Request for Additional Information

Cardinal Health – Ra-223 Radium Dichloride Xofigo® Manufacturing Facility Indianapolis, IN (CN 588680)

This RAI follows a site visit conducted on April 7, 2016.

NOTE: All references to the "letter" in the items below refer to Cardinal's additional information provided via letter dated March 16, 2016, unless otherwise indicated.

Participants:

NRC: *Patricia Pelke, Chief, Materials Licensing Branch, Region III*
Bryan Parker, Health Physicist, Materials Licensing Branch, Region III
Sara Forster, Health Physicist, Materials Licensing Branch, Region III

Applicant: *Scott Claunch, Corporate Radiation Safety Officer*
Glenn Sullivan, Corporate Health Physics Manager
Cami Still, Radiation Safety Officer (proposed)
Elizabeth Tindle, Senior Specialist, Radiation Safety

Other Cardinal Health personnel (Aaron Stevens, Margriet Hesser, and Derrick Alcaide) provided information during tour of the facility.

Also, 2 representatives from Bayer and 1 from Algeta were present: Chris Vasco (Bayer), Shaemus Gleason (Bayer), and Haavar Gausemel (Algeta).

DISCUSSION ITEMS

RADIOACTIVE MATERIALS USE:

1. Please clarify proposed revisions to the narrative overview of requested use of radioactive materials in your letter Item 2, as discussed:

   - Confirm that vial size and fill volume for Xofigo® will be limited to 10 milliliter vials with 6 milliliters per vial.

   - Update the maximum activity of actinium-227 to be contained in each A-generator to reflect actual anticipated needs.

   - In accordance with actual anticipated use, please update the maximum possession limits for radium-223 and actinium-227 to be authorized on the license.

   - For sealed source authorizations, please remove reference to Title 10 of the *Code of Federal Regulations* Section 35.65. Instead, please provide request for the needed quantities of byproduct material with atomic numbers 3-83, 84-95, 96-104, or other range as needed.

2. As needed, please clarify the proposed authorized uses of radium-223 and actinium-227 as described in your letter Item 2. The clarification should explicitly confirm that proposed use is for manufacturing, distribution of radiopharmaceutical for medical use under 10 CFR Part 32, validation, and any other needed activities. Please include your estimated timeframe(s) (i.e. – within 6, 12, 24 months, etc.) for using material as proposed.

3. As discussed and under separate cover from the other items in this record, please revise the 10 CFR 30.32(i)(1)(i) evaluation – including factors considered per 10 CFR 30.32(i)(2) – resubmitted in your letter Item 3 and originally submitted in your March 9, 2016 letter. As noted, the resubmitted evaluation should use a method appropriate for a short-term or instantaneous release, such as RASCAL.

PERSONNEL AND TRAINING:

4. Please provide a current description of the applicant's Health Physics group, including Ms. Still and Ms. Tindle. Include Ms. Tindle's position as well as training and experience.

5. Please confirm that any training assessment completed by "observation" – as specified in the letter Item 5 – permits the instructor to require remedial training or other action as the trainer deems appropriate. In the alternative, please specify the specific action that the trainer may take in the case where observation indicates that a trainee's understanding or competency may be inadequate.

6. Please define the meaning of an instructor listed as "Train the Trainer" in the letter Item 5. For example, state whether an individual listed as "Train the Trainer" must be an Authorized User listed on the license, must have training and experience equivalent to a named Authorized User, will have completed and demonstrated competency in the specific training component, or will have completed all training requirements for a specified workgroup, etc.

RADIATION SAFETY PROGRAM:

7. Please provide Xenon-133 testing results, verifying that the decay plenum will perform as designed by delaying the release of radioactive gaseous effluents (i.e., radon-219) for a minimum of 80 seconds as noted on page 9-19 of Item 9 to your August 28, 2015 application, and as specified in Item 17 to your January 11, 2016 letter.

8. Please expand the description in your letter Item 7 of how packages containing radioactive material other than A-generators will be received at the facility by providing a copy of your standard operating procedure for the receipt and opening of such packages.

Parker, Bryan

From:	Parker, Bryan
Sent:	Tuesday, April 12, 2016 8:57 AM
To:	Claunch, Scott; Sullivan, Glenn; Still, Cami
Cc:	Pelke, Patricia; Forster, Sara
Subject:	RAI from 4/7 site visit
Attachments:	Cardinal Health Ra-223 manuf license RAI from 04 07 2016 site visit.docx

Hey Scott,

Just to keep it "official," here is the RAI from our site visit last Thursday. Hope things are going well with the responses. Please take a look at this and let me know if you have any questions.

Reminder – please provide the E-plan response as a separate document.

Thanks.
Bryan