Texas Department of State Health Services
Radiation Safety Licensing Branch

Regulatory Guide 3.7

GUIDE FOR THE PREPARATION OF LICENSE APPLICATIONS FOR NUCLEAR PHARMACY OPERATIONS

I. Introduction

This guide describes the information required by the Texas Department of State Health Services Radiation Control Program (Agency) to evaluate license applications for the operation of a nuclear pharmacy.

II. License Fees

An application fee is required for all licenses and must be submitted with any NEW application. The applicant should refer to Title 25 Texas Administrative Code (TAC) Section (§) 289.204 to determine the amount of fee that should accompany the application. Review of the application will not begin until the proper fee is received by the Agency. The check or money order should be made payable to the Texas Department of State Health Service.

A fee should not be submitted with a request for renewal or amendment of a license. All current licensees will be billed according to the expiration date of their license.

III. Completing the Application

All items of the application, BRC Form 252-2, should be completed in sufficient detail to allow the Agency to make an accurate review of the program for safe use of radioactive material. The application and all attachments should be submitted in duplicate; an additional complete copy should be kept by the applicant because the license issued will require adherence to the procedures and limitations established in the application.

If radioactive waste is to be received from other licensees, a separate waste license must be sought from the Agency unless willing to comply with the exemption found in 25 TAC §289.254(e)(2)(B). Claims to operate under this exemption should be explicit.

Because the space on the application form is limited, additional sheets should be used when necessary. Specific items of the application are listed below with explanations.

October 2007

Items 1 through 4 - Self explanatory.

Item 5 - List all radiopharmacists who will dispense radiopharmaceuticals at the facility. Newly requested radiopharmacists must submit training records to demonstrate completion of the minimum training outlined in the Texas Board of Pharmacy's regulations for satisfying this sub-specialty.

Item 6 - The Radiation Safety Officer (RSO) is the person designated as responsible for the radiation safety program and maintenance of the license and associated records, and is the primary contact with the Agency in administering the license. The RSO should have the authority to enforce radiation safety policy, suspend activities deemed unsafe, and require and direct remedial action when necessary. See 25 TAC §289.252(f) for additional requirements and responsibilities.

Item 7 - Under this section of the application, insert the following for the first five entries, if appropriate, indicating the maximum activity in the blanks:

A. Any radioactive material with atomic number less than 84.	A. Any radiopharmaceutical except gases and aerosols	A. No single radionuclide to exceed ____ milliCuries except for Tc-99m not to exceed ____ Ci;	A. Receipt, storage, and dispensing upon prescription to authorized recipients.
B. Mo-99	B. FDA-approved Tc-99m generators	B. ____ Ci.	B. Production of Tc-99m. Redistribution of generators or eluate upon prescription to authorized recipients.
C. Any radioactive material with Atomic Number less than 84	C. Sealed calibration sources and reference sources	C. No single source to exceed ____ mCi. Total: ____ mCi	C. Storage, use and re-distribution of sealed calibration sources to authorized users and distribution of reference sources to medical users.
D. Xe-133	D. Any radiopharmaceutical	D. ____ Ci	D. Receipt, storage and dispensing upon prescription, without subdivision, to authorized recipients.
E. I-131	E. Any liquid or solid	E. ____ Ci	E. Receipt, storage, preparation, and dispensing to authorized recipients and in accordance with USP/NF requirements.

List the radioactive material that will be possessed in the form of sealed sources or other material not in the form of radiopharmaceuticals. For sealed sources you will need to identify the manufacturer and model number for each desired source, or request a broad authorization and commit to only acquiring those sources with evaluations compliant with 25 TAC §289.252(v) and commit to maintaining a copy of the Sealed Source and Device Registry sheets for each.

Material distributed under this type of license is to be dispensed upon prescription only to medical facilities. Other non-medical distributions (e.g., tracer materials) must be authorized on the license. However, such authorization will categorize the licensee as a distributor of radioactive material.

Item 8 - Submit a detailed, scaled drawing of the facility, and indicate the type of construction (e.g., wood, brick, etc.). If the building is multi-story, indicate the location of the radiopharmacy. Designate on the sketch restricted and unrestricted areas (e.g., restrooms, break room, clerical offices). Indicate the type and proximity of neighboring facilities. If I-125 and/or I-131 will be processed, include a detailed description of the hood and filter system to be used to prevent the spread of iodine inside or outside the facility. Also, show airflow patterns and supply/exhaust rates on the facility drawing, indicating locations of intake and exhaust. Describe the method for stack sampling and filter exchange. Describe segregation of air handling between restricted and non-restricted work areas.

It is recommended to locate this type of facility in an industrial park or similar out-of-the-way location. Residential areas and commercial area with heavy public access (e.g., shopping centers, office buildings) are not appropriate because there is a potential for accidents involving spread of radioactive contamination (e.g., loss, fire, explosion).

Item 9 - See Section IV for the content of the Radiation Safety Program procedures.

Item 10 - For survey instruments, describe the frequency and method, and indicate by whom the instruments will be calibrated. If they are to be calibrated in-house, give a detailed description of the method for calibrating the instruments for all meter scales. (Regulatory Guide 5.2, "Guide for the Preparation of Survey Instrument Calibration Applications," may be obtained from the Agency upon request.)

Describe the method for periodic calibration of dose calibrators and how they will be checked daily. These procedures should follow American National Standards Institute or U. S. Nuclear Regulatory Commission recommendations. Also, include what records shall be kept of these calibrations and checks. (Checks should include testing for constancy, linearity, accuracy, and geometry.) Identify any associated equipment or devices used in the testing or calibration of the dose calibrator.

Item 11 - Describe the method to be used for leak testing sealed sources. If they are to be tested by the applicant, a detailed description should be provided of the leak test procedure. (Regulatory Guide 5.1, "Guide for the Preparation of Leak Test

Applications," may be obtained from the Agency.) These tests are required each six months and records must be maintained of each test (25 TAC §289.201(g)).

Item 12 - Submit a complete resume of the education and experience of each radiopharmacist, with a confirmation that each is licensed in the State of Texas. If persons other than radiopharmacists are to handle or process radioactive material, a description of the minimum training that will be provided to them should be submitted with their job descriptions (see Appendix C).

Item 13 - Describe in detail how the pharmacy will handle and dispose of its own radioactive waste. Specifically address generator disposal and indicate how any releases to the environment or a sanitary sewer system will be controlled within regulatory limits.

Item 14 - The application should be signed and dated by the applicant or an individual duly authorized by the applicant to act for or on the applicant's behalf. Unsigned and undated applications will not be reviewed and will be returned to the applicant.

IV. Radiation Safety Procedures

The applicant should submit radiation safety procedures which will be followed by all persons using the radioactive material. The procedures should be in the form of an Operating, Safety and Emergency Procedures Manual, which has serially-numbered pages and a table of contents for easy reference. A copy of the procedures shall be provided to all named users and made available to all persons under their supervision who will use radioactive material (25 TAC §289.203(c)).

The radiation safety procedures should include the following items:

A. Procedures for the control and management of the radiation safety program, including a description of the duties and authority of the RSO. Also, indicate the daily staffing pattern, including the number of pharmacists and technicians per shift and the number of hours per person to be worked per day. Explain how the RSO will be contacted should a problem occur during routine operations.

B. Procedures for ordering radioactive material, receiving materials during normal business hours and at times other than normal business hours, and notifying responsible person(s) upon receipt of radioactive material. The procedures should be adequate to ensure that possession limits are not exceeded, that radioactive material is secured against unauthorized removal at all times, and that radiation levels in unrestricted areas do not exceed limits specified in 25 TAC §289.202(m).

C. Procedures for examining incoming packages for leakage, contamination, or damage, and for safely opening packages. The monitoring should be performed as soon as practicable after receiving the package of radioactive material (see 25 TAC §289.202(ee) for requirements). The procedures may vary depending upon the

quantity of radioactive material received or USDOT labeling, but as a minimum should include instructions for visual inspection for damage and lost integrity/containment, surveying labeled packages, wearing gloves while opening packages, and checking packing material for contamination after opening and prior to discarding or recirculating.

D. Method of restricting access to areas where radioactive materials are handled and stored.

E. General instructions to be followed by laboratory personnel and/or trainees while working with radioactive material. These instructions should:

1. Outline general laboratory procedures to be followed when handling radioactive material (see Appendix A).

2. Prescribe limitations, conditions, and laboratory equipment for handling gaseous or volatile radioactive material such as Xe-133, I-131, etc. For example, explain what materials and what operations should be confined to radiochemical fume hoods or glove boxes. Indicate what shielding or remote handling equipment will be employed when hard beta and/or gamma emitting materials are used.

3. Describe the routine radiation survey program, including the areas to be surveyed, acceptable levels of contamination, and provisions for maintaining survey records. For delivery operations, include a description of vehicle survey procedures (see Appendix B).

4. Explain procedures for storing radioactive material, labeling containers, and identifying areas where radioactive material is used. Describe the location and method for handling and storing contaminated articles and glassware.

5. Explain what records will be kept on radioactive material use and disposal.

6. Outline procedures for monitoring personnel for radiation exposure and maintaining exposure records. The procedures should indicate when extremity monitoring will be used.

7. Describe the bioassay procedures to be followed if millicurie amounts of iodine-131 will be handled or processed in non-encapsulated form. (Interim Guide 5.9, "Bioassay Guide," may be obtained from the Agency upon request.)

8. Describe procedures for operational and maintenance checks of fume hoods and glove boxes, including exhaust systems and monitoring procedures for release to the atmosphere. This should include engineered controls to ensure that gasses and airborne radioactive material contaminants will be contained. This is best accomplished by either having segregated air handling systems or negative pressure balance to the areas of highest radioactive material use and

storage.

9. Describe emergency procedures to be followed in the event of a radioactive material spill, a fire, or other emergency. Address special emergency considerations if locating in an area that is at high risk for hurricanes, tornadoes or flooding. Address emergency procedures for accidental releases of gases if bulk quantities of xenon-133 or xenon-127 are to be authorized. Also, address vehicle accident procedures, instructions to be carried on vehicles, and any emergency kits.

V. Procedures for Preparing and Dispensing Radiopharmaceuticals

In addition to the information required by the application, the applicant should also submit procedures for preparing and dispensing radiopharmaceuticals. These procedures should include at least the following:

A. A description of the methods for preparing, performing quality control testing on, and dispensing the various types of radiopharmaceuticals. Describe those to be bought in bulk and subdivided, those to be made from kits, etc.

B. A sample of the labeling to be put on the product and on the shipping container.

C. The method to be used to assure that the radiopharmaceutical is authorized to be received by the recipient. The applicant could commit to verifying, annually, that the applicant possesses current radioactive material licenses of their customers.

D. The method of providing the proper dose at the time of use and the method for calculating the dose expiration time.

E. Records to be kept of radiopharmaceuticals prepared and dispensed.

F. A sample of the prescription form to be used.

G. Records of the receipt and transfer of radioactive material.

H. Procedures for eluting Tc-99m generators and testing for Mo-99 breakthrough. Method for determining compliance with Mo-99 contamination requirements, including calculation of dose expiration time.

I. Quality control checks to be used to assure proper doses are dispensed.

J. Additional procedures for handling radioiodine, radioxenon, or other products that require special precautions. (The interim guide, "Supplemental Information Needed for Use of Xenon-133," may be obtained from the Agency upon request.)

K. A description of the method to be used for shipping and transporting radioactive material, and a statement that such procedures are in accordance with the U. S.

Department of Transportation regulations. See Appendix D for additional guidance.

L. Confirm that an authorized nuclear pharmacist will be physically present during the preparation and dispensing of all prescriptions.

M. Because commercial nuclear pharmacy operations begin early in the morning, continue throughout the day and often include after hour emergency call-back, describe sufficient authorized nuclear pharmacists to ensure that all shifts are covered and to allow for vacations, illness, etc.

N. Describe arrangements you have made with the local fire department to inform them of your operation and to instruct them in appropriate emergency procedures. An annual walk-through is generally considered acceptable.

O. Identify that the shielding provided for each product in its final source container for which you wish to distribute will be adequate for safe handling and storage of that product at physician offices and hospitals. Also identify the maximum exposure rates likely on any of the final shielded container surfaces that you might ship.

Appendix A

GENERAL GUIDELINES FOR SAFE USE OF
RADIOACTIVE MATERIAL IN A LABORATORY

The following is an example of rules that could be specified for a laboratory using or preparing radioactive material. The applicant is encouraged to develop a set of rules specific to individual needs and the actual laboratory situation. Use of material that may become airborne (aerosols, xenon-133, iodine-125/131) will require additional rules, as will use of sealed sources. Rules should be written in the form of directions to be followed by staff.

1. Wear laboratory coats or other protective clothing at all times in areas where radioactive material is used.

2. Wear disposable gloves at all times while handling radioactive material.

3. Monitor hands/clothing for contamination after each procedure and before leaving the area.

4. Do not eat, drink, smoke, or apply cosmetics in any area where radioactive material is stored or used.

5. Do not store food, drink, or personal belongings with radioactive material.

6. Wear personnel monitoring devices (film badge or TLD) at all times while in areas where radioactive material is used or stored. These devices should be worn at chest or waist level. Personnel monitoring devices, when not being worn to monitor occupational exposures, should be stored in a designated low background area as should the control badge.

7. Wear TLD finger badges during elution of generator and during preparation and assay of radiopharmaceuticals.

8. Dispose of radioactive waste only in specially labeled and properly shielded receptacles.

9. Never pipette by mouth.

10. Survey generator, kit preparation, and injection areas for contamination after each procedure or at the end of each working day. Decontaminate, if necessary.

11. Confine radioactive solutions in covered containers plainly identified and labeled with name of compound, radionuclide, date, activity, and radiation level, if applicable.

Appendix A (continued)

GENERAL GUIDELINES FOR SAFE USE OF
RADIOACTIVE MATERIAL IN A LABORATORY

12. Always transport radioactive material in shielded containers.

13. Work over surfaces that are easily cleaned or covered with disposable absorbent coverings when handling open solutions of radioactive material. Work only in designated restricted use areas. Process volatile radioactive material under fume hoods or in glove boxes when possible.

14. Use appropriate syringe shields, vial shields and remove tools during activities involving millicurie quantities of radioactive material.

15. Assay every vial, syringe and capsule in a calibrated dose calibrator or other appropriate instrument following either preparation or the opening of another manufacturer's container, and prior to dispensing for use in humans.

16. Monitor the first elution of technetium from each generator for molybdenum concentration (break-through) for an acceptable ratio carried throughout the elution's final expiration. Also retain such records for a period of three years.

17. Store and process volatile radioactive material under fume hoods or in glove boxes when possible.

Appendix B

FREQUENCY AND METHODS OF CONDUCTING RADIATION SURVEYS

I. Introduction

When radioactive material is handled in solution or powder form, both radiation surveys and contamination surveys should be performed to prevent unnecessary radiation exposure to personnel and to prevent the spread of contamination throughout the facility. Radiation area surveys are performed using an appropriate radiation survey instrument. Contamination surveys are performed by taking wipe samples from surfaces that are likely to be contaminated in the facility, and counting the samples with a suitable detector.

II. Frequencies of Surveys

Survey frequency depends on the amount and type of radioactive material used. Listed below are examples that may be useful in determining how often to perform surveys. The greater the workload, the more often the surveys should be performed.

A. Low-Level Areas - Not less than once a month - Areas where packages are received, doses are packaged, etc.

B. Medium-Level Areas - Not less than once a week - Areas where radio-pharmaceuticals are prepared, doses assayed, etc.

C. High-Level Areas - Not less than once a day - Areas used for storage of active solutions, elution of generators, preparation of therapeutic doses, fume hoods, etc.

III. Methods for Surveying

Suggested methods for performing two types of surveys are given below. Records of these surveys are required for inspection by the Agency and should be maintained for reference to determine whether the radiation levels or the contamination levels remain constant or increase over a period of time.

A. Radiation Area Surveys - A survey instrument capable of measuring levels as low as 0.1 mrem/hr should be used and the results recorded on a standard form showing location, date, person performing survey, instrument used, exposure levels, and corrective action taken, if any. Also, records should be kept of post-corrective action surveys. A sketch of the area should be used to make an easily prepared and easily understood survey record when annotated with this information.

FREQUENCY AND METHODS OF CONDUCTING RADIATION SURVEYS

B. Contamination Surveys - A series of wipes using filter papers or cloth swatches should be taken from those surfaces where contamination could be expected to exist or where radiation levels are fairly high. (Areas where doses are drawn up, incoming packages are received, pipetting is performed, etc., are areas that may be contaminated.) The wipes should be numbered or labeled, and the location where they are taken shown on the sketch as described above for the radiation survey. Each wipe should be rubbed over a surface area of about 100 square centimeters to maintain a consistent means of determining the amount of removable contamination. The wipes may be counted using a gamma scintillation well counter, a Geiger counter, or any other detector capable of detecting the small amount and type of contamination on the sample. The amount of removable activity should be recorded in activity units (dpm, bequerels, or microcuries) per unit area if above acceptable limits (see Section IV). Calculations for converting instrument readings to activity are usually required. If the reading is less than acceptable limits, the instrument reading should be recorded.

IV. Acceptable Limits

A. Radiation Levels - In no area that is unrestricted (uncontrolled) should radiation levels exist such that a person could receive 100 mrem in any one year or 2 merm in any one hour. If such areas are found to exist, measures should be taken to eliminate the excessive radiation levels. Additional shielding or relocation of radioactive material may be required.

In restricted areas, the exposure limits mentioned above do not apply because personnel are monitored to determine their exposure. Levels, however, should be reduced to the minimum where practicable to reduce exposure. If visitors are allowed in restricted areas, their exposure should be as low as reasonably achievable.

B. Contamination Limits - If the wipe samples of an approximately 100 square-centimeter area indicate more than 1,000 disintegrations per minute (dpm), the area should be cleaned until the contamination has been reduced to background activity. Since it is difficult to determine exactly when a wipe sample has 1,000 dpm, it is recommended that when samples show an easily detectable amount of activity above background, the areas sampled should be cleaned to remove all radioactive contamination. This action should prevent the spread of contamination and reduce the probability of ingestion of radioactive material by personnel who might otherwise become contaminated.

Appendix C

ACCEPTABLE TRAINING FOR USERS

I. Introduction

Every nuclear pharmacy shall have one nuclear pharmacist who shall be named on the nuclear pharmacy's Drug Distribution permit as a Nuclear Pharmacist-in-Charge. A Nuclear Pharmacist-in-Charge may not be in charge of more than one nuclear pharmacy. This person will usually serve as the facility's RSO and would be responsible for the radiopharmacy's compliance with state and federal laws and regulations pertaining to all aspects of the practice of nuclear pharmacy. The RSO/Nuclear Pharmacist-in-Charge should have the autonomy to suspend pharmacy operations should a condition exist which would compromise radiation safety.

Acceptable training of nuclear pharmacy personnel is outlined below.

II. Nuclear Pharmacist

Every licensed (Class B) nuclear pharmacy in Texas which receives, prepares, possesses, uses, transfers, owns, acquires and/or distributes radioactive materials must be staffed with a person or persons classified as a nuclear pharmacist. The nuclear pharmacist must be named as an authorized user by the Texas Department of State Health Services, Radiation Control Program and licensed by the Texas Board of Pharmacy. Minimum acceptable training and experience can be found in Title 22, Part 15 Texas Administrative Code Section 291.53 (rules of the Texas State Board of Pharmacy). Essentially there is a requirement to obtain 200 didactic hours and 500 hours of formal supervised on-the-job training (OJT).

III. Nuclear Pharmacy Technician

Nuclear pharmacy technicians should meet the following minimum criteria:

A. Training in basic radioisotope handling techniques, including the minimum of 200 hours of didactic and laboratory hours from an accredited college or university program. The minimum of 200 hours of didactic and laboratory training (involving theory, background and practical applications) to include:

1. Radiation Physics and instrumentation	85 hours
2. Radiation Protection	45 hours
3. Mathematics of Radioactivity	20 hours
4. Radiation Biology	20 hours
5. Radiopharmaceutical Chemistry	30 hours

ACCEPTABLE TRAINING FOR USERS

B. Successful completion of a minimum of one year on-the-job training in radiation safety at the nuclear pharmacy. The supportive personnel will be under the supervision of the Nuclear Pharmacist-in-Charge. The in-house experience the proper receipt, handling, preparation, usage, transfer and/or distribution of radioactive material as specified by 25 TAC §289.252. Dispensing of radiopharmaceuticals is a task clearly limited to the licensed Nuclear Pharmacist.

   Board Certification of Nuclear Medicine Technology by the NMTCB or ARRT is recognition of training and will satisfy requirement A and will reduce requirement B to a term of four months on-the-job training.

   Note: Trainees will not be listed on the radioactive material license until their training is complete. During training they must work under direct supervision of an authorized user.

Appendix D

PROCEDURES FOR PACKAGING AND TRANSPORTING RADIOACTIVE DRUGS

You should establish and implement written procedures that (1) ensure compliance with the DOT regulations set forth in 49 CFR Parts 170 through 189 and (2) ensure that radioactive material is secured at all times against unauthorized removal. You should keep adequate information available in the delivery vehicle for drivers, police or other civil authorities in case of traffic accidents, etc.

You should submit:

1. Your step-by-step procedures for packaging and transporting radiopharmaceuticals to customers.
2. A description or copy of the written instructions you will provide to drivers about radiation safety and delivery procedures. Your instructions should include directions to lock the vehicle whenever it is left unattended and to leave deliveries only in secured places that have been previously designated by your customers.
3. A description or copy of the written instructions you will keep conspicuously available in your delivery vehicles for drivers, police or other civil authorities in case of traffic accidents, etc. These instructions should describe, in general terms, the contents of the vehicle, provide telephone numbers of responsible nuclear pharmacy employees who can assist at the scene, and give general "common sense" instructions for the interim until an employee can reach the scene.
4. A description or copy of your written instructions to the customer for repackaging used or unused materials and containers for transport back to the commercial nuclear pharmacy.
5. An indication that the applicant has had the outer container tested and certified to meet DOT type 7A standards. The applicant should also address compliance with design requirements, including security seal (under paragraph 173.443) outlined in 49 CFR Part 173.

Note: If the pharmacy takes the responsibility of the shipper for returned materials, the pharmacy needs to ensure that the customer follows DOT rules in the return process. This includes the customer having the proper documentation to demonstrate that the shipping containers meet the DOT regulations.