APPENDIX J

DEPARTMENTAL QUALITY ASSURANCE PROCEDURES

NUCLEAR PHARMACY DEPARTMENT

NUCLEAR PHARMACY QUALITY ASSURANCE............................... 197-203
Title: NUCLEAR PHARMACY QUALITY ASSURANCE

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Policy:

1. The MUSC Nuclear Pharmacy shall monitor the quality of services provided on an ongoing basis. Variances from established standards are identified, appropriate actions taken for improvement and the results of these actions reviewed.
2. As part of the quality assurance program, appropriate quality control tests will be performed on all prepared radiopharmaceutical kits on a daily or regular basis.
3. Radiopharmaceuticals will only be dispensed for patient use after the results from the appropriate radiochemical purity control tests performed indicated the radiochemical purity of the specific preparation was within the acceptable limit as defined by the United States Pharmacopeia (USP) or recommended by the manufacturer of the product (packet inserts).
4. Quality control tests for instrumentation will be performed in accordance with the DHEC regulations (RHA).
5. The MUSC Nuclear Pharmacy also participates with the quality assurance program MUSC Nuclear Medicine Department, medical staff and other health care providers to evaluate and promote effective and safe use of radiopharmaceuticals.
6. Results of quality assurance activities are reviewed by the Director of Nuclear Pharmacy and the MUSC Radiation Safety Office on a daily or regular basis. The results will also be presented and discussed at the regular Nuclear Pharmacy staff meeting for appropriate actions to improve the quality of services. The results are kept on file in a manner that is readily available for inspection.
Procedures:

1. RADIOCHEMICAL PURITY TESTING OF RADIOPHARMACEUTICALS
   a. Radiochromatography will be used to identify and quantify radiochemical impurities before administration to patients.
   b. Based on the most current USP standards, manufacturers recommendations and other equivalent references (AphA Alternative Radiochemical Purity Testing Procedures for the Compounded Radiopharmaceuticals Approved from 1988-1997, etc.), a specific chromatographic medium, solvent and threshold of radiochemical purity will be chosen for the quality control test for each specific radiopharmaceutical.
   c. Every radiopharmaceutical kit prepared will be tested for radiochemical purity before any dose is dispensed for patient use. Radiopharmaceutical preparations with unacceptable radiochemical purity will be immediately discarded.

2. MOLYBDENUM-99 BREAKTHROUGH
   a. Each Tc-99m eluate obtained from the Mo-99/Tc-99m generator will be tested for possible Molybdenum-99 (Mo-99) contamination in accordance with DHEC regulation RHA 4.10.2 and USP.
   b. A properly calibrated dose calibrator and a Mo-99 assay kit will be used to detect the potential presence of Mo-99. The assay kit is a Capintec product which consists of a lead canister and insertion holder.
   c. The empty lead canister will be first measured at the Mo assay calibration setting. This represents the background activity (BG) in Ci.
   d. The eluate will then be measured inside the canister at the Mo assay calibration. This value will represent the Mo-99 (Mo) in Ci.
   e. The Tc-99m activity of the eluate will then be measured without the canister at the Tc-99m calibration setting (Tc) in mCi. (after background subtraction)
   f. The ratio of Mo-99 contamination will calculated as:

   \[
   \frac{\text{Mo} - \text{BG}}{\text{Tc}}
   \]

   g. The maximum allowable Mo-99 contamination should be no more than 0.15 microcuries of Mo-99 per millicurie of Tc-99m at the time of calibration or administration to the patient. This limit represents the maximum values of Mo-99 level will be kept as low as reasonable achievable below this limit. Any preparation of Tc-99m radiopharmaceutical with unacceptable Mo-99 level will be immediately discarded.
   h. The MUSC Nuclear Pharmacy shall report immediately to DHEC for each occurrence of Mo-99 concentration in the generator eluate exceeding the limit.
   i. All personnel performing Mo-99 breakthrough tests must be given a specific training in performing the test prior to conducting such a test. Their record of training will be kept on file for inspection.
   j. The record of each Mo-99 breakthrough test will be entered into the DuPont
Commercial Nuclear Pharmacy Program and a hard copy of the record will be kept on file for two years for inspection. The record will include the information of the measured Tc-99m activity in mCi, the measured activity of Mo in Ci, the ratio of the measures expressed as Ci of Mo per mCi of Tc-99m, the date and time of the test, and the initial of the individual who has performed the test.

3. DOSE CALIBRATOR QUALITY CONTROL TESTS

k. Each dose calibrator used in the MUSC Nuclear Pharmacy will be regularly tested in accordance with DHEC Regulation RHA 4.8 and 10 CFR Part 35.50, 10 CFR Part 35.52.

l. Constancy Check.

i. The constancy check is performed every morning prior to the use of each dose calibrator. The reference sources used are Cs-137 (minimum activity of 50 Ci) and Co-57 (minimum activity of 50 Ci).

ii. The two reference sources will be measured at their respective calibration settings. Instrument constancy means that there is a reproducibility within +/- 10% in measuring a constant activity over time.

iii. Measurements outside the +/- 10% limits indicate that the dose calibrator cannot be used for clinical applications and must be adjusted or repaired.

iv. The record of the daily constant check will be kept for two years. The record will contain information of the model, the serial number of the dose calibrator, the identity of the reference source, the date of the check, the activity measured and the individual who has performed the test.

m. Linearity Test.

i. Each dose calibrator will be tested for linearity upon installation and then every three months.

ii. The Calicheck Method (Nuclear Associates Model 34-210, Procedure Manual 1-390 34-210) will be used. The Calicheck kit consists of seven tubes, six of which are lead-lined to attenuate gamma radiation from radioactive sources, and a seventh, unlined tube. Each lead-lined tube varies in the thickness of lead so as to simulate various stages of radioactive decay. This method will be used for measuring Tc-99m activity ranging from 5000 mCi to 10 Ci.

iii. The data will be entered into the DuPont Commercial Nuclear Pharmacy Program. The data will be calculated by the Health Physics Program and a hard copy will be printed for record.

iv. Measurements outside the +/- 10% limits will require the dosage readings be mathematically corrected and the dose calibrator will require adjustment or repair.

v. The record will contain the model name, the serial number, the method, the calculated activities, the measured activities, the date of the test, and the signature of the Radiation Safety Officer.
n. Accuracy Test.
   i. Each dose calibrator will be tested for accuracy upon installation and then
      every year.
   ii. Two sealed sources of Co-57 and Cs-137 of greater than 50 mCi activities
      will be used.
   iii. The data will be entered into the DuPont Commercial Nuclear Pharmacy
      Program.
   iv. The dose calibrator with measurements outside the +/- 10% limits will be
      adjusted or repaired.
   v. The record will contain the model name, the serial number, the reference
      sealed sources and their calculated activities, the results of the tests, the
      date of the test, and the signature of the Radiation Safety Officer.

o. Geometry Test.
   i. Each dose calibrator will be tested for geometry dependence upon
      installation.
   ii. Each dose calibrator for geometry dependence over the range of 1 ml to 10
      ml.
   iii. The data will be entered into the DuPont Commercial Nuclear Pharmacy
      Program. The data will be calculated by the Health Physics Program and a
      hard copy will be printed for record.
   iv. Measurements outside the +/- 10% limits will require the dosage readings
      be mathematically corrected and the dose calibrator will require
      adjustment or repair.
   v. The record will contain the model name, the serial number, the
      configuration of the source measured, the calculated activities, the
      measured activities, the date of the test, and the signature of the Radiation
      Safety Officer.

4. STERILITY AND PYROGEN TESTS

   a. Sterility Testing
      i. Sterility testing of radiopharmaceuticals will be performed annually to
         ensure the sterility of the radiopharmaceuticals prepared by the MUSC
         Nuclear Pharmacy.
      ii. A minimum of three random samples will be required and the samples will
         be drawn in the same day.
      iii. The sterility test will be performed in accordance with the USP Sterility
         Testing Method.

   b. Pyrogen testing of radiopharmaceuticals will be performed annually to ensure the
      apyrogenicity of the radiopharmaceuticals prepared by the MUSC Nuclear
      Pharmacy.
c. A minimum of three random samples will be required and the samples will be drawn in three different days.
d. The Limulus Amebocyte Lysate (LAL) test will be used to detect the presence of gram negative bacterial endotoxins which are the most common source of pyrogen contamination.

5. MISCELLANEOUS QUALITY CONTROL TESTS.

a. Alumina breakthrough in Tc-99m eluates will be determined by use of an Alumina Ion Indicator Kit. The eluate should contain less than $10^{−6}$ g/ml.
b. Particle sizes of particulate radiopharmaceuticals such as Tc-99m MAA and Tc-99m SC will be determined using microscopic analysis periodically on randomly selected samples.
c. The pH of the final compounded radiopharmaceutical preparation will be periodically checked using randomly selected samples to ensure that its value is within the acceptable range as defined by the USP or the manufacturer’s package insert.
d. For non-technetium products, radionuclide purity will be determined with the use of a multi-channel analyzer (MCA) or a suitable counting assembly in accordance with USP guidelines.
e. All prepared radiopharmaceuticals will be inspected visually behind shielding to ensure the absence of a foreign matter and also to establish product identity by confirming that (1) a liquid product is a solution, a colloid, or a macroaggregated suspension, and that (2) a solid product has defined properties that identify it.

6. PREPARATION, DISPENSING, DISTRIBUTION AND CONTROL OF RADIOPHARMACEUTICALS

a. All radiopharmaceuticals will be assayed by a nuclear pharmacist in a properly calibrated dose calibrator prior to dispensing. The identity of each radiopharmaceutical and its activity will be checked by a second qualified staff prior to distribution for patient administration.
b. Nuclear Pharmacists will conduct monthly inspections of areas storing radiopharmaceuticals to ensure the quality and appropriateness of the storage of radiopharmaceuticals.
c. Nuclear Pharmacists will report all suspected adverse drug reactions on an ADR Notification Form and notify the FDA.

7. MOLYBDENUM-99 GENERATOR DISPOSAL

To dispose of the molybdenum-99 generator, an authorized, trained personnel dismantles the generator from the shielding. A series of wipe tests are performed to ensure no presence of contamination. The generator along with the appropriate packaging material is placed in the original shipping container. After final packaging, each package will be monitored to determine if labeling requirements are met, and any contamination removed. The date and time of disposal, Transport Index, wipe tests results, individual performing survey, and all other required
information (Ref 49 CFR 172.200-204) are recorded on the shipping papers and in the Generator Receipt/Disposal Log. The appropriate markings, symbols and information are applied to the package (Ref. 49 CFR 172.203 (c) and 49 CFR 172.324). The package is blocked and braced to prevent leakage, spillage, etc. during normal transport. Packages are then transported by nuclear pharmacy personnel or an authorized commercial delivery service to the company from which it was shipped (Mallinckrodt Medical Inc. or DuPont).