

From: Gabriel, Sandra
Sent: Wednesday, November 24, 2010 10:42 AM
To: adelmustafa@gmail.com
Subject: Additional information for NRC license amendment request(s) for St. Vincent's Medical Center (mail control 573795)
Attachments: Microsphere guidance Sept 08.pdf

Licensee: St. Vincent's Medical Center (SVMC)
License No: 06-00843-03
Docket No.: 03001245
Mail Control No.: 573795

To: Adel Mustafa, Ph.D., Radiation Safety Officer (RSO)

Please send a return e-mail to confirm that you received this message.

This is in response to SVMC's license amendment requests dated October 19 and October 28, 2010, which will be addressed together in mail control 573795.

The letter dated October 28 requested to add Chengyu Shi, Ph.D. as authorized medical physicist (AMP) for SVMC's high dose rate remote afterloader (HDR) unit. Please note that the submitted preceptor attestation was signed by an authorized user (AU) physician, not an AMP. However, we can authorize Dr. Shi as HDR AMP based on the letter SVMC provided from the UT Health Science Center RSO confirming that Dr. Shi is an HDR AMP under that broad scope license. We also obtained a copy of that Texas license for our records to document that it authorizes HDR.

The letter dated October 19 requested to authorize use of Yttrium-90 SIR-Spheres. In order to continue our review of this request, please provide the following additional information within 30 days, under signature of SVMC senior management:

- 1) SVMC requested to name Dr. Zinn and Dr. Williams as AUs for SIR-Spheres, and provided a copy of Bridgeport Hospital's NRC license. Please note that NRC's 35.1000 licensing guidance for microspheres (copy attached to this message) provides two pathways for qualifications of AUs. Dr. Zinn and Dr. Williams qualified to be listed on Bridgeport Hospital's license using pathway 2 (see bottom of first page of attachment) and have not yet completed the necessary three hands-on SIR-Spheres cases supervised in the presence of a manufacturer representative. NRC considers this to be a provisional authorization that is insufficient to qualify Drs. Zinn and Williams as SIR-Spheres AUS for SVMC's license.

SVMC's options are to name one or more other experienced AUs who qualify under pathway 1 of the attached document, or to commit to follow the process described in pathway 2. Please indicate which of these two options SVMC wishes to pursue.

If SVMC wishes to pursue pathway 2, please note that NRC has on file copies of Dr. Zinn's and Dr. Williams' training certificates from Sirtex showing completion of training in operation of the delivery system, safety procedures, clinical use, and three supervised, hands-on, in vitro simulated cases. SVMC would need to do 2 things for NRC to approve Dr. Zinn and Dr. Williams to begin using SIR-Spheres under a provisional authorization:

- a) Commit to having the first three patient cases for each of these individuals (Dr. Zinn and Dr. Williams) to be hands-on and supervised in the physical presence of a Sirtex representative, and
 - b) Commit to providing documentation to the NRC Region I office within 30 days after Dr. Zinn and Dr. Williams each complete three patient cases supervised by a Sirtex representative. After receiving this, we will change the provisional authorization to a permanent one.
- 2) SVMC committed to provide training in the manufacturer's procedures to all individuals involved in Y-90 microspheres use. Please confirm that SVMC will document the date(s), instructor(s), content, and attendance for this training, and that RSO will be trained.
 - 3) Confirm that SVMC will conduct microsphere treatments using a multi-disciplinary team approach. The authorized user will consult, as necessary, with individuals with expertise in cancer management (e.g., radiation and/or medical oncology), catheter placement, radiation dosimetry, and safe handling of unsealed byproduct material.
 - 4) Confirm that SVMC will follow the manufacturer's procedures for calculating/documenting the dose to the treatment site and other sites (e.g., lung), preparing the dose, and performing pre/post vial dose measurements; or submit alternative procedures.
 - 5) Identify the location(s) where SIR-Spheres will be prepared (e.g., Nuclear Medicine hot lab) and administered to patients (e.g., in a specific interventional radiology suite). Unless this has been previously submitted to the NRC, provide a facility diagram identifying the location(s) where SIR-Spheres will be prepared and administered, and surrounding areas.
 - 6) Confirm that SVMC will follow all the requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use except where replaced by the following commitments, as described in the September 2008 version of NRC's 35.1000 licensing guidance for Yttrium-90 microspheres (These items were taken from the document attached to this message. SVMC should repeat the full text of these items in the response to this e-mail):

- a) For the purpose of written directives and medical event reporting requirements for microsphere use, "prescribed dose" means the total dose (rad or Gy). Alternatively, prescribed activity (mCi or GBq) may be used in lieu of prescribed dose.
- b) The written directive will include the patient's name and two separate entries:
 - i) pre-administration: the date; signature of the AU; treatment site; radionuclide (including physical form [Y-90 microspheres]), prescribed dose/activity; and, if appropriate for the type of microsphere used, identify the manufacturer and include the statement "or dose/activity delivered at stasis"; and
 - ii) after administration but before the patient leaves the post-procedural recovery area: date; signature of the AU; and total dose/activity delivered to the treatment site. If the administration was terminated because of stasis, then the total dose/activity to the treatment site is the value of the total dose/activity administered when stasis occurred and the administration was terminated. Note: The post-administration entries into the written directive are not an amendment to the written directive; rather, these entries complete the written directive.
- c) The pre-administration written directive will specify the maximum dose(s)/activity(ies) that would be acceptable to the specified site(s) outside the primary treatment site due to shunting (e.g., lung and gastrointestinal tract). The post-implantation written directive should specify the dose(s)/activity(ies) delivered to the specified site(s) outside the primary treatment site due to shunting.
- d) Administration of Y-90 microspheres will be performed in accordance with the written directive. If the written directive is specified in dose (rad or Gray), SVMC procedures will describe how the total dose to the treatment site, as well as the doses to other sites, will be determined before and upon completion of the administration, to confirm that the administration is performed in accordance with the written directive.
- e) The semi-annual inventory of aggregates (e.g., vials) will include the radionuclide and physical form, unique identification of each vial in which the microspheres are contained, total activity contained in each of the vials, and location(s) of the vial(s).
- f) SVMC will have procedures to describe measures to be taken to ensure that radiation emissions, which may include bremsstrahlung, from each patient allow his/her release in accordance with 10 CFR 35.75.

- g) When Y-90 microspheres are placed in vials, syringes, or radiation shields that are not labeled by the manufacturer, labels will be placed on vials and vial radiation shields to indicate the radionuclide and form, and labels will be placed on syringes and syringe shields to indicate the radionuclide, form, and therapeutic procedure (e.g., Y-90 microspheres, brachytherapy).
- h) SVMC will report any event, except for an event that results from intervention of a patient, in which:
 - i) the administration of byproduct material results in a dose that exceeds 0.05 Sv (50 rem) to an organ or tissue from use of the wrong radionuclide; or
 - ii) the administration of Y-90 microspheres results in a dose:
 - a) that differs from the prescribed dose, as documented in the pre-administration written directive by more than 0.05 Sv (5 rem) effective dose equivalent or 0.5 Sv (50 rem) to an organ or tissue, and the total dose/activity administered differs from the prescribed dose/activity, as documented in the pre-administration written directive, by 20 percent or more; or
 - b) that exceeds 0.05 Sv (5 rem) effective dose equivalent or 0.5 Sv (50 rem) to an organ or tissue to the wrong individual, via the wrong route, or by the wrong mode of treatment; or
 - c) to an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) to an organ or tissue and by 50 percent or more of the prescribed dose/activity expected to that site from the administration of Y-90 microspheres, if carried out as specified in the pre-administration portion of the written directive.
- i) SVMC will comply with the medical event reporting and notification requirements as described in 10 CFR 35.3045(b)-(g).

Please submit the information described above within 30 days or we will presume that SVMC does wish to pursue this request. SVMC may mail this to the Region I office or by fax to my attention at 610-337-5269, referencing mail control 573795. You may contact me with any questions, however, please note that I will be out of the country beginning on December 6 and returning to the office on December 27. I will have no access to e-mail from December 6 until approximately December 22.

Thank you,

Sandy Gabriel

Senior Health Physicist
Medical Branch
NRC Region I
610-337-5182

E-mail Properties

Mail Envelope Properties ()

Subject: Additional information for NRC license amendment request(s) for St. Vincent's Medical Center (mail control 573795)

Sent Date: 11/22/2010 1:17:31 PM

Received Date: 11/24/2010 10:41:00 AM

From: Gabriel, Sandra

Created By: Sandra.Gabriel@nrc.gov

Recipients:

adelmustafa@gmail.com (adelmustafa@gmail.com)

Tracking Status: None

Post Office:

Files	Size	Date & Time
MESSAGE	91885	11/22/2010
Microsphere guidance Sept 08.pdf	47937	

Options

Expiration Date:

Priority: o!ImportanceNormal

ReplyRequested: False

Return Notification: False

Sensitivity: o!Normal

Recipients received:

Microsphere Brachytherapy Sources and Devices

REVISED SEPTEMBER 2008

Questions should be directed to: Ashley Tull (240) 888-7129 or
Ronald Zelac (301) 415-7635 or
MedicalQuestions.Resource@nrc.gov

Licensing Guidance – 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 10 CFR 35.1000 "Other Medical Uses of Byproduct Material or Radiation from Byproduct Material." Consistent with the direction in 10 CFR 35.1000, the NRC has evaluated these devices and determined that licensees must use Y-90 microspheres in accordance with the following requirements, which will be incorporated into the license either through license condition or through incorporation by reference to licensee submittals that include commitments consistent with these requirements. Applicants are reminded that licenses issued pursuant to 10 CFR 35.1000 must still meet the general requirements in 10 CFR Part 35, Subparts A, B, C, L, and M.

Training and Experience

The authorized user for Y-90 microspheres (AU) must meet the training and experience requirements of 10 CFR 35.390 or 10 CFR 35.490. Additionally, the AU 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 either:

- pathway 1) an AU 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 AU 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 AU 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 AU 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 the appropriate NRC Regional Office 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 NRC 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.

Leak Tests

Leak tests are not required for Y-90 microspheres based on the criteria in 10 CFR 35.67(f).

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

The applicant shall commit to follow all the requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use, except where replaced by the following licensing commitments:

- For the purpose of written directives and medical event reporting requirements in the Y-90 microsphere guidance, "prescribed dose" means the total dose (rad or Gy). Alternatively, prescribed activity (mCi or GBq) may be used in lieu of prescribed dose.
- The written directive shall include the patient or human research subject's name and two separate entries:
 - 1) pre-administration: the date; the signature of the AU; the treatment site; the radionuclide (including the physical form [Y-90 microspheres]); the prescribed dose/activity; and, if appropriate for the type of microsphere used, identify the manufacturer and include the statement "or dose/activity delivered at stasis"; and
 - 2) after administration but before the patient or human research subject leaves the post-procedural recovery area: the date; the signature of the AU; and the total dose/activity delivered to the

treatment site. If the administration was terminated because of stasis, then the total dose/activity to the treatment site is the value of the total dose/activity administered when stasis occurred and the administration was terminated. Note: The post-administration entries into the written directive are not an amendment to the written directive; rather, these entries complete the written directive.

- The pre-administration written directive should specify the maximum dose(s)/activity(ies) that would be acceptable to the specified site(s) outside the primary treatment site due to shunting (e.g. lung and gastrointestinal tract). The post-implantation written directive should specify the dose(s)/activity(ies) delivered to the specified site(s) outside the primary treatment site due to shunting.
- Administration of Y-90 microspheres must be performed in accordance with the written directive. If the written directive is specified in dose (rad or Gray), the licensee should describe how the total dose to the treatment site, as well as the doses to other sites, will be determined before and upon completion of the administration, to confirm that the administration is performed in accordance with the written directive.
- The semi-annual physical inventory of microspheres aggregates (e.g. vials) should include:
 - 1) the radionuclide and physical form; and
 - 2) unique identification of each vial in which the microspheres are contained; and
 - 3) the total activity contained in each of the vial(s); and
 - 4) the location(s) 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 10 CFR 35.75.
- 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:
 - 1) Label vials and vial radiation shields with radionuclide and form (e.g., Y-90 microspheres).
 - 2) Label syringes and syringe radiation shields with the radionuclide, form, and therapeutic procedure (e.g., Y-90 microspheres, brachytherapy).
- The licensee shall commit to report any event, except for an event that results from intervention of a patient or human research subject, in which:
 - 1) the administration of byproduct material results in a dose that exceeds 0.05 Sv (5 rem) effective dose equivalent or 0.5 Sv (50 rem) to an organ or tissue from the use of the wrong radionuclide; or
 - 2) the administration of Y-90 microspheres results in a dose:
 - a) that differs from the prescribed dose, as documented in the pre-administration written directive, by more than 0.05 Sv (5 rem) effective dose equivalent or 0.5 Sv (50 rem) to an organ or tissue, and the total dose/activity administered differs from the prescribed dose/activity, as documented in the pre-administration written directive, by 20 percent or more; or

- b) that exceeds 0.05 Sv (5 rem) effective dose equivalent or 0.5 Sv (50 rem) to an organ or tissue from an administration to the wrong individual or human research subject, via the wrong route, or by the wrong mode of treatment; or
 - c) to an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) to an organ or tissue and by 50 percent or more of the prescribed dose/activity expected to that site from the administration of Y-90 microspheres, if carried out as specified in the pre-administration portion of the written directive
- Additionally, the licensee shall comply with the medical event reporting and notification requirements as described in 10 CFR 35.3045(b)-(g).

Notes to Licensees

Team Approach

Microsphere brachytherapy treatment is usually conducted using a multi-disciplinary team approach. The AU 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.

Notification for AUs

NRC recognizes that if an AU satisfies the training and experience listed in NRC's licensing guidance for Y-90 microspheres and is currently listed on a Commission or Agreement State medical use license or permit for a specific type of microsphere, the AU should be allowed to work under a different license for the medical use of the same type of microsphere. A limited specific medical use applicant initially applying for authorization for the medical use of Y-90 microspheres or an existing licensee applying for an amendment may request authorization to notify the NRC in the future that it has permitted an AU to work at its facility without the need to request an additional license amendment, provided the following conditions are met:

- 1) the AU satisfies the training and experience listed in NRC's licensing guidance for Y-90 microspheres; and
- 2) the AU is currently listed on a Commission or Agreement State license, a permit issued by a Commission master material license, a permit issued by a Commission or Agreement State

licensee of a broad scope, or a permit issued by a Commission master material license broad scope permittee; and

- 3) the licensee provides NRC a copy of the license or permit on which the AU was originally listed for the specific microsphere use; and
- 4) the licensee provides documentation to NRC for each AU of the above listed conditions no later than 30 days after the date that the licensee allows the AU to work as an AU for the specific type of microsphere.

If this authorization is approved, these notification conditions will be incorporated as license conditions in the licensee's license.

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, and 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 NRC license relieves the licensee from complying with those FDA requirements.

If the Institutional Review Board 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 10 CFR 35.6, "Provisions for research involving human subjects." (Note: 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.)

Revision of Y-90 Microsphere Radiation Safety Programs to Conform to Changes in This Licensing Guidance

The above licensing guidance may be revised as additional experience is gained regarding the medical use of TheraSphere® and SIR-Spheres® Y-90 microspheres. A licensee currently authorized to use these products that is committed by license condition to following provisions in this guidance existing at the time of commitment must apply for and receive an amendment to its license in order to make changes to conform with the revised provisions.

An applicant initially applying for authorization for the medical use of TheraSphere® and SIR-Sphere® Y-90 microspheres, or a licensee applying for an amendment to conform with revisions may request to incorporate into its license a change process similar to 10 CFR 35.26. Such a change process can allow some future changes to radiation safety programs provided that the change process requires the following conditions to be met for revisions to the radiation safety program:

- 1) the revision is in compliance with the regulations; and
- 2) the revision is based upon NRC's current guidance for TheraSphere® and SIR-Spheres® Y-90 microspheres 35.1000 use posted on the NRC Web site; and
- 3) the revision has been reviewed and approved by the licensee's Radiation Safety Officer and licensee's management; and
- 4) the affected individuals are instructed on the revised program before the change is implemented; and
- 5) the licensee will retain a record of each change for five years; and
- 6) the record will include a copy of the appropriate website guidance, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee management that reviewed and approved the change.

If approved, these conditions for use of updated guidance will be incorporated as license conditions in the licensee's license.

Waste Disposal Issues

In March 2007 NRC staff issued an Information Notice (IN 2007-10) to alert all medical licensees of the presence of radioactive contaminants and possible disposal issues 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 10 CFR 35.92; or
- return the microspheres to the manufacturer, if the manufacturer is authorized to receive Y-90 microspheres; or
- transfer the microspheres to an authorized recipient.

IN 2007-10, *Yttrium-90 TheraSpheres[®] and SIRspheres[®] Impurities*, is available on the NRC public website at <http://www.nrc.gov/reading-rm/doc-collections/gen-comm/info-notices/2007/in200710.pdf>.