Reply to a Notice of Violation

November 22nd, 2005

U.S. Nuclear Regulatory Commission Materials License No. 44-30124-01MD

U.S. Nuclear Regulatory Commission
ATTN: Document Control Desk
Washington, D.C. 20555

Subject: Response to Docket No. 03033449

To Whom It May Concern:

Todd Jackson, of the U.S. Nuclear Regulatory Commission, conducted a safety inspection of our Pharmalogic, Ltd. facility in Williston, Vermont (hereafter referred to as Pharmalogic) on August 23rd, 2005. We received a Notice of Violation(s) on October 18th, 2005 from James P. Dwyer, Chief of the Commercial and R&D Branch, Division of Nuclear Materials Safety of Region I of the U.S. Nuclear Regulatory Commission, which was dated October 8th, 2005. In the Notice of Violation, there were three violations listed specifically for Pharmalogic, Ltd. Each violation will be addressed, with (1) the reason for the violation presented (copied directly from the Notice of Violation), (2) the corrective steps that have been taken and any results achieved noted, (3) the corrective steps that will be taken to avoid future violations, and (4) the date when full compliance will be achieved (e.g., Violation C, subpart 1 will be C1).

Violation A:

A1:

"10 CFR 20.1502(b)(1) requires that each licensee monitor the occupational intake of radioactive material by and assess the committed effective dose equivalent to adults likely to receive, in 1 year, an intake in excess of 10 percent of the applicable annual limit of intake (ALI) in Table 1, Columns 1 and 2, of Appendix B to 20.1001-20.2402.

10 CFR 20.1204(a) requires, for purposes of assessing dose used to determine compliance with occupational dose equivalent limits, that the licensee shall, when required under 20. 1502, take suitable and timely measurements of –

(1) Concentrations of radioactive materials in air in work areas;
(2) Quantities of radionuclides in the body
(3) Quantities of radionuclides excreted from the body;
(4) Combinations of these measurements.

IE07

Contrary to the above, as of August 23, 2005, the licensee did not monitor the occupational intake of radioactive material by and assess the committed effective dose equivalent to adults likely to receive, in 1 year, an intake in excess of 10 percent of the applicable ALI by making suitable and timely measurements of (1) concentrations of radioactive materials in air in work areas; (2) quantities of radionuclides in the body; (3) quantity between 3.2 and 4 curies of iodine-131 sodium iodide each month, and who therefore were likely to receive, in 1 year, an intake in excess of 10 percent of the inhalation ALI of 50 microcuries, by making measurements of the quantity of iodine-131 in the body in an inaccurate and irreproducible manner. For example:

(1) Calibration of the system used to monitor the thyroid is inadequate. Calibration utilized a small iodine-131 capsule that could be placed in a variable position relative to the detector resulting in calibration factors ranging from 2419 up to 13,123 cpm/microcurie. Additionally high voltage settings were not controlled by procedure, which could cause the calibration factor to change in an uncontrolled manner;

(2) Detector background count rate varied significantly and in an uncontrolled manner, based on the background count rates recorded. Background could vary between the time background was measured and the time the thyroid measurements were made. The detector, while collimated to focus on the thyroid and minimize background influences from elsewhere in the controlled area, was pointed at the table upon which receipt surveys for incoming packages containing radioactive material were performed. If packages are being surveyed or opened during some portion of the bioassay procedure, a short-term fluctuation in background could affect measurements in an undetermined amount.

(3) Background measurements were made with the detector placed on the chest. This practice may contribute to background variability because placement on the chest may be over muscle or lung tissue, each of which will likely produce different background count rates. An alternative practice widely used is to measure background with the detector placed against the large muscle of the thigh. This also reduces the influence on the background from any radioactive iodine in the thyroid since the thigh is farther away from the thyroid.

(4) Recorded measurement data was incomplete. Two different scalars were used with the bioassay detector since July 2003 to make bioassay measurements, although records only indicate one serial number for all measurements. The date when the scalars were exchanged is not recorded. Additionally, only average background and net thyroid counts were recorded, making it impossible to verify manual calculations."

A2:

Regarding the bioassay, the corrective steps taken by Pharmalogic, Ltd. are as follows:

1) The high voltage settings were calibrated for the bioassay detector.

2) Background measurements are now made with the detector placed against the large muscle of the thigh.
3) A concerted effort was made to be sure that readings were not conducted when the background was influenced by incoming radioactive packages were being delivered or surveyed.
4) The individual measurements of both background and net thyroid counts were recorded.

A3:

The following steps will be taken (in addition to the above) to correct the situation, which led to Violation A:

1) The high voltage on the bioassay detector will be calibrated annually.
2) Based on the provisions of NRC Regulatory Guide 8.20 with respect to the bioassay action levels, frequency, and personnel to be monitored, only authorized users (pharmacists) will subject themselves to a bioassay using the bioassay detector. This should minimize any effect of an incoming package affecting background readings, as the authorized user(s) will be more attentive to changes in background than regular personnel. The procedure for the bioassay will be under Appendix A (which will explain the action levels and frequency of the bioassay), and a copy of the new bioassay record will be in Appendix B.

A4: The corrective steps in A3 will be put into effect on December 1, 2005.

Violation B:

B1:

"10 CFR 20.1101 requires that the licensee periodically (at least annually) review the radiation protection program content and implementation.

Contrary to the above, as of August 23, 2005, no periodic audits of the radiation safety program had been performed since the last NRC inspection on July 2, 2003."

B2:

We have looked into having an experienced authorized user from outside of the pharmacy conduct annual reviews of the radiation protection program content and implementation and believe we have found at least one individual who can provide that service.

B3:

An experienced authorized user from outside the pharmacy shall conduct an annual review of the radiation protection program content and implementation.

B4:

The corrective steps in B3 will be put into effect on January 1, 2006.

Violation C:

C1:

"10 CFR 32.72 requires that a licensee that manufactures, prepares, or transfers for commercial distribution radioactive drugs containing byproduct material for use by persons authorized pursuant to 10 CFR Part 35: (1) possess and use instrumentation to measure the radioactivity of radioactive drugs; (2) have procedures for use of the instrumentation; and (3) measure, by direct measurement or by combination of measurements and calculations, the amount of radioactivity in dosages of alpha-, beta-, or photon-emitting radioactive drugs prior to transfer for commercial distribution. In addition, the licensee shall:

(1) Perform tests before initial use, periodically, and following repair, on each instrument for accuracy, linearity, and geometry dependence, as appropriate for the use of the instrument; and make adjustments when necessary; and
(2) Check each instrument for constancy and proper operation at the beginning of each day of use.

Contrary to the above, as of August 23, 2005, the licensee did not have procedures for use of the instrumentation to measure the radioactivity of radioactive drugs. Specifically, on two occasions the results of dose calibrator accuracy testing were greater than the indicated acceptance criteria of +- 5% and no corrective action was taken. The licensee was not able to provide a procedure defining corrective action was taken. The licensee was not able to provide a procedure defining corrective actions to be taken in response to measurements outside the acceptance criteria."

C2:

To correct the violation noted above, our new procedure would follow the example of NUREG-1556, Vol. 13 (Program-Specific Guidance About Commercial Radiopharmacy Licenses – Final Report), under Appendix O (Model Dose Calibrator Testing Program), subparts number 6-6.4.

C3: Please see C2 above.

C4: The corrective steps in C3 will be put into effect on January 1, 2006.

If my manager, Tom DeFranco, or I can be of more assistance to the NRC, please don't hesitate to contact us at Pharmalogic, Ltd. We can be reached by phone at 802-862-9944, or by e-mail at pharmalogicltd@yahoo.com.

Sincerely,

Stephen Sopchak, R.Ph., RSO
Pharmalogic, Ltd.
Williston, VT 05495

Appendix A

I131 PERSONNEL BIOASSAY

Thyroid bioassay will be performed in accordance with the provisions of NRC Regulatory Guide 8.20 with respect to action levels and the frequency specified in this guide. All individuals handling an open form of quantities of radioactive iodine that are equal to or exceeds those quantities shown in Table 1 of NRC guide 8.20 shall be required to have thyroid bioassay. Any worker sufficiently close to the handling process (within a few meters, and in the same room as the worker handling the material) will also have thyroid bioassay procedures performed. Individuals compounding Iodine-131 capsules will perform bioassay weekly.

1. Obtain an I131 capsule for counting purposes. (Activity of the I131 capsule must get at least 100,000 CPM). Insert the I131 capsule into the neck phantom. Position the probe directly in front of the capsule and count 3 times for one minute each and average the counts.
2. Determine the background of the counting system. Position the probe on your thigh and count 3 times for one minute each and average the counts.
3. Position the probe onto the front of your neck and count 3 times for one minute each and average the counts
4. Be aware of background radioactivity that may effect counts. (example: incoming packages, dose drawing etc.)
5. Record and enter the data in the Microsoft Excel Bioassay Record program in the computer to determine if there has been any I131 uptake in the thyroid. Measurements of the thyroid will be compared to the I131 capsule housed in the neck phantom to take into account tissue attenuation from the employees neck.

6. The action level of I131 uptake is 0.04 uCi.

7. To compute the amount of I131 uptake: if your average background in CPM's is larger than your thyroid counts then there is no uptake and no reason to take action. If your thyroid counts are larger than the background counts then you need to figure out the amount in uCi. Take the average thyroid counts and subtract the background. Multiply this by the size of the I131 capsule you used for counting in uCi. Now divide this number by the capsule counts in CPM minus the background. This gives you I131 uptake activity in uCi. If it is greater than 0.04 uCi, these results will be investigated by the RSO, documented and corrective actions taken place to prevent further uptake.

Appendix B

BioAssay Record

Date 11/23/2005 Person Being Assayed:

Equipement Used : Ludlum Model 2200 SCA with High energy Lud 44-10 probe

Activity of Capsule Used :		0	uCi	
Count of Capsule :		0	cpm	
Background Count		0	cpm	
Counts of Thyroid	1	0	cpm	
	2	0	cpm	Avg. CPM 0
	3	0	cpm	

$$\textbf{M.D.A.} = \frac{[(3.3)\ (\text{sq.rt.}((2Rb)/tb))]}{CF} = \textbf{\#DIV/0! uCi ***}$$

*** if not below .04 uCi recalibrate

MDA	minimum detectable activity
Rb	background counting rate
tb	time taken to count background
CF	calibration factor - the cpm per uCi of the capsule

$$\textbf{I-131 Thyroid Activity} = \frac{\text{(avg. neck cnt.- bkg. cnt.) (uCi capsule)}}{\text{(capsule CPM - bkg. cpm)}}$$

I-131 Thyroid Activity = #DIV/0! uCi in the thyroid If less than 0 uCi assume no uptake

NRC reporting limits : greater than ----------> 0.14 uCi/week
greater than or equal to ----> 1.4uCi/quarter

R.S.O. - _____

Action Necessary : YES NO