[7590-01-P]

NUCLEAR REGULATORY COMMISSION

[NRC-2017-0215]

Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres®

AGENCY: Nuclear Regulatory Commission.

ACTION: Draft guidance; request for comment.

SUMMARY: The U.S. Nuclear Regulatory Commission (NRC) is revising its licensing guidance for licenses authorizing the use of Yttrium-90 (Y-90) Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres®. The NRC is requesting public comment on the draft revision of the licensing guidance (Rev. 10). The document has been revised to significantly update the criteria for training and experience, medical event reporting, inventory requirement specifications, and waste disposal issues. The revised guidance document also provides new information regarding cremation and autopsy. This guidance is intended for use by NRC applicants, NRC licensees, and the NRC staff.

DATES: Submit comments by **[INSERT DATE 60 DAYS AFTER PUBLICATION IN THE *FEDERAL REGISTER*]**. Comments received after this date will be considered if it is practical to do so, but the NRC is only able to ensure consideration of comments received on or before this date.

ADDRESSES: You may submit comments by any of the following methods:

- **Federal Rulemaking Web Site:** Go to http://www.regulations.gov and search for Docket ID **NRC-2017-0215**. Address questions about NRC dockets to Carol Gallagher; telephone: 301-415-3463; e-mail: Carol.Gallagher@nrc.gov. For technical questions, contact the individual listed in the FOR FURTHER INFORMATION CONTACT section of this document.
- **Mail comments to:** May Ma, Office of Administration, Mail Stop: OWFN-2-A13, U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001.

For additional direction on obtaining information and submitting comments, see "Obtaining Information and Submitting Comments" in the SUPPLEMENTARY INFORMATION section of this document.

FOR FURTHER INFORMATION CONTACT: Lisa Dimmick, Office of Nuclear Material Safety and Safeguards; U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001; telephone: 301-415-0694; e-mail: Lisa.Dimmick@nrc.gov.

SUPPLEMENTARY INFORMATION:

I. Obtaining Information and Submitting Comments

A. Obtaining Information

Please refer to Docket ID **NRC-2017-0215** when contacting the NRC about the availability of information regarding this action. You may obtain publicly-available

information related to this action by the following methods:

- **Federal Rulemaking Web site:** Go to http://www.regulations.gov and search for Docket ID **NRC-2017-0215**.

- **NRC's Agencywide Documents Access and Management System (ADAMS):** You may obtain publicly-available documents online in the ADAMS Public Documents collection at http://www.nrc.gov/reading-rm/adams.html. To begin the search, select "ADAMS Public Documents" and then select "Begin Web-based ADAMS Search." For problems with ADAMS, please contact the NRC's Public Document Room (PDR) reference staff at 1-800-397-4209, 301-415-4737, or by e-mail to pdr.resource@nrc.gov. The draft Y-90 Microsphere Brachytherapy Sources and Devices Licensing Guidance, Revision 10, is available in ADAMS under Accession No. ML17107A375.

- **NRC's PDR:** You may examine and purchase copies of public documents at the NRC's PDR, Room O1-F21, One White Flint North, 11555 Rockville Pike, Rockville, Maryland 20852.

The draft Y-90 Microsphere Brachytherapy Sources and Devices Licensing Guidance, Revision 10, is also available on the NRC's public Web site on the "Medical Uses Licensee Toolkit" page at https://www.nrc.gov/materials/miau/med-use-toolkit.html.

B. Submitting Comments

Please include Docket ID **NRC-2017-0215** in your comment submission.

The NRC cautions you not to include identifying or contact information that you do not want publicly disclosed in your comment submission. The NRC will post all comment submissions at http://www.regulations.gov as well as enter the comment

submissions into ADAMS. The NRC does not routinely edit comment submissions to remove identifying or contact information.

If you are requesting or aggregating comments from other persons for submission to the NRC, then you should inform those persons not to include identifying or contact information that they do not want to be publicly disclosed in their comment submission. Your request should state that the NRC does not routinely edit comment submissions to remove such information before making the comment submissions available to the public or entering the comment submissions into ADAMS.

II. Background

The NRC is requesting public comment on the draft licensing guidance entitled "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance." This draft would be revision 10 to this licensing guidance. The licensing guidance provides medical use applicants with an acceptable means of satisfying the requirements for a license for the use of TheraSphere® and SIR-Spheres® and is not intended to be the only means of satisfying the requirements for a license. The licensing guidance provides the NRC with a set of standard criteria for evaluating a license application, although an applicant may submit alternative information and commitments for review by the NRC staff to make a licensing determination unless the information is specifically required by regulation. This guidance will also be available for voluntary use by Agreement States.

The licensing guidance for Y-90 microsphere brachytherapy was initially published in October 2002 and subsequently revised in 2004, 2007, 2008, 2011, 2012, and 2016. Following years of using the current licensing guidance, the NRC staff,

stakeholders, and the Advisory Committee on the Medical Uses of Isotopes (ACMUI) have identified numerous issues that need to be addressed. A working group comprised of Agreement State representatives and NRC staff was formed to address identified issues. The document has been revised to significantly update the criteria for training and experience, medical event reporting, inventory requirement specifications, and waste disposal issues. The revised guidance document also provides new information regarding cremation and autopsy.

As described in the draft licensing guidance, the NRC is recommending removal of the alternate, manufacturer provided clinical training pathway to complete the training and experience criteria listed in Section B of the training and experience section of the licensing guidance. During an ACMUI meeting on October 7, 2016 (ML16357A688), the ACMUI recommended that the NRC leave this alternate pathway in the Y-90 microsphere licensing guidance to allow access to Y-90 microsphere brachytherapy in areas where there may not already be approved AUs to supervise new physicians. However, after licensing Y-90 microspheres under 10 CFR 35.1000 for over 10 years, there should be substantial facilities and AUs available to offer training for Y-90 microspheres, similar to other therapeutic modalities, and therefore this pathway should be removed to bring Y-90 microsphere brachytherapy training and experience (T&E) in line with other T&E requirements in 10 CFR Part 35.

The manufacturers stated, during the same ACMUI meeting, that training under the supervision of a manufacturer representative should remain as a T&E pathway because their representatives are highly knowledgeable about their devices. The NRC agrees with the manufacturers that the individual who provides the training in the operation of the device should be knowledgeable about the device, and this could

include a manufacturer representative as well as the licensees' personnel. The proposed licensing guidance still requires the physician to receive training on the operation of the device. However, the clinical experience a physician received during the 3 patient cases should include more than operation of the device. At a minimum, the clinical experience should also include evaluation of dose and activity of Y-90 microspheres to be administered to each treatment site, calculating and measuring the activity and safely preparing the Y-90 microspheres to be delivered, using administrative controls to prevent a medical event, and following up and reviewing each patient's case history. During the ACMUI meeting, the ACMUI recommended that this type of training be provided by someone with defined medical experience, but left it up to the NRC to decide what medical experience would be necessary. As this T&E is specific to patient care and patient follow-up, the proposed licensing guidance recommends this type of training be provided by an AU for each type of Y-90 microsphere for which the individual is seeking AU status, similar to how other modalities are regulated in 10 CFR Part 35. Additionally, changing the criteria would not preclude the manufacturer representatives from providing training, as is normally done for other therapies.

III. Request for Comments

The NRC is requesting comments on the proposed licensing guidance, entitled, "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance, Revision 10." While the NRC is requesting comments on the entirety of the proposed guidance, the NRC is specifically seeking comments on several sections.

(1) Recommended Minimum Clinical Experience:

Due to the complexity of delivery of Y-90 microspheres, the licensing guidance historically and currently recommends that a prospective AU demonstrate he or she has clinical experience with the device. The current recommendation is that 3 patient cases for each type of microsphere should be completed for each prospective authorized user prior to approval. This recommendation is similar to requirements in other therapy modalities, such as section 35.390 of title 10 of the *Code of Federal Regulations* (10 CFR). The NRC is seeking specific comments on whether 3 patient cases provide adequate clinical experience for a physician to gain AU status for Y-90 microspheres.

(2) Adding Authorization for Other Microsphere Type:

The NRC is seeking comments to determine additional training needed when an AU who is already authorized to use one type of microsphere requests authorization for use of another type of microsphere. For instance, are 3 additional cases for the other type of microsphere necessary for the AU to gain the knowledge to safely administer the new microsphere, or should the number of cases be left to the discretion of the supervising AU?

(3) Written Attestation from Preceptor:

Historically, the NRC has not required a written attestation, signed by a preceptor AU, because there was not a sufficient number of AUs to supervise the training and sign the written attestation. However, given that the NRC and Agreement States have licensed Y-90 microsphere brachytherapy AUs for over 10 years, the

NRC is seeking comments to determine if there is anything unique about Y-90 microsphere brachytherapy compared to other types of manual brachytherapy that would obviate the need for a written attestation.

(4) Clinical Experience under the Supervision of a Manufacturer Representative:

The proposed licensing guidance removes the alternate pathway, which allows an individual to become an AU for Y-90 microsphere brachytherapy prior to completing any patient cases if the applicant commits that the first three patient cases completed by that AU will be hands-on and supervised in the physical presence of a manufacturer representative. This alternate pathway remained in the licensing guidance for several years because there were a limited number of AUs who were authorized for each type of Y-90 microsphere, which made it difficult for physicians who were seeking authorization to complete the necessary clinical experience described in Section B under the supervision of another AU already authorized for the use of Y-90 microspheres. The NRC is seeking comments on whether completing the recommended clinical experience under the supervision of AU(s) authorized for the type of microsphere for which the new physician is seeking authorization still presents an undue burden on physicians. Further, the NRC is seeking comments on whether any unique characteristics of Y-90 microsphere brachytherapy warrant continuation of this alternate training pathway. Additionally, the NRC is seeking comments on whether finding licensed facilities at which the physicians could complete this clinical experience would be difficult.

(5) Timeliness for Completion of In-Vivo Cases:

The NRC is seeking comments on whether the proposed one in-vivo case prior to treating patients would be appropriate if 6 months has passed to ensure recentness of training or whether this proposal could potentially lower licensee's safety standards for the patients being treated.

(6) Medical Event Definition:

The NRC is seeking comments on the definition of medical events (ME) for Y-90 microspheres as provided in the proposed guidance. A primary purpose of ME reporting is to identify the cause of the event in order to correct them and prevent their recurrence. In the last 2 years there have been several MEs reported where the administration of the Y-90 results in dose or activity to the lobe opposite the lobe documented in the written directive. The working group was informed that in some instances, the AU may determine in the interventional radiology suite that they may be unable to deliver the amount of Y-90 microspheres to the intended lobe, but still wish to perform the treatment knowing some dose or activity may go to the lobe opposite the lobe documented in the written directive. The NRC is seeking specific comments on whether the delivery of Y-90 microspheres can be controlled to a specific lobe or location as described in the written directive and, if not, whether flexibility in the written directive is necessary to avoid reporting of events that cannot be controlled using the current technology. If flexibility is necessary, the NRC is seeking comments on whether the use of dose or activity ranges in the written directive or an ability to change

the written directive in the interventional radiology suite prior to administering the Y-90 microspheres would be adequate. This type of revision could be made

verbally by the AU, as long as the revision is documented in writing and signed by the AU within 24 hours of providing the revision verbally, consistent with other uses in 10 CFR Part 35.

Dated at Rockville, Maryland, this 1st day of November, 2017.

For the U.S. Nuclear Regulatory Commission.

Daniel S. Collins, Director,
Division of Material Safety, State, Tribal and Rulemaking Programs,
Office of Nuclear Material Safety and Safeguards.

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