medical event based on the "wrong-location" criterion. The ACMUI is recommending that this subparagraph be revised to use the term "discontiguous." The term, "discontiguous," according to the ACMUI, means "disconnected or without contact," and is a term that is well understood in the radiation oncology community.

Staff Response: The NRC staff agrees with the ACMUI recommendation and has made this revision in the final rule. The NRC staff also revised this section based on a comment from an Agreement State. The phrase "…as defined in the written directive" was revised to "…as documented in the post-implantation portion of the written directive." Without this revision, it was not clear if the requirement was with respect to the pre- or post-implantation portion of the written directive.

Recommendation 7: The ACMUI recommends that NRC staff consider providing guidance in the NUREG-1556, Volume 9 update to licensees on the ways individuals with board certifications prior to NRC's board recognition date may seek authorization.

Issue: The ACMUI's recommendation is related to the Petition for Rulemaking, PRM-35-20, which was filed by E. Russell Ritenour, Ph.D., on behalf of the AAPM in September 2006 (Ritenour petition). The petitioner requested that the NRC amend its regulations that address training requirements for experienced RSOs and AMPs. The ACMUI recommended in 2012 that all individuals who were able to meet the requirements of the previous Subpart J within 10 CFR Part 35 before that subpart was eliminated as of October 24, 2005, be grandfathered, thus relieving them of meeting the current training and experience requirements. This applied to AUs, RSOs, AMPs or ANPs.

The ACMUI indicated that the impact of the date of recognition of a certifying board by the NRC remains unclear with respect to the Ritenour petition. Individuals who received board-certification prior to October 24, 2005, and were not named on a license for a given type of use, will continue to have difficulty knowing how to obtain approval for a new type of use. Therefore, the ACMUI recommends that guidance be included in the revision to NUREG-1556, Volume 9, to describe how these individuals can apply for a new type of use without having to repeat the entire training-and-experience pathway.

Staff Response: The ACMUI recommendation does not require a change to the rule text. The NRC will include additional guidance in NUREG-1556, "Consolidated Guidance about Materials Licenses," Volume 9, "Program-Specific Guidance about

Medical Use Licenses," to clarify the ways in which individuals with Board certification prior to the NRC's Board recognition dates may seek authorization. The NRC will explain why different Boards have different recognition dates and the information needed when an individual was certified outside of the NRC's Board recognition dates.

ACMUI Recommendations NRC Staff is Accepting in Part

Recommendation 11: The ACMUI does *not* endorse establishing a separate category of Authorized Users for parenteral administration of alpha-emitting radiopharmaceuticals but, instead, recommends deleting § 35.390(b)(1)(ii)(G)*(4)* in the current Draft Final Rule and revising the pertinent passage in § 35.390(b)(1)(ii)(G)*(3)* as follows, "Parenteral administration of any radioactive drug for which a written directive is required."

Issue: The ACMUI continues to disagree with maintaining a separate category for parenteral administration of alpha-emitting radiopharmaceuticals within § 35.390(b)(1)(ii)(G). The ACMUI continues to support its previous recommendations that alpha-emitting radiopharmaceuticals do not differ significantly in terms of clinical use and management, radiation safety, and logistics from currently approved radiopharmaceuticals. Therefore, physicians already authorized to use therapeutic radiopharmaceuticals under § 35.390 or § 35.396 have the requisite education, training, and experience to safely and effectively use alpha-emitting radiopharmaceuticals.

The ACMUI disagrees with the NRC's previous responses that there is a need to keep a separate category for parenteral administration of alpha-emitting radiopharmaceuticals because there are fundamental differences between the clinical uses and the radiation safety of the radioactive drugs used primarily for their alpha emission versus beta emission. The ACMUI believes that the NRC staff has not provided a sufficient basis to state that there are such "fundamental differences." The ACMUI provided a list of the physical properties of current or under-development therapeutic radionuclides. The ACMUI noted that each of the alpha-emitting radionuclides in this list emit gamma radiation and two also emit beta radiation; therefore, different radiation-detection equipment is not necessary.

The ACMUI recommends that § 35.390(b)(1)(ii)(G)(*3*) be revised as follows: "Parenteral administration of any radioactive drug for which a written directive is required."

Response: The rule text has been changed, in part, based on the ACMUI's recommendation. After reviewing the ACMUI's recommendation and supporting statements, the NRC has determined that an additional three cases of administering dosages of radioactive drugs for alpha-emitting radiopharmaceuticals for parenteral administration is not necessary. Therefore, in the final rule § 35.390(b)(1)(ii)(G)(*3*) was revised to read: "Parenteral administration of any radioactive drug that contains a radionuclide that is primarily used for its electron emission, beta radiation characteristics, alpha radiation characteristics, or for its photon energy of less than 150 keV, for which a written directive is required." Further, § 35.390(b)(1)(ii)(G)(*4*) is deleted in the final rule.

The NRC is not accepting the ACMUI recommendation to revise § 35.390(b)(1)(ii)(G)(*3*) as follows: "Parenteral administration of any radioactive drug for which a written directive is required." This revision would mean that any radioactive drug for parenteral administration could be encompassed within § 35.390(b)(1)(ii)(G)(*3*) with no opportunity for the NRC to evaluate new radionuclides that are developed for parenteral administration, including evaluating necessary training. While it may appear that all new radioactive drugs would be encompassed within the category of "primarily used for its electron emission, beta radiation characteristics, alpha radiation characteristics, or for its photon energy of less than 150 keV for which a written directive is required," the NRC would lose flexibility to review new radionuclides under § 35.1000, "Other medical uses of byproduct material or radiation from byproduct material," for health and safety issues. The NRC needs to maintain this flexibility for emerging medical uses.

ACMUI Recommendations NRC Staff is not Accepting

Recommendation 4: The ACMUI recommends revising the passage in § 35.3045(a)(2)(iii)(D) in the Draft Final Rule as follows, thereby eliminating the dose-based criteria for a "leaking-source" medical event

> "3) An administration that includes the wrong radionuclide; the wrong individual or human research subject; a leaking sealed source; or a sealed source or sources implanted into a location discontiguous from the treatment site, as defined in the written directive."

Issue: The ACMUI recommended removing the dose-based criteria for a leaking source in 10 CFR Part 35.3045(a)(2)(iii)(D) (exceeds 0.5 Sv (50 rem) to an organ or tissue). The ACMUI recommended this change for consistency with the new activity-based criteria for a medical event for permanent implant brachytherapy. The ACMUI also stated that it is difficult to estimate the dose to an organ or tissue from a leaking source.

Staff Response: The NRC acknowledges that measuring dose from leaking sealed sources can be difficult. However, no change was made to the rule text based on this recommendation. NRC has retained the dose-based criteria for leaking sealed sources. These calculations can and are made. Further, doses in excess of 50 rem to organs or tissues can cause deterministic effects. Doses below this threshold do not pose a risk to the patient sufficient to require reporting as a medical event.

Recommendation 8: The ACMUI does *not* endorse the new requirement in the Draft Final Rule that licensees report to the NRC as well as to the manufacturer/vendor generator elutions with out-of-tolerance parent-breakthrough but, instead, recommends a single reporting requirement to the manufacturer/vendor.

Issue: The ACMUI recommended removing the requirement in § 35.3204(a) for licensees to report radiopharmaceutical generator elutions that exceed permissible concentration levels in § 35.204(a) to both the NRC and the manufacturers/distributors.

Instead, the ACMUI recommended a single reporting requirement to the manufacturer/vendor.

Staff Response: No change was made to the rule text based on this comment. The NRC does not support the ACMUI recommendation of revising § 35.3204(a) to only retain the single reporting requirement to the manufacturer/vendor. This recommendation does not ensure all relevant information will be reported to the NRC. However, there are no requirements for manufacturers/distributors to report generator failures to the NRC in the current regulations or in the proposed rule. In order for the NRC to receive such information, a new rule would have to be proposed requiring manufacturers/distributors to make reports to the NRC. NRC believes it is important to retain the requirement that licensees report generator failures directly to the NRC because this will permit the NRC to identify if the failure is limited or more widespread and address the failure in a timely manner.

Recommendation 10: The ACMUI recommends that the designation of a board-certified authorized user, authorized medical physicist, or authorized nuclear pharmacist as the RSO or as an ARSO requires their board certification to include the designation "RSO Eligible."

Issue: The ACMUI noted that the draft final rule discusses the designation of an AU, an AMP, or an ANP as the RSO or ARSO on medical licenses. The ACMUI suggests that the NRC include in this discussion a statement that, for a board-certified AU, AMP, or ANP to be named as the RSO or as an ARSO, the Board certification of the AU, AMP, or ANP must include the designation "RSO Eligible."

Staff Response: The "RSO Eligible" designation is not needed for those individuals board-certified for their respective specialties because all AUs, AMPs, or ANPs are already eligible to be an RSO or ARSO under the training and experience provisions of § 35.50(c)(2) or (c)(3). The "RSO Eligible" designation is only needed for individuals who are board-certified under the American Board of Radiology and American Board of Medical Physics.

Recommendation 13: The ACMUI recommends changing the "medical-events" language in §35.3045(a) in the Draft Final Rule *from*, "A licensee shall report any event, except for an event that results from patient intervention…,"*back to the language in the Proposed Rule as presented for public comment,* "A licensee shall report as a medical event, any administration requiring a written directive, except for an event that results from patient intervention…." The Sub-Committee believes the wording change proposed in the current version of the Proposed Rule should not be made without further public review and opportunity for comment.

Issue: The ACMUI is referring to § 35.3045(a), which provides the criteria for reporting and notification of medical events. The ACMUI recommends that NRC instead retain the language in the proposed rule, which limited the reporting of medical events to any administration *requiring a written directive*.

Staff Response: The NRC is retaining the language in the draft final rule, "A licensee shall report any event as a medical event…." It is important for the NRC to learn of any

event that meets the criteria for a medical event, not just those for which a written directive is required. If the NRC were to accept the ACMUI's recommendation, then the NRC would not learn of events in which the administration did not require a written directive but otherwise met the criteria to be reported as a medical event.

The NRC deleted the phrase "any administration requiring a written directive" in § 35.3045(a) because its insertion into the proposed rule was an error. The Statement of Considerations (SOC) for the proposed rule did not identify limiting medical event reporting at § 35.3045(a)(1) to procedures requiring a written directive as a proposed revision nor did the SOC explain the NRC's regulatory basis for making such a revision.