UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

May 3, 2023

MEMORANDUM TO: Darlene Metter, M.D., Chair
Advisory Committee on the Medical Uses of Isotopes

FROM: Christian Einberg, Branch Chief
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Signed by Einberg, Christian
on 05/03/23

SUBJECT: RESPONSES TO THE COMMENTS OF THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES ON THE DRAFT REGULATORY BASIS FOR THE RULEMAKING TO ESTABLISH REQUIREMENTS FOR RUBIDIUM-82 GENERATORS AND EMERGING MEDICAL TECHNOLOGIES

The Advisory Committee on the Medical Uses of Isotopes (ACMUI) Subcommittee on Emerging Medical Technologies/Rubidium-82 Generator Rulemaking Draft Regulatory Basis was charged to review and comment on the U.S. Nuclear Regulatory Commission (NRC) staff's draft regulatory basis for the emerging medical technologies (EMT) and rubidium-82 generators rulemaking (ML22326A362). The Subcommittee provided comments in a draft report to the NRC on November 18, 2022 (ML22322A157) and presented these comments during a public meeting on December 5, 2022. The ACMUI unanimously approved the Subcommittee's report as presented and submitted a final version of the report to the NRC on December 19, 2022 (ML22353A053). Below are the ACMUI comment summaries and the NRC staff responses. The ACMUI final report includes responses to the questions posed in Appendix A of the draft regulatory basis document. The NRC staff will consider ACMUI's responses to the Appendix A questions during the rulemaking process.

ACMUI Comments and NRC Staff Responses:

1. **Comment:** The NRC should evaluate which emerging medical technologies are no longer being distributed in the United States. This information should be stated in Section 3.3 and reflected in the assumptions in Table 7. This information should also inform the proposed rule text.

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Response: Accepted. Section 3.3. was revised to state that NeoVista is no longer in business but that the Sealed Source and Device Registry remains active. Section 3.3 was further revised to state that the ViewRay™ System is no longer manufactured or distributed. Footnotes were added to Table 7 to identify devices that are no longer distributed and to clarify assumptions underlying the estimates of licensing hours saved. The NRC staff's estimate for each technology is an estimate for that device and similar types of EMTs that would be accommodated in Title 10 of the *Code of Federal Regulations* (10 CFR) part 35 through this rulemaking.

2. **Comment:** Some members of the Subcommittee believe the scope of the proposed rulemaking is ambitious, but reasonable. Other members of the Subcommittee believe the scope of the proposed rulemaking should be limited to products that are in broader use because time and clinical experience are needed to understand the technology and safety issues prior to being able to codify requirements via rulemaking.

   Response: Accepted. The NRC staff reviewed all the changes proposed in the regulatory basis considering the ACMUI comments. The staff also reviewed the operating experience of each technology, which includes the breadth of use and the maturity of the technology. After conducting this review, the staff revised the regulatory basis to eliminate certain technologies from inclusion in the rulemaking. Specifically, this rulemaking will not address manual brachytherapy using diffusing sources such as Alpha DaRT™, because of a lack of operating experience. Additionally, the staff may opt to reduce rulemaking efforts on ophthalmic sources if warranted based on public comment.

3. **Comment:** The Subcommittee supports the proposed changes to allow for the use of additional radionuclide generators. In addition, all Subcommittee members agree that gamma knife, microspheres, radioactive seed localization and intravascular brachytherapy (IVB) have extensive histories of clinical use and should be moved out of 10 CFR 35.1000 and into other subparts of 10 CFR part 35.

   Response: Accepted.

4. **Comment:** The Subcommittee believes that medical technologies presenting novel radiation safety hazards should default to 10 CFR 35.1000. NRC should assess the novelty, risk, and general clinical experience (i.e., beyond clinical trials) when determining whether to move a technology out of 10 CFR 35.1000 and into other parts of 10 CFR part 35.

   Response: Partially Accepted. Regulating novel technologies under 10 CFR 35.1000 was never intended to be a permanent regulatory framework for those technologies. This regulatory basis proposes moving certain novel technologies into other parts of 10 CFR part 35 based on the operating experience of each technology, which includes the breadth of use (including general clinical experience) and the maturity of the technology.

5. **Comment:** In any case, the Subcommittee cautions the NRC against putting specific requirements in 10 CFR part 35 which are particular to devices or products that aren't in widespread use (i.e., Alpha DaRT™).
   - The Subcommittee supports adding general requirements for contamination control for liquid or diffusing brachytherapy.
   - The Subcommittee discourages adding training and experience requirements to 10 CFR part 35 which were designed for products no longer being distributed (i.e., Epi-Rad90™ eye applicators).

Response: Partially Accepted. The NRC staff agrees that there is insufficient operating experience for Alpha DaRT™ and has opted to exclude manual brachytherapy using diffusing sources from this rulemaking. The NRC staff agrees that a general requirement for contamination control is necessary for liquid brachytherapy and diffusing brachytherapy. Currently, NRC guidance requests licensees to make general commitments regarding contamination control. Appendix A, Section A.3 was revised to propose a general contamination control requirement for all medical licensees. This proposed regulation would reduce the number of commitments needed by licensees during licensing**.** The NRC staff supports establishing regulations, including training and experience requirements, for devices and technologies that are no longer being distributed to capture operating experience that may inform future similar uses of those technologies.

6. **Comment:** The Subcommittee supports the proposed change to the 10 CFR 35.2 definition of “physician.”

   Response: Accepted.

7. **Comment:** The Subcommittee supports the proposed changes to 10 CFR 35.24. Radiation safety committees should include an authorized user (AU) representative for microsource therapy and any future therapeutic emerging medical technologies.

   Response: Accepted.

8. **Comment:** The Subcommittee cautions the NRC as it considers how to incorporate “treatment regimen” into the written directive regulations. A single written directive should not prescribe a radiopharmaceutical in cycles when the prescribed activity may vary from cycle to cycle, for example based on the patient’s weight, bone marrow reserve, or renal or hepatic function.

   Response: Partially Accepted. The proposed changes would provide the AU the ability to revise the dose for a specific administration that is part of a treatment regimen based on medical necessity, such as change in patient weight, bone marrow reserve, or organ function.

9. **Comment:** The Subcommittee recommends a wholesale re-evaluation of the ophthalmic brachytherapy requirements. The divergent training requirements for physicians and physicists are very complicated, and the Subcommittee recommends streamlining the training requirements. Of particular note, the Subcommittee believes it is not a good practice for a device’s applicable training requirements to depend on the prescribed dose. The NRC should consider regulating ophthalmic sources that are intraocular or have shorter half-lives under standard 10 CFR 35.400 manual brachytherapy regulations, since they are significantly more complex than the traditional strontium-90 pterygium applicators. The added complexities may include dose to a specified tissue depth and stricter criteria for source calibration due to rapid decay.

   Response: Not Accepted. The current regulatory structure provides reasonable assurance of public health and safety. The NRC staff’s position at this time is that a comprehensive revision of the requirements would place an undue burden on existing licensees using ophthalmic applicator systems under 10 CFR part 35, subpart F and would not result in significant radiation or public safety benefits. However, the NRC staff may choose to

conduct an evaluation of these requirements if warranted by additional feedback received during the public comment period.

10. **Comment:** NRC should re-evaluate when authorized medical physicists (AMPs) should be required. Why do some of the 10 CFR 35.400 uses require an AMP and some do not? What are the specific tasks or skills that must be performed by an AMP? It may be useful to pose this question during the public comment period.

    Response: Partially Accepted. The NRC staff believes the current structure is adequate and that AMPs should not be required for all manual brachytherapy procedures. However, the NRC staff understands that requiring AMPs for some but not all manual brachytherapy uses may be confusing. The NRC staff has added Question A.8.3 to solicit public comment on this topic, as suggested by the ACMUI.

11. **Comment:** Submission of procedures for patient immobilization should be part of the licensing process for licensees using gamma stereotactic radiosurgery devices in 10 CFR part 35, subpart H. The Subcommittee notes that immobilization methods can also impact emergency response.

    Response: Partially Accepted. Section A.6 was revised to require in 10 CFR 35.610 that licensees list in their emergency procedures the types of immobilization devices they will be using, as well as methods for removing immobilization devices in the event of an emergency. While the procedures for patient immobilization are important, the NRC staff believes the types of immobilization devices and procedures for removal are the critical elements to be reviewed during licensing. Full calibration procedures as required by 10 CFR 35.632 would need to be submitted during licensing to provide assurance of the functionality of the immobilization devices.

12. **Comment:** The Subcommittee supports the addition of 10 CFR part 35, subpart I (35.700) for microsource brachytherapy.

    Response: Accepted.

13. **Comment**: In multiple places, Appendix A states, “This section would be amended to require completion of device specific training by the medical physicist applying to be an AMP on a license authorizing use of this device.” The Subcommittee notes that device-specific training is already required for AMPs in 10 CFR 35.51(c).

    Response: Not Accepted. Currently, 10 CFR 35.51(c) requires AMPs to have training for the *types of use* for which authorization is sought. In the regulatory basis, the NRC staff is proposing *device specific* training. This shift is critical to account for the wide variety of devices within a specific type of use.

14. **Comment:** In Section 10 CFR 35.415 (page A-6), it states, “this section of the regulation will be amended to require licensees to lock storage of the IVB storage container and to house that storage container in a secure location.” The Subcommittee notes that 10 CFR 20.1801 already requires licensees to secure radioactive material from unauthorized access. What is the basis for the additional proposed security requirement?

Response: Accepted. The additional security requirement was removed. The NRC staff believes that 10 CFR 20.1801 and 10 CFR 20.1802 already provide sufficient assurance of adequate control of these devices.

15. **Comment:** In Section 10 CFR 35.3045 (page A-14), the Subcommittee recommends removing the requirement to report as a medical event a radioactive seed localization procedure that uses the wrong radionuclide. Based on the low implanted activity and the short implantation time, the dose effect of the wrong isotope is of minimal consequence.

    Response: Not Accepted. The inclusion of the radionuclide in this requirement is consistent with current reporting requirements for other modalities. Reporting of these events would ensure that the NRC can identify potential safety deficiencies in the use of radioactive material and require that corrective actions be taken to prevent recurrence. Such an event does not necessarily result in harm to the patient, but the NRC staff believes that reporting it would not place additional burden on the licensee and would provide useful operating experience.

16. **Comment:** In Section 10 CFR 35.610 (page A-24), it states, “This section will be revised to clarify that the AU and AMP, as well as any individual who will operate the unit, are required to have vendor operational and safety training.” The Subcommittee recommends also allowing the operational and safety training to be given by an approved AU or AMP.

    Response: Partially Accepted. The word “vendor” was removed from the sentence identified in the comment. The proposed change would clarify that AUs and AMPs, as well as individuals operating the unit, are required to have the training currently described in 10 CFR 35.610(d)(1) and 10 CFR 35.610(d)(2). Training from the device manufacturer or an individual certified by the device manufacturer would be required for training on new units or devices with upgrades that affect the operation and safety of the unit as currently outlined in 10 CFR 35.610(d)(1). Licensees would have flexibility to determine who may provide the annual training required by 10 CFR 35.610(d)(2).

Responses to ACMUI Comments on the Regulatory Basis for the Rulemaking to Establish Requirements for Rb-82 Generators and Emerging Medical Technologies DATE May 3, 2023

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