UNITED STATES
NUCLEAR REGULATORY COMMISSION
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December 13, 2021

ALL AGREEMENT STATES, CONNECTICUT, INDIANA

MANUFACTURER TRAINING PATHWAY FOR YTTRIUM-90 MICROSPHERES
(STC-21-083)

Purpose: To inform the Agreement States of U.S. Nuclear Regulatory Commission (NRC)'s actions regarding Boston Scientific request for a 1-year extension to the implementation date of the training and experience (T&E) criteria change found in the Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® licensing guidance.

Background: Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® licensing guidance provides applicants with acceptable means to satisfy the requirements for a license for the use of TheraSphere® and SIR-Spheres®. This licensing guidance was initially published in October 2002, with the last major revision, Revision 10, being issued in November 2019 (Agencywide Documents Access and Management System [ADAMS] Accession Number ML19338E099). In this last major revision, criteria for T&E for Authorized Users (AU) was significantly updated. As part of this update, the criteria was changed so clinical use training would include at least three hands-on patient cases, conducted in the physical presence of an AU or a physician who meets the T&E criteria listed in the guidance, for each type of yttrium-90 (Y-90) microsphere requested. This was a change from past revisions of the licensing guidance which allowed a new AU to complete their first three hands-on patient cases supervised by and in the physical presence of a manufacturer representative who did not have to be an AU or a physician. As stated in response to public comments (ADAMS Accession Number ML19030B536), this change was made as it is NRC's belief that training on the medical use of the Y-90 microspheres is best provided by a physician, specifically an AU, similar to training for all other therapy modalities regulated under Title10 of the *Code of Federal Regulations* (CFR) Part 35. However, the NRC staff delayed implementation of this T&E criteria until May 6, 2020, to allow physicians who were in the process of becoming AUs to complete ongoing casework.

On March 20, 2020, the NRC issued Revision 10.1 of the guidance (ADAMS Accession Number ML20080J208). In Revision 10.1, the NRC staff recommended delayed implementation of the change to the T&E criteria until November 8, 2021 due to concerns from Boston Scientific, the manufacturer for TheraSphere®, that requiring the first three hands-on patient cases to be conducted in the physical presence of an AU, or a physician who meets the T&E criteria could cause a delay in training future physicians.

Discussion: By letter dated October 6, 2021 (ADAMS Accession Number ML21314A422), Boston Scientific requested another 1-year extension to the implementation date of this T&E criteria revision. Boston Scientific stated in the letter that if the manufacturer representatives are not allowed to provide the supervision for the first three hands-on patient cases beyond November 8, 2021, this would directly impact patient cases as cases will be cancelled.

In response to Boston Scientific's request, SIRTeX, another manufacturer for Y-90 microspheres, provided a letter to the NRC dated November 2, 2021 (ADAMS Accession Number ML21314A398). In this letter, SIRTeX stated that further delay of implementation of this criteria would cause confusion regarding AU approvals and thus reduce patient access due to the variability of the implementation of the manufacturer's pathway between Agreement States. The letter further implied that AU to AU training reduces medical events and is critical for safe use of these products.

Due to the 2-year time period which the industry had to prepare for the implementation of the new T&E criteria, the NRC staff is currently not recommending a change to the licensing guidance to delay implementation again at this time. However, the conditions contained in the licensing guidance provide one acceptable means to satisfy the requirements for licensing. Applicants may submit alternative information and commitments for review by NRC staff to make a licensing determination. Therefore, if an applicant provides documentation that they cannot access an AU or a physician who meets the T&E criteria to provide physical presence for a physician's first three patient cases and this criteria would impact patient care, they can submit alternative information and commitments. In a memo to the NRC regions, the NRC staff recommended the following commitments to be found acceptable for licensing in this case (ADAMS Accession Number ML21106A291).

- The applicant has met all other training criteria listed in the licensing guidance including work experience or training under the supervision of an AU for the type of Y-90 microsphere brachytherapy the applicant is requesting. Note the supervision does not need to be in the physical presence of an AU. See 10 CFR 35.27, "Supervision" for more information regarding supervision.
- The applicant commits to ensuring the manufacturer representative has had training and work experience in topics described in T&E criteria 5.1.3.ii, iii, and iv and operation of the delivery system, safety procedures, and clinical use for the type of Y-90 microsphere they are providing training for. The manufacturer representative should have a minimum of 80 hours of combined training in these areas as documented by the manufacturer.

In addition to the alternative approach indicated above, the NRC is continuing to evaluate Boston Scientific's request. This evaluation may result in changes to the conditions deemed acceptable provided above or in the licensing guidance document itself. The NRC will inform the Regional Offices and Agreement States of the results of the evaluation when it has been completed. The NRC expects to complete the evaluation by February 2022.

The licensing guidance is available at http://www.nrc.gov/materials/miau/med-use-toolkit.html

If you have any questions regarding this correspondence, please contact me at 301-415-5422 or the individual named below:

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Sincerely,

Signed by Anderson, Brian
on 12/13/21

Brian C. Anderson, Chief
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