From: Gabriel, Sandra
Sent: Sunday, February 20, 2011 3:15 PM
To: Moore, Marleen M.
Subject: Additional information for NRC amendment request, mail control 574255

Licensee: Fletcher Allen Health Care
License Number: 44-10187-03
Docket Number: 03003289
Mail Control: 574255

To: Marleen Moore, RSO

This refers to the amendment request to authorize use of SIR-Spheres.

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

1) It appears that there may be a minor error in the third line of your request, which reads: "Byproduct material: Y-90 Therasphere microspheres under CFR 35.1000." Please confirm that this should be corrected to: "Byproduct material: Y-90 SIR-Spheres microspheres under 10 CFR 35.1000."

2) The letter dated December 21, 2010 from Sirtex certifying Dr. Kikut's training was unsigned. Please submit a signed copy.

3) As you know, the NRC licensing guidance for Y-90 microspheres was updated in January 2011. Further clarification is required to fully address several items in this guidance:

   a) The licensing guidance states: "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." In your letter dated September 12, 2008 requesting to use Therasphere, you stated: "For the purposes of written directives and medical event reporting, prescribed activity will be used in lieu of prescribed dose." Please restate this commitment and confirm that it will apply to your use of both Therasphere and SIR-Spheres.

   b) The licensing guidance states: "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 prescribed dose/activity; the manufacturer; and, if appropriate for the type of microsphere used, the statement 'or dose/activity delivered at stasis.'" Please confirm that your written directives for both Therasphere and SIR-Spheres will be in accordance with this guidance (restate the language from the licensing guidance in your response).

   c) The licensing guidance states: "The 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)." In your letter dated September 12, 2008 requesting to use Therasphere, you stated: "As noted on the proposed written directive that was submitted as part of this amendment,

the maximum acceptable activity outside the treatment site due to shunting is noted, with post implant specifications based on MAA imaging values." Please confirm that your written directives for both Therasphere and SIR-Spheres will specify the maximum dose(s)/activity(ies) to specified sites outside the primary treatment site due to shunting.

d) Your current request addressed the "post-implant" written directive to be completed and signed by the AU before the patient leaves the post-procedural recovery area. Please note that this section of the licensing guidance has been changed and now states "The licensee shall record the administered dose/activity delivered to the primary treatment site and to the other specified site(s). If the administration was terminated due to 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. 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 made the assessment, the date, and the signature of an AU for Y-90 microspheres, if terminated due to stasis." You may replace your statement about the "post-implant" written directive with a commitment to follow the language in the revised licensing guidance, indicating that this will apply to your use of Therasphere and SIR-Spheres (restate the language from the licensing guidance in your response).

e) The current licensing guidance states: "Administration of Y-90 microspheres must be performed in accordance with the written directive." Please confirm that your use of both Therasphere and SIR-Spheres will be in accordance with this guidance.

f) Please confirm that you will retain each semi-annual physical inventory record for both Therasphere and SIR-Spheres for three years.

g) In your current request, you committed to report any event involving total activity that differs from the prescribed activity in the written directive by more than 20% and results in a dose that differs from the intended dose by more than 50 rem to an organ or tissue (e.g., the intended treatment site). Please note that the wording in this section of the licensing guidance is now: "The licensee shall commit to report any event in which the administration of Y-90 microspheres results in a dose that differs from the prescribed dose or the dose that would have resulted from the prescribed activity, as documented in the written directive, by more than 0.5 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 written directive, by 20 percent or more." Please confirm that your use of both Therasphere and SIR-Spheres will be in accordance with this section of the guidance (restate the language from the licensing guidance in your response).

h) Please confirm that you will comply with the medical event reporting and notification requirements as described in 10 CFR 35.3045(b)-(g) for use of both Therasphere and SIR-Spheres.

Please provide a written response to these items within 30 days under signature of senior management. You may provide this to my attention by letter or fax (610-337-5269), referencing mail control 574255. If we do not receive a reply within 30 days, we will assume that you do not wish to pursue your application.

You may contact me by telephone or e-mail with any questions. Please note that I will be out of the office for most of the next 3 weeks, but will check e-mail and voicemail messages several times each week. Thank you.

Sandy Gabriel, Ph.D.
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