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ANSI/HPS N13.30-2011 (R2017)

Performance Criteria for Radiobioassay

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Performance Criteria for Radiobioassay

1.0 Purpose and Scope

1.1 Introduction

In the course of employment, individuals may work with radioactive materials that, under certain circumstances, could be taken into the body. Radiation protection programs may include means for direct or indirect measurements, or both, of radioactive material that has entered the body. The performance criteria required for such measurements usually depend upon the purpose for the radiobioassay measurement. Radiobioassay measurements are made for the purpose of determining the internal human burden of radioactive material, estimating doses and dose commitments for risk estimates, radiation protection management, medical management where appropriate, and providing the necessary data for legal and record-keeping requirements. Measurements that are made as part of a routine monitoring program are usually at a lower minimum detectable amount (MDA) or minimum detectable concentration (MDC) than those to be used for diagnostic purposes. Routine examination measurements may be made less frequently, and diagnostic measurements may sometimes require more rapid turnaround times.

Much of the information in this standard is contained in other internal dosimetry standards for individual radionuclides. This document collects, expands, and standardizes the performance criteria contained in the other standards. It also provides a consensus on the statistical definitions of the quantitative performance criteria of bias, precision, and MDA.

Section 2.0 provides normative references with direct impact on compliance with this standard. Definitions for certain words used in the text are included in Section 3.0. These definitions are included to give the precise meaning intended. Furthermore, the standard created unique terms; definitions for these terms are given in Section 3.0 as well as in the text. Sections 4.0 through 6.0 were written primarily to provide guidance

for radiobioassay service laboratories, whereas Section 7.0 relates to testing laboratories and provides criteria for performance testing. The information in these sections provides beneficial insight for service laboratories, for users of the laboratory's services, and for testing laboratories, and it provides a possible basis for an interlaboratory quality assurance program.

1.2 Purpose

The purpose of this standard is to provide criteria for quality assurance, evaluation of performance, and the accreditation of radiobioassay service laboratories. These criteria include bias, precision, and determination of the MDA or MDC.

1.3 Scope

Criteria and guidance for direct radiobioassay (*in vivo*) and indirect radiobioassay (*in vitro*) are given in separate sections of this standard. In addition, examples to clarify concepts and methods that are described in this standard, and information that may be useful in implementing this standard, are presented in annexes to the standard. The annexes are illustrative and are not a part of the standard.

This standard addresses the following:

1. the accuracy (bias and precision) of direct (*in vivo*) measurements of activity and quantities of selected important radionuclides in test phantoms and indirect (*in vitro*) measurements of activity and quantities of selected important radionuclides in test samples;
2. methods for determining the minimum detectable amount;
3. minimum testing levels and testing ranges;
4. requirements for reporting radiobioassay results by service laboratories;
5. quality assurance in service laboratories;
6. quality control in service laboratories;
7. protocol for reporting test evaluations by

service laboratories to the testing laboratory;

8. default procedures when the service laboratory customer does not specify the performance criteria.

The scope of this standard *does not include* the following:

1. detailed radiochemical methods for separating radionuclides from biological samples;
2. detailed procedures for *in vivo* and *in vitro* radioactivity measurements;
3. metabolic data and mathematical models for converting radiobioassay results into absorbed dose and equivalent dose;
4. any aspects of a service laboratory customer's radiation protection program;
5. procedures for the preparation and distribution of test samples and phantoms by the testing laboratories.

Analytical methods for radiobioassay are not currently standardized but are available in the literature. Some analytical methods are provided in references appended to this standard and in other American National Standards Institute (ANSI) standards for specific radionuclides. Guidance for converting radiobioassay results into dose are provided in publications of federal and state regulations and guides, the International Commission on Radiological Protection (ICRP), the National Council on Radiation Protection and Measurements (NCRP), and the International Commission on Radiological Units and Measurements (ICRU). Recommendations of the ICRP, NCRP, and ICRU, and experience with the practical application of these recommendations to the conduct of radiobioassay services and the interpretation and use of bioassay results in radiation protection programs, have been considered in the development of this standard.

2.0 Normative References

Application of this standard is contingent upon adherence to the following references:

ANSI N44.3-1973. Thyroid radioiodine uptake measurements using a neck phantom.

ANSI N42.23-1996. Measurement and associated instrument quality assurance for radioassay laboratories.

ANSI N13.35-2009. Specifications for the bottle manikin absorption phantom.

ANSI/NCSL Z540.2 R2002. American national standard for expressing uncertainty – U.S. guide to the expression of uncertainty in measurement.

ICRP Publication 89; 2001. Basic anatomical and physiological data for use in radiological protections: reference values.

ISO 17025; 2005. General requirements for the competence of testing and calibration laboratories.

ISO/IEC Guide 99; 2007. International vocabulary of metrology—Basic and general concepts and associated terms (VIM).

ISO 43; 1997. Proficiency testing by inter-laboratory comparisons.

NCRP Report No. 58; 1985. A handbook of radioactivity measurement procedures.

3.0 Definitions

Terms defined in ISO/IEC Guide 99, *International Vocabulary of Metrology—Basic and General Concepts and Associated Terms (VIM)* (ISO/IEC 2007) or the National Institute of Standards and Technology (NIST) Technical Note 1297 (Taylor and Kuyatt 1994), titled *Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement Results*, are not defined in this standard. A word or term requiring a more precise definition is redefined in this section even though it was included in one of the aforementioned references. The following terms are of a restricted nature for the purposes of this standard.

3.1 Special Word Usage

The word "shall" is used to denote a requirement; the word "should" is used to

denote a recommendation; and the word "may" is used to denote permission, neither a requirement nor a recommendation. To conform to this standard, all radiobioassays shall be performed in accordance with its requirements, but not necessarily in accordance with its recommendations; however, justification shall be documented for deviations from recommendations.

3.2 Specific Terms

Accuracy: The characteristics of an analysis or determination that ensures that both the bias and precision of the resulting quantity will remain within specified limits.

Activity: The transition rate of atomic nuclei stated in becquerels, curies, or other acceptable units.

Aliquot: A representative portion of a whole.

Analyte: The particular radionuclide to be determined in a sample of interest.

Appropriate Blank: A sample, person, or phantom that is, ideally, identical in physiochemical and radiologically significant ways to the sample, person, or phantom to be analyzed. When feasible the appropriate blank should not contain environmental quantities of the analyte.

Background: Ambient signal response recorded by measurement instruments that is independent of radioactivity contributed by the radionuclides being measured in the person or sample.

Bias: A fixed mean deviation from the expected value that remains constant over replicated measurements within the statistical precision of the measurement. (Synonyms: deterministic error, fixed error, systematic error.)

Bias Statistic: An estimation of bias calculated from a finite sample of data using a specified formula.

Bioassay: Another word for radiobioassay.

Blind Testing: Testing of capabilities when the service laboratory is not aware of the

activity of the analyte(s) in the test sample or phantom.

Coefficient of Variation (CV): The quotient of the estimated standard deviation of a series of determinations, $x_1, x_2, \dots, x_i, \dots, x_N$, of a quantity divided by the mean value of x_i ; i.e.,

$$CV = \frac{\sqrt{\sum_{i=1}^N (x_i - \bar{x})^2 / (N - 1)}}{\bar{x}}$$

where

$$\bar{x} = \sum_{i=1}^N x_i / N$$

or, for a single measurement, the quotient of the estimate of the standard deviation divided by the value of the single measurement (synonymous with the relative standard deviation, multiplied by 100 when expressed as a percentage).

Combined Standard Uncertainty (CSU, u_c): The estimated standard deviation of the result obtained by combining the individual standard uncertainties (and covariances as appropriate).

Concentration: The activity or mass per unit volume or per unit mass.

Confidence Interval: The interval about an estimate of a stated quantity within which the value of the quantity is expected to be found with repeated measurements with a specified probability.

Coverage Factor (k): The value k by which the combined standard uncertainty is multiplied to give the expanded uncertainty.

Critical Level: Same as decision level.

Decision Level (DL): The number of counts measured (L_c) or final instrument measurement of a quantity of analyte (D_c) at or above which a decision is made that the analyte is definitely present.

Diagnostic Measurements: Measurements performed to estimate the amount of radionuclide deposited in a person when an intake is known or is suspected to have occurred.

Direct Radiobioassay: The measurements of radioactive material in the human body using instrumentation that detects radiation emitted from the radioactive material in the body. (Synonymous with *in vivo* measurement.)

Expanded Uncertainty: The product of the combined standard uncertainty of a measured value and a coverage factor k chosen so that the desired interval has a high probability of containing the value of the measurand.

Indirect Radiobioassay: Measurements to determine the presence of or to estimate the amount of radioactive material in the excreta or in other biological materials removed from the body. (Synonymous with *in vitro* measurement.)

In Vitro Measurement: Synonymous with indirect bioassay.

In Vivo Measurement: Synonymous with direct bioassay.

Lower Limit of Detection (LLD): See MDA.

Matrix: The material within which the constituent of interest is contained.

Measurand: Particular quantity subject to measurement (ISO 2007).

Minimum Detectable Amount (MDA): The smallest amount (activity or mass) of an analyte in a sample that will be detected with a probability β of non-detection (Type II error) while accepting a probability α of erroneously deciding that a positive (non-zero) quantity of analyte is present in an appropriate blank sample (Type I error).

Minimum Detectable Concentration (MDC): The MDA expressed in units of concentration.

Minimum Testing Level (MTL): The minimum amount of radioactive material that the

testing laboratory should use to estimate relative bias and relative precision of the service laboratories participating in the performance testing program, assuming the sample(s) is(are) free of interference from other radionuclides unless specifically addressed. The MTL is a multiple of the expected procedural MDA.

Phantom: A simulated person or part of a person used for calibration of *in vivo* measurement systems. A phantom is constructed to allow placement of radionuclides in a geometry approximating internal depositions.

Precision: The closeness of agreement between independent measurement results obtained by applying the experimental procedure under stipulated conditions.

Precision Statistic: An estimator of precision calculated from a finite sample of data using a specified formula.

Quality Assurance: All those planned and systematic actions necessary to provide adequate confidence that an analysis, measurement, or surveillance program will perform satisfactorily in service.

Quality Control: The actions that control the attributes of the analytical process, standards, reagents, measurement equipment, components, system, or facility according to predetermined quality requirements.

Radiobioassay: Measurement of the amount or concentration of radionuclide material in the body or in biological material excreted or removed from the body and analyzed for purposes of estimating the quantity of radioactive material in the body.

Radiochemical Recovery: The fraction of the radioactive analyte in a sample collected by a chemical process. Synonymous terms in common usage are yield, radiochemical yield, chemical yield, recovery, and fractional yield.

Reagent or Method Blank: The contribution of the reagents to the measurement process determined by carrying the reagents through

all the operations that are used for the sample.

Relative Bias: The quotient of the bias divided by the expected value.

Relative Standard Deviation: Synonymous with coefficient of variation.

Relative Precision: The quotient of the precision divided by the expected value (see Section 4.3.2).

Root Mean Squared Error (RMSE): A measure of total error defined as the square root of the sum of the square of the relative precision and the square of the relative bias.

Routine Measurements: Radiobioassays conducted on a planned schedule to determine whether any intake might have occurred.

Screening Measurements: Measurements made to detect radioactive material under routine conditions but not used to quantify the amount of a given radionuclide.

Service Laboratory: Laboratory performing direct and/or indirect radiobioassay measurements.

Significance Level: The probability of rejecting the tested hypothesis when it is true.

Standard Deviation: The estimated dispersion of a set of measurements as given in the numerator of the equation for coefficient of variation.

Standard Error (Uncertainty): The standard deviation of the mean of a set of measurements. The standard error reduces to the standard deviation of the measurement when there is only one determination (see Annex A).

Standard Reference Material (SRM): Material characterized by the NIST for the activity of radionuclides and issued with a certificate that gives the results of the characterization.

Systematic Error: An error component that produces a fixed bias in the underlying

expected value of a determination, from measurement to measurement.

Testing Laboratory: A laboratory authorized to prepare measurement assessment bioassay specimens (excreta samples and phantoms) with known amounts of radioactive material and associated uncertainties for distribution to service laboratories. The testing laboratory is responsible for evaluating the measurement performance of the service laboratories in meeting the performance specifications of this standard.

Traceability (Measurement): Property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty. See also applicability notes in ISO/IEC Guide 99:2007 (ISO/IEC 2007).

Transfer Reference Standard (TRS): A material that contains radionuclide components of interest in chemical and physical forms similar to bioassay specimens and is used to certify the amount of activity present in a person or sample measured. The radionuclides used for the preparation of the TRS are, when possible, related to SRMs. The preparation procedures are verified and documented.

Unbiased: A measurement of a random variable is called unbiased if it has zero bias (i.e., if the measured value of the measurement is equal to the expected value of the property being determined).

Uncertainty Component: Type A: a component of uncertainty that may be evaluated based on a valid statistical method for treating data. Type B: a component of uncertainty based on scientific judgment using all of the relevant information available.

Validation: Defining the process of the method capability and determining whether it can be properly applied as intended (see Annex B).

Verification: An act of confirming, substantiating, or ensuring that an action, condition, or goal has been implemented,