GE Healthcare

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U.S. Nuclear Regulatory Commission - Region III
Materials Licensing Section
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

RE: NRC Material License No. 21-26707-01MD

To Whom It May Concern:

The GE Healthcare nuclear pharmacy located at 4380 Brockton SE, Suite 3, Kentwood, MI 49512 has received numerous requests from customer licensees (i.e. Nuclear Medicine Departments) to supply Iodine-123 whole body diagnostic capsules. To complete this request, GE Healthcare would need to purchase liquid Iodine-123 and compound the capsules in our nuclear pharmacy. The liquid radiochemical Iodine-123 would be provided by our GE Healthcare manufacturing site in Arlington Heights, Illinois which is registered with the U.S. Food and Drug Administration as a drug manufacturer under 21 CFR 207.20(a).

Please allow this letter to serve as notice that Medi-Physics, Inc., dba GE Healthcare wishes to amend the above referenced radioactive materials license and application to reflect the following modifications to allow for the compounding of Iodine-123 diagnostic capsules:

1. Amend Radioactive Materials License Condition 8(K) to increase the Iodine-123 radionuclide possession limit to 2 curies (74 GBq).

2. Amend the Radioactive Materials License Application Item 10.6 – Safe Use of Radionuclides and Emergency Procedures specific to "Precautionary Measures for Handling Millicurie Quantities of Radioiodine" as indicated in Attachment A. Revisions to Item 10.6 of the license application are in italic print for ease of reference.

GE Healthcare conducted a health physics assessment to determine the intake potential when handling unsealed Iodine-123 in the radiopharmacy to determine the need for air sampling and occupational worker bioassays. Based on the results of the assessment, there is no justification for performing air sampling or occupational worker bioassays. Refer to Attachment B for a summary of the health physics assessment.

All other aspects of our Radiation Safety Program remain unchanged at this time. Should you require any further information on this request, please feel free to contact me at (616) 554-5717.

Sincerely,

Stephen M. Williams, R.Ph.
Radiation Safety Officer

Enc. Attachments A & B

Appropriate Legal Entity

Attachment A

Item 10.6: Safe Use of Radionuclides and Emergency Procedures – Precautionary Measures for Handling Millicurie Quantities of Radioiodine

Precautionary Measures for Handling Millicurie Quantities of Radioiodine

Compounding and Dispensing Iodine-131

A) Precautionary Measures.

The iodine fume hood will be located in the radioiodine room as shown on the attached floor plan (Appendix B). Iodine-131 capsules will be manually or mechanically compounded utilizing a professionally engineered custom capsule compounding machine. This compounding device will allow for hands free compounding of any size/volume/activity capsules from high-concentrated stock Iodine-131. Provisions for the use of this device are included within this license application.

Ventilation keeps the radioiodine hood at negative pressure with respect to the rest of the room. The design of the hood precludes releases into the room and prevents the operator from disrupting the airflow. The hood is designed to provide a minimum airflow rate of 100 linear feet per minute.

B) Equipment.

The iodine fume hood is provided with small openings on the front face of the hood where airflow enters and exhausts via a dedicated carbon filtration system before effluents are released to the environment. The hood exhaust stack extends above the fume hood and beyond the building roofline.

Iodine-131 capsules will be compounded either manually within the iodine fume hood, or by using a professionally engineered custom capsule compounding machine such as the DRAXIMAGE Smart-Fill™ (DSF) capsule-filling system or other device. The DSF capsule-filling system is a computer-controlled dispensing unit and, if utilized, would be ducted directly into the iodine fume hood.

Sealed containers of volatile forms of Iodine-131 will be stored and dispensed within the fume hood, equivalent glove box, or the DSF capsule-filling system. Iodine-131 will be manipulated within the DSF as well as the iodine fume hood. Additional shielding will be provided when necessary.

The effluent sampling system will operate continuously and will be utilized to determine the concentration of radioactivity in the effluent air. Carbon cartridge sampling filters will be used to collect and analyze samples from the effluent air stream. Sampling cartridges will be analyzed weekly for the concentration of radioiodine in air compared to the values specified in rule 10 CFR Part 20, Appendix B. The air sample results are reported as a percentage of the effluent concentration values and used to determine compliance with the dose limits as defined in 10 CFR Part 20, Appendix B, for Iodine-131 (2 x 10-10 μCi/ml).

These air flow measurements will be evaluated at least semi-annually in order to verify proper air flows for this dedicated ventilation system and adjusted as necessary. Proper residence time of airflow through the carbon filter will be maintained. Assumptions and calculations are provided in Appendix F of this application for residence time determinations.

The site RSO shall be notified when measured effluent samples exceed the established action level. The site RSO will be responsible for conducting an evaluation and determine whether or not corrective actions are necessary. The evaluation may include such items as verification of handling procedures, counting techniques, and mathematical calculation, as well as functionality of equipment, product utilization and prior trends in effluent monitoring results.

Effluent results will be compared with annualized average concentration values in order to demonstrate compliance with rule 10 CFR 20.1302(b).

C) Thyroid Bioassay Program.

A thyroid bioassay program will be implemented and a baseline bioassay will be performed on all occupational personnel, who dispense, process, manipulate, or otherwise handle open containers of radioiodine. Bioassay measurements will be performed using a Single Channel Analyzer (SCA), or equivalent instrument, which is interfaced with an uptake probe.

The thyroid bioassay program will be a weekly evaluation for all individuals that dispense radioiodine from open containers. Thyroid bioassay measurements may be conducted on other individuals, who work in the nuclear pharmacy. Otherwise, the bioassay program to be implemented will be based upon the guidance given in Regulatory Guide 8.9, "Acceptable Concepts, Models, Equations, and Assumptions for a Bioassay Program".

The Annual Limit on Intake (ALI) for Iodine I-131 is 50 microcuries. Under normal operation, cumulative exposure to volatilized Iodine I-131 will not exceed 0.02 ALI (1 μCi) in one month.

Bioassay will be performed within 72 hours only after an accidental release and results will be compared to a baseline value.

The values for the Evaluation Level and Investigation Level are based on the ALI of 50 μCi for Iodine. The Evaluation Level, as described in Regulatory Guide 8.9, will be 1.0 μCi (2% ALI). The Investigation Level as described in this same document will be 5.0 μCi (10% ALI).

Action Level	Description	Intake Amount
Level I	Evaluation	1.0 μCi
Level II	Investigation	5.0 μCi

If any single measurement exceeds1.0 μCi (Level I), the RSO will evaluate methods, techniques and calculations. Repeat bioassays may be made to verify measurements and obtain a better measurement of the intake. If any single measurement exceeds 5.0 μCi (Level II), the RSO will institute a thorough investigation. Multiple measurements over several days may be performed.

Air sampling and surveys will also be evaluated and compared to the bioassay. Preventive actions will be taken if confirmed. When the total thyroid uptake for an individual reaches 3 μCi in a year, consideration will be given to removing the individuals from Iodine I-131 handling responsibilities. Individuals shall be removed from Iodine I-131 handling responsibilities prior to reaching a total intake of 6 μCi for the year.

D) Calibration of Thyroid Bioassay Equipment

Calibration of the instrumentation will be performed using a NIST Barium-133 source of known activity as a reference standard. A neck phantom will be utilized to evaluate the reference standard as well as for evaluating background measurements. The reference source will be placed in a neck phantom and positioned with the phantom to obtain reproducible geometry with respect to the detector. The reference standard will be counted for at least 2 minutes and the count rate recorded.
The reference standard will be removed from the phantom and the source will be adequately shielded. Background counts will be collected for at least 2 minutes with the neck phantom in place, and the count rate recorded.

The instrument calibration factor (CF) will be determined by dividing the reference standard's activity by its net count rate,

CF = net source activity (μCi) ÷ net source count rate (cpm)

E) Thyroid Uptake Measurement

The hand-held scintillation detector will be positioned over the center of the thyroid and counted for a two-minute interval. The net thyroid count rate should be obtained by subtracting the background count rate from the thyroid count rate.

If the Thyroid count rate is significant (i.e., greater than minimum detectable activity), the Thyroid Activity (A), in microcuries (μCi), will be calculated by multiplying the net thyroid count rate (cpm) by the calibration factor (CF = μCi/cpm).

Activity (A) = net thyroid count rate (cpm) x CF (μCi/cpm)

For calculations of Minimal Detectable Activity, refer to Appendix G.

The thyroid Activity may also be calculated by placing the appropriate data in the pharmacy computer program.

Compounding and Dispensing Iodine-123

All Iodine-123 high activity capsule compounding (~1-5 mCi) will be performed manually by, or under the direct supervision of an Authorized Nuclear Pharmacist (ANP) in accordance with State Board of Pharmacy regulations and GE Healthcare standard operating procedures for the preparation and dispensing of Iodine -123.

Iodine-123 high activity capsule compounding will take place in a functioning, certified Biological Safety Cabinet (BSC), fume hood, or equivalent device within the restricted area of the radiopharmacy. The BSC or fume hood are ductless hoods designed for handling radioiodine by recirculating carbon filtered exhaust back into the general room air. The BSC or fume hood with carbon filtered exhaust will provide adequate containment for Iodine-123 high activity capsule compounding activities to keep worker exposure to Iodine-123 ALARA.

Sealed containers of Iodine-123 radiochemical and prepared Iodine-123 high activity capsules will be stored in shielded containers within the BSC, fume hood, or equivalent device.

Attachment B

Assessment for Handling Unsealed Iodine-123
Within the Radiopharmacy

Handling Unsealed Iodine-123 in Radiopharmacies
Intake Potential, Air Sampling, Bioassay Assessment
August 20, 2014
Adam Becker, Health Physicist

Intake Potential

To determine the extent of airborne contamination that may be present from compounding Iodine-123 capsules, the potential intake is calculated following the guidance in NUREG 1400, Air Sampling in the Workplace, and is compared to the ALI for Iodine-123. The potential intake is a calculated value based on empirical experimental data on a wide range of nuclear licensed activities. Its premise is that when normal precautions are taken, the amount of radioactivity inhaled by a worker is generally less than one millionth (10^{-6}) of the amount of radioactive material processed.

The following equation[1] is used to calculate the potential intake as a fraction of the ALI (I_f) assuming **1 Ci Iodine-123 is handled per week**:

$$I_f = \frac{Q \times 10^{-6} \times R \times C \times D}{ALI}$$

Where:

I_f = Potential intake as a fraction of the ALI (I-123)
Q = Curies per year (1Ci/week x 52 weeks per year) = 52 Curies
10^{-6} = Fractional amount of material processed inhaled by worker
R = Release fraction (1.0 for gases or volatile material)
C = Confinement factor (0.1 for handling in a fume hood)
D = Dispersibility (1.0, no grinding, boiling or exothermic reactions)
ALI = Annual limit on intake (0.006 Curies per 10 CFR 20, Appendix B)

So,

$$I_f = \frac{52Ci \times 10^{-6} \times 1.0 \times 0.1 \times 1.0}{0.006Ci}$$

$$I_f = 0.0009$$

Using the variables above, the fractional potential intake for Iodine-123 is 0.0009 ALI or 0.09% ALI.

Assessment for Need of Air Sampling

Guidance for considering the need for air sampling is provided in NRC Regulatory Guide 8.25. This guidance explains that, as a general rule, any license who handles or processes unsealed

[1] The fractional intake potential (I_f) is adapted from NUREG 1400, equation 1.2.

or loose radioactive materials in quantities that during a year will total more than 10,000 times the ALI for inhalation should evaluate the need for air sampling. When quantities handled in a year are less than 10,000 times the ALI, air sampling generally is not needed. The basis for this value is that experience has shown that worker intakes are unlikely to exceed one one-millionth of the material being handled or processed, as discussed in NUREG-1400.

Iodine-123 ALI = 0.006 Ci
Consideration for the need for air sampling = 0.006 Ci x 10,000 = 60 Ci
Actual handling per year = 52 Ci Iodine-123

The annual Iodine-123 activity handled as part of this assessment is 52 Ci. Because this amount is less than 10,000 times the Iodine-123 ALI (60 Ci), air sampling is not warranted.

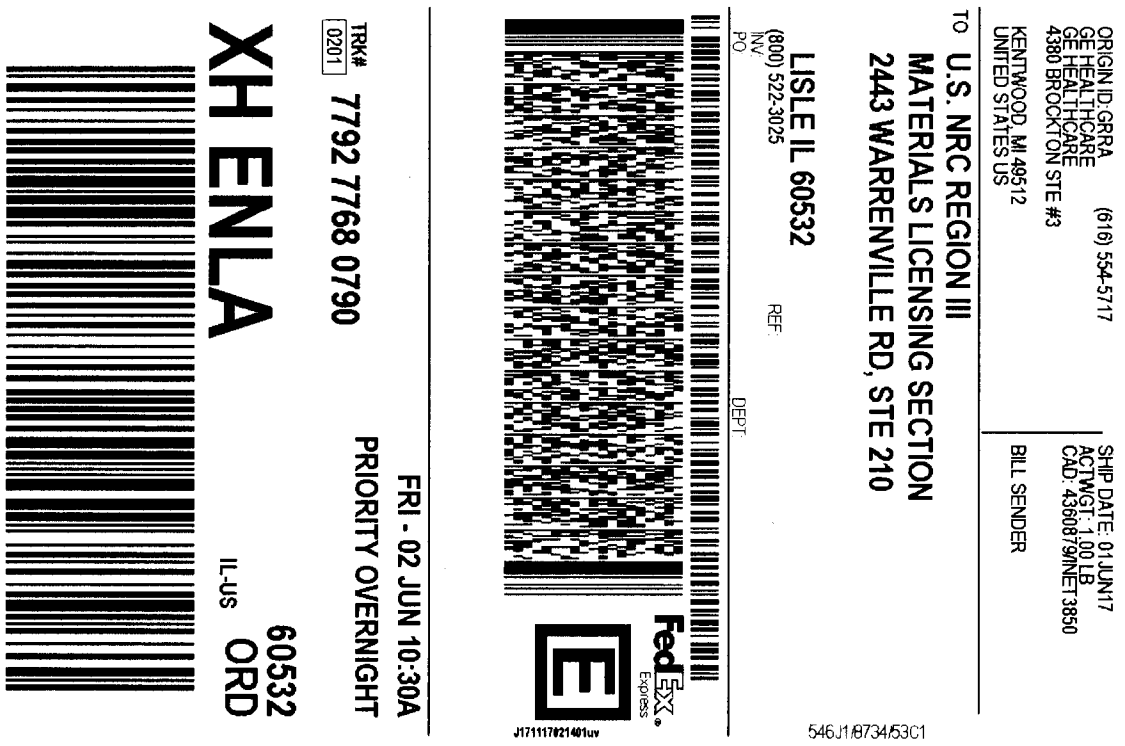
Impact on Dose to Members of the Public

EPA's COMPLY code is used to determine compliance with public dose limits within the radiopharmacies. Utilizing a maximum annual handling of 52 Ci Iodine-123 and comparing it to the possession table found in COMPLY guidance[2], the dose to a member of public would be less than 1 mrem (52 Ci / 490 Ci x 10 mrem). This estimate is considered to be very conservative.

Assessment for Need of Bioassays

NUREG-1556 Vol. 13, Rev. 1, Appendix R states that personnel with potential intakes of 10% of the ALI should be considered for bioassay. Based on the potential intake of 0.09% calculated above, the need for personnel bioassays is not warranted.

[2] "A Guide for Determining Compliance with the Clean Air Act Standards for Radionuclide Emissions from NRC-Licensed and Non-DOE Federal Facilities", October 1989, Table 3-1. This method can be used if the facility meets both of the following conditions: 1) There is no receptor within 10 meters of any release point; and 2) No milk, meat, or vegetables are produced within 100 meters of any release point.



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