

Republic of the Philippines
PHILIPPINE NUCLEAR RESEARCH INSTITUTE
Department of Science and Technology
Address: Commonwealth Avenue Tel. No.: 97-60-11 to 15
Diliman, Quezon City Fax No.: 95-16-46

NRLSD BULLETIN 93-04

DOSE CALIBRATOR QUALITY CONTROL

A. ADDRESSEES

All licensees using radioactive material for use in nuclear medicine.

B. PURPOSE

This Bulletin is issued to alert radiopharmaceutical licensees to problems concerning dose calibrators identified by PNRI inspectors during inspections of medical programs, quality control tests for dose calibrators, and also to emphasize the importance of quality control procedures for equipment used to assay patient dosage.

It is expected that licensees will review this bulletin for applicability to their program and to preclude abnormal situation from occurring at their facilities.

C. DESCRIPTION OF CIRCUMSTANCES

It has been observed during regulatory inspections that some nuclear medicine facilities using radiopharmaceuticals do not have records to show that they are performing quality control tests of dose calibrators.

Quality control checks of dose calibrators used to assay patient dosages are essential to ensure that the dosage administered to a patient is the prescribed dosage.

D. DISCUSSION

Authorized users and technologists administering radioactive dosages should be aware of the applicable PNRI regulations and related requirement specified in the license conditions. Written procedures should be developed and followed to assure that the correct dosage is administered. The regulatory body provides model procedures for meeting these requirements. From these model procedures the licensee can develop his own procedures that may be acceptable to the Institute.

Licensees are responsible for providing instructions and supervision of the staff to ensure the proper and correct use of the procedures for dose calibrator tests.

The regulatory position with respect to the test and check procedures for the use of dose calibrator are the following:

1. Constancy Checks

Constancy means reproducibility in measuring the activity of a known source over a long period of time. The dose calibrator is required to be checked for constancy with a dedicated check source at the beginning of each day of use. This includes weekends and holidays, if radiopharmaceuticals are administered to patients.

A long-lived sealed medium-energy gamma radiation source such as Cs-137, Co-60 or Ra-226 is suitable for this purpose. The reproducibility of performance should be such that all individual measured activities are within $\pm 5\%$ of the mean measured activity.

2. Accuracy Test

The accuracy test ensures that the activity is within 10 percent of a given calculated reference source whose activity has been determined by the manufacturer to be within 5 percent of the activity stated in the Standards set in the country where the source was purchased or by the supplier who has compared that source to a source that was calibrated by the standards in the country of origin. At least one sealed source with a principal energy between 100 keV and 500 keV, must be used to determine accuracy upon installation, and at least quarterly thereafter. The activity is at least 10 μCi of Cs-137 or any other photon-emitting radionuclide. For best accuracy, the lower energy reference standards should be in vials of similar thickness to those for actual samples. The requirement states that if the error exceeds 10 percent then the dose calibrator must be repaired or replaced.

3. Linearity Tests

The linearity test ensures that the dose calibrator can indicate the correct activity over the range for which it is to be used. The dose calibrator is to be tested for linearity upon installation and at least quarterly thereafter. Technetium-99m is most frequently used for the linearity test because of its availability and short half-life. If the percent deviation exceeds 10 percent, dosage readings must be mathematically corrected.

4. Geometry Independence

Testing for geometry independence ensures that the indicated activity does not change with volume or configuration. This test must be performed upon installation, over the range of volumes and volume configurations for which it will be used, and should be done using a syringe that is normally used for injections. Licensees who use generators and radiopharmaceutical kits should also do the test using a vial similar in size, shape, and

construction to the radiopharmaceutical kit vials normally used. Geometry testing performed by the manufacturer may be acceptable, provided that the manufacturer has included all volumes and volume configurations for which the dose calibrator will be used at the licensee's facility and the licensee keeps a record of this test.

Licenseses are also required to perform appropriate checks and tests following adjustment (e.g., a constancy check after battery replacement) or repair of the dose calibrator. Whereas it is not necessary to check geometry dependence if the dose calibrator is physically relocated within the department or following minor repairs to the instrument panel, it is appropriate to do the geometry check if repairs are done that might affect the response of the chamber. It is appropriate to conduct linearity and accuracy tests following any repairs to the dose calibrator.

It is the responsibility of the Radiological Health and Safety Officer (RHSO) and the Medical Isotopes Committee (MIC) to ensure that these tests are performed. The RHSO shall be responsible for implementing the radiation safety program and ensuring that radiation safety activities are being performed in accordance with approved procedures and regulatory requirements in the daily operation of the licensee's radiopharmaceutical program. In addition, the Medical Isotopes Committee (MIC) shall perform reviews to oversee the use of radioactive materials and see to it that a copy of all records and reports required by the regulations are kept.

E. REQUIRED LICENSEE ACTION

All licenseses who possess and use dose calibrators are required to respond to this bulletin describing their compliance, or otherwise, to this bulletin.

If there are questions about this Bulletin, please contact the person listed below.

Enclosures: Model Procedures

June 14, 1993

TECHNICAL CONTACT:

OSROXZON L. AMPARO

Head, Standards Development Section
Nuclear Regulations, Licensing and Safeguards Division
Tel. No. 97-60-11 to 15 local 227
96-73-43 Direct Line

MODEL PROCEDURES FOR CALIBRATING DOSE CALIBRATOR

1. CONSTANCY

Constancy means reproducibility in measuring a constant source over a long period of time. Assay at least one relatively long- lived source such as Cs-137, Co-60, Co-57 or Ra-226 using reproducible geometry each day before using the calibrator. Use the following procedure:

- a. Assay each reference source using the appropriate dose calibrator setting (i.e., use the Cs-137 setting to assay Cs-137);
- b. Note the background reading to be subtracted from subsequently measured activities. Alternatively, if an adjustable zero control is provided, adjust this for zero reading;
- c. Insert the gamma-radiation source into the source holder by means of the remote handling device and introduce the source holder into the instrument;
- d. Allow sufficient time for the reading to stabilize;
- e. Measure and record the apparent activity, subtracting the background reading if necessary;
- f. Remove the source from the instrument and extract the source by means of the remote handling device;
- g. Repeat steps a. to f. under operating conditions appropriate to each other radionuclide in common use. Plot or log the results.

2. TEST OF PRECISION AND ACCURACY

Purpose of Test

To test the precision and accuracy of a radionuclide calibrator in activity measurements in standard geometry at selected gamma-radiation energies.

Materials

Sealed low, medium and high-energy gamma radiation sources (standard vial-type), certified to $\pm 5\%$ overall uncertainty or less, e.g. Co-57, Ba-133, Cs-137 and Co-60.

Source holder
Remote handling device for sources

Procedure

For each gamma-radiation source in turn:

1. Select the operational conditions appropriate to the radionuclide concerned;
2. Note the background reading to be subtracted from subsequently measured activities. Alternatively, if an adjustable zero control is provided, adjust this for zero reading;
3. Insert the source into the source holder by means of the remote handling device and introduce the source holder into the instrument;
4. Allow sufficient time for the reading to stabilize;
5. Measure and record the activity, subtracting the background reading if necessary;
6. Repeat step 5 to a total of 10 successive measurements;
7. Remove the source holder from the instrument and extract the source by means of the remote handling device.

Data Analysis

1. To assess precision, calculate for each source the percentage differences between the individual measured activities, A_i , and their mean, A , that is:

Record results of calculations.

2. To assess accuracy, calculate for each source the percentage difference between the mean measured activity, A , and the certified activity of the source corrected for radioactive decay to the day of measurement, C , that is:

Record results of calculations.

Limits of acceptability

The limits of acceptability for the results of the test are determined by the precision and accuracy of the instrument specified by the manufacturer. In general, however, for measurements on sources such as those specified, the precision should be such that all individual measured activities on any source are within $\pm 5\%$ of the mean measured activity, provided that radioactive decay has a negligible effect over the measurement period, and the accuracy should be such that the mean measured activity is within $\pm 10\%$ of the certified value corrected for radioactive decay to the day of measurement.

3. TEST OF LINEARITY OF ACTIVITY RESPONSE

Purpose of Test

To test the linearity of the activity response of a radionuclide calibrator over the range of activities for which it is to be used.

METHOD 1: DECAYING SOURCE METHOD

Materials

Short-lived radionuclide (e.g., Tc-99m or In-113m) in solution, initial activity equal to or greater than the highest activity for which the instrument is to be used (e.g., 3.7 GBq (100 mCi)).

Sample vial
Remote pipetting device
Source holder
Remote handling device for sample vial
Log-linear graph paper (3- or 4-cycle)

Procedure

1. Transfer the radionuclide solution to the sample vial by means of the remote pipetting device. Cap the vial firmly.
2. Select the operational conditions appropriate to the radionuclide concerned.
3. Note the background reading to be subtracted from subsequently measured activities. Alternatively, if an adjustable zero control is provided, adjust this for zero reading.
4. Insert the sample vial into the source holder by means of the remote handling device and introduce the source holder into the instrument.

5. Allow sufficient time for the reading to stabilize.
6. Measure and record the activity, subtracting the background reading if necessary. Record the exact time of day corresponding to the measurement.
7. Remove the source holder from the instrument and extract the sample vial by means of the remote handling device.
8. Repeat steps 2-7 regularly over a period several times greater than the physical half-life of the radio-nuclide, sufficient for the source to decay to an activity equal to or less than the lowest activity for which the instrument is to be used.
9. Record the results on a graph showing measured activity against lapsed time on 3 or 4-cycle log-linear paper (see Figure 1).
10. With the aid of a transparent ruler, fit the best straight line possible to the data points in the lower activity region. Extrapolate this line upward to obtain an activity value corresponding to the time of the initial reading measurement.
11. Check the negative slope of the line to ensure that it is consistent with the known physical half-life of the radionuclide. This may conveniently be done by dividing the time for the measured activity to fall to 1/10 of its initial value, determine in step 10, by 3.32 and comparing the result with the physical half-life.
12. Examine the graph for systematic departures of the data points from the fitted straight line; such discrepancies indicate non-linearity of the activity response of the instrument.

Limits of acceptability

In general, the linearity of the activity response should be such that all individual activities measured in the test are within $\pm 10\%$ of the values corresponding to the straight line fitted to the data points.

METHOD 2: GRADED SOURCES METHOD

Materials

Radionuclide of moderate half-life (e.g., I-131) in solution, activity equal to or

greater than twice the highest activity for which the instrument is to be used (e.g., 7.4 GBq (200 mCi)).

Sample vials
Remote pipetting device
Source holder
Remote handling device for sample vials
Log-log graph

Procedure

Caution: The extensive handling of a large amount of radioactive material in this method necessitates the use of gloves, radiation shields and remote pipetting and handling devices. If I-131 is used, it must be pipetted and stored for decay in a fume hood with adequate air flow. If these protective devices are not available, do not proceed.

1. Pipette into a series of sample vials by means of the remote pipetting device decreasing volumes of the radionuclide solution, with activities covering the range of interest (e.g. 10, 5, 2, 1, 0.5, 0.2, 0.1 ml of a solution having an activity about 370 MBq/ml (10 mCi/ml). Bring up the total volume in each vial to the same volume (e.g. 20 ml) with water. Cap the vials firmly.
2. Select the operating conditions appropriate to the radionuclide concerned.
3. Note the background reading to be subtracted from subsequently measured activities. Alternatively, if an adjustable zero control is provided, adjust this zero for zero reading.
4. Insert the sample vial having the highest activity into the source holder by means of the remote handling device and introduce the source holder into the instrument.
5. Allow sufficient time for the reading to stabilize.
6. Measure and record the activity, subtracting the background reading if necessary.
7. Remove the source holder from the instrument and extract the sample vial by means of the remote handling device.
8. Repeat steps 4-7 for each of the other sample vials in turn.
9. Record the results on a graph showing measured activity against volume of

radionuclide solution on log-log paper (see Figure 2).

10. With the aid of a transparent ruler, fit the best straight line possible to the data points in the lower activity region.
11. Extrapolate the line to cover the full range of measured activities.
12. Examine the graph for systematic departures of the data points from the fitted straight line: such discrepancies indicate non-linearity of the activity response of the instrument.

4. GEOMETRY INDEPENDENCE

The following test assumes injections are done with 3-cc plastic syringes and that radiopharmaceutical kits are made in 30-cc glass vials. If you do not use these, change the procedure so that your syringes and vials are tested throughout the range of volumes commonly used.

- a. In a small beaker or vial, mix 2 cc of a solution of Tc-99m with an activity concentration between 1 and 10 mCi/ml. Set out a second small beaker or vial with nonradioactive saline. You may also use tap water.
- b. Draw 0.5 cc of the Tc-99m solution into the syringe and assay it. Record the volume and millicuries indicated on the Dose Calibrator Geometry and Accuracy Form (see Form).
- c. Remove the syringe from the calibrator, draw an additional 0.5 cc of nonradioactive saline or tap water, and assay again. Record the volume and millicuries indicated.
- d. Repeat the process until you have assayed a 2.0-cc volume.
- e. Select as a standard the volume closest to that normally used for injections. For all the other volumes, divide the standard millicuries by the millicuries indicated for each volume. The quotient is a volume correction factor. Alternatively, you may graph the data and draw horizontal 5 percent error lines above and below the chosen "standard volume".
- f. If any correction factors are greater than 1.05 or less than 0.95 or if any data points lie outside the 5 percent error lines, it will be necessary to make a correction table or graph that will allow you to convert from "indicated activity" to "true activity". If this is necessary, be sure to label the table or graph "syringe geometry dependence", and note the date of the test and the

model number and serial number of the calibrator.

- g. To test the geometry dependence for a 30-cc glass vial, draw 1.0 cc of the Tc-99m solution into a syringe and then inject it into the vial. Assay the vial. Record the volume and millicuries indicated.
- h. Remove the vial from the calibrator and, using a clean syringe, inject 2.0 cc of nonradioactive saline or tap water, and assay again. Record the volume and millicuries indicated.
- i. Repeat the process until you have assayed a 19.0-cc volume. The entire process must be completed within 10 minutes.
- j. Select as a standard the volume closest to that normally used for mixing radiopharmaceutical kits. For all the other volumes, divide the standard millicuries by the millicuries indicated for each volume. The quotient is a volume correction factor. Alternatively, you may graph the data and draw horizontal 5 percent error lines above and below the chosen "standard volume".
- k. If any correction factors are greater than 1.05 or less than 0.95 or if any data points lie outside the 5 percent error lines, it will be necessary to make a correction table or graph that will allow you to convert from "indicated activity" to "true activity". If this is necessary, be sure to label the table or graph "vial geometry dependence", and note the date of the test and the model number and serial number of the calibrator.