Recommended Procedures for Performance Testing of Radiobioassay Laboratories

Volume 3: In Vivo Test Phantoms

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November 1988

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RECOMMENDED PROCEDURES FOR PERFORMANCE
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FOREWORD

In recent years, extensive research has been conducted to improve occupational radiation protection. Of particular concern to the U.S. Department of Energy (DOE) and U.S. Nuclear Regulatory Commission (NRC) have been the accuracy, quality control, and performance of personnel radiation dosimeters, radiation survey instruments, and bioassay laboratories.

The U.S. Department of Energy Order 5480.1, Chapter XI (DOE 1983) and Title 10, Part 20 of the U.S. Code of Federal Regulations (NRC 1982) require assessment of occupational radiation exposures. Accurate bioassay measurements are necessary to correctly assess internal exposure to radioactive materials. However, a concern of both DOE and NRC is that bioassay laboratories may not be providing accurate and consistent results. To address this concern a Health Physics Society working group was formed to prepare a draft American National Standards Institute (ANSI) standard on bioassay laboratory performance. The resultant document was designated draft ANSI N13.30, Performance Criteria for Radiobioassay.^(a)

Draft ANSI N13.30 provides performance criteria in the form of the minimum numerical values necessary to meet an acceptable minimum detectable amount, relative bias, and relative precision. The acceptance values for these criteria have been reviewed and revised throughout the process of developing the draft standard.

The testing procedures described in this document were developed as a part of a project to evaluate the performance criteria of draft ANSI N13.30 by testing the current measurement capabilities of various in vivo bioassay laboratories. Included in the project was a nationwide, two-round bioassay intercomparison study to test the analytical performance of in vivo (external measurement) bioassay laboratories and evaluate their ability to meet the minimum performance criteria specified in the standard.

(a) Copies of published draft ANSI N13.30 are available from the Executive Secretary, Health Physics Society, 8000 Westpark Drive, Suite 400, McLean, VA 22102.

The procedures used to prepare in vivo samples have been described in a previous report of this research project, Performance Testing of Radiobioassay Laboratories: In Vivo Measurements, Pilot Study Report (Robinson et al. 1986).

The purpose of this report is to provide recommended procedures for
1) preparing standard radionuclide solutions for in vivo test phantoms,
2) preparing and distributing test phantoms, and 3) evaluating the measurement performance of in vivo counting facilities.

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SUMMARY

Draft American National Standards Institute (ANSI) Standard N13.30 (Performance Criteria for Radiobioassay) was developed for the U.S. Department of Energy and the U.S. Nuclear Regulatory Commission to help ensure that bioassay laboratories provide accurate and consistent results. The draft standard describes the procedures necessary to establish a bioassay performance-testing laboratory and program. The bioassay performance-testing laboratory will conduct tests to evaluate the performance of service laboratories.

Pacific Northwest Laboratory^(a) helped develop testing procedures as part of an effort to evaluate the draft ANSI N13.30 performance criteria by testing the existing measurement capabilities of various bioassay laboratories. This report recommends guidelines for the preparation, handling, storage, distribution, shipping, and documentation of test phantoms used for calibration of measurement systems for direct bioassay. The data base and recommended records system for documenting radiobioassay performance at the service laboratories are also presented.

(a) Pacific Northwest Laboratory is operated for the U.S. Department of Energy under Contract DE-AC06-76RLD 1830 by Battelle Memorial Institute.

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ACRONYMS

AMDA	acceptable minimum detectable amount
ANSI	American National Standards Institute
CFR	U.S. Code of Federal Regulations
CUS	concentration of the uranium solution
DOE	U.S. Department of Energy
DTPA	diethylenetriaminepentaacetate
EDTA	ethylenediaminetetraacetic acid
HPSSC	Health Physics Society Standards Committee
MDA	minimum detectable amount
NBS	National Bureau of Standards
NCRP	National Council on Radiation Protection and Measurement
NRC	U.S. Nuclear Regulatory Commission
QA	quality assurance
TQ	test quantity

1.0 INTRODUCTION

1.1 PURPOSE

This report provides recommended procedures for: 1) preparing standard radionuclide solutions for in vivo test phantoms, 2) preparing and distributing test phantoms for the bioassay performance-testing program, and 3) evaluating the performance of bioassay service laboratories. The overall goal of this report is to specify the content of the procedures that are necessary to establish a bioassay performance-testing laboratory. The purpose of the testing laboratory is to help the service laboratories establish acceptable radiobioassay practices.

1.2 SCOPE

The procedures recommended in this report are based on technical specifications given in the American National Standards Institute (ANSI) Standard N13.30, Performance Criteria for Radiobioassay.^(a) This performance standard was prepared by Working Group 2.5 of the Health Physics Society Standards Committee (HPSSC). The U.S. Department of Energy (DOE) and the U.S. Nuclear Regulatory Commission (NRC) asked the HPSSC to provide guidance on acceptable criteria for bioassay laboratory measurements, and the draft performance standard resulted from the Committee's efforts.

The procedures given in this report apply only to the performance testing of direct (in vivo) bioassay measurements. Metabolic data and mathematical models for converting radiobioassay results into depositions or into absorbed dose and dose equivalent are beyond the scope of this report.

1.3 PROCEDURE REVISION

Revisions of the testing procedure may be necessary. The revision process should conform to instructions given in Section 1.3 of Volume 1 of this report.

(a) Copies of published draft ANSI N13.30 are available from the Executive Secretary, Health Physics Society, 8000 Westpark Drive, Suite 400, McLean, VA 22102.

1.4 DEFINITION OF TERMS

The definitions of the terms used in this report conform to those given in Section 2 of draft ANSI N13.30. Additional terms are defined in Section 1.4 of Volume 1 of this report.

2.0 PREPARATION OF TEST PHANTOMS FOR INDIRECT BIOASSAY

The following procedures for the preparation of test phantoms were established to evaluate the performance of in vivo bioassay service laboratories.

2.1 STANDARDS OF THE NATIONAL BUREAU OF STANDARDS

Standardized radionuclide solutions used in the preparation of test phantoms should be certified by the National Bureau of Standards (NBS), either directly or by traceability through the demonstrated-measurement-capability pathway. The certificates should be kept in the Quality Assurance (QA) notebook or in a file that is referenced in the QA notebook. Radioactive standard solutions are normally stored in a radiation work area. The supervisor of the testing laboratory should keep an inventory of these radioactive materials.

2.2 SELECTION OF TEST RADIONUCLIDES

Each service laboratory has the option of being tested and evaluated for an entire category of draft ANSI N13.30 or for a specific radionuclide in a category. If the service laboratory elects to be tested for an entire category, a test radionuclide will be selected by the performance-testing laboratory from the radionuclides listed for the category in Table 3 of the standard. If the service laboratory designates a specific radionuclide for which they wish to be tested, only that radionuclide may be used for testing and evaluation, and accreditation will be for that radionuclide only.

2.3 PREPARATION OF TEST PHANTOMS OF KNOWN RADIOACTIVITY

The performance-testing laboratory should prepare two types of phantoms. The first type of phantom is an appropriate blank as described in draft ANSI N13.30. This phantom contains only ⁴⁰K. The second type of phantom, a test phantom, will be identical to the blank phantom except for the addition of the radionuclides that are specified in the various test categories. The purpose of the blank phantom is to allow for estimation of the minimum detectable amount (MDA) of the service laboratory. The test phantom should be used to

estimate the bias and precision of the service laboratory. The performance-testing laboratory may also prepare and distribute phantoms that contain radionuclides less than 10 times the acceptable minimum detectable amount (AMDA). These phantoms may be used to evaluate the performance of the service laboratory near the AMDA for the given procedure and for verification of the MDA calculations. The service laboratory will be requested to make five replicate analyses of each phantom, removing and repositioning the phantom after each analysis.

2.3.1 Whole Body Phantom Preparation

Draft ANSI N13.30 requires that the whole body phantom used for testing purposes be commercially available and that the activity be uniformly distributed throughout the phantom. In this report we assume that the phantoms used will be equivalent to those used during the intercomparison studies conducted during development of the draft standard. Any phantom that meets the criteria of the standard may be used by the performance-testing laboratory.

A BOMAB whole body bottle phantom, consisting of 10 sturdy polyethylene circular or elliptical right cylinders, was used during intercomparison testing (EMI Gencom, Inc., Plainview, New York). Each cylinder was fitted with a sturdy screw-cap for filling. The bottles of the phantom were of various sizes and volumes that approximated the whole body proportions of an adult male of average stature. The dimensions and volumes of the phantom are given in Table 1. The volume of each part is the volume that can be filled with tissue-equivalent test matrix.

Each of the bottles of the phantom should be filled with a solution that contains the appropriate quantity of radionuclides and ^{40}K . The potassium included in the phantom approximates the potassium content of an adult, which is included for its ^{40}K content.

TABLE 1. Dimensions of Phantom Bottles Representing Human Body Parts

<u>Part</u>	<u>Shape</u>	<u>Cross Section, cm</u>	<u>Length, cm</u>	<u>Vol, mL</u>	<u>Percent of Total</u>
Head	Ellipse	19 x 14	20	3,244	5.8
Neck	Circle	13	10	900	1.6
Thorax	Ellipse	30 x 20	40	16,370	29.1
Abdomen	Ellipse	36 x 20	20	9,118	16.2
Arms (2)	Circle	10	60	7,305	13.0
Thighs (2)	Circle	15	40	11,970	21.3
Legs (2)	Circle	12	40	<u>7,362</u>	<u>13.0</u>
Total				56,269	100

Preparation of Phantom Solutions

The amount of radioactivity to be placed in the test phantoms is provided in draft ANSI N13.30. The quantity of radionuclide placed in the whole body phantom for purposes of testing relative precision and relative bias must exceed 10 x AMDA for the particular radionuclide. The testing quantity of each radionuclide to be included in the phantom is called the TQ.

A solution containing the TQ of each radionuclide should be prepared and the solutions combined to form a phantom stock solution. During the preparation of the phantom stock solution, the dilutions of individual radionuclides should not exceed a factor of about 1:1000. During dilution of the radionuclides, precautions must be taken to ensure that the radionuclide does not adhere to the surface of the container. Surface plateout may be prevented by diluting the radionuclide with nitric acid, with a solution that contains a chelating agent such as ethylenediaminetetraacetic acid (EDTA) or diethylenetriaminepentaacetate (DTPA), or with a carrier solution. The carrier solution method is best suited for activation fission products.

An excess amount of phantom stock solution should be prepared so that an aliquant is reserved for radionuclide analysis. The concentration of the phantom stock solution should be low enough so that the dilution from the stock solution to the phantom is not too great. The reason for a small

dilution factor is that the mixing process for the phantom takes place in the phantom body segment and is not very efficient. We recommend that the dilution factor not exceed about 1:100. Aliquants of the phantom stock in proportion to the "percent of total" column in Table 1, are pre-weighed into plastic containers; one for each phantom segment.

Preparation of Phantom Body Parts

A warm gelatin mixture is prepared by dissolving 300 g of gelatin in 2.5 L of water. The gelatin solution is poured into the phantom section until the section is about half full. The pre-weighed radionuclide solution is neutralized with an appropriate volume of KOH solution and poured into the phantom segment. The radionuclide bottle is rinsed several times and the rinsate is poured into the body segment. Benzalkonium chloride (17% solution or 16 mL/L) is also added to the phantom segment to inhibit the growth of microorganisms, and sodium metabisulfate (5 g/L) is added to retard the oxidation of the gelatin. The phantom segments are tilted back and forth until complete mixing of the solution is achieved. Food coloring may be added to the segment prior to the mixing process; the distribution of the food coloring will aid in gauging the degree of mixing that has been achieved.

Draft ANSI N13.30 states that the phantom shall contain ^{40}K in an amount equivalent to that contained in a person of average stature (0.08-0.16 μCi). If enriched ^{40}K is not readily available, the requisite activity can be obtained using a potassium salt. Assuming an isotopic abundance of 1.2% for ^{40}K in potassium, 0.08-0.16 μCi of ^{40}K will be found in 95 to 190 g of potassium. If KCl is used as the source of the potassium, the required amount is 181 to 362 g KCl. The potassium should be distributed among the phantom segments in proportion to the "percent of total" column of Table 1.

The segment should be filled by adding gelatin solution in small increments. The solution is mixed after each addition. When the segment is filled and well mixed, it should be placed in a refrigerator to cool and solidify. The purpose of the gelatin is to stabilize the radionuclide solution to reduce leakage if a segment is dropped and broken.

A second phantom is required for estimating the MDA. This phantom is identical to the phantom that contains the test radionuclides, except that the

quantity of the test radionuclides is at the single AMDA level. The ^{40}K content should be the same as that of the test phantom. This phantom should be identified by a different color of food coloring so the parts do not become interchanged.

2.3.2 Lung Phantom Preparation

The lung phantom specified by draft ANSI N13.30 is one that is a realistic simulation of the torso, skeleton, and lungs of a man of average stature. The phantom should have a chest wall over the lungs that simulates muscle tissue with a thickness in the range of 1.4 to 1.7 cm. The simulated tissues of the phantom should have transmission and scatter characteristics for low-energy photons that closely approximate those for normal tissue. The torso phantom should have interchangeable pairs of simulated lungs in which the test radionuclide is uniformly distributed. Also, the phantom should be commercially available. Any phantom that meets the above criteria is acceptable for purposes of the draft standard.

The phantom used during intercomparison testing was a realistic torso phantom developed at Lawrence Livermore National Laboratory and marketed commercially by the Humanoid Systems, Inc. The phantom was constructed of tissue-equivalent plastic materials and plastic bone. The phantom contains an interchangeable pair of simulated lungs with a density of 0.3 g/cm^3 . For the final round of the intercomparison study, kits were obtained from the manufacturer that allowed custom fabrication of lung sets. The kit material consisted of two parts; a black urethane plastic and a catalyst. The radionuclide solution was mixed with the plastic component prior to polymerization. Addition of the catalyst causes polymerization and foaming of the urethane material. After the lungs were formed they were sealed with a polyurethane coating. The final product was a lung-shaped object that contained a uniform distribution of radioactivity the total quantity of which is well known.

Preparation of the Lung Solution

Draft ANSI N13.30 states that for testing the bias and precision of the service laboratory, the radionuclides shall be in the lungs in a quantity at least 10 times the AMDA for the particular radionuclide and within the range

of activity listed in Table 3 of the draft standard. The testing quantity can be any quantity chosen by the performance-testing laboratory and will be labeled TQ.

A solution containing the TQ of each radionuclide should be prepared and the solutions should be combined to form a phantom stock solution. During the preparation of the phantom stock solution the dilutions of individual radionuclides should not exceed a factor of about 1:1000. During dilution of the radionuclides, precautions must be taken to ensure that the radionuclide does not adhere to the surface of the container. This may be effected in one of at least three ways. First, the radionuclide may be diluted with nitric acid. Second, the radionuclide may be diluted with a solution that contains a chelating agent, such as EDTA or DTPA, which has an affinity for the test radionuclides. Lastly, the radionuclide solution may be diluted with a carrier solution. The carrier solution method is best suited for activation/fission products because these radionuclides have stable isotopes that may be used for carriers.

The TQ must be partitioned between the right and the left lung; these quantities will be referred to as TQ-R and TQ-L, respectively. The activity in the right and left lungs should be proportional to the relative mass of each lung (of the phantom). The quantities are:

$$\text{TQ-R} = 0.56 \text{ TQ}$$

$$\text{TQ-L} = 0.44 \text{ TQ.}$$

The test solutions should be prepared using gravimetric means rather than volumetric means. The reason for this is that Standard Reference Materials (SRMs) are calibrated for gravimetric dispensing and gravimetric methods avoid the necessity of temperature corrections for the volumes. The balances used by the performance-testing laboratory should be calibrated; the weight calibrations should be traceable to the NBS.

When preparing the testing quantities of the radionuclides, the performance-testing laboratory should weigh the test solutions in non-wetting plastic vials. Also, it is recommended that during any dilutions the testing

laboratory prepare greater quantities of material than required so that the testing laboratory can analyze the solutions at each dilution.

^{238}Pu Solutions. Standard Reference Material solutions of ^{238}Pu can be ordered from the NBS. The material should be ordered so that it is packaged in the desired quantity in separate vials. The procedure is then to open the vial, weigh the vial, empty the contents of the vial into the lung material, and then reweigh the vial. The loss in mass of the vial is the mass of the material dispensed into the lung material.

Activation/Fission Product Solutions. Standard Reference Material solutions can be obtained from the NBS for the test and interference radionuclides that are to be in the lungs. Alternately, Reference Standards for the radionuclides can be obtained from commercial suppliers.

The lungs will normally contain four radionuclides; two test radionuclides and two interference radionuclides. Each radionuclide should be diluted so that TQ-L and TQ-R will be in a volume from 0.12 to no more than 1.2 mL. The solutions should be prepared so that the testing quantity is in the smallest possible volume. After each dilution of the radionuclides an aliquant should be reserved for confirmation of the radionuclide concentration. The test and interference radionuclides are then pooled. An aliquant of the pooled radionuclides should be taken for analysis to confirm that the solution contains all the desired radionuclides in the desired quantities.

Natural Uranium Solutions. Standard Reference Materials of natural uranium metal are available from the New Brunswick Laboratory, Argonne, Illinois. The metal must be prepared as a solution using the method described here. Dip the metal in 1:1 HNO_3 for about 10 minutes to remove the surface oxide on the metal. Rinse the metal in distilled water. Etch the metal in 1:3 HCl for 5 minutes. Rinse the metal thoroughly in distilled water. Pat dry the metal with a lint-free wiper, then place the metal chip in a vacuum desiccator. Removal of surface moisture is accelerated and reoxidation of the metal is retarded by drying the chip under vacuum for a suitable length of time (evacuation for a 1/2-hour is sufficient). After about 30 minutes, periodically reweigh the metal chip until a constant weight has been achieved. During the

cleaning process it is important that the metal not be touched with the fingers; use only clean stainless steel forceps for handling the metal. The weighing should be done on a calibrated balance.

After a constant weight has been achieved for the uranium metal place it in a tared pyrex flask. Add enough 1:1 HNO_3 /3N HCl to dissolve the metal. The solution can be diluted with distilled water; if a precipitate forms the material can be resolubilized by the addition of a small quantity of 3N HCl. After the metal has been solubilized, reweigh the flask. The formula for the concentration of the uranium solution (CUS) is:

$$\text{CUS} = \frac{\text{mass of uranium chip}}{\text{MF2W} - \text{MF1W}} \quad (1)$$

where MF2W is the mass of the flask after the second weighing and MF1W is the mass of the flask after the first weighing. The quantity of the solution that is to be placed into each lung is:

$$\text{Mass of solution for left lung} = \text{TQ-L/CUS} \quad (2)$$

$$\text{Mass of solution for right lung} = \text{TQ-R/CUS}. \quad (3)$$

Preparation of the Lungs

The lung material is a two-component kit. One component is a black plastic, the other is a clear catalyst. Only a very small volume of the radionuclide solution can be incorporated into the plastic component. The manufacturer recommends that the volume be less than 0.5 mL, although we have been able to incorporate up to 5 mL of radionuclide solution with some degradation of the quality of the plastic. Record the mass of the black plastic material that is in the mixing container.

The radionuclide solution is added to the plastic component. Although human lung actually contains very little potassium, draft ANSI N13.30 specifies that KCl is also added to the lung material; 89.6 g for the right lung, 70.4 g for the left lung. The KCl should be sprinkled over the surface of the material in an attempt to prevent clumping and to aid in effecting a uniform mixture. The plastic component is then thoroughly mixed with a paint

stirrer attached to a hand-held power drill. This is not a time-critical process, so sufficient time can be taken to ensure the uniform distribution of the radionuclide.

The lung molds are prepared by first cleaning them with acetone and then lubricating them with a silicone grease (Dow Corning #4 silicone grease works well).

Mix the catalyst component well, then draw the material into two 50-mL syringes that have luer fittings. Record the mass of the syringes after they have been filled with catalyst material.

The next step is best performed by two persons. One individual operates a hand-held drill and paint stirrer, mixing the black plastic component. The second person adds the catalyst using the syringe. The streams from the syringes should be moved back and forth to aid in the mixing of the catalyst. The plastic-catalyst mixture is mixed for about 10 seconds. The mixture is then poured into the bottom half of the lung mold. The mixture can be scraped out of the mixing container with a tongue depressor.

The top of the lung mold is clamped into place. The vent hole of the top portion of the lung mold should be closed with a stopper when plastic material begins to exude from the hole. Record the mass of the catalyst syringes after the catalyst has been injected into the black plastic.

Allow the lung to set for at least 1 hour before removing it from the mold. Trim the edges of the lung of all material that leaked between the two halves of the lung mold, then weigh the lung to determine the mass of the lung. After removing the lung from the mold, clean the lung with acetone and paint it with a polyethylene coating material. White model paint is used to mark the lungs.

The marking on the lungs is of the type "nnnnn-xx," where nnnnn is the laboratory notebook number, and xx is the page number of the notebook that contains the data recorded during the manufacture of the lung material.

The radionuclide concentration (C) in the lung material is given by the following equation:

$$C = \frac{A_S}{(M_B + M_C + M_R + M_K)} \quad (4)$$

where M_B = Mass of black plastic (the mass of the material placed into the mixing container)

A_S = Activity of added test radionuclide solution in nanocuries

M_C = Mass of catalyst (the mass of the full catalyst syringes minus the mass of the emptied catalyst syringes)

M_R = Mass of the radionuclide solution

M_K = Mass of KCl.

The activity in the lung material (A_L) is given by the equation:

$$A_L = M_L \times C \quad (5)$$

where M_L equals the mass of the lungs after trimming excess material and before applying a sealant.

2.3.3 Thyroid Phantom Preparation

Draft ANSI N13.30 specifies that the thyroid phantom shall be that described in ANSI N44.3-1973, American National Standard: Thyroid Radioiodine Uptake Measurements using a Neck Phantom (ANSI 1973). This phantom is a right cylinder of polymethacrylate. The dimensions are 12.7 cm (5 in.) in height and diameter. The phantom contains a cavity in which a polyethylene bottle can be placed. The bottle dimensions are 3 cm (1.2 in.) in diameter and 7.5 cm (3 in.) in height, and it has a nominal volume of 30 mL.

Preparation of the Iodine Solution

Draft ANSI N13.30 states that for testing the bias and precision of the service laboratory the radionuclides in the thyroid shall be in a quantity of at least 10 times the AMDA for the particular radionuclide and within the range of activity listed in Table 3 of the draft standard. The testing quantity of the iodine can be any quantity chosen by the performance-testing laboratory and is designated TQ.

Following the recommendations in ANSI N44.3-1973, the iodine activity is prepared to contain a TQ volume of 30 mL and is dispensed in polyethylene bottles. The solutions are prepared with a carrier solution of sodium iodide containing 200 g/mL of sodium thiosulfate; the purpose of the sodium

thiosulfate is to prevent volatilization of the iodine. The dispensing should be done gravimetrically using a calibrated balance.

The bottles of iodine solution are sealed by placing an adhesive sealing compound around the cap screws prior to closing the vial. The bottles may also be sealed with tape. An aliquant of the iodine solution should be retained for measurement of total iodine content.

2.3.4 Certification of Activity

The amount(s) of activity of the test radionuclide(s) in the test phantoms should be estimated with an overall propagated standard deviation of 5% or less using the methods given in the appendix. An aliquant of each test sample batch should be analyzed by a laboratory with demonstrated measurement traceability to the NBS as described in Report No. 58 of the National Council on Radiation Protection and Measurements (NCRP 1985). The amount estimated by the testing laboratory shall not differ from the analyzed amount by more than 5%. If the estimated uncertainty or difference between the estimated and measured activity exceeds 5%, the test-sample batch should not be used in the accreditation program.

2.4 LABELING AND PACKAGING

Samples should be labeled and packaged in a manner that allows for proper documentation of chain of custody and sample identification. Shipping cases should be sturdy enough to withstand normal handling during shipping.

2.5 STORAGE

If samples are not shipped immediately to the bioassay service laboratory, they should be stored in a designated storage area. This storage area should be separate from any other radioactive materials use to avoid external contamination of the shipping container.

2.6 SHIPPING

The test radionuclide activity levels qualify under the "limited quantity" designation of Section 173421 of Title 49 of the U.S. Code of Federal Regulations, Transportation (CFR 1986). The sample containers are packaged

and labeled in compliance with federal regulations for packaging and shipping nonradioactive materials. The shipping of "limited quantity" activity levels does not require any external radiation labeling of the box. Samples are generally shipped by surface carrier.

2.7 DOCUMENTATION AND RECORD KEEPING

The QA notebook should contain or reference the storage location of the NBS certificates for the standard radionuclide solutions used in the preparation of the test samples. Worksheets that are not included in the QA notebook should be referenced and their storage location recorded. It is important that individual weights be recorded so that checks can be made on the calculations of radionuclide concentrations. All information from the individual sample labels, as well as the known radionuclide concentration for the samples, should be maintained within the process control data base.

3.0 ANALYSIS REPORT EVALUATION

Following the receipt of analysis data for all samples sent to a service laboratory, the test statistics for the performance report should be calculated. The test statistics include the relative bias (B_r), relative precision (S_A and S_B), and the MDA for each test nuclide analyzed by the service laboratory. Test statistics are calculated in accordance with draft ANSI N13.30.

3.1 RELATIVE BIAS AND RELATIVE PRECISION

The B_r , S_A , and S_B are easily calculated from the analysis data reported by the service laboratory using the following equations:

$$B_{rij} = \frac{A_{ij} - A_{ai}}{A_{ai}} \quad (6)$$

$$B_r = \sum B_{rij} = \sum_{i=1}^M \sum_{j=1}^N B_{rij} / N \cdot M \quad (7)$$

$$S_A = \left[\sum_{i=1}^M \sum_{j=1}^N (A_{ij}/A_i - 1)^2 / (N \cdot M - 1) \right]^{1/2} \quad (8)$$

$$S_B = \left[\sum_{i=1}^M \sum_{j=1}^N (B_{rij} - B_r)^2 / (N \cdot M - 1) \right]^{1/2} \quad (9)$$

where B_{rij} = the relative bias (B_r) of the j th sample in the i th activity category

A_{ij} = the reported result for the j th sample in the i th activity category

A_{ai} = the true activity for the i th activity category

N = the number of samples per activity category

M = the number of activity categories

$A_i = \sum A_{ij} / N$ = the mean reported result for the i th activity category.

3.2 MINIMUM DETECTABLE AMOUNT

Estimation of the MDA requires the evaluation of the variability observed in the measurement of the appropriate blanks. The specific form of the MDA equation will depend on the assumptions made about the count distribution. If the performance test identifies a relative bias for the reported analysis data, the calculated MDA must be multiplied by $1/(1+Br)$ to obtain the bias-corrected MDA.

3.2.1 Sample Distribution

The goodness of fit of the data to the Poisson distribution should be tested using the Chi-squared test (Remington and Schork 1970):

$$\chi^2 = \sum_{i=1}^n (x_i - \bar{x})^2 / \bar{x} \quad (10)$$

where $n = N \cdot M$ and χ^2 has $n-1$ degrees of freedom.

The sample variance equals $\sum (x_i - \bar{x})^2 / (n-1)$ and the variance of a Poisson distribution equals the mean. Therefore, the above equation may be rewritten as follows:

$$s^2 / \sigma^2 = \chi^2 / (n-1) \quad (11)$$

Because we are usually only concerned when there is variability in excess of the Poisson estimate, a one-sided test for significance is appropriate. The hypothesis that the distribution is Poisson will then be rejected when the ratio of the sample variance and the mean exceeds the value in the third column of Table 2.

The power of this test (probability of detecting a true variance that is greater than the mean) may be estimated using the data in Table 3.

3.2.2 Poisson-Based Minimum Detectable Amount

If the hypothesis that the distribution is Poisson is not rejected the MDA should be calculated using the following equation, which is equivalent to the equation of Section 4.3.1.2 of draft ANSI N13.30.

$$\text{MDA} = (1 + \Delta_K) [3.29 S_0 + \Delta_B B + 3]/KT \quad (12)$$

where K = the calibration factor supplied by the performance laboratory for the measurement process in counts per minute per nanocurie

Δ_K = the estimated fractional systematic error in the calibration factor K (assumed to have an upper bound of 10%)

B = the baseline count for the spectrum in the region of interest

Δ_B = the estimated fractional systematic error in determining the baseline count B (assumed to have an upper bound of 5% when no higher energy interference nuclides are present and 1% when higher energy nuclides are present).

$s_0 = s_B(n)$ = the standard deviation of the net blank count

T = the sample count time.

TABLE 2. Five Percent Rejection Levels for Poisson Goodness of Fit

<u>Sample Size</u>	<u>Chi-Squared</u>	<u>Chi-Squared/ (n-1)</u>
3	5.991	3.00
4	7.815	2.61
5	9.488	2.37
6	11.070	2.21
7	12.592	2.21
8	14.067	2.01
9	15.507	1.94
10	16.919	1.88

TABLE 3. Power of Chi-Squared Test to Identify Non-Poisson Variability

<u>Sample Size</u>	<u>σ^2/mean</u>		
	<u>1.1</u>	<u>1.4</u>	<u>1.54</u>
5	0.69	0.90	0.95
10	0.72	0.96	0.99

The value of the net blank standard deviation equals the sample standard deviation times a factor (n), which depends on the ratio (b) of the background and sample count times. If better estimates for Δ_K and Δ_B are not available the assumed upper bounds may be used.

$$n = (1+1/b)^{1/2} \quad (13)$$

The MDA equations therefore reduce to

$$MDA = (3.62(n)s_b + 0.11B + 3)/KT \quad (14)$$

when no interference nuclides are present, and

$$MDA = (3.62(n)s_b + 0.02B + 3)/KT \quad (15)$$

when interference nuclides are present. For paired observations (each sample compared to a single blank) the equations reduce further to

$$MDA = (5.12s_b + 0.11)/KT \quad (16)$$

and

$$MDA = (5.12s_b + 0.06B + 3)/KT \quad (17)$$

The calibration factor, K , is equal to the product of the detector counting efficiency, sample volume, and the physical conversion factor for nuclear transformations per unit activity (i.e., decays per minute per nanocurie). Use the lower 5% bound of the estimate of K based on the t distribution (i.e., $K(1-t S_k)$).

3.2.3 Non-Poisson-Based Minimum Detectable Amount

If the hypothesis that the distribution is Poisson is rejected, the standard deviation must be estimated from the sample distribution. The replicate based estimate of the standard deviation is best represented by a t -distribution rather than the normal distribution (Remington and Schork 1970). Also, the replicate-based estimate includes all components of the

error, including those estimated by Δ_K and Δ_B . With a one-tailed test the MDA equation then becomes

$$MDA = [2(t)(n)s_b + 3]/KT. \quad (18)$$

When the total baseline counts exceed about 1000 counts, the 3 term will be insignificant and may be dropped from the equation.

The first term of the above equation may be determined using the data in Table 4.

The sample size for the t term refers to the number of replicate blank counts in the performance test, while the sample size for the n term refers to the number of replicate counts used to determine the background for the service laboratory.

TABLE 4. Student's t (5%) and n Terms for the Direct Bioassay MDA Equation

<u>Sample Size</u>	<u>t</u>	<u>n</u>
1	-	1.414
2	6.3138	1.225
3	2.9200	1.155
4	2.3534	1.118
5	2.1318	1.095
6	2.0150	1.080
7	1.9432	1.069
8	1.8946	1.061
9	1.8595	1.054
10	1.8331	1.049
large	1.645	1.000

For the normal case using five replicate counts of the appropriate blank and a single background count for comparison the MDA equations reduce to

$$MDA = (6.03s_b + 3)/KT \quad (19)$$

and

$$MDA = (6.03s_b + 3)/KT \quad (20)$$

3.2.4 Minimum Detectable Amount Based on the Laboratory-Estimated Standard Deviation

The MDA should be calculated using Equation (18) (Section 3.2.2) and the standard deviation estimate supplied by the service laboratory.

3.3 PERFORMANCE REPORTS

The performance report returned to the service laboratory by the testing laboratory should include for each replicate count the sample code, the reported activity, the true activity, and the individual relative bias. For each group of counts with the same spike activity the relative precision (S_A and S_B), and the mean relative bias (B_r) should be listed. The report should also specify the calculated standard deviation for the appropriate blank, whether Poisson statistics were rejected, and the calculated MDA. The MDA calculated from the standard deviation of the blank supplied by the service laboratory supplied should also be included.

If the service laboratory passes all criteria except the MDA based on the performance test, passes the MDA criterion when the MDA is calculated based on the blank standard deviation they supplied, and has reported no false negatives for samples spiked at a level near the AMDA, a site visit may be scheduled to determine the validity of their estimate. If the laboratory-supplied estimates of the blank standard deviation are determined to be valid following the site visit, the laboratory will be considered to have passed the MDA criterion. If the calculated value for any test statistic exceeds the acceptance criteria of draft ANSI N13.30, the service laboratory shall not be accredited for that category.

4.0 REFERENCES

American National Standards Institute (ANSI). 1973. American National Standard: Thyroid Radioiodine Uptake Measurements Using a Neck Phantom. ANSI N44.3-1973, American National Standards Institute, New York, New York.

National Council on Radiation Protection and Measurements (NCRP). 1985. A Handbook of Radioactivity Measurements Procedures. NCRP Report No. 58, Second Edition, pp. 336-342, National Council on Radiation Protection, Bethesda, Maryland.

Remington, R. D., and M. A. Schork. 1970. Statistics with Applications to the Biological and Health Sciences. Prentice-Hall, Inc., Englewood Cliffs, New Jersey.

Robinson, A. V., D. R. Fisher, W. D. Reece, and J. A. MacLellan. 1986. Performance Testing of Radiobioassay Laboratories: In Vivo Measurements, Pilot Study Report. PNL-5820, Pacific Northwest Laboratory, Richland, Washington.

U.S. Code of Federal Regulations. 1986. Transportation, "Shippers - General Requirements for Shipments and Packagings." Title 49, Part 173 (49CFR173), U.S. Government Printing Office, Washington D.C.

U.S. Department of Energy (DOE). 1983. Environmental Protection, Safety, and Health Protection Program for DOE Operations. "Requirements for Radiation Protection." DOE 5480.1, Change 5, Chapter XI, U.S. Department of Energy, Washington, D.C.

U.S. Nuclear Regulatory Commission. 1982. Rules and Regulations, "Standards for Protection Against Radiation." U.S. Code of Federal Regulations, Title 10, Part 20 (10CFR20), U.S. Nuclear Regulatory Commission, Washington, D.C.

APPENDIX

PROPAGATION OF ERROR IN SPIKED IN VIVO SAMPLES

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PROPAGATION OF ERROR IN SPIKED IN VIVO SAMPLES

The methods used to estimate the total error in the analysis of in vivo phantoms shall be the same as those discussed by Kanipe (1977). Assume that the individual components of the total error are independent, normally distributed variables and that propagation for the manipulation of various functions is expressed as below.

<u>Function</u>	<u>Error Formula</u>
$Q = X \pm Y$	$\sigma_Q = (\sigma_x^2 + \sigma_y^2)^{\frac{1}{2}}$
$Q = aX \pm bY$	$\sigma_Q = (a^2 \sigma_x^2 + b^2 \sigma_y^2)^{\frac{1}{2}}$
$Q = XY$	$\sigma_Q = XY (\sigma_x^2/X^2 + \sigma_y^2/Y^2)^{\frac{1}{2}}$
$Q = X/Y$	$\sigma_Q = X/Y (\sigma_x^2/X^2 + \sigma_y^2/Y^2)^{\frac{1}{2}}$

Using the error formulas above, the equations detailed in the procedure, and the error estimates quoted in the solution certificates supplied for each nuclide, the total error in the prepared samples may be estimated.

REFERENCE

Kanipe, L. G. 1977. Handbook for Analytical Quality Control in Radioanalytical Laboratories. PB-277-254, U.S. Department of Commerce, National Technical Information Service, Springfield, Virginia.

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