UNITED STATES
NUCLEAR REGULATORY COMMISSION
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September 27, 2024

MEMORANDUM TO: Hossein Jadvar, M.D., Ph.D., Chair
Advisory Committee on the Medical Uses of Isotopes

FROM: Christian Einberg, Branch Chief
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Signed by Einberg, Christian
on 09/27/24

SUBJECT: RESPONSES TO THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPE'S RECOMMENDATIONS ON EYE90 MICROSPHERES® 10 CFR 35.1000 LICENSING GUIDANCE

Below are the U.S. Nuclear Regulatory Commission's (NRC) staff responses to the recommendations and comments from the Advisory Committee on the Medical Uses of Isotopes (ACMUI) on the draft Eye90 microspheres® Title 10 of the *Code of Federal Regulations* (10 CFR) 35.1000 licensing guidance. In the ACMUI report, the ACMUI supported the staff recommendation to license the use of Eye90 microspheres® under 10 CFR 35.1000 and to draw on existing licensing guidance for other Y-90 microsphere technologies. The ACMUI provided the following recommendations and comments to the NRC staff on April 8, 2024. The full report from the ACMUI can be found at Agencywide Documents Access and Management System (ADAMS) Accession No. ML24120A245.

Recommendations

1. **ACMUI recommendation:** Use of the term "dose" alone may be ambiguous. In this and other therapeutic application guidance from the NRC, should be consistent in terms of the dose definition used, specified target and organs at risk, and units. Likewise, use of "dose equivalent" vs "equivalent dose" in reporting of medical events/exposures.

   NRC Response: Accepted. This comment has been noted and kept in mind when revising this document and for development/revision of documents in the future. Appropriate changes have been made for consistency.

2. **ACMUI recommendation:** Background section, 2nd paragraph: add "Following angiographic pre-therapy evaluation for extrahepatic shunting."

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NRC Response: Accepted.

3. **ACMUI recommendation:** Training and experience, section 5.1.A.3.ii.b: add “and” to note that in addition to the experience and classroom/laboratory training requirement, the relevant supervised work experience is also required.

   Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

4. **ACMUI Recommendation**: Training and experience, section 5.1.B: change “should” to “must” as the consensus of the group is that there must be hands on training in the Eye90 microspheres® product by an AU, vendor training alone would be insufficient.

   NRC Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

5. **ACMUI Recommendation:** Training and experience, section 5.1.B: note that the hands-on cases are “conducted in the physical presence of an AU”.

   NRC Response: Accepted. This change is already included in the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

6. **ACMUI Recommendation:** Training and experience, section 5.1.B: change “above, including case work” to “at the beginning of this section” to reduce redundancy.

   NRC Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

7. **ACMUI Recommendation:** Training and experience, section 5.1.C: include “fellowship” as an addition/alternative to residency training throughout.

   NRC Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

8. **ACMUI Recommendation:** Team approach, section 5.4: add “ordering” to the participating individuals to whom training must be provided.

   NRC Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

9. **ACMUI Recommendation:** Written directives, section 6.2 written directive condition: removed “or manufacturer” as the Eye90 microspheres® product could change ownership.

   NRC Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

10. **ACMUI Recommendation:** Written directives, section 6.2: for clarity, in the written directive, “prescribed activity (mCi or GBq) means the total activity administered whereas “prescribed dose” means the total planned dose (rad or Gy). The choice of prescribed activity or prescribed dose should be used consistently for all subsequent documentation and evaluations.”

    NRC Response: Accepted. This change has also been noted for future revisions to the Y-90 Microsphere Brachytherapy Sources and Devices Therasphere® and Sir-Spheres® Licensing Guidance.

11. **ACMUI Recommendation:** Written directives, section 6.2: Reported dose should indicate absorbed dose to the treatment site (liver, liver lobe, liver segment, or liver lesion) or to the dose limiting structure (liver absorbed dose or lung absorbed dose).

    NRC Response: Partially accepted. The recommendation was moved to section 6.1: Procedures for Administration where recording administered dose is already addressed.

12. **ACMUI Recommendation:** Medical event reporting, Section 6.3: “0.5 Sv (50 rem) dose equivalent to an organ or tissue per 10 CFR 35.3045”; use of “dose equivalent” vs “equivalent dose” uniformity throughout NRC guidance recommended. Added “equivalent” to dose to skin/organ/tissue.

    NRC Response: Accepted.

13. **ACMUI Recommendation:** Surveys, section 6.8: changed to “As the Eye90 microspheres® are too small to be seen, licensees should survey, with an appropriate calibrated radiation detection survey instrument (per 10 CFR 35.61),”.

    NRC Response: Accepted.

14. **ACMUI Recommendation:** Section 7.4: changed heading to “Explanted Tissues, Autopsy and Cremation“ and added language about management of explanted tissues as patients may undergo removal of the treated liver as part of a liver transplant: “However, when managing explanted tissues treated with Eye90 microspheres, or in the case of autopsy or cremation, a radiation hazard exists for individuals who handle tissues that may contain radioactive material, especially if the event of explantation or death occurs within 1 month after treatment with Eye90 microspheres®.” One month was specified as this would allow sufficient decay of an yttrium-90 source.

    NRC Response: Accepted. This comment is especially valuable, because this category of therapy may be used while a patient awaits transplant. This guidance has been modified to incorporate the suggested inclusion of explantation, and the comment has been noted for possible inclusion in other microsphere guidance.

RESPONSES TO THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES RECOMMENDATIONS ON EYE90 MICROSPHERES® 10 CFR 35.1000 LICENSING GUIDANCE DATE September 27, 2024

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