



05/25/94

United States Nuclear Regulatory Commission  
Region I  
475 Allendale Road  
King of Prussia, Pennsylvania 19406-1415

License No. **44-30124-01MD**  
Docket No. 030-33449  
Control No. 119277

Dear Sir,

PharmaLogic Ltd. is requesting amendments to License number **44-30124-01MD** for:

1. Item **9.4** Special Equipment for Handling Millicuries Quantities of Liquid Radioiodine.
2. Item **10.10** Precautionary Measures for Handling Millicurie Quantities of Liquid Radioiodine.
3. Authorization for distribution of used generators to **PharmaLogic** customers.

Enclosed, please find written procedures for **Item 9.4**, **Item 10.10**, and written description as described in **Draft Regulatory Guide FC 410-4**, dates **August 1985**, page **42(4.2)** for distribution of used generators.

Also, find enclosed the appropriate amendment fee.

If you have any **further** questions or comments, please call me at 1-802-862-9944.

Sincerely,

William Chatoff R.Ph., BCNP

Log	June 13
Remit for	
Check No.	1120
Amount	\$490
Pay to the order of	30
Special Instructions	Amo
Date	6/20/94
By:	[Signature]

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PharmaLogic Ltd. 9 Krupp Drive Williston, Vermont 05495

**Item 9.4 Special Equipment for Handling Millicurie Quantities of Liquid Radioiodine**

A radioiodine **fume** hood will be utilized for dispensing liquid <sup>131</sup>-Sodium Iodine and compounding Iodine-131 therapy capsules. The effluent **from** this **fume** hood will be connected directly into the standard laboratory **fume** hood.

**Two(2)** charcoal filters **will** be used in the Iodine-131 fume hood. Each filter is one foot square and one inch thick. One filter **will** be stacked on top of the other so that the Iodine-131 **will** be exhausted through two inches of charcoal. This ensures a trapping efficiency of 98%. Measurements with an anemometer of air flow at the arm ports for this Iodine-131 fume hood show a minimum linear air flow of 50-70 **feet/min** with a minimum total exhaust of 25 CFM.

The efficiency of this trapping system is checked weekly using a survey meter. The filters are removed and the radiation levels at their surfaces is measured with a pancake probe type survey meter. When the **mr/hr** level of the top filter is equal to or greater than **10%** of the *m r h* level of the bottom filter, the bottom filter will be replaced. Air sampling for volatile <sup>131</sup>-Iodine will be performed in conjunction with the use of the radioiodine **fume** hood.

## **Procedures for Completion of 131-I Air Monitoring**

The following pages give detailed instructions for performing 131-Iodine air **monitoring**, including operating procedures for air filters. This is followed by installation instructions.

### **Procedures for 131-Iodine Air Monitoring**

#### A. Discussion

1. The handling of certain volatile radioactive materials may require that air sampling be performed to document that Derived Air **Concentrations(DAC)** are not exceeded in either restricted or unrestricted areas.
2. Acceptable methods include:
  - a. Air sampling data **and/or**
  - b. Calculations (if those calculations can demonstrate that the DAC for a particular substance is not exceeded.) A good example of the use of calculations for this **purpose** is the information which is submitted for authorization to use 133-Xenon. If calculations are submitted, it is necessary to document those specifications and measurements (such as **fume** hood flow in CFM, etc.) and check them periodically to ensure that the conclusions made **from** the calculations have not changed.
3. For volatile 131-Iodine, the approach of using calculations may be taken to document that the DAC is not exceeded. The concentration of volatile 131-Iodine will be calculated using the "**Worksheet** for Radioactive Air Monitoring" which is enclosed.

#### B. Equipment

1. Vacuum pump with air flow gauges.  
Because **PharmaLogic** will operate its air sampling equipment **continually**, evaluation of the **effluent** concentration should be done in **24** hour increments or multiples of **24** hour increments. The activity in the filters must be measured within **24** hours **from** the time that liquid Iodine-131 is handled for liquid doses or therapy capsules.
2. Appropriate tubing.
3. Filter holders.

4. Charcoal impregnated filter or filter paper.
5. Scintillation well counter assembly and appropriate counting vials.

#### C. Operating Procedure for Air Filters

1. Mount the air sampling apparatus in a manner which **will** ensure that effluents being released to both restricted and unrestricted areas **will** be sampled. Sampling may be done in the exhaust vent pipe on the up **stream** side of any additional air filtering system.
2. The activity in the filter must be **measured** within 24 hours after handling the last 131-Iodine Solution.
3. To measure the activity in the filter from each holder:
  - a. Fold or roll up the filter if applicable using clean disposable gloves;
  - b. Place the filter in a counting vial or in the same geometrical **configuration** as the standard source; and,
  - c. Count it in the gamma-well. Make sure that the analyzer window is set for 131-**Iodine** and that a efficiency **factor** ( $F_{131\text{-Iodine}}$ ) for this analyzer setting **has** been calculated.
4. Record the well counter background and net 131-Iodine count on the "Worksheet for Radioactive Air Monitoring".
5. Record the sampling pump air flow in ml from measured flow of vacuum pump.

#### D. Procedure for Calculating Concentration of Volatile Iodine.

1. The following calculations may be used to determine the concentration of volatile iodine in **uCi/ml** in the restricted and unrestricted areas.
  - a. Calculate "pump on **duration**" from pump on and **off** times.
  - b. Determine **uCi** of 131-**Iodine** present on filter using:

$$131\text{-Iodine uCi} = \frac{\text{Net cpm(Filter)}}{2.2 \times 10^6 \text{ dpm/uCi} \times F_e \text{ 131-I}}$$

- c. Determine ml air flow through sampling pump **from**:
- (i) Direct **pump** flow data **x** time
  - (ii) Pump flow data converted to ml/min x time
- d. Calculate **uCi/ml** of 131-Iodine concentration using formula below:

$$\frac{\text{uCi 131-I}}{\text{ml of flow through pump}}$$

- e. The **maximum permissible** Derived Air Concentrations (**DAC**) are:
- (i) For occupational limits  $\text{DAC} = 2 \times 10^{-8} \text{ uCi/ml}$
  - (ii) For effluent limits  $\text{DAC} = 2 \times 10^{-10} \text{ uCi/ml}$

2. **Useful** conversion factors are:

- a.  $1 \text{ ft}^3 = 2.832 \times 10^{-2} \text{ M}^3 = 2.832 \times 10^4 \text{ ml}$
- b.  $1 \text{ ft}^3/\text{min} = 2.832 \times 10^4 \text{ ml/min}$
- c.  $1 \text{ ft}^3/\text{min} = 28.3 \text{ liters/min}$
- d. ratio of Photon yield  $\frac{\text{I-131}}{\text{Ba-133}} = R_p$

### Procedures for Installation

A. Filter holder #1 should be mounted on the **OUTSIDE** of the 131-Iodine hood above the area where an individual would be working. This filter monitors the air in a **RESTRICTED** area.

B. Filter holder #2 should be mounted to sample air **from** the fume hood stack. This filter monitors the **air** in an **UNRESTRICTED** area, i.e., the air being vented to the environment.

If a barium-133 standard is used,  $F_c$  may be corrected for photon yield. However, the actual correction factor is dependent on the equipment used to obtain your data. The theoretical rate peak abundance is:

$$\frac{\text{I-131(E)} \quad 82.0}{\text{Ba-133(E)} \quad 61.6} = \frac{\quad}{\quad} = 1.33$$

**WORKSHEET FOR RADIOIODINE AIR MONITORING**

Date: \_\_\_\_\_  
 Instrument: \_\_\_\_\_ Bkg: \_\_\_\_\_ cpm  
 Well Counter Setting: \_\_\_\_\_ KeV to \_\_\_\_\_ KeV (range of 100 KeV)

A uCi of Iodine in Filter:

1) Restricted Filter:

Net sample count(cpm) X uCi of Standard

$$= \frac{\text{Net Standard Count(cpm)} \times 1.33}{1.33 \times \text{cpm}} \text{ uCi}$$

2) Unrestricted Filter:

Net sample count (cpm) X \_\_\_\_\_ X uCi of Standard

$$= \frac{\text{Net Standard Count (cpm)} \times 1.33}{1.33 \times \text{cpm}} \text{ uCi}$$

B. Air Flow Through Sampling Pump:

Measured Pump Flow (ml/min) X Pump Duration (min)

\_\_\_\_\_ ml/min X \_\_\_\_\_ min = \_\_\_\_\_ ml

C. Concentration of Iodine in Air:

1) Restricted Air Filter:

\_\_\_\_\_ uCi (A.1)  
 ----- = \_\_\_\_\_ uCi/ml  
 \_\_\_\_\_ ml (B.)

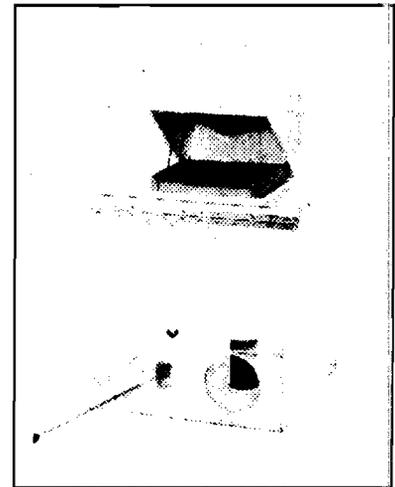
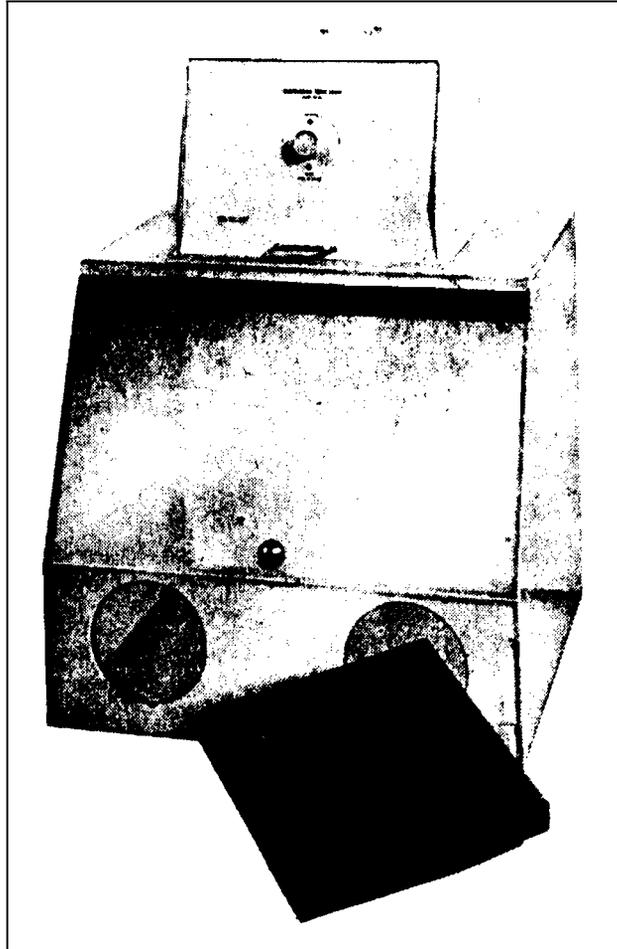
2) Unrestricted Air Filter:

\_\_\_\_\_ uCi (A.2)  
 ----- = \_\_\_\_\_ uCi/ml  
 \_\_\_\_\_ ml (B.)

Signature: \_\_\_\_\_

**Action Level: RESTRICTED:  $2 \times 10^{-8}$  uCi/ml**  
**UNRESTRICTED AREA:  $2 \times 10^{-10}$  uCi/ml**

# Radioiodine Fume Hood



Constructed of 3/8" clear plexiglass, this rugged Radioiodine Fume Hood is designed to meet the problems associated with iodination procedures. The large internal work area and spacious arm ports allow maximum uninhibited manipulation of material within the unit. A 24" x 13" swing-away front door permits easy placement and retrieval of items. An air baffle assures an even flow speed of air out of the box. Negative air flow speed can be adjusted from 0 to a maximum of 80 CFM. The motor is a UL approved induction type. The disposable charcoal filter traps 90% of the radioiodine produced. Each unit can accommodate up to two filters. One 12" x 12" x 1" activated charcoal filter is supplied with the system.

## SPECIFICATIONS:

**Motor:** 1/45" H P . 61 Watts, 3/4 Amps. 110 VAC, 50.60 Hz  
**Glove Box:** 24" x 20" base x 36" height (61 cm x 51 cm x 91.4 cm)  
**Shipping Weight:** 90 lbs (41 kgs )

NOTE: The radioiodine fume hood pictured above, or equivalent, will be used to dispense liquid 1-131 sodium iodine solution and capsules.

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## Sodium Iodine 1-131 Capsule Preparation

\*\*\*Compounding Procedures\*\*\*

1. Turn on the **fume** hood and **1-131** glove box **if** not already operating. Check to make sure the equipment is operating properly.
2. Turn on the vacuum pump for air monitoring if not already operating. Check to make sure the gauges and vacuum pump are operating properly.
3. **Wear two(2) pair(s)** of gloves. Put on pair of shoulder length plastic gloves next. Put on a pair of latex gloves over the shoulder length gloves you are wearing.
4. Perform an area **survey** of the **I-131** glove box and work area to assure that it is contamination free. If not decontaminate the work area before you start. Always use ALARA principles!  
*A survey meter equipped with a pancake probe is ideal for isolating I-131 contamination. This probe is extra sensitive to Beta-Rdation; more so than a GM sidewall probe.*
5. Calculate the amount of **1-131** solution needed to fill the prescription. Remember to take into consideration "**decay**" if the therapy is for the next day. Also residual volume left in the **LO-DOSE** syringe will be approximately **200-400uCi**. This must also be taken into consideration especially when very low **millicurie** capsules are made.
6. In the iodine glove box, vent the **1-131** solution through a charcoal syringe. Next, draw up the activity needed in a shielded **LO-DOSE** syringe and assay.
7. Place the shielded **1-131 LO-DOSE** syringe and **I-131** solution **in** the **fume** hood so it is out of the way.
8. Set up the orange NEN lead vial with the **Squibb gen.** lead piece on top. This set-up will be referred to as the "lead capsule holder".
9. Take a small piece of saran wrap (approx. **3" X 3"**) and place on top of the lead capsule holder.
10. Separate a size "0" gelatin capsule. Take the long end and push the plastic wrap into the lead capsule holder.
11. Place a sodium phosphate capsule capsule (from the **freezer**) into the shielded size "0" capsule.

12. Take an empty LO-DOSE syringe and bore a pilot hole through the center top of the **sodium** phosphate capsule.
13. **Insert** the needle of the shielded **I-131** dose into the hole as far as it will go. Inject the capsule with a slow but constant injection.
14. Once the injection is complete, remove the needle from the capsule and cap. Place the empty **1-131** syringe in its holder and store in the **fume** hood out of the way.
15. Using a modified straw, pick up the other size "0" capsule **half** and place the empty **I-131** syringe in its' holder and store in the **fume** hood out of the way.
16. Remove the capsule by inverting the Squibb gen. lead piece onto a second orange lead container that has a "dispensing **container**" within. With an empty LO-DOSE syringe push the capsule through the Squibb gen. lead piece so it drops into the dispensing container.
17. Remove the Squibb gen. lead piece and cap the dispensing container inside. Cover the orange lead container with it's lead top.
18. Assay the **1-131** therapy capsule; account for decay; and assure that the **finished** capsule strength is not greater than **10%** which was ordered.
19. Remove your latex gloves and replace with new ones.
20. Dispense the **I-131** therapy capsule in a heavy lead container.
21. Remove the shielded **I-131** syringe from the fume hood and place in the **I-131** Glove Box. Rinse the syringe into a shielded 10cc or 20cc **saline** wash vial. Store the **1-131** wash vial **in** the fume hood for **future** use. Dispose of the **1-131** syringe in the appropriate radioactive waste bin.
22. Perform an **area** survey of the **1-131** glove box and other immediate **work areas** to assure it is contamination **free**. Decontaminate if necessary.
23. Follow the **air** monitoring procedure as outlined in your NRC or Agreement State License.

## **Item 10.10    Precautionary Measures for Handling Millicurie Quantities of Liquid Radioiodine**

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 or more **frequently**. 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.

### In-Vivo Thyroid Bioassay

#### 1. Equipment Necessary

- a. Scintillation counting system with
- b. Thyroid neck phantom
- c. I-131 capsule

#### 2. Procedure:

131-I energy = 364 KEV  
Analyzer **window** = 100 KEV

With the 131-I capsule, **peak** the analyzer by adjusting the detector voltage until **maximum** count rate is achieved.

- a. Determine background of counting system.
- b. Determine standard count by placing neck phantom containing capsule centered on detector face.
- c. Obtain counts over the thyroid. Place the detector against the **front** of the neck at midline in three vertical positions. For your calculations use the positions which give you the highest count rate.
- d. Calculate thyroid activity **from**:

$$\frac{131\text{-I thyroid activity} = (\text{neck CPM} \cdot \text{Bg CPM}) (\text{uCi of capsule})}{\text{Capsule CPM} \cdot \text{Bg CPM}} = \text{uCi in thyroid}$$

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3. Comment: Since **NRC Guide 8.20** specifies an action level with respect to thyroid burden of **0.12 uCi**, it will be necessary for you to determine the sensitivity of the equipment, and the thyroid counting time necessary to demonstrate a level of **0.12 uCi** in the thyroid. This may be done in the following manner:

a. From the data obtained when counting the 1-131 capsule for thyroid bioassay, express the sensitivity of your counting system in CPM per **uCi**. Example: a **5.0 uCi 131-I** capsule is counted in the thyroid neck phantom on the detector face and counts **20,000 CPM**, then:

$$CF = \frac{20,000 \text{ CPM}}{5 \text{ uCi}} = 4000 \text{ CPM/uCi}$$

b. Sample calculations: Minimum Detectable activity

Prior to any thyroid bioassay procedure, it is necessary to **verify** that the requisite MDA can be achieved. The MDA is given by:

$$MDA = \frac{3.3 * \sqrt{2R_b/t_b}}{CF}$$

$R_b$  = the background counting rate

$t_b$  = time taken to count the background

CF = calibration factor, **i.e.**, the counts per minute per **uCi** of a standard source

In the above example, CF = **4000 CPM/uCi**

If background was counted for **one(1)** minute and yielded **240** total counts, then the **MDA** is determined to be:

$$MDA = 3.3 * \frac{\sqrt{(2 * 240 \text{ cpm})/1 \text{ min.}}}{4000 \text{ cpm/uCi}} = MDA = 0.0057 \text{ uCi}$$

which satisfies the requisite sensitivity.

It is apparent that this thyroid counting system would be capable of detecting quantities of **131-I** below that required for adequate monitoring of health and safety.

The quantity of radioactive material (Q) **deposited** in the thyroid is simply:

$$Q = \frac{\text{Net thyroid cpm}}{CF}$$

4. For our bioassay programs, action levels, **frequency** of bioassay, and actions to be taken if those levels are exceeded **will** be in accordance with U.S. NRC Regulatory Guide 8.20, Application of Bioassay for <sup>125</sup>I and <sup>131</sup>I-**I**. **Bioassays** for thyroid uptake will be obtained with a **Ludlum** 2200 and Scintillation Probe, or equivalent. Measurements of the thyroid **will** be compared to an Iodine 131 capsule housed in a appropriate thyroid phantom to take into account tissue attenuation **from** the employees neck.

A record of bioassay results on the above test will be maintained. Records **will** contain the name of the individual, results of testing, and date. **All** positive bioassay results **will** be investigated. Corrective actions taken to prevent **further** uptake will be documented in accordance with Section **20.103, 10 CFR, Part 20**.

\* DERIVATION OF MDA FORMULAE

$$A. \quad LLD = \frac{2.71}{T_s + 3.3} \left[ \frac{R_b}{T_b} \left( 1 + \frac{T_b}{T_s} \right) \right]^{\frac{1}{2}}$$

Where:  $T_s$  = sample count time

$T_b$  = background count time

$R_b$  = background count rate (CPM)

LLD = lowest level detectable activity in CPM

When  $T_s = T_b$ , the term  $\frac{2.71}{T_s}$  may be neglected and the

above formulae becomes:

$$B. \quad LLD = 3.3 \sqrt{\text{————}}$$

Also:

$$C. \quad MDA = \frac{LLD}{(2.22 \times 10^6 \text{ DPM/uCi}) F_e}$$

Where:  $F_e$  = efficiency factor of counting system

MDA = minimum detectable activity in uCi

However:  $(2.22 \times 10^6) F_e = CF$  where  $CF = \text{CPM/uCi}$  of a standard source

Therefore, MDA may be expressed as:

$$MDA = \frac{3.3 \sqrt{2 R_b/T_b}}{CF}$$

When  $T_b = T_s$

\*HASL Procedures Manual (HASL-300, Suppl-2)

CURRENT LIST OF  
PERSONNEL IN BIOASSAY PROGRAM

Location: \_\_\_\_\_

Month: \_\_\_\_\_ Year: \_\_\_\_\_

INSTRUCTIONS: The following employees are listed as participants in the Bioassay program for the above location and month. To verify this, please:  
1) Give the name and date added for any new employees in the Program.  
2) Line through the name of any employee deleted from the Program and give the date deleted. 3) IF THERE ARE NO CHANGES, sign and date the "No Changes?" line.

Name

Date Added or Deleted

NO CHANGES? Name: \_\_\_\_\_

Date: \_\_\_\_\_

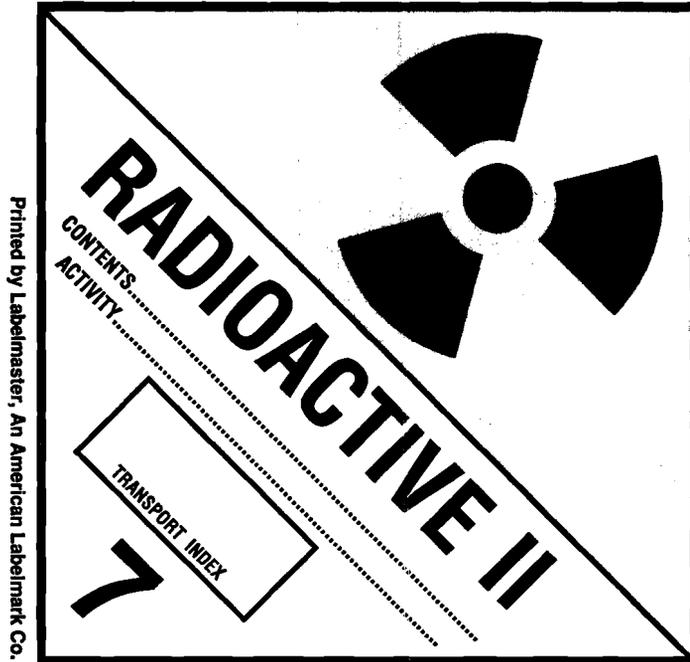




## **REDISTRIBUTION OF USED GENERATORS**

- (a) During the time the generator is being used by PharmaLogic Ltd., the generator will be used **only** in accordance with the manufacturer's instructions.
- (b) At the end of **PharmaLogic's** Ltd. use of **the** generator, the generator will be repackaged in its original shipping container in accordance with NRC and DOT regulations (**e.g.**, wipe test, measurements of radiation levels at the surface of and 1 meter **from** the package, security seal, appropriate DOT labels, shipping papers).
- (c) Enclosed please find actual sample labels that PharmaLogic Ltd. will affix to the generator shield. (*Please note that the labels **fulfill the color, symbol, and wording requirements of 20.203 of 10CFR Part 20 and paragraphs 32.73(a)(4) and (a)(5)(ii) of 10 CFR Part 32.***)
- (d) PharmaLogic will ensure that each redistributed generator is accompanied by the **manufacturer-supplied package insert, leaflet, or brochure** that describes the procedures to be followed and the equipment and shielding to be used when using the generator.
- (e) **PharmaLogic Ltd. will not** redistribute generators beyond the expiration date shown on the generator label.
- (f) Please note that **PharmaLogic Ltd. has begun** correspondence with the Food and Drug Administration (FDA). PharmaLogic has corresponded with a **John Levchuk Ph.D., phone number 1-301-594-0094, Elden Lusinger Ph.D., phone number 301-443-1560** and an independent Board Certified Nuclear Pharmacist who is a leader in the field of Nuclear Pharmacy, **William Hladick, phone number 505-277-6104 or 505-277-6625.**

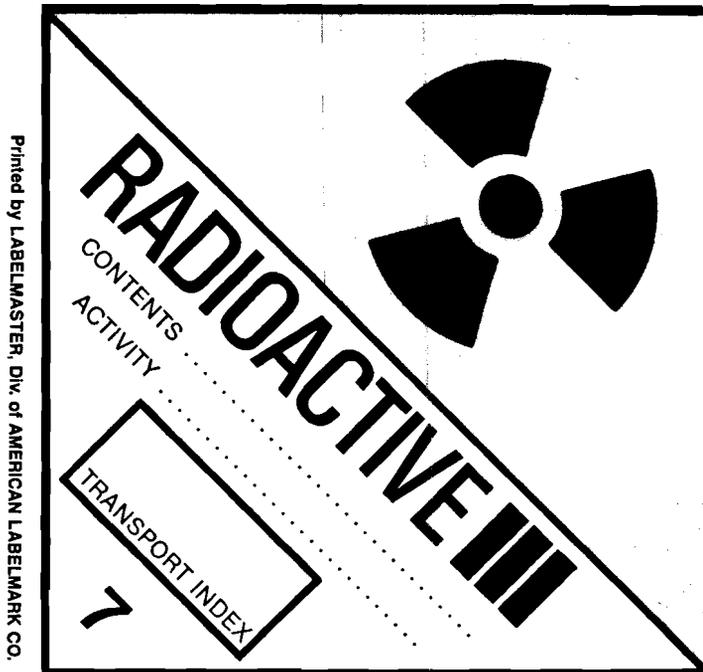
**Actual sample labels that will be affixed to the generator shield.**



Printed by Labelmaster, An American Labelmark Co.

Chicago, IL 60646 (800) 621-5808 HML15

OR



Printed by LABELMASTER, DIV. OF AMERICAN LABELMARK CO.

CHICAGO, IL 60646 (800)621-5808 L16

OFFICIAL RECORD COPY ML 10

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