Tomczak, Tammy

From: Pelke, Patricia
Sent: Monday, April 20, 2015 11:02 AM
To: Tomczak, Tammy
Cc: Parker, Bryan
Subject: FW: New License Application Dated 1/5/2015 To Manufacture Ra-223 (Control No. 585731)
Attachments: Cardinal Health 414 LLC CN 585731 void.docx

Importance: High

Tammy,
Here is the email and attachment that needs to be included with the voided application (CN 585731). Let me know if you have any questions. Thanks - Patty

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From: Pelke, Patricia
Sent: Thursday, April 09, 2015 3:46 PM
To: 'Sullivan, Glenn'
Cc: 'Claunch, Scott'; 'Stacy Sternberg (radcondiva@aol.com)'; 'Even, Greg'; 'Ellert, Benjamin'; 'Benson, Katherine'; 'WRegits@gmail.com'; 'Hasselkus, Rick'; Parker, Bryan; Tomczak, Tammy
Subject: New License Application Dated 1/5/2015 To Manufacture Ra-223 (Control No. 585731)

Glenn,
As you are aware, my staff has been working to resolve the remaining deficient items related to the application submitted for the radium-223 nuclear pharmacy license (Control No. 584197) and we have a conference call scheduled tomorrow (4/10/15 at 9 am central time) to discuss the remaining items. We are optimistic and feel that we have a defined success path to issue the license, once we wrap up a couple of issues.

Moving on - I have reviewed the application submitted for the manufacturing license and identified several significant deficiencies, which I have described in the attached document. This new license will include the manufacture of radium-223 generators and highly risk significant radionuclides will be involved in the process. After reviewing your application, there is not sufficient information or level of detail provided for us to complete a thorough radiation safety evaluation of your proposed manufacturing and distribution process. The decision to void the application was based on the observations identified in the attachment, which are limited, but serve to represent the lack of detailed information provided in your application.

Please resubmit your application as a result of the information provided in the attachment, include current diagrams of facilities and associated equipment, provide a timeline for completion of major milestones regarding construction of the manufacturing facility so that the NRC can schedule a site visit to evaluate the constructed facility and address any safety issues/inconsistencies identified with your application. Your resubmittal needs to include sufficient detailed information for us to evaluate the hazards associated with your proposed manufacturing facility. Refer to Voided Control No. 585731 in your resubmittal.

If you and or others at Cardinal would like to discuss this further, please let me know and we can schedule a separate call. If you have any questions, please contact me at directly at 630-829-9868. We appreciate your demonstrated desire to work collaboratively to resolve outstanding issues - Patty

Patricia J. Pelke
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630-515-1259 (fax)

As a result of findings identified during an acceptance review of the application (Control No. 585731) dated 1/5/2015 Cardinal Health 414, LLC (Nuclear Pharmacy Services and Manufacturing Services) submitted for a new license for radiopharmaceutical manufacturing, we have voided the application. We understand that this new license will include the manufacture of radium-223 generators and that highly risk significant radionuclides are involved in this process. After reviewing your application, there is not sufficient information or level of detail provided for us to complete a thorough radiation safety evaluation of your proposed manufacturing and distribution process. Our decision to void the application was based on the following observations, which are limited, but serve to represent the lack of detailed information provided in your application.

The application did not include or discuss financial assurance for decommissioning in support of your request to possess 8 curies of Actinium-227 and other radionuclides with half-lives that exceed 120 days in unsealed forms. Please refer to 10 CFR, Section 30.35 regarding financial assurance requirements. Based on our review, you are required to develop a decommissioning funding plan (DFP) and providing financial assurance in the amounts driven by the DFP. You should refer to NUREG 1757, Volume 3 for guidance on developing the DFP and for acceptable financial assurance mechanisms. Additionally, we cannot issue the license until we have received these documents.

Item 5 of the application included a list of the radioactive materials you are requesting; however, the information is not provided in a manner that facilitates our understanding of your planned activities and the hazards involved. For example, the application did not include any details regarding the types and quantities of radioactive materials that would be handled day-to-day at this facility (e.g., typical quantities and maximum quantities processed on a daily/weekly/monthly basis), volatility, special handling precautions/equipment, etc. The application discusses production/storage/preparation and/or transfer of bulk radioactive drugs and reference sources-with no discussion regarding quantities (with the exception of the total possession limits included in Item 5). You also discuss calibration and reference sources – but it's not clear whether or not you intend to manufacture them as well, or merely possess them for use at your facility to calibrate your instruments. Also included is leak test, wipe test or samples for analytical testing and instrument calibration – what do you mean by "samples" and "analytical testing" and will you be performing these in-house only or as a service to customers?

Item 7&8 of the application discuss a Manufacturing RSO (MRSO) and the application identifies a Corporate RSO. There are statements in this section stating the MRSO has corporate responsibility at the local level and the MRSO has authorization from the Corporate Radiation Safety Committee to cease any unsafe activities. Additionally, this section also includes a paragraph indicating that "in the absence of the MRSO, another authorized user must assume the duties of the MRSO." You also included an organization chart in Attachment A – but without further discussion, it is difficult to determine who will have ultimate responsibility over the ra-223 manufacturing facility. The application must clearly delineate roles and responsibilities and if the MRSO has ultimate responsibility for the ra-223 manufacturing facility and NRC licensed

requirements, that position cannot be replaced by merely designating "another authorized user" and including an MRSO delegation of authority in your license application.

Item 9 very generally describes facilities. You state that access is restricted to authorized personnel who have work to perform in this area – you need to define these individuals or identify by category of worker, who has access to which areas within your facilities and that these individuals receive training commensurate with their roles & responsibilities relative to the ra-223 production. Additionally, this section includes statements such as "a robot arm or similar picks up ..." if not a robot arm, then what will accomplish this task; the finished product will be moved to Warehouse for final distribution – how will this transfer be accomplished; the HC 1/5 Carousel will store actinium generators that have been pre-processed elsewhere – this statement requires further clarification – "elsewhere within the ra-223 manufacturing facility, offsite by another vendor, etc.; there is a statement regarding the dedicated transfer of the shielded Pig from elsewhere in the building to the Hot Cells – again define where elsewhere is within the ra-223 manufacturing facility; there are no diagrams included in Attachment C (as described); and you indicate architectural drawings are available upon request, but we understand these facilities have not been finalized and continue to be reviewed/revised. We want to see perfected diagrams that represent your final facilities.

Based on these observations, we would expect to identify additional deficiencies related to the bioassay program, air sampling and effluent monitoring system, surveys, emergency procedures, details of the final products you intend to distribute, and your program to maintain specialized equipment in support of the radiation risk associated with your proposed manufacturing process.

Please resubmit your application as a result of the information provided above, include current diagrams of facilities and associated equipment, provide a timeline for completion of major milestones regarding construction of the manufacturing facility so that the NRC can schedule a site visit to evaluate the constructed facility and address any safety issues/inconsistencies identified with your application. Your resubmittal needs to include sufficient detailed information for us to evaluate the hazards associated with your proposed manufacturing facility. Refer to Voided Control No. 585731 in your resubmittal.