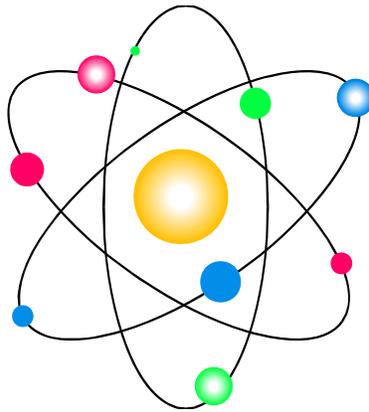




RADIOACTIVE MATERIALS REGULATORY GUIDE



MICROSPHERE BRACHYTHERAPY SOURCES AND DEVICES



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REGULATORY GUIDE FOR MICROSPHERE BRACHYTHERAPY SOURCES AND DEVICES

TheraSphere® and SIR-Spheres® Yttrium-90 Microspheres

Yttrium-90 (Y-90) microspheres are manual brachytherapy sources used for permanent implantation therapy. Y-90 microspheres are regulated under 4731.4404 "Other Medical Uses." The following requirements are necessary to ensure the public health and safety.

Training and Experience

The authorized user for Y-90 microspheres must meet the training and experience requirements of 4731.4443 or 4731.4458. Additionally, the authorized user must have successfully completed training in the operation of the delivery system, safety procedures, and clinical use for each type of Y-90 microspheres for which authorization is sought. The additional Y-90 microsphere specific training and experience requirements may be satisfied by satisfactory completion of a training program provided by:

Pathway 1: an authorized user who is authorized for the type of microsphere for which the individual is seeking authorization. The clinical use experience should include at least three supervised hands-on cases for each type of Y-90 microsphere for which the individual is seeking authorized user status;

or

Pathway 2: a Y-90 microsphere manufacturer. The clinical use experience should include at least three supervised hands-on *in-vitro* simulated cases for each type of Y-90 microsphere for which the individual is seeking authorized user status. *In-vitro* simulated cases should demonstrate issues that are encountered during Y-90 microsphere administration procedures. Following the license amendment that names the individual as an authorized user for Y-90 microsphere use, the first three patient cases completed by the individual should be hands-on and supervised in the physical presence of a manufacturer representative for each type of Y-90 microsphere for which the individual is authorized.

The applicant must submit documentation for the above training and experience. For individuals obtaining clinical use experience under Pathway 1 above, this documentation includes the clinical use cases. For individuals obtaining clinical use experience under Pathway 2 above, this documentation includes the *in-vitro* simulated cases and a commitment that each individual will complete the first three hands-on patient cases supervised in the physical presence of a manufacturer representative for each type of Y-90 microsphere for which authorization is sought. Additionally for Pathway 2, the licensee's commitment will include submitting documentation to MDH within 30 days of when these three patient cases have been completed.

In addition, the applicant shall commit to provide training in the manufacturer's procedures to all individuals involved in Y-90 microsphere use, commensurate with the individual's duties to be performed. This training must be provided to all individuals preparing, measuring, performing dosimetry calculations, or administering Y-90 microspheres.

If the MDH staff revises the training and experience criteria, physicians who were authorized for the medical use of a specific type of Y-90 microsphere under these criteria or previous criteria, do not have to meet the revised criteria for that type of microsphere.

MDH recognizes that if an authorized user satisfies the training and experience listed above and is currently listed on an NRC or Agreement State medical use license or permit for a specific type of microsphere, the authorized user should be allowed to work under a different license for the medical use of the same type of microsphere. However, a facility must request a license amendment if it wishes to add users that have not previously been authorized for the use of Y-90 microspheres.

Leak Tests

Leak tests are not required for Y-90 microspheres.

License Commitments - Written Directives, Inventory, Patient Release, Labeling, & Medical Event Reporting

The licensee shall follow all the requirements for brachytherapy sources and manual brachytherapy use except where the following licensing commitments provide regulatory relief:

For Y-90 microspheres, "prescribed dose" means the total dose documented in the written directive. The written directive should include:

- before implantation: the treatment site, the radionuclide (including the chemical/physical form [Y-90 microspheres]), the manufacturer, the dose in rad/Gray, and, if appropriate for the type of microsphere used, the statement "dose delivered at stasis"; and
- after implantation but before completion of the procedure: the radionuclide (including the chemical/physical form [Y-90 microspheres]), the manufacturer, treatment site, and the total dose to the treatment site. If the implantation was terminated because of stasis, then the total dose is the value of the total dose delivered when stasis occurred and the implantation was terminated.

The written directive should specify the maximum dose that would be acceptable for a specified site (or sites) outside the primary treatment site to which the microspheres could be shunted (e.g. lung and gastrointestinal tract). The post-implantation written directive should specify the dose that will result to the specified site (or sites) due to shunting.

The semi-annual physical inventory of microspheres aggregates (e.g. vials) should include:

- the radionuclide and physical form,
- unique identification of each vial in which the microspheres are contained,
- the total activity of the vial(s), and
- the location of the vial(s).

Procedures should describe measures taken to ensure that radiation emissions, which may include bremsstrahlung, from each patient or human research subject permits his/her release in accordance with 4731.4427.

The following additional guidance applies when the Y-90 microspheres are placed in vials, syringes, or radiation shields that are not labeled by the manufacturer:

- Label vials and vial radiation shields with radionuclide and form (e.g., Y-90 microspheres).
- Label syringes and syringe radiation shields with the radionuclide, form, and therapeutic procedure (e.g., Y-90 microspheres, brachytherapy).

Microsphere brachytherapy treatment is usually conducted using a multi-disciplinary team approach. The authorized user should consult, as necessary, with individuals with expertise in:

- Cancer management (e.g. radiation or medical oncology)
- Catheter placement
- Radiation dosimetry
- Safe handling of unsealed byproduct material

One individual may satisfy more than one of the listed areas of expertise.

Change in Physical Conditions of Use

If the physical conditions of use exceed those reported in the Sealed Source and Device (SSD) certificate, the limited specific medical use licensee should request an amendment for the new conditions. A broad scope licensee should perform its own engineering and radiation safety evaluation addressing those differences.

Use of Other Y-90 microspheres

The SSD safety evaluation for a specific manufacturer's Y-90 microspheres does not cover the use of any other Y-90 microspheres, including the preparation of Y-90 on other microspheres by a commercial nuclear pharmacy, the medical use licensee's authorized nuclear pharmacist, or a physician authorized user qualified to prepare radioactive drugs. The medical use of such a source will require a new SSD certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use, safety of the new Y-90 microspheres, and compatibility of the new microspheres with microsphere delivery system(s).

The SSD safety evaluation for a manufacturer's Y-90 microsphere delivery system does not cover the use of any other delivery system with the Y-90 microsphere brachytherapy device. Before authorization, the medical use of such a delivery system will require a new SSD certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use, safety of the microsphere delivery system, and compatibility of the new delivery system with the Y-90 microspheres.

TheraSphere® Use Outside Humanitarian Device Exemption (HDE) Restrictions

The MDS Nordion TheraSphere® Y-90 microspheres are approved by the U.S. Food and Drug Administration (FDA) under the provisions of a "Humanitarian Device Exemption" (HDE No. H9800006), which includes unique restrictions on the medical use of the devices. Nothing in the MDH license relieves the licensee from complying with those FDA requirements.

If the Institutional Review Board¹ that is required to approve and monitor the use of the MDS Nordion TheraSphere® Y-90 microspheres determines that the particular use of TheraSphere® Y-90 microspheres is for research purposes, the licensee must meet the requirements in 4731.4401, "Protection of human research subjects."

Waste Disposal Issues

Medical licensees should be aware of the presence of radioactive contaminants and possible issues with disposal with the two variations of commercially available Y-90 labeled microspheres, TheraSphere® and SIR-Spheres®. Depending on the contaminants, licensees may need to:

- hold the remaining microspheres longer in decay-in-storage in accordance with 4731.4429;
- return the microspheres to the manufacturer, if the manufacturer is authorized to receive Y-90 microspheres; or

¹ One of the conditions of approval for an HDE is that there be an Institutional Review Board initial review and approval before a humanitarian use device is used at a facility, as well as continuing review of its use.

- transfer the microspheres to an authorized recipient.

