A QUALITY-CONTROL SYSTEM FOR SHORT-LIVED RADIOPHARMACEUTICALS

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The availability of generator systems for the production of short-lived radionuclides in hospital laboratories has introduced new problems into the field of nuclear medicine. Chief among these is quality control of these newer nuclides and their compounds. Although after the fact bacteriological and pyrogen testing does not insure the safety of the materials at the time of injection, it is presently the only feasible method for dealing with nuclides that have half-lives on the order of hours. Some system of quality control must be instituted at an earlier stage of production so that compounds meet certain specified standards before injection. Because there are no standards for radiopharmaceuticals set forth in *USP XVII* (*1*), the individual laboratory must set up its own system using the specifications of the *USP XVII* as a guideline.

In the Nuclear Medicine Department at Chicago Wesley Memorial Hospital we have instituted a system of quality control for compounds of ^{99m}Tc and ^{113m}In along these lines, which allows some testing before injection to assure the bacteriological purity, nonpyrogenicity, radiochemical purity and identity of all the compounds produced in our laboratory.

This system involves bacteriological and pyrogen testing of all reagents, sterile storage of reagents and periodic testing of preparation methods as well as a system of record keeping which allows every component of all injected materials to be traced.

A Master Control Book is used to assign each batch of reagents and compounds a lot number. This book lists the lot numbers in numerical order along with the date and identity of the reagent or compound.

Reagent _____ Amount _____ Lot _____

Chemical	Formula	Manufacturer	Lot	Amount

Procedure:

Label _____

Date _____ Amount/vial _____ Made By_____

FIG. 1. Radiopharmacy Manufacturing Form used to record all information relevant to reagents used in radiopharmaceutical preparation.

REAGENT PREPARATION

Reagents are prepared in lots large enough to last a reasonable amount of time, both in regard to retention of sterility and to chemical stability. Reagent-grade chemicals and sterile, pyrogen-free distilled water are used to prepare all reagents to minimize the chances of introducing chemical pyrogens into the final compound by way of the reagents. Every time a batch of reagent is prepared, a Radiopharmaceutical Manufacturing Form (Fig. 1) is filled out recording all information pertinent to the preparation procedure. The reagents are sterilized either by autoclaving or membrane filtration depending on which method is consistent with reagent stability. They are stored in clean serum vials in amounts sufficient for use for 1 week or less to lessen the number of repeated entries into a vial. Radiopharmacy labels are affixed to each vial identifying the contents, concentration and lot number. Samples of each sterilized batch are sent for both bacteriological and pyrogen testing according to the testing standards of *USP XVII* (*2*). Some reagents are also tested by chemical methods to be sure that they conform to specifications. The reagent is held until all these tests are completed and the results show that the reagent preparation is acceptable on all grounds. The testing results are attached to the rear of the manufacturing forms and filed for future reference.

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PREPARATION OF COMPOUNDS

All compounds are prepared by a registered pharmacist using standard preparation methods set up in our laboratory. These methods are checked on a regular basis by testing the final compound by various physical and analytical methods. A lot number is assigned from the Master Control Book and a Radiopharmaceutical Control Form (Fig. 2) is filled out for each batch of compound. This form records all data pertinent to the compound. The compounds are prepared either in a closed system using sterile reagents and aseptic technique or in an open system with sterilization of the final product. After preparation the product is assayed for activity. Every time a generator is eluted for injection without further processing the same form is filled out.

The eluents from the generators are checked for radionuclidic purity using chemical and physical methods. If contamination is above legal limits, the contaminant is removed or the eluent is not used. Labels (Fig. 3) are affixed to each vial of compound identifying the nuclide, chemical form, lot number and radioassay data.

Closed generators offer no problems in regard to protection of the column from bacterial or pyrogen contamination because the system is sealed and in use for a short time, but open generators that are in use for several months require precautions so that the generator itself does not become contaminated. To protect our open generator from airborne contamination, it is kept capped at all times. Eluting solution is added to the generator through a tube from an eluting solution reservoir through the cap. The eluent from this generator is checked periodically for bacteria to be sure that the generator has not become contaminated despite these precautions.

Bacteriological tests are run on pooled samples of all compounds and generator eluents after the radioactivity has decayed. The samples which comprise the pool are kept until results are reported so that should the pooled sample show the presence of bacterial growth, the individual samples can be tested to pin down the contaminated lot of compound.

The control forms, bacteriological and pyrogen test results, and the usual isotope distribution sheets are kept on file. These files allow every compound to be traced from its source to its final destination.

The standards we have set for our quality-control system follow the specifications set by the *USP XVII* in regard to sterility and pyrogen testing. We have set up other aspects of our system with consideration to acceptable chemical and pharmaceutical testing procedures.

This system has worked well in our hands. Since it was started in May 1967, we have had no bacteriological contamination of any injected compound in over 1,500 lots of material.

Radiopharmaceutical Control Form

Compound _____ Lot _____

Isotope Source _____

Reagent	Lot	Amount

Time _____ _____ mc./ml.

Date _____ _____ ml.

Made by _____ _____ mc.

FIG. 2. Radiopharmaceutical Control Form on which is recorded all data relevant to preparation of radiopharmaceuticals.

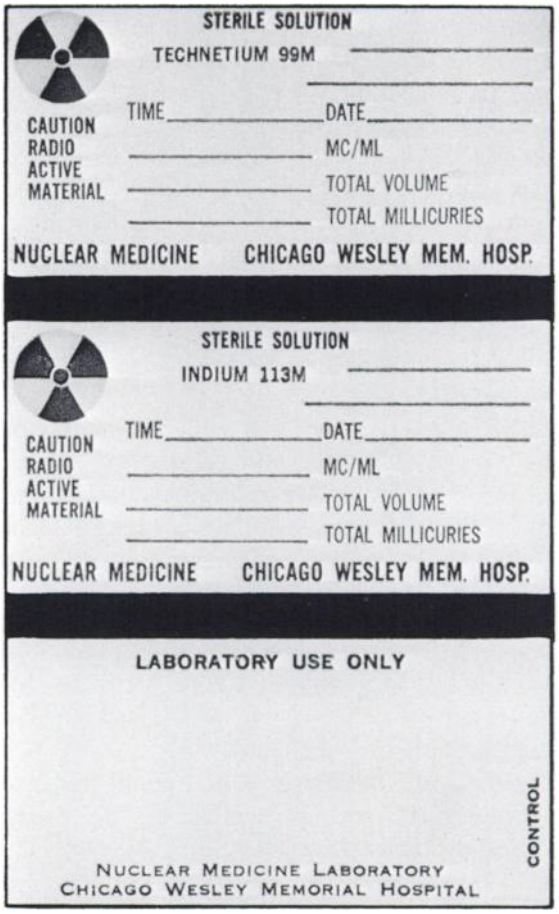

FIG. 3. Specimen labels for ^{99m}Tc, ^{113m}In and reagents used in radiopharmaceutical preparation.

REFERENCES

1. *The United States Pharmacopeia,* Seventeenth Revision, Mack Publishing Company, Easton, Pa., 1965.
2. Ibid., pp. 827, 863.