August 16, 1989

Troy Radiopharmacy
1555 W. Big Beaver Road
Troy, Michigan 48084
313/649-3682

U.S. NUCLEAR REGULATORY COMMISSION
MATERIALS LICENSING SECTION
799 ROOSEVELT ROAD
GLEN ELLYN, ILLINOIS 60137

SUBJECT: ADDITIONAL INFORMATION TO SUPPORT AMENDMENT REQUEST DATED APRIL 20, 1989 (FOR NRC LICENSE NO. 21-24305-01) CONTROL NO. 87307

Dear Dr. Adam,

1. We wish to be approved to redistribute the following sealed sources all of which shall be purchased from Amersham:

Model No.	Radionuclide	Activity
IMC 61029	I-125	200 mCi
IMC 71029	I-125	200 mCi
IMC 81029	I-125	200 mCi
IMC 21235	I-125	800 mCi
GDC 10413	Gd-153	1000 mCi
GDC 10414	Gd-153	1000 mCi
GDC 10415	Gd-153	1000 mCi
GDC 10416	Gd-153	1000 mCi
GDC 10417	Gd-153	1000 mCi
GDC 10417	Gd-153	1000 mCi
GDC 10418	Gd-153	1000 mCi

2. (a) Please increase our possession limit of I-131 to include a maximum of 300 millicuries of LIQUID sodium iodide solution. We request that our maximum possession limit for both liquid and capsule form of I-131 sodium iodide be increased to 600 millicuries to enable us to provide full service radiopharmacy products to the larger Detroit area hospitals.

(b) The purpose of the use of this I-131 is the same as stated in Subitem 9.c. of our current license. We plan to redistribute the I-131 sodium iodide solution and capsules for the purpose of diagnostic and therapeutic patient care to authorized NRC licensees.

(c) The procedures for handling liquid I-131 are attached. See the Procedure For Dispensing Sodium Iodide I-131 Therapy Solutions.

(d) The bioassay procedures that were previously submitted will be applied.

3. (a) The hood face velocity will be measured at six-month intervals with a calibrated velometer. Records of the flow rates measured will be available for NRC review.

(b) "Worst case" calculations for release concentration at the

point of release from the hood to an unrestricted area are as follows:

1. The "worst case" calculation will assume that the activated charcoal filter in the hood traps zero percent of the radioiodine produced. Note that the disposable charcoal filter used is rated by the manufacturer to trap 98% of radioiodine produced. See the attached description of the Radioiodine Fume Hood.

2. Maximum amount of I-131 released in "worst case" situation per week, A, is equal to the product of the total possession limit and loss factor. The loss factor is based on published values of volatility of I-131 therapy solutions. (Clanton JA, Chilton HM, Laven DL, Slater JB, and Strane TR: Volatility of I-131 Therapy Solutions for Oral Administration: A Multi-Center Study. Holker & Barry, Inc., Brooklyn, NY, 1989). All liquid I-131 solution shall be purchased from Mallinckrodt or Squibb. The maximum solution volatility reported in this s 0.491 nCi/mCi for Mallinckrodt, and 4.97 nCi/mCi for Squibb's I-131. The loss factor for this calculation is assumed to be 0.005 uCi/mCi of I-131.

The possession limit requested is 300 millicuries for I-131 in liquid solution.

$A = 300\ mCi/week \times 0.005\ uCi/mCi = 1.5\ uCi/week$

3. The airflow measured by A-OK Cooling and Heating on 6/29/89 through the fume hood was 100 cfm through the charcoal filter to the outside vents. The manufacturer specifies a maximum airflow of 80 cfm. The lower value of 80 cfm will be used for the calculation.

$V = 80\ cfm \times 2.832 \times 10^{4}\ ml/ft^{3} \times 7200\ min/week$

$= 1.6 \times 10^{10}\ ml/week$

4. Average concentration for unrestricted areas from worst case, C

$C = A/V$

$$C = \frac{1.5\ uCi/week}{1.6 \times 10^{10}\ ml/week}$$

$C = 9.2 \times 10^{-11}\ uCi/ml$

5. This is below the maximum permissible concentration of

1×10^{-10} uCi/ml for unrestricted area.

(c) The records of the results of tests verifying the performance of the radioiodine fume hood will be available for NRC review. The results of the flow rate measurments and calculations performed on

6/29/89 are attached for your review.

(d) The charcoal filter is activated with Teda and contains about 3 - 4 pounds of activated charcoal capable of absorbing the maximum amount of volatile radioiodine that could be released in our "worst case". The exposure rate at the surface and at 3 feet from the charcoal filter shall be measured and recorded every six weeks. When the exposure at 3 feet exceeds 2 mR/hr, the disposable filter shall be removed from the hood and stored for decay in the 'hot locker' in accordance with our NRC license. A new filter will be available prior to replacement of a used filter, so that the hood shall always be operated with properly-fitting activated charcoal filter when volatile radioiodine is present in the radiopharmacy.

3. Please change the Radiation Safety Officer on our license from Mike Slugaj to Earl Hussett, B.S. Earl has been an authorized user on our license since August of 1988. He is an excellent record keeper and radiopharmacist. Ms. Cheryl Culver, M.S. has recommended that Earl Hussett, B.S. assume the responsibility of the Radiation Safety Officer, which will permit me more time for managing the business.

Please call me at 313/649-3682 if you have any questions. Or, if you prefer, call my consultant physicist, Cheryl Culver, M.S. at 313/551-4118.

Thank you for your consideration.

Sincerely,

MIKE SLUGAJ, R.T.
Radiation Safety Officer

PROCEDURE FOR DISPENSING SODIUM IODIDE I-131 THERAPY SOLUTIONS

Precautions

Disposable gloves must be worn throughout the dispensing procedure.

Pipette bulb must be used to pipette. NO PIPETTING BY MOUTH.

Remote handling tools must be used to transfer dose bottles from lead shielding to dose calibrator.

Work in the radioiodine fume hood while preparing I-131 therapy solutions. Store all sodium iodide I-131 therapy solutions and capsules in its shielding in the radioiodine fume hood.

Dispensing Procedures

1. Using the tool supplied by the manufacturer, remove cap from the bottle containing the I-131 solution and allow it to stand opened in the hood (this will allow any volatile I-131 to be dispersed up the hood) for 1-10 minutes.

2. Fill out all dispensing forms at this time.

3. Determine if any transfer of solution is necessary. Transfers should be made so that the amount of radioactivity being pipetted is minimized. Example: If 3 mCi is needed from a 10 mCi source, pipette 3 mCi from the 10 mCi vial and transfer to a shielded dispensing vial. If 140 mCi is needed from a 150 mCi source, pipette 10 mCi from the 150 mCi vial and transfer to a shielded, pre-labeled vial, and use the remaining 140 mCi as the dose container.

4. Working in the exhaust hood, prepare the dose.

5. Cap the dose bottle and transfer to the dose calibrator. Remote handling tools must be used to remove the dose bottle from the shielding and transferring to the dose calibrator. Dose calibrator reading must be within 10% of required radioactivity.

6. Carefully dispose of the contaminated pipette tip and other contaminated waste in the appropriate waste storage bin.

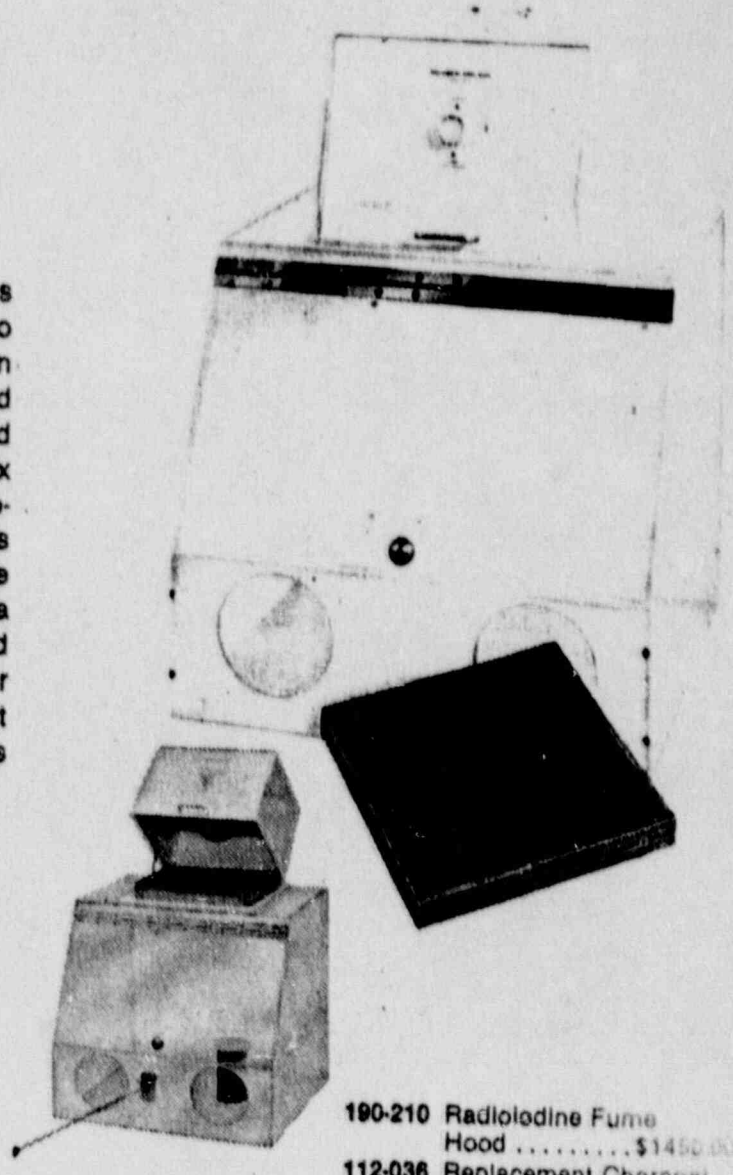
7. I-131 shall be transported for commercial distribution in the original shipping materials whenever possible. In the event that more than one dose is to be drawn from the original shipping vial, equivalent lead shielding (from old doses of I-131) shall be used. The I-131 will be packed in DOT approved shipping containers and labeled according to NRC/DOT regulations.

8. The drivers shall be carefully instructed about the delivery of I-131 to designated, locked areas only, and emergency procedures.

9. All personnel involved in the preparation and dispensing of sodium iodide I-131 therapy solutions are required to have a bioassay performed in accordance with USNRC Regulatory Guide 8.23.

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 of air out of the box. Negative air flow speed can be adjusted from O to a maximum of 80 CFM. The motor is a UL approved induction type. The disposable charcoal filter traps 98% of the radioiodine produced. Each unit can accommodate up to two filters. One filter is suppiled with the system.



SPECIFICATIONS:

Motor:	1/45 H.P. 61 Watts, 3/4 Amps, 110 V.A.C. 50/60 Hz.
Glove Box:	24" x 20" base 36" height

190-210 Radioiodine Fume Hood $1450.00

112-036 Replacement Charcoal Filter 95.00

H-OK Cooling & Heating
775-5400 Doug Heiberg

6-29-8

SECOND LAB AREA

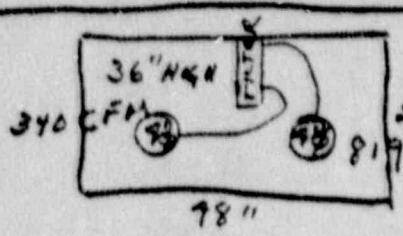
MAIN LAB ROOM $22\frac{1}{2}' \times 12\frac{3}{4}' \times 8' = 2295$ CU. FT
2- 12"X12" SUPPLY DIFFUSERS, 1-245 CFM
2- 130 CFM = TOTAL 375 CFM = 9.8 AIR CHANGES PER HOUR

OFFICE $9\frac{1}{4}' \times 7\frac{3}{4}' \times 8' = 573$ CU. FT
1- 6"ϕ SUPPLY DIFFUSER AT 58 CFM
= 6 AIR CHANGES PER HOUR

HOT LAB $8\frac{3}{4}' \times 7\frac{3}{4}' \times 8' = 542$ CU. FT
1- 6"ϕ SUPPLY DIFFUSER AT 45 CFM
= 5 AIR CHANGES PER HOUR

HOOD U.S. TESTING CO. 48"X22"X36" =
21.96 CU. FT ÷ (OF .366 CFM = 1 AIR CHANGE PER HOUR)
2- SMALL UTILITY FANS 4"ϕ FLEX DISCHARG HOSE THROUGH ONE 12"X12"X4" CHAR-COAL FILTER
1- HOSE 4"ϕ 72 CFM
2- HOSE 4"ϕ 28 CFM
100 TOTAL EXHAUST THROU FILTER TO OUT SIDE VENTS (2-4"ϕ)
273 AIR CHANGE IN HOOD PER HOUR

EARL



- 72 CFM

1 - 820 - 72 CFM
2 - 340 - 28 CFM
100 CFM

21.96 CU. FT. ÷ 60 = .366 ÷ 100 CFM EXHAUST
273 AIR CHANGES PER HOUR

VOLATILITY OF I-131 THERAPY SOLUTIONS FOR ORAL ADMINISTRATION: A MULTI-CENTER STUDY

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D.L. Laven, C.R.Ph., FASCP, V.A. Medical Center, Bay Pines, Fla.
J.B. Slater, Ph.D., R.Ph., Loma Linda University Medical Center, Loma Linda, Calif.
T.R. Strane, M.S., R.Ph., St. Lukes Hospital, Milwaukee, Wisc.

Produced by: Holker & Barry, inc. 608 SIXTH STREET BOX NO. 159029 BROOKLYN, NY 11215-9029 (718) 788-3001

INTRODUCTION

Diagnostic and therapeutic forms of I-131 have the potential of creating significant amounts of contamination in the work place (1-4). This potential is increased dramatically if the I-131 is contained in a dosage form that is highly volatile. It is general knowledge that I-131 therapeutic solutions are volatile; however, it is not well known if differences in formulation affect volatility. Similarly, it has been suggested (10) that therapeutic I-131 capsular forms may contain removable contamination. In addition, the extent of volatility of this contamination, or possible differences in the volatility of I-131 in capsular form among different products, has not been established. Therefore, the purpose of this study was to test all commercially available forms of therapeutic oral I-131 and determine the volatility of each product at five different test sites. A multicenter approach was used because generic I-131 therapy capsules are prepared at many different locations by Syncor pharmacies.

MATERIALS AND METHODS

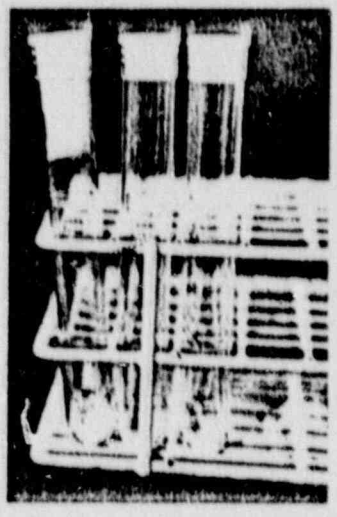
Five different lots of therapeutic oral solution and capsules were obtained from each vendor (Table 1) over a six-month evaluation period at each test site.

Table 1 **Iodine Products Tested and Their Formulations**

Capsules:			
Mallinckrodt (a)	**Squibb (b)**	**Syncor (c)**	
Solutions:			
Mallinckrodt (a)	**Squibb (b)**	**Syncor (c)**	

Volatility of the capsules was determined by placing a capsule (up to 15 mCi) in a small test tube. The small test tube was then placed in a larger tube and a 0.5 gm activated charcoal bag' was placed in the mouth of the larger tube. The larger tube was then sealed for a 24-hour period. The volatility of the oral solutions was measured by placing three 5 mCi doses into three small test tubes. The small tubes were placed into larger tubes in the same fashion as the capsules. A 0.5 gm activated charcoal bag was placed in the tube mouths and the tubes were sealed for a 2-hour period (Fig. 1).

Figure 1

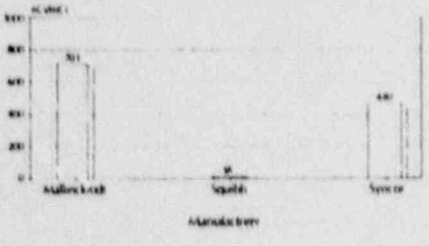


All charcoal bags were counted using a single or multichannel analyzer attached to a shielded NaI crystal with an integrated region of interest at the 364 KeV energy peak. The counts were then corrected for background and scintillation efficiency using a known I-131 standard. In all cases, care was taken to exclude the 163.9 KeV peak of Xe-131m. All counting information was collected at a central site and compiled for analysis.

RESULTS

The average volatility (nCi released/mCi of I-131) of the therapeutic capsules is presented in Figure 2. The mean volatility of Squibb's therapy capsules is statistically different ($p < 10^{-6}$) from the other commercially available products. However, there is no statistical difference ($p = .07$) in the means of Syncor's and Mallinckrodt's capsules. When comparing products, Syncor's therapeutic capsules are 25 times more volatile than Squibb's product, and Mallinckrodt's capsules are 40 times more volatile than Squibb's capsules.

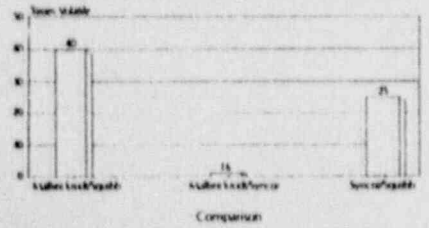
Figure 2 CAPSULE VOLATILITY



Capsule Volatility (nCi/mCi)

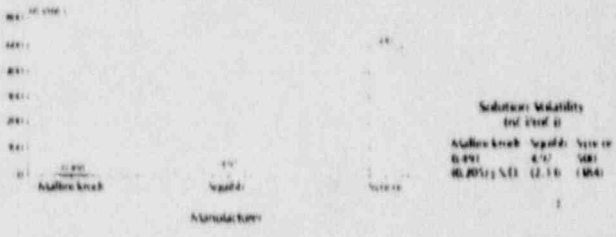
Mallinckrodt	Squibb	Syncor
702.6	17.7	440.2
(419) ± S.D.	(21.6)	(168.8)

CAPSULE VOLATILITY COMPARISON

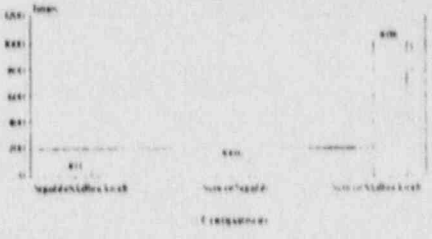


The average volatility of the oral solutions is presented in Figure 3. All means are statistically different, with a $p < 10^{-6}$. If a comparison of oral solutions is made, Squibb's iodine is 10 times more volatile than Mallinckrodt's, Syncor's iodine is 1,018 times more volatile than Mallinckrodt's, and Syncor's iodine is 101 times more volatile than Squibb's I-131 oral solution.

Figure 3 SOLUTION VOLATILITY



SOLUTION VOLATILITY COMPARISON



DISCUSSION

The accumulation of I-131 in the thyroid gland of personnel handling oral dosage forms of I-131 sodium iodine is well documented (3,7,8,10,11). In 1979, Jackson and Macintyre noted differences in personnel thyroid uptakes based on the vendor who supplied the I-131 therapy solution (3). This concern led to the reformulation of Mallinckrodt's oral I-131 therapy solution in 1979. This reformulation may explain the fact that Mallinckrodt's oral solution is the ieast volatile commercially available oral solution on the market.

The use of therapeutic I-131 oral solutions has been recognized historically as a source for personnel radiocontamination. Recently, however, it has been pointed out that therapeutic I-131 capsules are as potentially dangerous as the oral therapy I-131 solution in terms of external contamination (10). The results from this study indicate that there is a high quantity of volatile I-131 released from therapy capsules as well as from the oral solutions.

The significance of this volatility can be demonstrated by applying the data obtained in this study to the use of a 10 mCi therapy dose in a model treatment room that is 10 x 15 x 7 feet with the usual hospital ventilation air exchange of ten times per hour. Under these conditions, would the maximum permissable concentration (mpc) of 9.0 x 10^{-9} uCi/cc be exceeded with the use of any I-131 product upon administration? When we apply this simplistic model to the oral solutions, Syncor's oral therapy solution exceeds the mpc, releasing 1.0 x 10^{-7} uCi/cc into the model environment. When applying this model to the therapeutic capsules, Mallinckrodt's as well as Syncor's I-131 therapy capsules exceed the mpc, releasing 1.3 x 10^{-7} and 0.9 x 10^{-7} uCi/cc, respectively, into the room.

CONCLUSIONS

The results of this study indicate I-1 products have significant volatility that not limited to therapeutic solutions onl Additionally, these findings indicate notable variability of I-131 volatility amo the different commercial formulatio For example, Syncor's oral solution considerably more volatile than oth commercially available solutions, an Syncor's capsules, as well as Malli ckrodt's, are significantly more volati than Squibb's product. Therefore, th improper use and storage of these ther peutic dosage forms may significant increase the risk of personnel, equipme and patient administration areas to radi contamination. Extreme care in the handling (9) is prudent and necessa Careful consideration should also b given, whenever selecting a particul product, to ensure that the chose product optimizes patient manageme while minimizing personnel and enviro mental contamination.

I-131 therapy has important clinic benefits, and these therapeutic drugs ca be used safely and effectively if prop care is taken in their storage, dispensi and administration.

REFERENCES

1. [illegible] Letter to all medical licensees concerning radioactive iodine volatility from sodium iodide oral solution. U.S. Nuclear Regulatory Commission, Washington, DC, [illegible]
2. [illegible] Thyroid contamination from airborne I-131. J Nucl Med [illegible]
3. Jackson GL and Macintyre [illegible] Accumulation of radioiodide in staff members. J Nucl Med [illegible]
4. [illegible] Airborne Radioiodide Contamination [illegible] I-131 Treatment [illegible]
5. [illegible] Safe handling of radioiodide. J Nucl Med [illegible]
6. [illegible] Reply to accumulation of radioiodide in staff members. J Nucl Med [illegible]
7. [illegible] Airborne concentrations of I-131 in a nuclear medicine laboratory. J Nucl Med [illegible]
8. [illegible] Radioiodide volatilization from [illegible] sodium iodide I-131 solutions. J Nucl Med [illegible]
9. [illegible] Safe handling of radioiodinated solutions. J Nucl Med [illegible]
10. [illegible] Contamination from therapeutic I-131 Capsules. Health Physics [illegible]
11. [illegible] The Radioactive Patient. [illegible] Nucl Med [illegible]

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