U.S. Nuclear Regulatory Commission (NRC)
Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Subcommittee Review and Comments on

Draft Licensing Guidance for Yttrium-90 Microsphere Brachytherapy Eye90 Microspheres Device

Final Report
Submitted: April 24, 2024

Subcommittee Membership:

Michael Folkert, MD PhD (chair)
Rebecca Allen, MS
Andrew Einstein, MD PhD
Darlene Metter, MD
Zoubir Ouhib, MS

Consultant to Subcommittee: John Angle, MD
NRC Technical Staff Resource: Sarah Spence, CHP

Charge

On November 3rd, 2023, the ACMUI Chair, Dr. Darlene Metter, charged the Eye90 Y-90 Microsphere Subcommittee to review and comment on the NRC staff's draft licensing guidance for the ABK Biomedical, Inc. Eye90 microspheres® manual brachytherapy device for hepatocellular carcinoma.

Background

The liver is a common site for malignant involvement, including primary cancers such as hepatocellular carcinoma and cholangiocarcinoma, and secondary cancers metastasizing from other organs such as the colon and rectum, pancreas, small intestine, and breast. Transarterial radioembolization is an interventional technique used to treat hepatic sites of disease with permanent implantable radiopaque glass Y-90 microspheres. The microspheres are delivered to tumor vasculature via an intra-arterial catheter placed under fluoroscopic guidance, usually by an interventional radiologist.

A new yttrium-90 microsphere brachytherapy device called Eye90 microspheres® has recently been approved by the Food and Drug Administration (FDA) under an Investigational Device Exemption (IDE) for use in a clinical trial. It uses a proprietary delivery system comprised of a sterile, single-use delivery device and a re-useable, nonsterile system container. This product is unique to the existing FDA-approved yttrium-90 microsphere products at the time of publication, due to the radiopaque quality of the microspheres. The authorized user (AU) may choose to use fluoroscopy to directly image the radiopaque microspheres in the tumor vasculature during administration and via any x-ray imaging modality thereafter.

The NRC staff have determined that this product needs to be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices. The NRC staff developed the draft licensing guidance to support future licensing, adapted from the existing guidance for other microsphere brachytherapy, "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance" (ML21089A364) revised in April 2021.

General Comments:

1. The subcommittee agrees that the Eye90 microspheres® product needs to be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices.
2. The guidance reviewed is substantially similar to that previously issued for other Yttrium-90 microsphere therapy devices (TheraSpheres and SIR-Spheres): "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance" (ML21089A364), which is appropriate due to the similarity of these devices, their indications and the technical approaches used in administration.
3. 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.

Specific Comments:

1. Background section, 2nd paragraph: add "Following angiographic pre-therapy evaluation for extrahepatic shunting,"
2. 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.
3. 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.
4. Training and experience, section 5.1.B: note that the hands-on cases are "conducted in the physical presence of an AU".
5. Training and experience, section 5.1.B: change "above, including case work" to "at the beginning of this section" to reduce redundancy.
6. Training and experience, section 5.1.C: include "fellowship" as an addition/alternative to residency training throughout.
7. Team approach, section 5.4: add "ordering" to the participating individuals to whom training must be provided.
8. Written directives, section 6.2 written directive condition: removed "or manufacturer" as the Eye90 microspheres® product could change ownership.
9. 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."
10. 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).

11. 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.
12. 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),”.
13. 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 explanation 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.

Respectfully submitted on March 16, 2024

Subcommittee on “Draft Licensing Guidance for Yttrium-90 Microsphere Brachytherapy Eye90 Microspheres Device”
Advisory Committee on the Medical Use of Isotopes
U.S. Nuclear Regulatory Commission

The ACMUI unanimously approved this report as presented during its public meeting on April 8, 2024