UNITED STATES
NUCLEAR REGULATORY COMMISSION
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March 10, 2022

MEMORANDUM TO: Darlene Metter, MD, Chairman
Advisory Committee on the Medical Uses of Isotopes

FROM: Christian E. Einberg, Branch Chief
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Assessments Branch
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Signed by Einberg, Christi
on 03/10/22

SUBJECT: RESPONSES TO THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPE'S RECOMMENDATIONS ON DRAFT ALPHA TAU ALPHA DART™ MANUAL BRACHYTHERAPY LICENSING GUIDANCE

Below are the U.S. Nuclear Regulatory Commission's (NRC) staff responses to the recommendations and comments on the Draft Alpha Tau Alpha DaRT™ Manual Brachytherapy Licensing Guidance from the Advisory Committee on the Medical Uses of Isotopes (ACMUI). The ACMUI provided these recommendations and comments to the NRC staff on December 15, 2021, following review of the draft guidance (Agencywide Documents Access and Management System [ADAMS] Accession No. ML21326A170). The full report from the ACMUI can be found at the ADAMS Accession No. ML21341A561

1. **ACMUI Comment:** The subcommittee does not support any specified role for an authorized medical physicist (AMP) in acceptance testing of software for treatment planning (Section 6.3). This opinion aligns Alpha DaRT™ with brachytherapy treatment planning software requirements in 35.400.

Staff Response: Accepted. The staff agrees with the ACMUI that acceptance testing requirements should align with those in Title 10 *Code of Federal Regulations* (CFR) 35.400. However, the staff will continue to review the need for future requirements and guidance regarding treatment planning software for all uses of byproduct material in medicine with emerging software uses.

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2. **ACMUI Recommendation:** The ACMUI does not believe an AMP has any role in training the radiation safety officers (RSOs) (Section 5.2.2). The RSO training should come from the vendor or an RSO already trained in Alpha DaRT™.

   Staff Response: Accepted.

3. **ACMUI Recommendation:** The ACMUI sees no role for an authorized nuclear pharmacist for this device (Section 5.2.2). There is no liquid or pill for a pharmacist to manage.

   Staff Response: Accepted.

4. **ACMUI Recommendation:** The subcommittee does not support an assessment to assure the sources are not leaking outside the body (Section 6.1, 6.5). Since the radioactive particles are traveling through tissue in all directions, it is impossible to assess leakage as opposed to intended radiation distribution from treatment. The concept of leakage does not apply since Alpha DaRT™ is not a sealed source, rather the Ra-224 is adherent to the surface of the source with the Rn-220 gas and subsequent daughters readily diffusing off the device.

   Staff Response: Accepted. The staff removed references to leakage outside the patients' body in Sections 6.1 and 6.5. However, the staff retained the commitment to verify that the seeds are fully contained within the patient's body during treatment to avoid significant leakage and contamination from daughter products.

5. **ACMUI Recommendation:** Regarding the required surveys required by 10 CFR 35.70 and 35.404 (Section 6.5), the subcommittee notes that unlike sealed source brachytherapy, there is a potential of room contamination after the procedure due to the fact that sources are not sealed, but rather, the radioactivity is adherent to the surface of the source and the daughter products diffuse from the source. These two features create the possibility of contamination in the procedure room. Following both the ambient radiation level and contamination survey guidance in NUREG-1556, Volume 9 is recommended. In addition, the subcommittee recommends changing the phrase "survey instrument used" to "radiation detection instrument" to keep this more generic.

   Staff Response: Accepted. Updated guidance to clearly identify that both ambient and contamination surveys should be performed.

6. **ACMUI Recommendation:** The subcommittee does not support assessing the integrity of the source seal (Section 6.7). In the subcommittee's opinion, even if the integrity were broken and equilibrium were not reached, the dose delivery would not be affected.

   Staff Response: Accepted. Due to the significantly longer decay time of the Ra-224 compared to the daughters, there would be minimum effect on the patient's dose if the source is not in equilibrium at time of administration. In addition, while there could be contamination concerns if the seal is broken, the commitment to perform surveys with an appropriate radiation detection survey instrument in all areas where Alpha DaRT™ seeds were prepared for use or administered after each administration should identify any contamination.

7. **ACMUI Recommendation:** Regarding patient release (Section 7.3), the subcommittee recommends changing the following language. Patients should not be released from the licensed facility "if it is possible under normal conditions for a seed or seal has a potential to become dislodged" to "if it is likely under normal conditions for a seed or seal to become dislodged."

Staff Response: Accepted.

8. **ACMUI Recommendation:** The subcommittee agrees with the definition of Medical Event (Section 6.2) for temporary applications of Alpha DaRT™. However, if in the future permanent implants are performed, the subcommittee recommends the definition of Medical Event for that application be defined like other permanent brachytherapy as stated in 10 CFR 35.3045.

Staff Response: No change necessary. The staff will evaluate the guidance for necessary changes should the Alpha DaRT™ be approved for permanent brachytherapy.

9. **ACMUI Recommendation:** The requirement that locations where the patient will spend significant time be documented (Section 7.4) does not add any clear safety benefit. It is unclear what the clinical and safety team at the treating facility will do with this information to enhance radiation safety. The subcommittee recommends removal of the requirement.

Staff Response: Accepted.
The purpose of the staff adding this commitment is to help the licensee locate a source if it becomes missing. However, as sources are implanted into the body, it is unlikely a source would be lost without a patient's knowledge and therefore, the staff agrees this commitment is not necessary for Alpha DaRT™.

Alpha DaRT Manual Brachytherapy Licensing Guidance DATE March 10, 2022

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