UNITED STATES
NUCLEAR REGULATORY COMMISSION
REGION I
475 ALLENDALE ROAD
KING OF PRUSSIA, PENNSYLVANIA 19406-1415

August 24, 2010

Docket No. 030-38331 License No. 34-32780-02
Control No. 573262

Willie Regits, Ph.D.
Director, Health Physics, Nuclear Pharmacy Services
Cardinal Health
Nuclear Pharmacy Services
7000 Cardinal Place
Dublin, OH 43017

SUBJECT: CARDINAL HEALTH, REQUEST FOR ADDITIONAL INFORMATION CONCERNING APPLICATION FOR NEW LICENSE, CONTROL NO. 573262

Dear Dr. Regits:

This is in reference to your letter and application dated July 23, 2010, applying for a Nuclear Regulatory Commission license. In order to continue our review, we need the following additional information:

1. Your letter states that the production and drug manufacturing processes are linked together for synthesis of radioactive drugs, according to the U. S. Food and Drug Administration (FDA) requirements. Please note that the NRC issues separate licenses for the production of radionuclides in an accelerator, and for the production of radiopharmaceuticals (a radiopharmacy license). Your License No. 34-29200-01MD authorizes radiopharmaceutical production and distribution at the East Hartford, Connecticut location. Your application for this license to produce radionuclides in an accelerator at that same location should not include activities that are covered by the radiopharmacy license. In addition, please note that the NRC does not regulate the operation of the accelerator itself, but only with the activities that involve the radionuclides produced by activation (purposefully and incidentally) due to the operation of the accelerator.

   a. Please state the point in your production and processing of the radionuclides from the accelerator at which those radionuclides would be considered to be transferred to the radiopharmacy license.

   b. The following sections of you application appear to refer to activities which are either associated with accelerator operation, or radiopharmacy. Confirm which of these sections should be commitments in your license, and which are for information only; alternately, you may re-submit your application with only the applicable information: Item 9.2, General Description – it is difficult to determine which of the described areas would be under the cyclotron license and which under the radiopharmacy; Item 9, Figure 4; Item 9.3, Cyclotron and Safety Features; Item 9.7.IV, Calibration of Dose Calibrators; Items 10.8 and 10.9,

procedures for receiving wastes from customers; Items 10.13 and 10.14, product labeling and containers; Item 10.17, Cyclotron Operation.

2. Your "Radioactive Materials License Application" cover sheet contains a box titled "Confidential and/or Proprietary Information Notice." If you believe that your application contains material that should be withheld from public disclosure, you must follow the requirements in 10 CFR 2.390 "Public inspections, exemptions, and requests for withholding." The information must be submitted with an affidavit and marked in accordance with 10 CFR 2.390(b), and the NRC will inform you if the request is granted or denied as described in 10 CFR 2.390(c). If you believe that the application you submitted contains such information, you must provide this information required by 10 CFR 2.390 immediately, or retract the application and submit an application that does not contain proprietary information.

3. Item 5.E of your application request 5 curies of radionuclides with atomic numbers 3 through 83, as incidental radioactive material, foils, etcetera. Please specify the maximum quantity for individual radionuclides (for example "1 curie per radionuclide and 5 curies total").'

4. Item 5. E of your application requires the provision of financial assurance for decommissioning. 10 CFR 30.35 requires that licensees authorized to possess and use unsealed licensed material with a half-life greater than 120 days in quantities greater than those described in 10 CFR 30.35(d) must submit certification for financial assurance or a decommissioning funding plan (DFP) in any new or renewal application. This plan must include an actual estimate of the costs for decommissioning your facility and a mechanism to fund the Plan. The appropriate level of detail for the cost estimate is discussed in Appendix A.3 of NUREG-1757, "Consolidated NMSS Decommissioning Guidance," Volume 3, "Financial Assurance, Recordkeeping, and Timeliness" (NUREG-1757, Vol. 3). Please follow closely the recommended wording for financial assurance mechanisms found in Appendix A to NUREG-1757, Vol. 3. The current NUREG-1757, Vol. 3 guidance can be found on the NRC website using the following URL: http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1757/v3/. Please note that you may submit your DFP and cost estimate for review and acceptance, prior to obtaining the financial assurance instrument.

5. For Item 5.F of your application, in accordance with NUREG-1556, "Consolidated Guidance About Materials Licenses," Volume 21, "Program Specific Guidance About Licenses for Production of Radioactive Materials Using an Accelerator," (NUREG-1556, Vol. 21) Section 8.5.1, identify all the sealed sources you wish to possess by radioisotope, manufacturer, model number and the maximum amount of licensed material in the source.

6. Item 7 of your application states that the facility radiation safety officer (RSO) will be James Matthews, the Manufacturing RSO (MRSO). However, it shows his location as St. Louis, Missouri. Please name an individual who will be on site in East Hartford as the RSO for this license, and submit their qualifications.

7. Beginning in Item 7 and throughout other sections of the application, you refer to

compliance with State regulations. Please confirm that, in each location which refers to "State regulations", it should read "State and/or federal regulations".

8. Item 8.7.2, "Individuals Authorized to Handle Licensed Material,": in NUREG-1556, Vol. 21, guidance about "Possession Licenses for Production of Radioactive Material Using an Accelerator," states that authorized users should have: (1) a college degree at the Bachelor's level, or equivalent training and experience in physical, chemical, or biological sciences or in engineering; and (2) training and experience commensurate with the scope of proposed activities such as handling of activated targets and products associated with accelerator activities.

   a. You did not provide any information regarding academic qualifications for any of the proposed authorized users. Please provide information for each proposed authorized user which indicates that the individuals have either a college degree, or equivalent training and experience in sciences or engineering.

   b. The only information provided in support for Robert Droege was the experience in handling materials produced in an accelerator. Please provide information that demonstrates he has had training in (a) principles and practices of radiation protection, (b) radioactivity measurements, standardization, and monitoring techniques and instruments (c) mathematics and calculations basic to the use and measurement of radioactivity, and (d) biological effects of radiation.

   c. The information provided in support of William Rahardjo did not include any training or education in the biological effects of radiation. Please provide documentation which indicates that he was provided training in this area.

9. Item 8 of your application did not describe a training program for ancillary personnel (maintenance, security, clerical staff, etc.) who may need to work in the vicinity of radioactive materials. The training given to each group should be commensurate with the duties and responsibilities of the group. The training program must assure that personnel are instructed before assuming duties with, or in the vicinity of, licensed materials and specify a frequency for periodic refresher training. Appendix F of NUREG-1556, Vol. 21 addresses radiation safety training topics and may be helpful in developing your response.

10. In accordance with NUREG-1556, Volume 21, Section 8.9. "Facilities and Equipment," provide diagrams of your facility that show the locations of the accelerator, delivery lines, shielded areas and equipment (hot cells, waste storage bunkers, materials storage vaults, etc), the proximity of radiation sources to unrestricted areas, and other items related to radiation safety (target transfer lines, radiation monitors, restricted areas, etc). Diagrams should be drawn to scale. In addition, please describe the type and amount of shielding used in the various areas, and confirm that you have, or will establish, a preventative maintenance program for the facilities and equipment used for production, transport and handling of the licensed materials.

11. In accordance with NUREG-1556, Volume 21, Section 8.9, "Facilities and Equipment,", provide a diagram of the ventilation system, including ventilation for equipment such as

hot cells, glove boxes, or fume hoods; air supply and exhaust lines; and filtration and monitoring systems. Describe pertinent air flow rates, differential pressures, and/or performance to be achieved, if such information is not already described in Item 9.6. In addition, verify that the ventilation systems ensure that effluents are ALARA, that effluents are within the limits of 10 CFR 20.1301, and that effluents are within the ALARA constraints for air emissions established in 10 CFR 20.1101(d).

12. Item 9 of the application did not include descriptions of the instrumentation used for air sampling measurements, air monitoring for occupational dose assessment, or for monitoring effluent releases. In accordance with NUREG-1556, Vol. 21, Section 8.10.2, please provide this information.

13. Item 9 of the application does not address systems for target transfer and processing, hot cells or remote handling systems and/or equipment for processing targets. If target processing is performed under the radiopharmacy license, you should confirm this and ensure that those activities are included in your authorized activities under the radiopharmacy license. If target processing is performed under this accelerator license, you should provide the information requested as requested in NUREG-1556, Vol. 21, Section 8.10.2.

14. In accordance with NUREG-1556, Vol. 21, Section 8.10.3, confirm that you have developed, and will implements and maintain written procedures for licensed material accountability and control to ensure that 1) license possession limits are not exceeded, 2) licensed material ion storage is secured from unauthorized access or removal, 3) licensed material not in storage is maintained under constant surveillance and control, and 4) records of receipt, production, transfer and disposal of licensed material will be maintained. A discussion of issues related to these procedures may be found in Section 8.10.6.

15. Item 9.7 of the application includes the “Neutron and Photon Survey of the Cyclotron Vault…East Hartford, CT.” This survey appears to be provided to demonstrate that radiation exposures to members of the public are not likely to exceed 100 millirem in a year, although this information is not required to be submitted with the application. Based on the review of this information, please address the following:

    a. The neutron survey results, based on one simulated production run lasting 2 hours, does not appear to be valid because the Landauer CR-39 neutron dosimeter is not sensitive enough to detect doses of less than 10 millrem. Therefore, the “zero” results that you reported for the dosimeters is not correct because, in fact, the dosimeters cannot detect doses below 10 millirem. If you wish to use the dosimeters to demonstrate that no neutron doses are received, the dosimeters should be left in place for much longer periods of time. Please confirm that you will not base you public dose on the dosimeter results reported in this application.

    b. Please correct the diagram and/or dosimeter location descriptions, because dosimeter locations 8, 9,and 13 do not appear to match the descriptions.

    c. The NRC limits to the public are 2 millirem in any one hour, and 100 millirem in

any one year. You did not specify the number of runs you would do in a year, but based on your dose rate survey measurements, several of your public areas (Supply Room and roof) have gamma dose rates of greater than 1 millirem in an hour, and location 29 had a gamma dose rate of 3 millirem per hour and a neutron dose rate of 0.3 millirem per hour. Explain how you will know if public access to these areas occurs during a run, or how you will limit public access to these areas during a run to confirm that members of the public do not receive more than 2 millirem in any one hour, or more than 100 millirem in any one year.

16. Item 10.1.2 of your application, Table 1, lists the ALARA investigation levels and states that the Radiation Safety Committee will review occupational exposures that exceed the Level II investigation level "trimesterly". Please state what you mean by "trimesterly" (for example, 4-month intervals, or 3 times each year, or once every 4 months, etcetera).

17. Item 10.1.3 of your application states that the Corporate RSO will review occupational exposures quarterly. Item 10.6 stats that the Corporate RSO or the Manufacturing RSO will investigate doses to individuals which exceed the ALARA investigation levels in a quarter. Table 1 in Item 10.1.2 of your application states that, for extremities, the ALARA Level I investigation dose is 25 rem and the ALARA Level II investigation dose is 40 rem. These investigation levels are large fractions of the total annual dose limit of 50 rem to extremities. Explain how you will prevent workers from exceeding the annual dose limit to extremities, since it appears that there is no review of total annual dose to date, and an individual could exceed the annual dose in three or more quarters without exceeding the Level I investigation level. Also, explain why the review will be performed quarterly, considering that Item 10.2 states that extremity monitors will be exchanged at least monthly.

18. Item 10.2 "Personnel Monitoring Program" states that whole body dosimetry will be provided to "personnel who enter restricted areas under the circumstances described in State regulations…" Confirm if these circumstances include activities in which personnel may be handling targets or working in areas that contain activated materials. Confirm that persons who handle or work in the vicinity of targets, foils, transfer lines or other activated materials that may cause an extremity dose greater than 10% of the limit will be provided with extremity monitors.

19. Item 10.7, "Emergency Procedure," of your application refers only to spill procedures. In accordance with NUREG-1556, Volume 21, Section 8.10.6, confirm that you will develop written emergency procedures to use for accelerator-specific emergencies, such as target failures, malfunctions of transfer lines, malfunctions of air supply or exhaust systems, or alarms or other identification of high radiation levels in exhaust monitors or systems. Some of this information is stated in Item 9, "Facilities and Equipment" of your application.

20. Item 10.8 of your application is "Procedures for Returning Radioactive Waste from Customers" and Item 10.9 is "Customer Procedures for Return…to Cardinal Health Nuclear Pharmacies." These procedures appear to refer to items that would be distributed under the radiopharmacy license, not the accelerator production license. Confirm that you will not be receiving radioactive wastes under the accelerator

production license, and that these procedures are not applicable to this application. In addition, revise Item 11.1, "Waste Generated" to remove the references to waste accepted from customers.

21. Item 10.10, "Area Survey Procedures," refers to compliance with NUREG-1556, Volume 13, "Program-Specific Guidance About Commercial Radiopharmacy Licenses." These procedures are equivalent to those in Appendix M of NUREG-1556, Vol. 21 and their use would be consistent with your radiopharmacy license. Please note, however, that your minimum survey sensitivity of 0.1 millirem per hour may make it difficult to demonstrate that public dose limits are less than 100 millirem in a year. Assuming that dose rates are constant over 2000 work-hours in a year, a dose rate of 0.05 millirem per hour would need to be detected, unless run-time and occupancy is controlled. No response to this item is required.

22. Item 10.11, "Distribution Procedures," states that "Transportation will be an act licensed under the nuclear pharmacy or transferee licensee in all cases." There is no "licensing' of transportation activities. In addition, this statement is contradicted by Item 10.12, "Procedure for Package and Transporting Radioactive Materials" and Item 11.4, "Waste Disposal Procedures." Confirm that persons who prepare packages for shipment and/or transport material will be trained in accordance with DOT requirements, and that any packages offered for transport will be prepared in accordance with DOT requirements.

23. Items 10.13, "Container Labeling," 10.14, "Product Shielding," and 10.18, "PET Compound Production," appear to overlap with your radiopharmacy license. If this is not true, and these sections refer to activities that will be performed ONLY under the radiopharmacy license, confirm that these sections are not applicable to this license application. Alternately, you may re-submit your application with only the required sections.

24. Item 11.4, "Waste Disposal Procedures," states in sub-item 1.h. that certain wastes that are surveyed but not yet able to be released "...may be placed within the waste container or outside of the waste container for further decay in storage." Explain how you will maintain tracking of these wastes, given the "container emptying rotation cycle" that is described Item 11.3.

Current NRC regulations and guidance are included on the NRC's website at www.nrc.gov; select **Nuclear Materials; Medical, Academic, and Industrial Uses of Nuclear Material;** then **Regulations, Guidance, and Communications.** You may also obtain these documents by contacting the Government Printing Office (GPO) toll-free at 1-866-512-1800. The GPO is open from 7:00 a.m. to 6:30 p.m. EST, Monday through Friday (except Federal holidays).

We will continue our review upon receipt of this information. Please reply to my attention at the Region I Office and refer to Mail Control No. 573262. If you have any technical questions regarding this deficiency letter, please call me at (610) 337-5040.

If we do not receive a reply from you within 30 calendar days from the date of this letter, we will assume that you do not wish to pursue your application.

Sincerely,

Original signed by Elizabeth Ullrich

Betsy Ullrich
Senior Health Physicist
Commercial and R&D Branch
Division of Nuclear Materials Safety

cc:
James R. Matthews, Radiation Safety Officer

DOCUMENT NAME: G:\WordDocs\Current\Lic Def Letter\L34-32780-02.573262.doc

SUNSI Review Complete: EUllrich

After declaring this document "An Official Agency Record" it **will** be released to the Public.

To receive a copy of this document, indicate in the box: "**C**" = Copy w/o attach/encl "**E**" = Copy w/ attach/encl "**N**" = No copy

OFFICE	DNMS/RI	N	DNMS/RI		DNMS/RI			
NAME	EUllrich/EU							
DATE	8/24/2010							

OFFICIAL RECORD COPY