From: Nguyen, Janice
To: Reid Gadziala
Subject: NRC Request for Additional Information for PharmaLogic Ltd. (Mail Control Number 612086)
Date: Tuesday, July 23, 2019 2:15:00 PM

Licensee: PharmaLogic Ltd.
License No.: 44-30124-01MD
Docket No.: 030-33449
Control No.: 612086

PLEASE CONFIRM RECEIPT OF THIS REQUEST FOR ADDITIONAL INFORMATION BY RETURN EMAIL

Dear Dr. Gadziala:

In the letter dated April 25, 2019, you requested a license amendment to add a new manufacturer of Ge-68/Ga-68 generator, the IRE Galli-Eo. In order to continue our review, please provide the following additional information:

1. Please commit to the following statements regarding each manufacturer of Ge-68/Ga-68 generator:

    - We will provide instructions and/or training on the manufacturer's procedures to all individuals involved in Ge-68/Ga-68 generator use, commensurate with the individual's duties to be performed;
    - We will not open, breach, or physically modify the Ge-68/Ga-68 generator in any way;
    - We will follow the manufacturer's procedures, including: generator set-up; generator elution; Ge-68 breakthrough testing and frequency when in use; and final disposition;
    - We will elute the generator in accordance with the manufacturer's stated frequency and procedures to minimize the concentration of Ge-68 in the eluate;
    - We will not use an expired generator for preparation of materials that will be administered to patients or human research subjects;
    - We will only use a generator that has a clearly marked expiration date;
    - After installation, we will perform the conditioning procedure following the manufacturer's instructions properly disposing of the conditioning eluates prior to the first use of eluate for testing or human use;
    - We will develop and implement written procedures for the determination of breakthrough that will detect whether the eluate exceeds the manufacturer's 0.001 percent breakthrough limit, i.e., the presence of Ge-68 in excess of a ratio of 0.01 uCi Ge-68 per 1 mCi Ga-68;
    - During the course of breakthrough testing, if the eluate exceeds 0.001 percent breakthrough limit, the eluate will not be distributed or administered to a patient or human research subject;
    - We will maintain a record of the breakthrough tests for at least 3 years. These tests should include the ratio of the measured activity of Ge-68 per Ga-68 corrected for the time of elution, time and date of the elution, time and

date of the measurement, and the name of the individual who made the measurement;

- We will notify by telephone the NRC Operations Center (301-816-5100) and the manufacturer/distributor of the generator within 7 calendar days after discovery of a generator that is unable to meet the manufacturer's stated Ge-68 breakthrough limits. A failed generator effective date will be when the breakthrough calculation was performed, which should be no more than 7 days from the date of the previous breakthrough calculation;
- We will include in the report to the NRC Operations Center the manufacturer, model number, and serial number (or lot number) of the generator; the results of the measurement; the date of the measurement; whether dosages were administered to patients or human research subjects; when the manufacturer/distributor was notified; and the action taken;
- We will send a written report to the appropriate NRC Regional Office within 30 days after discovery of a generator that is unable to meet the manufacturer's stated breakthrough limits of Ge-68 on multiple occasions rendering the generator unusable in human patients and research subjects;
- We will include in the written report the action taken by the licensee; probable cause and assessment of failure in the licensee's equipment, procedures, or training that contributed to the excessive readings if an error occurred in the licensee's breakthrough determination, and the information in the telephone report made as described above;
- We will conduct surveys of all areas of licensed material use, including the generator storage and kit preparation areas, for contamination each day of use; and
- We will develop and implement written emergency procedures for leaking or damaged generators.

2. Please note that the NRC is considering issuing revised licensing guidance for Germanium-68/Gallium-68 Pharmaceutical Grade Generators. Therefore, please confirm if you wish to be authorized to make minor revisions to your Ge-68/Ga-68 generator program, and that you will follow the conditions below. An applicant initially applying for authorization for use of a Ge-68/Ga-68 generator for preparation of Ga-68 radiopharmaceuticals for imaging and localization studies 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 protection program:

   a. The revision does not require a license amendment under 10 CFR 35.13;
   b. The revision is based upon NRC's current guidance for use of the Ge-68/Ga-68 generator to prepare Ga-68 radiopharmaceuticals for imaging and localization studies under 10 CFR 35.1000 posted on the NRC Medical Uses Licensee Toolkit;
   c. The revision has been reviewed and approved by the licensee's Radiation Safety Officer and management;
   d. The affected individuals are instructed on the revised program before the change is implemented;
   e. The licensee shall retain a record of each change for 5 years; and

f. The record will include a copy of the current guidance for use of the Ge-68/Ga-68 generator to prepare Ga-68 radiopharmaceuticals for imaging and localization studies under 10 CFR 35.1000, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee management representative who 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.

3. As referenced in NRC Memorandum, "Revision of Technical Basis for Granting Specific Exemption from Decommissioning Funding Plan Requirement for Germanium-68/Gallium-68 Generators," issued on July 13, 2017 (Accession No. ML17075A487), Regional Administrators can issue an exemption from having a decommissioning funding plan, when requested, only for Ge-68/Ga-68 generators and only if a legally binding agreement is in place for the licensee to return the generators to the manufacturer or distributor when the generators are no longer used. Per the memorandum, the legally binding agreement should be dated.

   Please note that the legally binding agreement was not dated by the Cardinal Health management representative. Please resubmit this agreement, with signatures and dates for both parties.

We will continue our review upon receipt of the requested information. You may respond to my attention in writing by letter, email (if letter is signed by senior management and scanned into a pdf format), or fax (610-337-5269), referencing mail control number 612086. Please provide a response as soon as possible. If you have any questions regarding this deficiency letter, please call me at (610) 337-5006.

Current NRC regulations and guidance are included on the NRC's website at www.nrc.gov; select **Nuclear Materials; Med, Ind, & Academic Uses;**then **Licensee Toolkits, see our toolkit index page.** 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 8:00 a.m. to 5:30 p.m. EST, Monday through Friday (except Federal holidays).

Thank you in advance for your help!

Sincerely,

Jan

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