UNITED STATES
NUCLEAR REGULATORY COMMISSION
REGION III
2443 WARRENVILLE ROAD, SUITE 210
LISLE, ILLINOIS 60532-4352

OCT 2 5 2017

Wallace Fuhrman
Radiation Safety Officer
SSM Cardinal Glennon Children's Hospital
Radiology Department
1465 South Grand Boulevard
St. Louis, MO 63104

Dear Mr. Fuhrman:

We have reviewed your application dated August 1, 2017, requesting new authorization for yttrium-90 SIRSpheres permitted by 10 CFR 35.1000, and find that we will need additional information to complete our review.

This also refers to the email message I sent to you at Wally.Fuhrman@ssmhealth.com on October 23, 2017, requesting a telephone call with you to discuss the deficient items in your application before I finalized my correspondence with you.

However, as of the close of business on October 25, 2017, I have not heard back from you. I have a "read receipt" email from October 24, 2017 only.

Therefore, I am "voiding" the current request, because it is insufficient to complete my review. If or when you submit a written response, we will re-activate your request and continue our review. "Void" just means that we take it out of our active pending casework database. It is an administrative procedure that we do.

Please see the enclosed "marked up" pages from the Licensing Guidance for Y-90 SIRSpheres in 10 CFR 35.1000, from our website. I have marked the sections that we need you to explicitly commit to, in the same level of detail as shown.

Please do not make statements, such as "We commit to xxxxxxxxxxxxxxx in accordance with NRC's February 2016 Licensing Guidance." This type of blanket statement does not constitute actual, detailed commitments, statements and representations. If such statements were "approvable," our Licensing Guidance would state as much and it does not.

Please do not resubmit any information you have already sent us in the August 1, 2017, application, that we have not asked for additional information now. To do so will likely delay the review of your written response.

We are not considering in our review the following documents that you submitted with the August 1, 2017, that we did not ask for in our Licensing Guidance:

- The Sirtex Training Manual;
- The Sirtex Package Insert; and,
- The Y-90 SIR-Spheres Preparation and Verification Procedure.

Please do not resubmit these, or other, similar, documents. Please also note that such documents do not constitute the actual, explicit, specific commitments, statements and representations that are requested in our Licensing Guidance.

In Item 7 of your application dated August 1, 2017, you made several statements regarding compliance with 10 CFR 35.75 that appeared to resemble a kind of "exemption" from 10 CFR 35.75, and we also noted that it appeared to resemble a kind of "exemption" from 10 CFR 20.1501, although the latter regulation was not stated in your application.

If or when you respond to this request for additional information and if we are eventually able to approve the Y-90 SIRSpheres modality in 10 CFR 35.1000 for your license, we will be excluding all of the information in Item 7, and you must comply with 10 CFR 35.75 and 20.1501.

Item 7 also included information about your survey instrument. We did not request information about your survey instrument in our Licensing Guidance and we do not need it to consider your licensing request in this instance. If we had needed it, we would have asked for it in the Guidance.

Further, please do not provide "serial numbers" for your survey instruments. If we needed information about your survey instruments (and we do not), we would ask for the manufacturer's names and model numbers, and information demonstrating compliance with 10 CFR 35.60 and 35.61.

Please address your written response to my attention at the address shown at the top of page 1 of this application and reference it as "additional information to control number 600335."

If you have any questions or comments concerning this amendment, please contact me at (630) 829-9841. My fax number is (630) 515-1078.

In accordance with 10 CFR 2.390 of the NRC's "Rules of Practice," a copy of this letter will be available electronically for public inspection in the NRC Public Document Room or from the NRC's Agencywide Documents Access and Management System (ADAMS), accessible from the NRC Web site at http://www.nrc.gov/reading-rm/adams.html.

Sincerely,

Colleen Carol Casey

Colleen Carol Casey
Materials Licensing Branch

License No. 24-32264-01
Docket No. 030-35553
Control No. 600335

Enclosure: As stated

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

Notification

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 requesting 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 for the same type of Y-90 microsphere use 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 to the NRC a copy of the license or permit on which the AU is listed for the specific microsphere use; and
4. the licensee provides documentation of the above listed conditions to NRC for each AU 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.

Grandfathering COMMIT TO THIS EXPLICITLY - IN SAME DETAIL AS SHOWN.

If a licensee adopts this revision of Y-90 microsphere training and experience criteria, physicians who are currently authorized for the medical use of a specific type of Y-90 microsphere under previous criteria do not have to meet the revised criteria for that type of microsphere.

License Commitments

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:

Training

The applicant shall commit to provide training in the licensee'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.

Procedures for Administration

The licensee shall commit to following the manufacturer's procedures for calculating and documenting the dose or activity to the treatment site; preparing the dose for administration; determining shunting to non-treatment sites; and performing pre- and post-vial dose measurements; or submit alternative methods.

Administration of Y-90 microspheres must be performed in accordance with the written directive. The licensee shall record the dose or activity delivered to the treatment site. The record should be prepared within 24 hours after the completion or termination of the administration and must include the name of the individual who determined the administered dose or activity and the date.

COMMIT TO THIS EXPLICITLY - IN SAME DETAIL AS SHOWN.

Written Directives

For the purpose of written directive 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. If prescribed activity is used in lieu of prescribed dose, activity should be used for all documentation and evaluations.

The written directive shall include the patient or human research subject's name; the date; the signature of an AU for Y-90 microspheres; the treatment site; the radionuclide (including the physical form [Y-90 microspheres]); the manufacturer; the prescribed dose or activity; and, if appropriate for the type of microsphere used, the statement "or dose or activity delivered at stasis."

Termination of Treatment Due to Stasis

If the administration was terminated because of stasis, then the total dose or activity to the treatment site is the value of the total dose or activity administered when stasis occurred and the administration was terminated. The record should be prepared within 24 hours after the completion or termination of the administration and must include the name of the individual who determined the administered dose or activity, the date, and the signature of an AU for Y-90 microspheres.

Emergent Patient Conditions

If the procedure must be modified due to emergent patient conditions that prevent administration in accordance with the written directive (e.g., artery spasm or sudden change in blood pressure), the AU should document such changes in the written directive within 24 hours after the completion or termination of the administration. The modification to the written directive should include the reason for not administering the intended dose or activity, the date, and the signature of an AU for Y-90 microspheres.

Medical Event Reporting

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:

- 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
- the administration of byproduct material: to the wrong individual or human research subject; via the wrong route; or by the wrong mode of treatment; or

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COMMIT TO THIS EXPLICITLY- IN SAME DETAIL AS SHOWN.

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- the total dose or activity administered differs from the prescribed dose or activity, as documented in the written directive, by 20 percent or more, except when stasis or emergent patient conditions are documented and resulted in a total dose or activity administered that was less than that prescribed; or
- the administration of byproduct material results in dose or activity to an organ or tissue other than the treatment site, as documented in the written directive, except for shunting when shunting was evaluated prior to the treatment in accordance with the manufacturer's procedures.

Additionally, the licensee shall comply with the medical event reporting and notification requirements as described in 10 CFR 35.3045(b)-(g).

Inventory

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

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

The licensee shall retain each semi-annual physical inventory record for three years.

Labeling

The licensee should commit to the following 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).

Patient Release

The licensee should commit to develop procedures that describe measures taken to ensure that radiation emissions, which may include bremsstrahlung, from each patient or human research subject permits his or her release in accordance with 10 CFR 35.75.

Radiation Protection Program Changes

This 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 a previous revision of this guidance may request a license amendment to commit to following this revision of the guidance instead. The licensee must apply for and receive this license amendment in order to make program changes to conform to this revision of the guidance.

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 this revision of the guidance 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 Medical Uses Licensee Toolkit;
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

COMMIT TO THIS EXPLICITLY- IN SAME DETAIL AS SHOWN.

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.

COMMIT TO THIS EXPLICITLY - IN SAME DETAIL AS SHOWN.

Notes to Licensees

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 or in 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 given manufacturer's Y-90 microsphere delivery system does not cover the use of that manufacturer's Y-90 microspheres with another manufacturer's delivery system or the use of another manufacturer's Y-90 microspheres with the given manufacturer's delivery system. 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.