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

JUL 27 2016

Paul Jursinic, Ph.D.
Radiation Safety Officer
Borgess Medical Center
1521 Gull Road
Kalamazoo, MI 49048

Dear Dr. Jursinic:

Enclosed is Amendment No. 104 to your NRC Material License No. 21-12275-02 in accordance with your request.

Please review the enclosed document carefully and be sure that you understand all conditions. If there are any errors or questions, please notify the U.S. Nuclear Regulatory Commission, Region III office at (630) 829-9887 so that we can provide appropriate corrections and answers.

If you have any questions concerning this amendment please contact me at either (630) 829-9841 or (800) 522-3025, ext. 9841. My fax number is 630-515-1078.

We were unable to approve your request for the use of yttrium-90 TheraSpheres, permitted by 10 CFR 35.1000, because the information in your letter dated May 9, 2016, received May 26, 2016, was insufficient to complete our review.

If you wish to pursue this request, please submit a written, currently dated and signed response addressing the deficient items marked in handwritten red ink on the enclosed copy of NRC's guidance for yttrium-90 TheraSpheres, permitted by 10 CFR 35.1000.

Please include in your written response documentation that you, as the RSO, have obtained the requisite training in the radiation safety, regulatory issues and emergency procedures for the proposed new type of use for which you are seeking approval. This is similar to the training described in 10 CFR 35.50(e), as modified for the emerging technology permitted by 10 CFR 35.1000.

Some wording was also missing from two commitments made in your letter. The relevant excerpt page from your letter is also attached and the missing wording is marked in handwritten red ink. Please make these corrections in your written response also.

You do not need to, and you should not, resubmit the commitments that have already been accepted, i.e., they are not requested to be addressed in response. Doing so will only serve to delay the completion of our review. Please limit your response to only the issues we have requested additional information on.

The enclosed license document contains sensitive security-related information. When separated from the license, this cover letter and attachments 2 and 3 are uncontrolled.

Please address your written response to my attention at the address shown above as "additional information to control number 590932." We will then resume our review.

In addition, we noted that only you, the RSO for this license, signed the letter above requesting the addition of this new therapeutic modality. Please note the following advice and regulations for appropriate signatories for your licensing correspondence. It would be best to have your response to this letter signed by a senior management representative, as a senior management representative did not sign the initiating letter for this request above.

Signatures required for Materials Licensing Correspondence and Best Practices

To help ensure that an application for a new, amendment or renewal materials licensing request is complete and may be acted upon by NRC, all incoming licensing correspondence must be signed by an appropriate certifying officer for the materials licensee in question.

An applicant's or licensee's legal representative, administrative assistant, outside consultant, etc. will not suffice as a certifying officer.

As enumerated below, for all materials applicants and licensees, and as noted for medical/human use applicants and licensees, all initial requests for licensing requests must be signed, in order to comply with the regulatory requirements listed below.

If a certifying officer/management representative signs an "initial" licensing request that names someone else as a "point of contact," then the designated point of contact may be the sole signatory for any written responses related to that initial licensing request only, unless the NRC reviewer requests otherwise.

All subsequent "new/initial" licensing requests must then be signed appropriately.

Please *always* sign every licensing document and communication submitted, even if you sign an email and transmit it to us via email/PDF or fax.

Unsigned email messages, electronically generated or imposed "signatures," stamped signatures, etc. are not acceptable substitutes for an actual, physically hand-written signature.

Submitting any licensing correspondence without a signature, or with an unacceptable signature, may delay the review process until an acceptable signature is obtained on the document(s) in question.

Please be reminded that 10 CFR 30.32(a) and (c) require:

" (a) A person may file an application on NRC Form 313, "Application for Material License," in accordance with the instructions in § 30.6 of this chapter." And,

"(c) Each application shall be signed by the applicant or licensee or a person duly authorized to act for and on his behalf."

Please note that the NRC Form 313 requires the typed or printed name and signature of a certifying officer. The NRC Form 313 can be found at:

http://www.nrc.gov/reading-rm/doc-collections/forms/nrc313.pdf

If the NRC Form 313 is not used, then a business letter containing all of the information on the NRC Form 313 may be used instead.

In addition, please be reminded that 10 CFR 30.9(a) requires:

" (a) Information provided to the Commission by an applicant for a license or by a licensee or information required by statute or by the Commission's regulations, orders, or license conditions to be maintained by the applicant or the licensee shall be complete and accurate in all material respects."

This is important because several items in your letter dated May 9, 2016, were incomplete or failed to address sections in the guidance. Also, the device-specific and modality-specific training and experience for your two proposed authorized users had not been completed at the time you submitted the request. As of July 20, 2016, documentation of this training and experience had not been received by the reviewer.

Prior to submitting licensing requests, all pertinent training and experience must already be completed and documentation included with the submission so NRC may commence the review.

For medical/human use applicants and licensees:

10 CFR 35.12 Application for license, amendment, or renewal requires:

"(a) An application must be signed by the applicant's or licensee's management."

10 CFR 35.2, "Definitions" states, in part:

"Management means the chief executive officer or other individual having the authority to manage, direct, or administer the licensee's activities, or those persons' delegate or delegates."

For medical licensees, please also see "NRC INFORMATION NOTICE 2007-38: ENSURING COMPLETE AND ACCURATE INFORMATION IN THE DOCUMENTATION OF TRAINING AND EXPERIENCE FOR INDIVIDUALS SEEKING APPROVAL AS MEDICAL AUTHORIZED USERS," dated December 14, 2007, located on our website at:

http://pbadupws.nrc.gov/docs/ML0722/ML072270127.pdf

This document describes the importance of providing information that complies with 10 CFR 30.9.

Please address all licensing correspondence to: "ATTN: Materials Licensing Branch Chief" at the address shown below.

If you have any questions or comments please contact me at either (800) 829-9500, ext. 9841 or (630) 829-9841. My fax number is (630) 515-1078. My email address is colleen.casey@nrc.gov.

NRC's Regulatory Issue Summary (RIS) 2005-31 provides criteria to identify security-related sensitive information and guidance for handling and marking of such documents. This ensures that potentially sensitive information is not made publicly available through ADAMS, the NRC's electronic document system.

Pursuant to NRC's RIS 2005-31 and in accordance with 10 CFR 2.390, the enclosed license is exempt from public disclosure because its disclosure to unauthorized individuals could present a security vulnerability.

The RIS may be located on the NRC Web site at: http://www.nrc.gov/reading-rm/doc-collections/gen-comm/reg-issues/2005/ri200531.pdf and the link for frequently asked questions regarding protection of security related sensitive information may be located at: http://www.nrc.gov/reading-rm/sensitive-info/faq.html.

A copy of this letter and the two attachments will be available electronically for public inspection in the NRC Public Document Room or from the Publicly Available Records (PARS) component of NRC's document system (ADAMS).

The NRC's document system is accessible from the NRC Web site at http://www.nrc.gov/reading-rm/adams.html (the Public Electronic Reading Room).

You will be periodically inspected by NRC. Failure to conduct your program in accordance with NRC regulations, license conditions, and representations made in your license application and supplemental correspondence with NRC will result in enforcement action against you.

This could include issuance of a notice of violation, or imposition of a civil penalty, or an order suspending, modifying or revoking your license as specified in the General Statement of Policy and Procedure for NRC Enforcement Actions.

Since serious consequences to employees and the public can result from failure to comply with NRC requirements, prompt and vigorous enforcement action will be taken when dealing with licensees who do not achieve the necessary meticulous attention to detail and the high standard of compliance which NRC expects of its licensees.

The NRC's Safety Culture Policy Statement became effective in June 2011. While a policy statement and not a regulation, it sets forth the agency's *expectations* for individuals and organizations to establish and maintain a positive safety culture.

You can access the policy statement and supporting material that may benefit your organization on NRC's safety culture Web site at http://www.nrc.gov/about-nrc/regulatory/enforcement/safety-culture.html.

We strongly encourage you to review this material and adapt it to your particular needs in order to develop and maintain a positive safety culture as you engage in NRC-regulated activities.

Sincerely,

Colleen Carol Casey

Colleen Carol Casey
Materials Licensing Branch

License No. 21-12275-02
Docket No. 030-02115

Enclosures:

1. Amendment No. 104
2. Yttrium-90 TheraSpheres guidance, marked up
3. Excerpt from letter dated May 9, 2016, marked up

ATTACHMENT 2

Yttrium-90 Microsphere Brachytherapy Sources and Devices
TheraSphere® and SIR-Spheres®
Licensing Guidance

February 12, 2016, Revision 9

NRC Contact
Katie Tapp (301) 415-0236
MedicalQuestions.Resource@nrc.gov

Table of Contents

10 CFR 35.1000 Use

Although yttrium-90 (Y-90) microspheres are manual brachytherapy sources used for permanent implantation therapy, Y-90 microspheres have many unique properties that merit radiation safety considerations other than those required by 10 CFR Part 35, Subpart F, "Manual Brachytherapy." These unique properties include their small size; the large number of microspheres used in a treatment; the route of administration; and their use by physician authorized users (AU) in addition to radiation oncologists, including nuclear medicine physicians and interventional radiologists. As a result, Y-90 microspheres are regulated under 10 CFR 35.1000 "Other Medical Uses of Byproduct Material or Radiation from Byproduct Material."

Licensing Guidance

This guidance provides applicants with an acceptable means of satisfying the requirements for a license for the use of TheraSphere® and SIR-Spheres® and is not intended to be the only means of satisfying the requirements for a license. The applicant must submit the information required by 10 CFR 30.33 and 35.12, as described below. The applicant should submit additional information and commitments requested below or may, unless the information is specifically required by regulation, submit alternative information and commitments for review by the U.S. Nuclear Regulatory Commission (NRC) staff to make a licensing determination. The commitments incorporated into the applicant's license by license condition will be reviewed during routine inspections. Applicants are reminded that licenses issued pursuant to 10 CFR 35.1000 must still meet the general requirements in Part 35, Subparts A, B, C, L, and M, except as specified in this guidance. Additionally, applicants must meet applicable requirements of 10 CFR Part 30.

General

Radionuclides, Form, Possession Limits, and Purpose of Use

The applicant shall identify the radionuclides, chemical/physical form, requested maximum possession limit, and purpose of use. NRC Form 313 may be used to submit this information. For example, the following provides the format for an acceptable request.

	TheraSphere®	SIR-Sphere
Radionuclides (Authorization 6)	Yttrium-90	Yttrium-90
Chemical/Physical Form (Authorization 7)	Glass microsphere (manufacturer as listed in Sealed Source and Device Registry NR-0220-D-131-S, TheraSphere®)	Resin microsphere (manufacturer as listed in Sealed Source and Device Registry MA-1229-D-101-S, SIR-Sphere®)
Maximum Possession Limit (Authorization 8)	540 mCi/vial, 2 Ci total	189 mCi/vial, 2 Ci total
Authorized Use (Authorization 9)	TheraSphere® for permanent brachytherapy using delivery system as listed in Sealed Source and Device Registry NR-0220-D-131-S	SIR-Spheres® for permanent brachytherapy using delivery system as listed in Sealed Source and Device Registry MA-1229-D-101-S.

Leak Tests

Leak tests are not required for Y-90 microspheres. The small size and large number of Y-90 microspheres makes leak testing as required by 10 CFR 35.67(b) impractical. Further, if leak testing were practical, licensees would not be required to leak test individual microspheres because the activity of each microsphere is below the threshold in 10 CFR 35.67(f)(3).

Authorized Individuals

NRC has determined that individuals meeting the guidance provided in both A and B below will be considered qualified and can be authorized for the use of Y-90 microspheres. Applicants may also submit alternative training and experience commitments to be reviewed on a case-by-case basis by NRC staff. The alternative information should include an explanation of why the applicant believes the alternative information demonstrates that the individuals are qualified to be authorized individuals.

Training and Experience

The authorized user for Y-90 microspheres:

A.

1. Is identified as an authorized user for medical uses in 10 CFR 35.400, "Use of sources for manual brachytherapy," or for medical uses in 35.300, "Use of unsealed byproduct material for which a written directive is required," that include the uses described in paragraphs (1), (2), and (3) of 10 CFR 35.390(b)(1)(ii)(G) on one of the following licenses or permits that permit the medical use of byproduct material: A Commission or Agreement State license, a permit issued by a Commission master materials licensee, a permit issued by a Commission or Agreement State specific licensee of broad scope, or a permit issued by a Commission master materials license broad scope permittee; or
2. Meets the training and experience requirements of 10 CFR 35.390 or 10 CFR 35.490; or
3. Meets the training and experience guidelines as follows:

   i.

      a. Board certification in diagnostic radiology and subspecialty certification in interventional radiology by either the American Board of Radiology or the American Osteopathic Board of Radiology; or
      b. Three years supervised clinical experience in diagnostic radiology and one additional year of supervised clinical experience in interventional radiology; and

   ii. has 80 hours of classroom and laboratory training for byproduct material, including Y-90 microspheres, which may be concurrent with training received in accordance with Item A.3.i. in:

      a. Radiation physics and instrumentation;

b. Radiation protection;

c. Mathematics pertaining to the use and measurement of radioactivity;

d. Radiation biology; and

iii. has work experience under the supervision of an AU for Y-90 microspheres or training provided by a Y-90 microsphere manufacturer representative involving:

a. Ordering, receiving, and unpacking radioactive materials safely and performing the related radiation surveys;

b. Performing quality control procedures on instruments used to determine the activity of Y-90 microspheres and performing checks for proper operation of survey meters;

c. Evaluation of each patient or human research subject for the dose and activity of Y-90 microspheres to be administered to each treatment site;

d. Calculating and measuring the activity and safely preparing the Y-90 microspheres to be delivered to the patient or human research subject;

e. Using administrative controls to prevent a medical event involving the use of byproduct material (Appendix S to NUREG-1556, Volume 9 provides additional guidance on this subject);

f. Using procedures to control and to contain spilled byproduct material, including Y-90 microspheres, safely and using proper decontamination procedures (Appendix N to NUREG-1556, Volume 9 provides additional guidance on this subject. The procedures should address any special circumstances that may be encountered, such as electrostatic charge of microspheres and proper survey instrument and survey technique for beta emitters); and

g. Follow up and review of each patient's or human research subject's case history for Y-90 microspheres; and

DEFICIENT ITEM

Training for both proposed AU's is incomplete. Please submit in response.

B. has successfully completed training in the operation of the delivery system, safety procedures, and clinical use for each type of Y-90 microsphere for which authorization is sought. This requirement may be satisfied by satisfactory completion of a training program provided by either:

1. (Pathway 1) an AU who is authorized for the type of microsphere for which the individual is seeking authorization. This 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

2. (Pathway 2) a Y-90 microsphere manufacturer. This 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.

Training and Experience Documentation

The applicant must submit documentation of the above training and experience. For individuals obtaining clinical use experience under B.1 (pathway 1) above, this documentation shall include the clinical use cases. For individuals obtaining clinical use experience under B.2 (pathway 2) above, this documentation shall include the *in-vitro* simulated cases and a commitment that each individual will complete at least 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 B.2 (pathway 2), the licensee's commitment will include submitting documentation from the manufacturer to the appropriate NRC Regional Office within 30 days of when these three patient cases have been satisfactorily completed.

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, and
- safe handling of unsealed byproduct material.

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

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.

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

- 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).

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Inventory

Submission of a form is not a substitute for explicit commitments. Please make these commitments.

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. — OK.

Labeling

DEFICIENT ITEM

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).

Please make these explicit commitments. You can add a unique identification number but you cannot substitute that number for these commitments.

Patient Release DEFICIENT ITEM Please address this in response.

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

DEFICIENT ITEM

your Radiation Safety Committee can review changes in addition to your management, but not "instead of" your management. Please make the appropriate commitment.

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.

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.

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.)

Waste Disposal Issues DEFICIENT ITEM

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.

Your Attachment 2 Inventory Form does not take the place of explicit commitments contained here. Your Form is incomplete also. Please make these commitments explicitly in response.

ATTACHMENT 3

[EXCERPT FROM 5/9/16 LETTER]

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 will document such changes in the written directive within 24 hours after the completion or termination of the administration. The modification to the written directive will 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 commits to report any event, except for an event that results from intervention of a patient, in which any of the following occurs:

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
2. The administration of byproduct material: to the wrong individual or human research subject; via the wrong route ? material
3. The administration ~~of by product~~ by the wrong mode of treatment;
4. 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 result in a total dose or activity administered that was less than that prescribed
5. 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.

Please Correct these

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

Inventory

Stored microsphere aggregates (e.g., vials) will be physically inventoried semi-annually. This inventory will be retained for 3 years.

The inventory form to be used is Attachment 2.

Labeling

The licensee commits to the following: all Y-90 microspheres in vials, syringes, connecting tubes, and radiation shields will be placed in a container that is labeled with unique identification number. This container will be put in the radiation decay room in nuclear medicine department. The container will be logged on to the inventory form, Attachment 2.

If you have any questions, please contact me at 269-373-7407 or pjursinic@wmcc.org.

Regards,

Paul Jursinic

Paul Jursinic, Ph.D.
Radiation Safety Officer