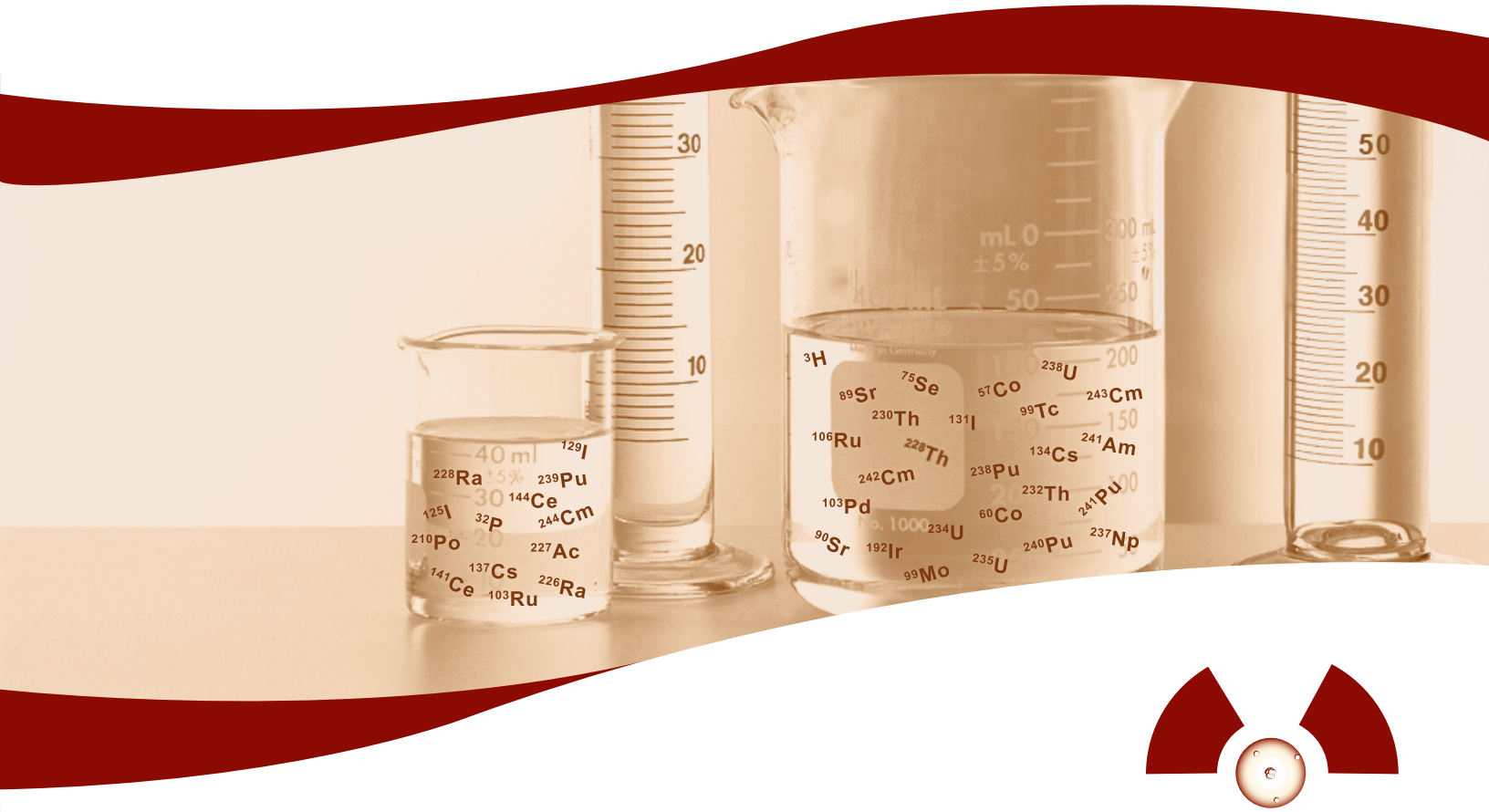
United States
Environmental Protection
Agency

Office of Radiation and Indoor Air
National Air and Radiation
Environmental Laboratory

EPA 402-R-09-006
June 2009
www.epa.gov/narel

Disclaimer - For assistance accessing this document or additional information, please contact radiation.questions@epa.gov.

Method Validation Guide for Qualifying Methods Used by Radiological Laboratories Participating in Incident Response Activities



EPA 402-R-09-006
www.epa.gov
June 2009
Revision 0

Method Validation Guide for Qualifying Methods Used by Radiological Laboratories Participating in Incident Response Activities

U.S. Environmental Protection Agency
Office of Air and Radiation
Office of Radiation and Indoor Air
National Air and Radiation Environmental Laboratory
Montgomery, AL 36115

This report was prepared for the National Air and Radiation Environmental Laboratory of the Office of Radiation and Indoor Air, United States Environmental Protection Agency. It was prepared by Environmental Management Support, Inc., of Silver Spring, Maryland, under contracts 68-W-03-038, work assignment 35, and EP-W-07-037, work assignments B-33 and I-33, all managed by David Garman. Mention of trade names or specific applications does not imply endorsement or acceptance by EPA.

Preface

This document describes project method validation guidance that a radioanalytical laboratory should comply with in order to validate methods used to process samples submitted during a radiological or nuclear incident, such as that caused by a terrorist attack. EPA laboratories using radioanalytical processes consistent with the guidance provided in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* should first validate their methods according to the guidance provided in this document. The use of the guidance in this document, as well as in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance*, will assist in fulfilling EPA's responsibilities as outlined in the *National Response Framework Nuclear/ Radiological Incident Annex*. These responsibilities include response and recovery actions to detect and identify radioactive substances, and to coordinate federal radiological monitoring and assessment activities. Additionally this document identifies a formalized process for the development (Section 4.0) and testing (Section 5.0) of a new method so that there is confidence that radioanalytical results meet project-specific data requirements.

The need to ensure adequate laboratory infrastructure to support response and recovery actions following a major radiological incident has been recognized by a number of federal agencies. The Integrated Consortium of Laboratory Networks (ICLN), created in 2005 by 10 federal agencies[1], consists of existing laboratory networks across the Federal Government. The ICLN is designed to provide a national infrastructure with a coordinated and operational system of laboratory networks that provide timely, high quality, and interpretable results for early detection and effective consequence management of acts of terrorism and other events requiring an integrated laboratory response. It also designates responsible federal agencies (RFAs) to provide laboratory support across response phases for chemical, biological, and radiological agents. To meet its RFA responsibilities for environmental samples, EPA has established the Environmental Response Laboratory Network (ERLN) to address chemical, biological, and radiological threats. For radiological agents, EPA is the RFA for monitoring, surveillance, and remediation, and will share responsibility for overall incident response with the U.S. Department of Energy (DOE). As part of the ERLN, EPA's Office of Radiation and Indoor Air is leading an initiative to ensure that sufficient environmental radioanalytical capability and competency exists across a core set of laboratories to carry out EPA's designated RFA responsibilities.

Laboratories that support EPA's incident-response mission will undergo training and should adopt the use of the material presented in this document, with emphasis on validating methods for expected radionuclide and matrix combinations in the event of a terrorism incident involving radioactive materials. As soon as reasonably possible, rapid radioanalytical methods expected to be used to process anticipated radionuclide and matrix combinations from the early to intermediate phases of a radiological incident should be validated according to the guidance of the document. During these early phases of an incident response, there may be insufficient time to validate methods. Therefore, it is prudent to validate the applicable radioanalytical methods for various sample matrices as part of the preparatory actions that are necessary to respond properly to a possible radiological incident.

[1] Departments of Agriculture, Commerce, Defense, Energy, Health and Human Services, Homeland Security, Interior, Justice, and State, and the U.S. Environmental Protection Agency.

Laboratories developing new methods and operational protocols should review the detailed guidance on recommended radioanalytical practices found in the *Multi-Agency Radiological Laboratory Analytical Protocols Manual* (MARLAP) referenced in this document. Familiarity with Chapters 6 and 7 of MARLAP will benefit readers of this document.

This document is one in a planned series designed to present radioanalytical laboratory personnel, Incident Commanders (and their designees), and other field response personnel with key laboratory operational considerations and likely radioanalytical requirements, decision paths, and default data quality and measurement quality objectives for samples taken after a radiological or nuclear incident, including incidents caused by a terrorist attack. Documents currently completed or in preparation include:

- *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance – Radionuclides in Water* (EPA 402-R-07-007, January 2008)
- *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance – Radionuclides in Air* (EPA 402-R-09-007, June 2009)
- *Radiological Laboratory Sample Screening Analysis Guide for Incidents of National Significance* (EPA 402-R-09-008, June 2009)
- *Method Validation Guide for Qualifying Methods Used by Radiological Laboratories Participating in Incident Response Activities* (EPA 402-R-09-006, June 2009)
- *Guide for Radiological Laboratories for the Identification, Preparation, and Implementation of Core Operations for Radiological Incident Response* (in preparation)
- *Guide for Radiological Laboratories for the Control of Radioactive Contamination and Radiation* (in preparation)
- *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance – Radionuclides in Soil* (in preparation)

Comments on this document, or suggestions for future editions, should be addressed to:

Dr. John Griggs
U.S. Environmental Protection Agency
Office of Radiation and Indoor Air
National Air and Radiation Environmental Laboratory
540 South Morris Avenue
Montgomery, AL 36115-2601
(334) 270-3450
Griggs.John@epa.gov

Acknowledgments

This manual was developed by the National Air and Radiation Environmental Laboratory (NAREL) of EPA's Office of Radiation and Indoor Air (ORIA).

Dr. John Griggs served as project lead for this document. Several individuals provided valuable support and input to this document throughout its development. Special acknowledgment and appreciation are extended to Dr. Keith McCroan, ORIA/NAREL; Mr. Daniel Mackney for his support of instrumental analysis, ORIA/NAREL; Dr. Lowell Ralston and Mr. Edward Tupin, CHP, both of ORIA/Radiation Protection Division; Ms. Schatzi Fitz-James, Office of Emergency Management, Homeland Security Laboratory Response Center; and Mr. David Garman, ORIA/NAREL. We also wish to acknowledge the peer reviews conducted by Carolyn Wong, David Burns, and Jack Bennett, whose thoughtful comments contributed greatly to the understanding and quality of the report. Numerous other individuals both inside and outside of EPA provided peer review of this document, and their suggestions contributed greatly to the quality and consistency of the final document. Technical support was provided by Dr. N. Jay Bassin, Dr. Carl V. Gogolak, Dr. Robert Litman, Dr. David McCurdy, Mr. Robert Shannon, and Dr. Anna Berne of Environmental Management Support, Inc.

Contents

Figures

Tables

Acronyms, Abbreviations, Units, and Symbols

(Excluding chemical symbols and formulas)

α . . . . . alpha particle
α . . . . . probability of a Type I decision error
AAL . . . . . analytical action level
AL . . . . . action level
APS . . . . . analytical protocol specification
β . . . . . beta particle
β . . . . . probability of a Type II decision error
Bq . . . . . becquerel (1 dps)
CL_{NC} . . . . . critical net concentration level
CSU . . . . . combined standard uncertainty
d . . . . . day
DAC . . . . . derived air concentration
DP . . . . . decay product(s)
dpm . . . . . disintegration per minute
dps . . . . . disintegration per second
DQO . . . . . data quality objective
DRC . . . . . derived radionuclide concentration
DWC . . . . . derived water concentration
EPA . . . . . [United States] Environmental Protection Agency
γ . . . . . gamma ray
g . . . . . gram
Gy . . . . . gray [unit of absorbed radiation dose in materials; 1 gray = 100 rad]
h . . . . . hour
IC . . . . . Incident Commander [or designee]
ISO . . . . . International Organization for Standardization
keV . . . . . thousand electron volts
L . . . . . liter
m . . . . . meter
MARLAP . . . . *Multi-Agency Radiological Laboratory Analytical Protocols Manual*
MARSSIM . . . *Multi-Agency Radiation Survey and Site Investigation Manual*
MDB . . . . . minimum detectable bias
MDC . . . . . minimum detectable concentration
MeV . . . . . million electron volts
min . . . . . minute
mL . . . . . milliliter (10^{-3} L)
MQO . . . . . measurement quality objective
mrem . . . . . millirem (10^{-3} rem)
MSE . . . . . mean squared error
MV . . . . . method validation
MVRM . . . . . method validation reference material
PAG . . . . . protective action guide
pCi . . . . . picocurie (10^{-12} Ci)
PE . . . . . performance evaluation

PT . . . . . proficiency test/testing
QC . . . . . quality control
rad . . . . . unit of absorbed radiation dose in materials; 100 rad = gray
RDD . . . . . radiological dispersal device (i.e., "dirty bomb")
rem . . . . . roentgen equivalent man (traditional units; 1 rem = 0.01 Sv)
RSD . . . . . relative standard deviation
s . . . . . second
s_{Blanks} . . . . . standard deviation of blank sample net results
SI . . . . . International System of Units
Sv . . . . . sievert (1 sievert = 100 rem)
u_{MR} . . . . . required method uncertainty
φ_{MR} . . . . . relative required method uncertainty
y . . . . . year

Radiometric and General Unit Conversions

To Convert	To	Multiply by	To Convert	To	Multiply by
years (y)	seconds (s) minutes (min) hours (h) days (d)	3.16×10^{7} 5.26×10^{5} 8.77×10^{3} 3.65×10^{2}	s min h d	y	3.17×10^{-8} 1.90×10^{-6} 1.14×10^{-4} 2.74×10^{-3}
disintegrations per second (dps)	becquerels (Bq)	1	Bq	dps	1
Bq Bq/kg Bq/m^3 Bq/m^3	picocuries (pCi) pCi/g pCi/L Bq/L	27.0 2.70×10^{-2} 2.70×10^{-2} 10^{-3}	pCi pCi/g pCi/L Bq/L	Bq Bq/kg Bq/m^3 Bq/m^3	3.70×10^{-2} 37.0 37.0 10^{3}
microcuries per milliliter (μCi/mL)	pCi/L	10^{9}	pCi/L	μCi/mL	10^{-9}
disintegrations per minute (dpm)	μCi pCi	4.50×10^{-7} 4.50×10^{-1}	pCi	dpm	2.22
cubic feet (ft^3)	cubic meters (m^3)	2.83×10^{-2}	cubic meters (m^3)	cubic feet (ft^3)	35.3
gallons (gal)	liters (L)	3.78	L	gal	0.264
gray (Gy)	rad	10^{2}	rad	Gy	10^{-2}
roentgen equivalent man (rem)	sievert (Sv)	10^{-2}	Sv	rem	10^{2}

NOTE: Traditional units are used throughout this document instead of International System of Units (SI) units. Protective Action Guides (PAGs) and their derived concentrations appear in official documents in the traditional units and are in common usage. Conversion to SI units will be aided by the unit conversions in this table. Conversions are exact to three significant figures, consistent with their intended application.

1.0 Introduction

The United States Environmental Protection Agency (EPA) is responsible for assessing the extent of environmental contamination and human health consequences in the event of a radiological incident such as a terrorist incident involving radioactive materials. Although EPA will be mainly involved in the intermediate and recovery phases of an incident response, there also may be involvement in some activities in the early phase. For a terrorist event such as a radiological dispersion device, the radionuclide(s) and the types and number of sample matrices that may be collected and analyzed can vary dramatically depending on the type of device used and radioactive material incorporated. The radioanalytical laboratories used to process the samples must not only be capable of identifying and quantifying the radionuclide(s) in various matrices, but they must also have the capacity to process a large number of samples in a short time (thousands of samples per week). Sufficient laboratory capacity is a balance of adequate facility processing areas and nuclear instrumentation, validated radioanalytical methods available, and trained staff.

In order to make proper assessments and decisions in the event of a radiological incident, EPA will utilize only qualified radioanalytical laboratories that have the capability, capacity and quality needed to process samples taken from affected areas. Analytical protocol specifications (APSs), including measurement quality objectives (MQOs), will be preestablished to define the expected quality of the data for incident situations. The objective of this document is to establish systematic and objective methodologies and acceptance criteria for validating analytical methods, based on the stated quality requirements of a specific incident-response project, such as recovery from a radiological dispersal device. Laboratories developing new methods and operational protocols should review the detailed guidance on recommended radioanalytical practices found in current editions of MARLAP and MARSSIM.

Several radiological sample analysis guides for incident response have been developed that provide information on the expected radionuclides of concern and MQOs to make decisions relative to sample processing priorities for the water, air particulate filter, and soil/solid matrices. As part of the laboratory qualifying process, laboratories must demonstrate their ability to meet the APSs and MQOs for the methods used to analyze each radionuclide and sample-matrix combination. EPA will require an initial project method validation and a subsequent participation in a performance evaluation (PE) program as a means to demonstrate that the methods used by a laboratory are capable of meeting the MQOs for incident response applications. For incident-response applications, project method validation will be required and applied to methods currently being used by the laboratories, including EPA Safe Drinking Water Act required methods, as well as to newly developed methods and methods that have been modified for incident response. Project method validation and participation in a PE program will be required for gross alpha and beta screening methods as well.

In this document, the term “project method validation” is synonymous with “incident response method validation.”

2.0 Method Validation Description

The *Multi-Agency Radiological Laboratory Analytical Protocols Manual* (MARLAP) Chapter 6 discusses two distinct applications of method validation: general method validation and project

method validation. General method validation is the process of demonstrating that a method is suitable for its general intended use, such as routine radioanalytical processing of samples for the determination of environmental levels of a given radionuclide. For general method validation, the methods would address internal measurement quality objectives, and typical sample matrix constituents and nominally interfering concentrations of expected chemical and radionuclide interferences. EPA has developed a draft general method validation process document (EPA 2006, *Validation and Peer Review of U.S. EPA Radiochemical Methods of Analysis*) that covers the method validation parameters for radioanalytical methods. That document provides guidance to satisfy EPA requirements for general method validation for measurement uncertainty, method bias and trueness, precision, detection capability, analyte concentration range, specificity and ruggedness.

In contrast, this document provides guidance on project method validation applicable to methods for processing samples during a response to a radiological incident, including radiological incidents of national significance. Project method validation demonstrates that a method is capable of meeting project-specific MQOs (in other words, a required method uncertainty at a specific radionuclide concentration). The method selected for a project needs to address specific sample matrix characteristics, chemical and radionuclide interferences, special sample preparation requirements, sample-processing turnaround times, and MQOs defined in an analytical protocol specification (APS). This document addresses the method validation expectations for an incident response for the MQOs of the required method uncertainty and the required minimum detectable concentration (MDC). The method validation procedures for the method uncertainty MQO follow the guidance provided in MARLAP Chapter 6. As discussed in MARLAP, the principal MQO is the required method uncertainty at an action level. Although the MDC MQO normally would not be specified as an MQO for incidence response applications, this document provides method validation guidance for a "required MDC" MQO.

Even though a laboratory has a method that has undergone general method validation, use of the method for the incident response application will require project method validation. The degree of effort and required level of project method validation will depend on the degree of method development or use, and the MQOs of the project, as included in the APSs.

Proper planning is critical for successful method validation because many method validation parameters must be considered, evaluated and documented. Method development and method validation generally are not separate processes. The types of experiments conducted during method development and the types of tests performed during method validation have many similarities.

3.0 Method Description

The components of a method or measurement process requiring validation should be clearly described. Generally, a laboratory method includes all physical, chemical and radiometric processes conducted at a laboratory in order to provide an analytical result. The processes for radiochemical methods may include sample preparation or dissolution, chemical separations, preparation of sample test sources, nuclear counting, analytical calculations, data review and qualification, and data reporting (MARLAP Chapter 6). Method validation efforts should evaluate all process components combined. Some radiochemical methods may also include procedures for sampling (e.g., methods for radon in air analysis or for volatile radioactive organic compounds in soils and other solid matrices), in which case the sampling procedures should be included in the validation tests. The

measurement process components validated, and the combination of procedures comprising a method, must be clearly and completely stated.

The purpose of a method (i.e., measurement objectives) and the intended use of the data must be clearly defined. In addition, method scope and applicability must be well defined and clearly described and consistent with the documented performance of the method. These measures will help minimize misapplication by the users. Method scope and applicability include the following:

- The measurement process components validated (e.g., sample preparation, dissolution, chemical isolation, precipitation, final product for counting, radiation measurement process, etc.)
- The nature (chemical-physical form, type of radiation and quantity measured) of the radionuclides and matrices (chemical and physical form) studied
- The range of analyte concentration levels for which the method is claimed to be suitable
- A description of any known limitations and any assumptions upon which a method is based (e.g., radiological and non-radiological interferences, minimum sample size, etc.)
- A description of how the method and analytical parameters chosen meet the measurement quality objectives for the intended application, when applicable
- Aliquant sample size for processing

4.0 Method Performance Characteristics

The performance characteristics of a radiochemical method that may be evaluated in method validation include:

- Method uncertainty at a specific radionuclide concentration (action level)
- Detection capability (minimum detectable concentration)
- Bias/trueness
- Analyte concentration range
- Method specificity
- Method ruggedness

A brief discussion of each of these performance characteristics will be covered in the following sections. For more detailed information on a characteristic, the reader is referred to MARLAP (Chapters 3 and 6); EPA (2006) *Validation and Peer Review of U.S. EPA Radiochemical Methods of Analysis*; EURACHEM Guide (1998) *The Fitness for Purpose of Analytical Methods, A Laboratory Guide to Method Validation and Related Topics*; ISO 17025; and ANSI N42.23.

4.1 Method Uncertainty

MARLAP defines method uncertainty as follows:

> Method uncertainty refers to the predicted uncertainty of the result that would be measured if the method were applied to a hypothetical laboratory sample with a specified analyte concentration. Although individual measurement uncertainties will vary from one measured result to another, the required method uncertainty is a target value for the individual measurement uncertainties, and is an estimate of uncertainty (of measurement) before the sample is actually measured.

Method uncertainty can be thought of as an estimate of the expected analytical standard deviation at a specified radionuclide concentration. For certain projects, including incident response, a required method uncertainty should be specified. An example of a required method uncertainty specification would be "...at a ^{137}Cs soil concentration of 10 pCi/g, the required method uncertainty is 1 pCi/g." In many applications, including incident response laboratory analyses, the specified radionuclide concentration is referred to as the analytical action level (AAL) and may be based on either incident-specific, risk-based or regulatory mandated value, such as a protective action guide (PAG) as presented in the *Radiological Laboratory Sample Analysis Guides for Incidents of National Significance*. Radioanalytical results from an incident response are compared to action level concentrations, and thus it is very important to have results that are of sufficient quality to support decisions to be made. Specifying a required method uncertainty at the AAL ensures the data quality needed to make decisions.

To be consistent with MARLAP, certain nomenclature for the required method uncertainty is used for incident response applications. The notation "u_{MR}" is specified for the absolute required method uncertainty at or below the action level and has units of activity or activity concentration that match the AAL value. Above the action level, a relative required method uncertainty φ_{MR}, defined as the u_{MR}/AAL, is specified (φ_{MR} is unitless). For the ^{137}Cs soil example provided above, φ_{MR} would be equal to:

$$= \frac{1 \text{ pCi/g}}{10 \text{ pCi/g}} = 0.10 \text{ (10\%) at concentrations greater than 10 pCi/g}$$

Method uncertainty should not be confused with measurement uncertainty, which MARLAP and the International Organization for Standardization (ISO) (1993a) defined as:

> "Parameter associated with the result of a measurement that characterizes the dispersion of the values that could reasonably be attributed to the measurand."

Each radioanalytical method that will be used by a laboratory processing samples from an incident response will be evaluated to determine if its uncertainty meets the required method uncertainty. The result of each test sample processed during the method validation process is compared to the limits of acceptability established for the specific validation level, i.e., a multiple of the required method uncertainty. A method will be considered acceptable if it meets the method validation criteria provided in Section 5.4 for the appropriate level of validation. Derived radionuclide concentrations (DRCs) corresponding to the AAL for the water, air filter and soil matrices can be found in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* (see Appendix A for summary tables). For project method validation, MARLAP recommends that the uncertainty of a method be evaluated at or near an action level radionuclide concentration. In the absence of defined AALs and required method uncertainties (either by the Incident Commander [IC][2] or other project manager), default AALs and corresponding required method uncertainties for the method validation test samples provided in Sections 5.2 and 5.4 can be used. The default values in Appendix A may be considered "acceptable" starting levels. The IC may develop and require other

[2] Throughout this guide, the term "Incident Commander" (or "IC") includes his or her designee.

AALs and required method uncertainties. If so, the IC should verify whether the laboratory can meet the new method uncertainty requirements for the updated AALs.

4.2 Detection Capability

In some cases, the detection capability of a method, rather than the required method uncertainty, is the important MQO of a project. Detection capability for this guide uses the concept of the minimum detectable concentration (MDC) or minimum detectable value. MARLAP defines the minimum detectable value of the analyte concentration in a sample as:

> An estimate of the smallest true value of the measurand that ensures a specified high probability, $1 - \beta$, of detection.[3]

For radioanalytical processes, the probability of detection ($1 - \beta$) of 0.95 is commonly used. The definition of the minimum detectable value presupposes that an appropriate detection criterion has been specified, i.e., "critical net concentration" for this document. This approach assumes that the measured radionuclide net concentration in a sample will be above the critical net concentration 95% of the time if the true concentration is equal to the MDC.

MARLAP (Chapter 20) provides a detailed discussion on how to calculate the critical net concentration and MDC using a number of equations for various applications. The equations provided in MARLAP calculate estimates of these method detection parameters for a given method based on either a measured signal response of a single blank sample or from a population of sample blanks that have been processed by the method under evaluation. For those applications when a required MDC for a method has been specified as an MQO, the detection capability of the method should be evaluated during method validation.

4.3 Bias and Trueness

Bias refers to the overall magnitude of systematic errors associated with the use of an analytical method. The presence of systematic errors can be determined only by comparison of the average of many results with a reliable, accepted reference value. Method bias may be estimated by measuring materials whose composition is reasonably well known, such as reference materials, by comparing results to those from at least one alternate method or procedure, or by analyzing spiked materials.

ISO (1993a) defines bias as:

> "[T]he mean value that would result from an infinite number of measurements of the same measurand carried out under repeatability conditions minus a true value of the measurand."

According to MARLAP (Chapter 6), bias typically cannot be accurately determined from a single result or a few results because of the uncertainty in the measurement process to determine the measurand. Bias is normally expressed as the absolute or relative deviation of the average of a group of samples from the "true" or "known" value. Since it is a calculated estimate, a bias should be

[3] Here, β means the probability of a Type II decision error.

reported with a combined standard uncertainty and include the number of data points used to calculate the bias.

It is assumed that the mean response of the method is essentially a linear function of analyte concentration over the useful range of the method. As defined in MARLAP, "this function can be characterized by its *y*-intercept, which reflects the mean response at zero concentration, and its slope, which reflects the ratio of the change in the mean response to a change in sample analyte concentration." The "absolute bias" of a method can be thought of as the difference between the average concentration of the radionuclide at the y-intercept and the true concentration of zero.

The IC will specify a method bias limit as an APS when method bias is considered an important method performance characteristic for the method or a quality parameter for the project. Method bias must be evaluated during method development, general and project method validation processes, and subsequently, the processing of batch quality control (QC) samples processed with the incident response samples (MARLAP Chapter 7).

The method uncertainty acceptance criteria provided in MARLAP (Chapter 6), as well as for project method validation in Section 5.4, assume that laboratories would not use a method that has a significant bias. When a method has excessive bias, the method validation test results for the required method uncertainty will be unacceptable. Appendices D and E provide information on bias evaluation methods as related to the method validation acceptance criteria.

4.4 Analyte Concentration Range

The analyte concentration range of a method is a method performance characteristic that defines the span of radionuclide activity levels, as contained in a sample matrix, for which method performance has been tested and data quality deemed acceptable for their intended use. However, not all sample matrices encountered during an incident response will have preestablished analytical action levels with corresponding required method uncertainty values or required MDCs. Therefore, incident response method validation must be sufficiently flexible to address not only those typical sample matrices (liquids, air filters, swipes, and soil/solids) for which there are action levels, but also those matrices for which there are no specified action levels. The subsequent subsections discuss the analytical concentration range options for method validation for both situations. For both options, the method is to be tested at a low, mid and upper validation test concentration/activity except when noted.

4.4.1 Derived Radionuclide Concentrations Corresponding to Established Action Levels

MARLAP (Chapter 6) recommends that a method be validated at the expected action level for a radionuclide and matrix combination. Therefore, an analyte concentration range should include either an established regulatory limit or a defined action level, typically near the midpoint of the radionuclide activity (concentration) range for a project. For a radiological incident response application, the established AAL would normally be a derived radionuclide concentration corresponding to a PAG or a risk-based dose as designated by an agency representative. There may be four or five action levels for the various matrices contaminated, with the range of concentrations as great as four orders of magnitude. Derived radionuclide concentrations for the various established AALs have been generated for water and air-filter matrices (AALs for soils/sediments and building

materials are being developed), and can be found in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* series. Summary tables of the established AALs for these three matrices can be found in Appendix A. AALs vary according to the matrix, phase of the incident and applied PAG.

At most laboratories, samples that have been screened and found to contain very high radionuclide activities probably will be subdivided (when possible) prior to specific radioanalytical processing. Also, samples requiring multiple radionuclide analyses should be subdivided. Both situations will result in lower-activity subsamples (aliquants) for processing. For example, when a sample that has a very high radionuclide concentration or activity is received by a laboratory, the sample likely will be subdivided (possibly into five parts) so that a different radioanalytical pathway for each radionuclide may be performed in parallel. For aqueous and soil samples, the radionuclide concentration of the radionuclides in the aliquants would be the same as the original aqueous and soil concentrations, but the aliquant activity available for processing will be reduced proportionally from the original sample size. For air-filters, the total activity on the filter matrix represents the activity in a volume of air collected. For swipe samples, the activity on the sample represents the activity removed from a surface area swiped. Air filter and swipe samples may be digested prior to radiochemical processing and the digestate volume generated represents the total activity on the original sample for the air volume collected or surface area swiped. Aliquanting these digestates to obtain a lower subsample activity or for multiple analyses is also a common practice. Thus, it is important to know the exact fraction of the original sample taken so that the analysts know that a sufficient sub-sample quantity has been processed to ensure that the MQOs have been met.

When developing incident response methods for high activity samples, it is important to note that the analytical concentration range and detection capability specifications will be significantly higher than what is usually found in normal procedures for environmental monitoring sample processing. This difference in concentration range should be emphasized in the procedure's scope.

4.4.2 Default Analytical Action Levels

Established AALs based on PAG-derived radionuclide concentrations may not be available for all matrices encountered in an incident response, such as concrete or asphalt. In the absence of established PAG action levels, default AALs may be used for the validation test concentration or activity levels. Section 5.4 provides guidance on selecting default AALs applicable to method validation for the three general matrix categories of liquids, air sampling media/swipes and solids. The default AALs approximate the expected derived radionuclide activity level for a sample volume or mass for a 100-mrem or 10^{-4} risk-based AAL. These AAL levels were chosen because they can be conveniently scaled to other possible project-specific AALs for the various matrices. For example, if a specific project had an AAL at 20 mrem (one-fifth of a 100 mrem AAL), the table values for the AALs can be scaled down simply by dividing the listed values by five.

4.5 Method Specificity

MARLAP defines "method specificity" as "the ability of the method to measure the analyte of concern in the presence of interferences." EURACHEM (1998) defines selectivity or specificity as "the ability of a method to determine accurately and specifically the analyte of interest in the presence of other components in a sample matrix under the stated conditions of the test."

By extension, this guide defines method specificity as:

> The ability to correctly identify and quantify the radionuclide(s) of interest in the presence of other interferences in a sample under stated conditions of the test.

Method specificity should be evaluated during method development and the general and project method validation processes for the applicable matrices, radionuclide(s) of interest and known interfering radionuclides. Method specificity may be evaluated during method validation by analyzing:

- Matrix samples that have been characterized in terms of radionuclide and chemical constituent content;
- Appropriate matrix blanks; and
- Matrix blanks spiked with interferences.

Each specific sample matrix should be tested for method specificity, e.g., concrete, asphalt, soil, etc. Matrix samples and blanks should be chosen to be as representative of the target matrix as is practical. When possible, matrix blanks should contain the chemical species and potential interfering radionuclides, other than the radionuclide(s) of interest, at concentrations that are reasonably expected to be present in an actual sample. Each of the three options to determine method specificity may provide insight into the relative degree of expected quantitative effect that the interferences will have on the identification and quantification of the radionuclide(s) of interest at different concentrations.

Method specificity is typically expressed qualitatively and quantitatively. A radiochemical method specificity statement would include descriptions of parameters, such as:

- Expected radionuclide and chemical interferences
- Effects of the interfering substances on the measurement process
- Measurement information that substantiates the identity of the analyte (e.g., half-life, or decay emission and energy)
- Effects of oxidation or molecular state of the target or interfering radionuclides
- Chemical processes that can remove interfering materials (e.g., ion exchange, solvent extraction)
- Summary of results from analysis of standards, reference materials and matrix blanks

4.6 Method Ruggedness

MARLAP defines “method ruggedness” as “the relative stability of method performance for small variations in method parameter values.” EURACHEM (1998) discusses the concept of method ruggedness and robustness interchangeably. Ruggedness is a measure of how well a method’s performance stands up to less than perfect implementation. In any method there are certain steps which if not carried out sufficiently, exactly or carefully may have a significant effect on method performance and the reliability of the results. Typically, these critical steps are identified during the method development process, and annotations are made in the method description that provide limiting conditions and an allowable range of application. It is advantageous to identify the variables in the method that have the most significant effect on the analytical results so that they are closely

controlled. Ruggedness or robustness tests have been developed which involve experimental designs for examining method performance when minor changes are made in operating steps or in some cases environmental conditions (EPA 2006, *Validation and Peer Review of the U.S. EPA Radiochemical Methods of Analysis*). The tests involve making deliberate variations to the method, and investigating the subsequent effect on performance.

An example of method ruggedness is the adjustment of pH during the separation of strontium from calcium in the analysis of milk for ^{90}Sr. The pH of the milk is buffered at 5.4 and disodium EDTA is added prior to passing the solution through a cation exchange column. The calcium will effectively complex with EDTA at this pH, forming an anion, while the strontium remains a cation. A pH lower than about 5.2 will not provide enough EDTA anion to effectively complex calcium, and a pH greater than about 5.5 will begin to effectively complex strontium. Thus for this analysis method, ruggedness deals with pH control in the range of 5.2 to 5.5.

Method ruggedness is typically evaluated during method development and prior to method validation. Therefore, no specific tests for ruggedness will be included in this document for project method validation of the radioanalytical methods used for incident response.

5.0 Incident Response Method Validation Guidance, Tests, and Requirements

This section provides guidance, specific tests and minimum requirements for project method validation for methods used to process samples from a radiological incident. This section addresses the following selected method performance characteristics:

- Method specificity
- Analyte concentration range
- Method validation levels for testing the required method uncertainty
- Verification of required detection limit specification

Discussion of matrix considerations and method bias tests are also included in this section. Before initiating the method validation process, a validation plan should be prepared that incorporates the various guidance and requirements specified in this section and Section 6, Method Validation Documentation.

5.1 Method Specificity

Method specificity is evaluated during general method validation for normal routine applications, e.g., environmental surveillance programs. During general method validation, the method should be evaluated for the applicable matrices and radionuclide(s) of interest and known interfering chemical constituents and radionuclides over a typical expected range. For some incident response applications, method validation testing for method specificity may be more focused than general method validation. Incident response scenarios may involve one or many radionuclides and a multitude of matrices. To ensure method specificity for the incident response application have been met, the proficiency testing (PT) samples used for incident response method validation should contain the known or expected concentration levels of the matrix chemical species and potential interfering radionuclides. Adequate method specificity during project method validation should be evaluated by analyzing:

- Matrix PT samples that have been characterized in terms of expected radionuclide and chemical constituent content;
- Appropriate matrix blanks containing the applicable radionuclide and chemical interferences; and
- Matrix blanks spiked with interferences.

During method development, decontamination factors[4] should be evaluated for the more commonly expected radionuclide interferences so that the final method can improve method performance and adequately address radionuclide interferences. Also, the concentration of the interfering radionuclides should be added during method development at their 100 mrem AAL-derived radionuclide concentrations. Matrix blank results having no absolute bias would indicate adequate method specificity. Excessive absolute or relative bias, erroneous chemical or radiotracer yields, or possibly excessive method uncertainty may be indications of inadequate method specificity.

5.2 Analyte Concentration Range

The radionuclide concentration range applicable to method validation for radiological incident response should extend from a lower bound (~0.5 AAL) to an upper bound (3 AAL) that are both a multiple of an incident response action level. For radiological incident response applications, the analyte concentration range for the method validation process and validation test levels should be established based on the established PAG or risk-based derived radionuclide concentrations as designated by a representative of the responsible government agency. If the laboratory has not been provided with action levels by the IC, default values listed in Table 1 may be used. Also, derived radionuclide concentrations for the various AALs for water, air filter and soil matrices can be found in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance*. Summary tables of the AAL-derived radionuclide concentrations for the water and air filter matrices can be found in Appendix A[5] of this document. These tables list the expected AALs for various media mainly for the late intermediate and recovery phases, but also for the early phase. The AAL-derived radionuclide concentrations will vary according to the matrix, phase of the incident and applied PAG. For air filters, an activity per sample corresponding to an AAL concentration for an assumed air volume sampled should be used.

The validation test concentration/activity values should be adjusted to reflect the typical sample aliquant size that would be analyzed. In some cases, the original sample may be aliquanted directly, but in other cases the sample must be completely digested before sample aliquanting. When the radionuclide(s) identity is known, the number of aliquants may be small, but when the identity is not known, the number of aliquants may be three or more depending on the decay particle emission type.

[4] The term "decontamination factor" is defined as the amount of interferent in the sample before chemical separation divided by the measured amount in the sample after chemical separation.

[5] The IC may develop and require other AALs and required method uncertainties. If so, the IC should verify whether the laboratory can meet the new method uncertainty requirements for the updated AALs. Calculating the test levels for method validation should be consistent with Table 2.

In the absence of established PAG AALs, default AALs may be used. Default AALs (activity per sample aliquant) for three general matrix categories and radionuclide emission type are provided in Table 1. Default AALs can be used for similar matrix categories, as discussed in Section 5.3 (for all solutions, use water; for swipes, use air-filter materials; and for pulverized concrete, use soil). It should be noted that these default AALs and associated required method uncertainty values (Table 4) for the stated general matrix categories do not have a dosimetric basis but may be considered adequate for method validation purposes.

TABLE 1 – Default Analytical Action Levels for General Matrix Categories

		Default Test Level Activity in Each Sample Aliquant (Total pCi) [1]		
Matrix Category	Size Assumptions for Values	Alpha (^{241}Am)	Pure Beta (^{90}Sr)	Gamma (^{60}Co)
Liquids	5-mL Screen	2.0	12	33
	100-mL Nuclide-Specific	40	240	660
Air Sampling Media/Swipe	68 m^3 Screen	22	1,900	8,400
	68 m^3 (4 aliquants [2]) Nuclide-Specific	5.5	480	2,100
Solids – soil, etc.	2 g	TBD [3]		
	100 g			
	500 g			

[1] Test-level activity corresponds closely to 100-mrem dose-derived concentration values for water and 10^{-4} risk-based DAC for air (Appendix A). The table values were calculated for the noted radionuclides. To calculate air sampling default AALs for 10^{-6} risk-based applications, the 10^{-4} risk-based values in the table can be scaled down by a factor of 100. Table values for the solids and soil are pending.

[2] Test-level activity assumes that the air filter has been split into four aliquants after sample digestion.

[3] TBD: To be determined pending development of *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Soils and Solids.*

For each matrix category, default AALs are provided for both screening and specific radionuclide methods requiring validation. The test level values stated in Table 1 were calculated using the DRC for the 100-mrem AAL values for the gross alpha, beta, and gamma screening levels and for ^{241}Am, ^{90}Sr, and ^{60}Co for the specific alpha and beta/gamma radionuclide categories. The default AALs have been adjusted to reflect the typical sample aliquant size (column 2 of Table 1) that would be analyzed by a laboratory.

For practical reasons and to prevent potential laboratory/instrumentation contamination and radiological safety issues, the test levels for incident response method validation purposes are limited to three levels related to the designated (established) PAG AALs (derived radionuclide concentrations) or default AALs. The use of three test levels is consistent with the specifications indicated in Table 3 and Section 5.4. For incident response method validation, the validation test levels are denoted as lower, mid, and upper. For method validation levels B, C, D, and E (Section 5.4), the recommended three concentration test levels for the replicate PT samples are presented in Table 2. The lower level test level of ~0.5 AAL was chosen to avoid detectability issues that could occur at lower test concentrations. The mid test level corresponds to the established PAG AAL or default AAL test level. It is assumed that a laboratory will use the same sample aliquant size and

counting time to analyze the test samples for all three test-level concentrations (values typically selected to meet the required method uncertainty at the mid test level, or AAL).

TABLE 2 – Method Validation Test Concentrations

Test Level	Relative Concentration
Upper	~3 AAL
Mid	~1 AAL
Lower	~ 0.5 AAL

5.3 Matrix Considerations

For method validation, the method under consideration shall address a specific radionuclide and matrix combination. In many applications, a matrix may be described by a general name or type, such as water or air particulate. However, when developing and documenting the applicability of a method, a description of the sample matrix should be specific and address possible variations in the matrix that may be encountered when such will impact method performance. In addition, validation of a method applies only to the specifically defined matrix described in the method validation plan, which must be consistent with the matrix description in the method applicability statement. Listed below are some specific matrices that may be encountered for radioanalytical processing during an incident:

- Liquids
  - Fresh water
  - Surface water
  - Groundwater
  - Rain
  - Salt/brackish water
  - Aqueous suspensions
  - Aqueous solutions
  - Sewer and water treatment effluents or discharges
  - Collection of volatiles
  - Organic liquids
  - Liquids generated during decontamination activities

- Air sampling media
  - Glass fiber, cellulose, acetate filters
  - Charcoal canisters or loose particles
  - Molecular sieve
  - Silica gel

- Swipes
  - Glass fiber, cellulose, acetate filter paper

- Solids
  - Soil, sediment, stone, sod, vegetation, wood
  - Manufactured/construction

- Concrete, asphalt, brick, ceramics, plaster, plastics, metals, clothes, paper, stone, wood, etc.
- Sludges
- Sewer and water treatment
- Solids generated during decontamination activities

5.4 Method Validation Levels for Testing the Required Method Uncertainty

The primary method validation approach used in this document follows the concepts presented in MARLAP Chapter 6 for the required method uncertainty MQO. The MARLAP method validation approach and validation acceptance criteria assume that the laboratory method being validated has no significant bias. However, this may not always be the case. Appendix D provides an insight into the effect of method bias on the probability of failing the MARLAP validation acceptance criteria.

An alternate approach that may be used to determine if a method has acceptable method validation performance is presented in Appendix E. This approach is based on the mean squared error (MSE) or root mean squared error concept and has a greater power to detect excessive imprecision or bias in many cases.

If a method fails to meet the method validation acceptance criteria as presented in the subsequent sections, the laboratory should:

- Evaluate the possible reasons for the failure;
- Identify the root causes for the failure; and
- Update the method with the appropriate corrections or additions to ensure the method will meet the specified MQOs.

The updated method must go through another validation process using the same requirements applied to the first attempt at method validation.

5.4.1. Method Validation Requirements Based on MARLAP Concepts

Similar to the MARLAP (Chapter 6) graded approach to project method validation, there are four proposed tiers or "levels" of method validation (Levels B, C, D, E) to demonstrate a method's capability of meeting the required method uncertainty MQO applicable to a radiological incident. For this guide, the MARLAP method validation Level A for the *same* radionuclide and matrix combination has been combined with validation Level B (see Table 3). The level(s) of method validation needed should be designated by the IC. The laboratory will select a method based on various operational aspects and the status of it's existing methods to meet the required method uncertainty u_{MR} or φ_{MR} specification for a designated (established) AAL (Appendix A) or a required method uncertainty for a default AAL (Section 5.2). The u_{MR} is specified in the units of the AAL. The φ_{MR} is a fractional unitless value (e.g., 0.13) and is calculated by dividing the u_{MR} by the AAL. Appendix A contains tables listing the required method uncertainties for screening and nuclide-specific methods for certain established AALs and sample matrices related to a potential radiological incident.

The four levels (B-E) of method validation for testing compliance with the required method uncertainty using specified PT samples cover the following:

Level B – Existing methods for radionuclide and matrix combinations for same, similar or slightly different matrices (internal PT samples);

Level C – Existing methods that require modification to accommodate matrix differences (internal or external PT samples);

Level D – Adapted or newly developed methods (internal and external PT samples); and

Level E – Adapted or newly developed methods using method validation reference materials (method validation reference materials).

During the method validation process, the laboratory shall evaluate the method as to the required method uncertainty and relative bias for the three test concentrations (Table 2) for the specified method validation level, as well as the absolute bias through the use of at least seven blanks (Section 5.6 and Appendix E). The acceptable performance of a method to meet the required method uncertainty will vary according to the level of validation as described in subsequent subsections. It should be noted that the probability of acceptable performance for meeting a required method uncertainty specification is dependent on the magnitude of existing method bias. The greater the magnitude of the method bias, the more likely the method will not meet the required method uncertainty specification. If excessive bias is measured during the method validation process, the method should be revised to eliminate the bias as much as possible.

For radiological incident response applications, the analyte concentration range for the method validation process, and thus the validation test levels, should be established based on the established PAG or risk-based derived radionuclide concentrations as designated by an agency representative. Derived radionuclide concentrations corresponding to the various established AALs (PAG or risk-based) for water, air particulate and soil matrices have been provided in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* and summarized in the Appendix A. In the absence of validation test activity levels based on established AALs (PAG or risk-based), default AALs specified in Section 5.2 may be used. Validation test activity/sample levels (designated established AALs or default AALs) are to be used in conjunction with all method validation levels stated in Table 3 and the required method uncertainty values for the radionuclide and matrix combinations provided in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* (Appendix A) or in Section 5.2.

A method is considered validated for a project when it has met the required method uncertainty acceptance criteria stated in Table 3 and the acceptance criteria for other method characteristics such as bias and required MDC, as may be stated by the IC. When the required method uncertainty specifications in Table 3 are met for default AALs, it will be assumed that the method has met the required method uncertainty acceptance criteria for all PAG or risk-based action levels above the default AALs.

All method validation levels require replicate samples at three different validation test concentration/ activity levels below, at, and above the derived radionuclide concentration corresponding to an AAL (designated, established, or default). To ensure testing for sufficient method specificity, the known concentration levels of potentially interfering radionuclides should be included in the test samples.

TABLE 3 – Method Validation Requirements and Applicable to Required Method Uncertainty

Validation Level [1]	Application	Sample Type	Acceptance Criterion [2]	Levels [4] (Concentration)	Replicates [3]	# of Analyses
B	Existing Method Radionuclide – Same, Similar or Slightly Different Matrix	Internal PT	Measured Value Within ±2.8 u_{MR} or ± 2.8 φ_{MR} of Validation Value	3	3	9
C	Similar Matrix: New Application	Internal or External PT	Measured Value Within ±2.9 u_{MR} or ± 2.9 φ_{MR} of Validation Value	3	5	15
D	Adapted, Newly Developed, Rapid Methods	Internal or External PT	Measured Value Within ±3.0 u_{MR} or ± 3.0 φ_{MR} of Validation Value	3	7	21
E	Adapted, Newly Developed, Rapid Methods	Method Validation Reference Materials	Measured Value Within ±3.0 u_{MR} or ± 3.0 φ_{MR} of Validation Value	3	7	21

[1] MARLAP method validation Level A for the *same* radionuclide and matrix combination has been included into validation Level B.

[2] The acceptance criterion is applied to each analysis/test sample used for method validation, not the mean of the analyses. u_{MR} and φ_{MR} values are the required absolute and relative method uncertainty specifications stipulated in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* for gross screening concentrations and quantification of individual radionuclide concentrations in various matrices. The acceptance criteria are chosen to give a false rejection rate of ~5% when the measurement process is unbiased, with a standard deviation equal to the required method uncertainty (u_{MR} or φ_{MR}). The stated multiplier (k = 2.8, 2.9, 3.0) for the required method uncertainty was calculated using the formula $k = z_{0.5 + 0.5(1-\alpha)^{1/N}}$ where N is the number of measurements, α is the desired false rejection rate, and, for any p, z_p denotes the p-quantile ($0 < p < 1$) of the standard normal distribution (MARLAP Appendix G, Table G.1). The u_{MR} or φ_{MR} values are provided in Appendix A or Table 4.

[3] For certain matrices, not all samples in a given test level can be spiked with the same known radionuclide activity or concentration. In such cases, the measured activity or concentration in the test sample should be compared to the known value for that test sample.

[4] At least seven blank samples should be analyzed as part of method validation but are not considered part of the three required concentration test levels.

5.4.2 Required Method Uncertainty Acceptance Criteria

For all four method validation levels for method uncertainty, acceptable method validation is determined by comparing each test sample result for a given test concentration or activity with the required method uncertainty specification ($k \times u_{MR}$ or $k \times \varphi_{MR}$) provided in Table 3. The values for u_{MR} or φ_{MR} are stipulated in the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* (Appendix A) for the three basic incident response matrices of water, air filter/swipes, and soil. A "k" value can be either 2.8, 2.9, or 3.0. It should be noted that the required method uncertainty specification and AAL-derived radionuclide concentrations may vary according to the matrix, the phase of the incident response and applied PAG.

Appendix B provides examples for testing a method's acceptability to meet validation Level D for an established PAG AAL and a default AAL test level in a water matrix.

5.4.2.1 Level B Method Validation: Same, Similar, or Slightly Different Matrix

Most qualified laboratories will have existing methods to analyze for the radionuclides of interest in the three most common matrices of water, air particulate filters and soil/sediment. Under method validation Level B, a method that has been previously validated for a different project and used for one matrix may be used for that same matrix or modified for use for a very similar matrix. An example of a slightly different matrix might be a method used for water samples having low dissolved solids, modified for water samples containing high dissolved solids. Level B requires the laboratory to conduct a method validation study for the radionuclide and matrix combination where three replicate samples from each of the three concentration levels are analyzed according to the method. Table 2 is to be used to determine the lower, middle, and upper testing levels for the replicate analyses. The test samples are internal PT samples prepared at the laboratory. In order to determine if a proposed method meets the project MQO requirements for the required method uncertainty, each internal PT sample result is compared with the method uncertainty acceptance criteria in Table 3. The acceptance criteria in Table 3 for Level B validation stipulate that, for each test sample analyzed, the measured value must be within ±2.8 u_{MR} for test-level concentrations at or less than the AAL or ± 2.8 φ_{MR} for the test-level concentration above the AAL. These acceptance criteria apply to either established AALs stated in Appendix A or default AALs (Section 5.2). The values of u_{MR} and φ_{MR} for select radionuclide and matrix combinations are provided in Appendix A for established PAG AALs or in Table 4 for default AALs. The required method uncertainty values for the established PAG AALs are based on the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance* for the three basic matrices addressed: water, air and soil. The Table 4 values for u_{MR} are base on the default AALs stated in Table 1, and the φ_{MR} values are taken from the air and water editions of the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance*. For example, in Table 4 the u_{MR} value of 5.2 pCi/sample for specific alpha-emitting nuclides in a water matrix (column two, row two) is calculated by multiplying the relative required method uncertainty (φ_{MR}) of 0.13 (column three, row two) for this radionuclide and matrix combination by the default AAL in Table 1 (column three, row two) of 40 pCi/sample value. The φ_{MR} values used in Table 4 are 0.30 for screening measurements and 0.13 for specific radionuclide analyses. The u_{MR} values listed are in units of pCi per sample, assuming the aliquant sample sizes that will be used in the method validation process given in Table 1.

TABLE 4 – Required Method Uncertainty (u_{MR} and φ_{MR}) Values for Default AAL Test Levels

Radionuclide [1]	Water [2,6]		Air Sampling Media/Swipes [3,6]		Solids [5,6]	
	u_{MR} (pCi/ sample)	φ_{MR}	u_{MR} (pCi/ sample)	φ_{MR}	u_{MR} (pCi/ sample)	φ_{MR}
Gross α Screen	0.60	0.30	6.7	0.30	TBD	TBD
Specific Alpha-Emitting[4] Nuclides - based on ^{241}Am	5.2	0.13	0.73	0.13	TBD	TBD
Gross β Screen	3.6	0.30	580	0.30	TBD	TBD
Specific Beta-Emitting[4] Nuclides - based on ^{90}Sr	31	0.13	63	0.13	TBD	TBD
Gamma Screen	9.9	0.30	2,500	0.30	TBD	TBD
Specific Gamma-Emitting[4] Nuclides - based on ^{60}Co	86	0.13	270	0.13	TBD	TBD

Notes:

[1] For each radionuclide category, the absolute required method uncertainty (u_{MR}) is applied to the lower and mid test levels. The relative required method uncertainty (φ_{MR}) is to be used for the upper test level.

[2] Required method uncertainty values for water correspond to the 100-mrem dose-derived concentration values from Scenario 1 of the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Water* (EPA 2008).

[3] Required method uncertainty values for air sampling media correspond to the 10^{-4} risk-based derived air concentration values from Scenario 1 of the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Air* (EPA 2009a).

[4] The default values stated in the specific emitting nuclide rows apply to all radionuclides in the designated emission category. The reference to a radionuclide is presented only as information indicating the basis for the specific emission category.

[5] TBD: To be determined pending development of *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Soils* (In preparation).

[6] Table values have been rounded after calculations.

5.4.2.2 Level C Method Validation: New Application of an Existing Method to a Different Matrix

When a laboratory has a validated method for a radionuclide in one matrix but not others, the method may require modification to accommodate a completely different media/matrix (water versus soil) or a very different similar matrix (two soils of different physicochemical compositions). The degree of adaptation or modification needed will vary according to chemical and physical differences in the two matrices. Because of the extent of these differences, a laboratory may choose to validate the method for the radionuclide and matrix combination through method validation Level C. Level C method validation requires the laboratory to conduct a method validation study wherein five replicate samples from each of the three concentration levels are analyzed according to the method. Table 2 is to be used to determine the lower, mid and upper testing levels for the replicate analyses. The test samples are internal PT samples prepared at the laboratory. In order to determine if a proposed method meets the project MQO requirements for the required method uncertainty, each internal PT sample result is compared with the method uncertainty acceptance criteria of Table 3. The acceptance criteria stated in Table 3 for Level C for new applications stipulate that, for each test sample analyzed, the measured value must be within $\pm 2.9\, u_{MR}$ for test level concentrations at or less than the AAL or $\pm\, 2.9\varphi_{MR}$ for the test level concentration above the AAL. These acceptance criteria apply to either established PAG AALs stated in Appendix A or default AALs (see Section 5.2). The values of u_{MR} and φ_{MR} for select radionuclide and matrix combinations are provided in Appendix A for established PAG AALs or in Table 4 for default AALs.

5.4.2.3 Level D Method Validation: Adapted or Newly Developed Methods, Including Rapid Methods

In some cases, a laboratory may not have a method for a certain radionuclide and matrix combination. For such situations, the laboratory may either develop a new method internally or adapt a method from the literature. In this case, the new method should undergo general method validation first and then incident response method validation. A laboratory would validate the new method for the radionuclide and matrix combination through method validation Level D or E (Section 5.4.2.4). Level D method validation requires the laboratory to conduct a method validation study wherein seven replicate samples from each of the three concentration levels are analyzed according to the method. Table 2 is to be used to determine the lower, mid and upper testing levels for the replicate

analyses. For validation Level D, the test samples are internal PT samples prepared at the laboratory. In order to determine if a proposed method meets the project MQO requirements for the required method uncertainty, each internal PT sample result is compared with the method uncertainty acceptance criteria in Table 3. The acceptance criteria stated in Table 3 for Level D validation stipulate that, for each test sample analyzed, the measured value must be within ±3.0 u_{MR} for test level concentrations at or less than the AAL or ± 3.0 φ_{MR} for the test level concentration above the AAL. These acceptance criteria apply to either established PAG AALs stated in Appendix A or default AALs (Section 5.2). The values of u_{MR} and φ_{MR} for select radionuclide and matrix combinations are provided in Appendix A for established AALs or in Table 4 for default AALs.

5.4.2.4 Level E Method Validation: Adapted or Newly Developed Methods, Including Rapid Methods, Using Method Validation Reference Materials

Methods developed by the laboratory or adapted from the literature that have undergone general method validation but not project method validation for an incident response are to be validated according to Levels D or E of Table 3. Both of these method validation levels have the same number of required test sample replicates and validation acceptance criteria. However, validation Level E is used when the sample matrix under consideration is unique and the IC determines that the method should be validated using the same matrix as the expected sample matrix. In this case, special method validation reference material (MVRM) would be used in the method validation process. The use of MVRM may be important for unique non-potable water matrices, soils or sediments, and manufactured type sample matrices.

Level E method validation requires the laboratory to conduct a method validation study wherein seven replicate samples from each of the three concentration levels are analyzed according to the method. Table 2 is to be used to determine the lower, mid and upper testing levels for the replicate analyses. The test samples are external MVRM samples prepared for the laboratory. In order to determine if a proposed method meets the project MQO requirements for the required method uncertainty, each MVRM sample result is compared with the method uncertainty acceptance criteria of Table 3. The acceptance criteria stated in Table 3 for Level E validation stipulate that, for each test sample analyzed, the measured value must be within ±3.0 u_{MR} for test level concentrations at or less than the AAL or ± 3.0φ_{MR} for the test level concentration above the AAL. These acceptance criteria apply to either established PAG AALs stated in Appendix A or default AALs (See Section 5.2). The values of u_{MR} and φ_{MR} for select radionuclide and matrix combinations are provided in Appendix A for established AALs or in Table 4 for default AALs.

Figure 1 (page 20) identifies the general approach to the method validation path that needs to be taken for a specific combination of radionuclide and matrix. Laboratories should use this chart to see where they are in the method validation process. It may be helpful for laboratories to create a similar flowchart in their method validation documentation to assist reviewers, auditors, and training personnel in recognizing the thought process used by the laboratory to validate methods.

5.5 Verification of Required Detection Limit (MDC) Specification

This section provides specifications for the method validation process to verify the required MDC specification MQO. Figure 2 (page 20) illustrates the process used to verify the required MDC for a method. The specifications presented are separate requirements with respect to the project method

validation process for the required method uncertainty MQO. General method validation requirements are to be met prior to the initiation of this verification process. The specifications given in this section are distinct from those given for the required method uncertainty MQO method-validation process.

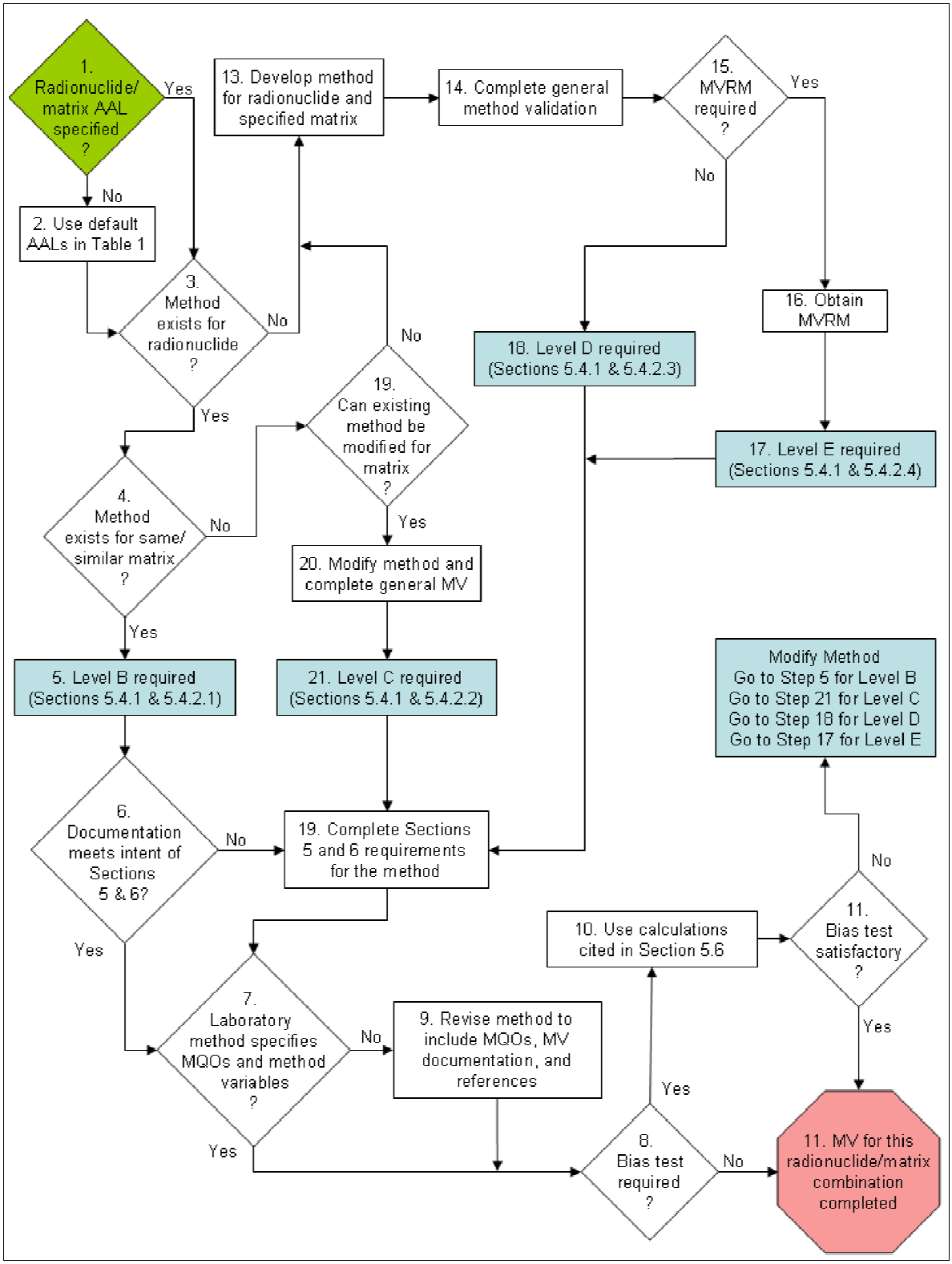


Figure 1 – Method Validation Process for the Required Method Uncertainty MQO

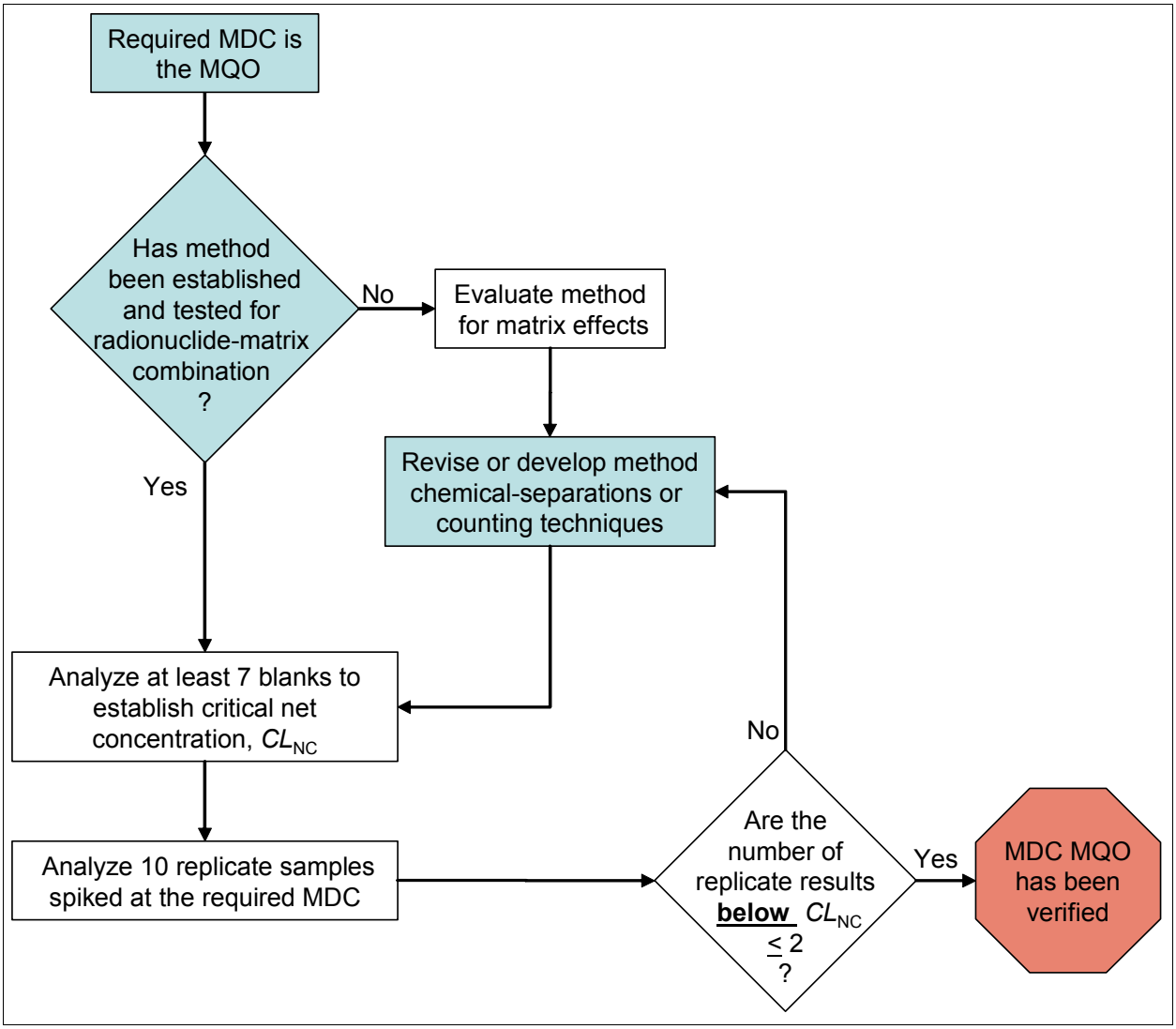


Figure 2 – Validation Process for Verifying the Required MDC MQO

5.5.1 Calculation of the Critical Net Concentration

The critical net concentration shall be calculated for the required MDC method validation process. The calculation of the critical net concentration for the method is based on the analytical results of the blank matrix samples used in the MDC validation process. A minimum of seven blank samples is required. To ensure testing for sufficient method specificity, the matrix blanks should contain the anticipated concentration levels of chemical interferences and the potential interfering radionuclides (naturally occurring and incident response-related).

The critical net concentration (CL_{NC}), with a Type I error probability of $\alpha = 0.05$, is calculated using the following equation (consistent with MARLAP, Chapter 20, Equation 20.35):

$$CL_{NC}\,(\text{pCi/unit}) = t_{1-\alpha}(n-1) \times s_{\text{Blanks}} \quad (1)$$

where s_{Blanks} is the standard deviation of the n blank-sample net results (corrected for instrument background) in radionuclide concentration units of pCi/sample, and $t_{1-\alpha}(n-1)$ is the $(1-\alpha)$-quantile of the t-distribution with $n-1$ degrees of freedom (see MARLAP Table G.2 in Appendix G). Although the Type I error rate of 0.05 is routinely used and accepted, it is possible that other error rates may be used in incident response situations.

For seven (minimum) blank results (six degrees of freedom) and a Type I error probability of 0.05, Equation (1) reduces to:

$$CL_{NC}\,(\text{pCi/unit}) = 1.94 \times s_{Blanks} \tag{2}$$

If the number of blank samples is different than the minimum value of seven, refer to MARLAP Chapter 20, Attachment 20A for appropriate guidance. Care must be taken to ensure that all samples and blanks are analyzed under conditions that are typical of those used for routine analyses using the same sample weight or volume and with the same instruments with representative counting efficiencies and background levels. The calculated critical net concentration will be used in the verification process to determine if a method is capable of meeting the required MDC specification as described in Section 5.5.2.

5.5.2 Testing for the Required MDC

When a required MDC specification for a radionuclide and matrix combination is given as an MQO rather than the required method uncertainty, the method should be validated by verifying that the method can meet the required MDC. As noted in Table 5, method validation for the required MDC specifies that ten replicate samples, each spiked at the required MDC, should be analyzed and evaluated. In addition, the results of at least seven blank samples are used to determine the critical net concentration of the method (Section 5.5.1). The ten replicate spiked samples and seven blanks should contain the chemical species and potential interfering radionuclides which are reasonably expected to be present in an actual sample. To ensure the testing for sufficient method specificity, the expected concentration levels of the chemical species and potential interfering radionuclides should be used during testing. Figure 2 (page 20) provides an overview of the method validation process for verifying the required MDC MQO.

Testing for the required MDC verification is based on the null hypothesis that the true MDC for the method is at or below the required MDC. If the true MDC of the method has been calculated properly and is equal to or less than the required MDC, the probability of failing to detect the radionuclide at or above the critical net concentration is at most β. For project method validation related to incident response, β is assumed to be 0.05. The number of "non-detects" (sample results below the critical net concentration) for a set of n samples spiked at the required MDC is assumed to have a binomial distribution with parameters β and n. For a set of ten samples spiked at the required MDC, the number of Y sample results expected to be below the critical net concentration is not more than two (2) for a β of 0.05. If Y is greater than two, the null hypothesis is rejected.

The following protocol should be used to verify a method's capability to meet the required method MDC for each radionuclide (including gross screening)-matrix combination:

1. Analyze a minimum of seven blank samples (representing the matrix of interest) for the radionuclide under consideration.

2. From the blank sample net results, calculate the estimated *Critical Net Concentration* (Section 5.5.1), CL_{NC}.

3. Analyze ten replicate samples (representing the matrix of interest) spiked at the required MDC for the radionuclide under consideration.

4. From the results of the ten replicate samples spiked at the required MDC, determine the number (Y) of sample results at or below the estimated *Critical Net Concentration*.

5. If $Y \leq 2$, the method evaluated at the required MDC passes the test for the required MDC specification.

6. If $Y > 2$, the method evaluated at the required MDC fails the test for the required MDC specification.

Appendix C provides an example for testing a method's capability to meet a required MDC specification.

TABLE 5 – Method Validation Requirements Applicable to Required MDC Verification

Method Characteristic	Application	Sample Type	Acceptance Criterion	Levels (Concentrations)	Replicates	# of Analyses
Detection Capability	Required MDC Specification	Internal PT	Number of Sample Results Below Critical Net Concentration Value ≤ 2	Single Concentration at the Required MDC Value	10	10

Note: At least seven blank samples should be analyzed to estimate the critical net concentration as part of the required MDC verification.

5.6 Method Bias Tests

In order to provide quality data, a method should not have a significant bias. Depending on the radiological incident, acceptable absolute and relative bias criteria for a method may be specified by the IC. Since the degree of acceptability of method bias depends on many parameters and circumstances, specific acceptance criteria for method bias have not been included for this method validation process. However, because the acceptance criteria for method uncertainty and required MDC verification will not tolerate a significant method bias or measurement uncertainty, acceptable method bias is indirectly evaluated when evaluating method uncertainty and the required MDC. Appendix D provides an example of the effect of bias on the probability of failing the required method uncertainty validation acceptance criteria for method validation Level D.

Method bias is initially evaluated during method development, general and project method validation processes, and then continuously during the processing of incident response samples using batch QC samples (MARLAP Chapter 7). Tests for absolute and relative biases shall be made for the method

validation level specified by the IC. The absolute bias shall be evaluated using the blank sample results and the relative bias evaluated for each test level (lower, mid and upper) using the results of the replicates.

When there is a significant absolute or relative bias, the probability of failing the required method uncertainty acceptance criteria of Section 5.4.2 may become significant depending on the magnitude of the actual method uncertainty. Appendix D provides an example of the probability of failing method validation Level D for three actual method uncertainty values (as compared to the required method uncertainty) as a function of relative bias up to 20%. In general, to avoid failure to meet the method validation acceptance criteria, it is best to have an actual method uncertainty at the AAL that is a fraction of the required method uncertainty.

The following equations, taken from MARLAP Chapter 6 (Attachment 6A) and other statistical references, are used to test for absolute and relative biases.

5.6.1 Absolute Bias Testing

The protocol for testing for absolute bias is the following:

1. Calculate the mean ($\overline{X}$) for "N" (at least seven) blank sample net results using Equation 3.

$$\overline{X} = \frac{1}{N}\sum_{i=1}^{N} X_i \tag{3}$$

   where N should be at least seven blank sample results.

2. Calculate the experimental standard deviation (s_x) of the same results[6] using Equation 4.

$$S_X = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(X_i - \overline{X})^2} \tag{4}$$

3. Use Equation 5 to calculate the |T| value:

$$|T| = \frac{|\overline{X}|}{s_X/\sqrt{N}} \tag{5}$$

[6] Notice that the sum under the radical in equation 4 is divided by the number of degrees of freedom, $N - 1$, not the number of results, N. When calculated in this manner, s_X^2 is an unbiased estimator for the variance of the results. If the true mean of the results, μ_X, were known, a better estimate of the variance would be $\frac{1}{N}\sum_{i=1}^{N}(X_i - \mu_x)$, but because the mean is estimated from the data, the number of degrees of freedom is reduced by 1. Notice also that the expression in the denominator of the right-hand side of Equation 5 gives the *experimental standard deviation of the mean*, more commonly known as the "standard error of the mean." The division by $\sqrt{N}$ in this case accounts for the effect of averaging N independent results.

4. An absolute bias in the measurement process is indicated if

$$|T| > t_{1-\alpha/2}\ (N-1) \tag{6}$$

where, $t_{1-\alpha/2}$ (N-1) represents the (1 - α/2)-quantile of the *t*-distribution with *N*-1 degrees of freedom. For seven blanks, an absolute bias is identified at a significance level of 0.05, when |T| > 2.447.

5.6.2 Relative Bias Testing

5.6.2.1 Test Level Samples with Same Known Value

When the samples for a test level have the same concentration (e.g., water) or activity, the protocol for testing relative bias for each method validation test level is the following:

1. Calculate the mean ($\bar{X}$) and estimated standard deviation (s_X) of the replicate results for each method validation test level using Equations 3 and 4, respectively.

2. Use Equation 7 to calculate the |T| value

$$|T| = \frac{|\bar{X} - K|}{\sqrt{s_X^2 / N + u^2(K)}} \tag{7}$$

where:

$\bar{X}$	is the average measured value
s_X	is the experimental standard deviation of the measured values
N	is the number of replicates
K	is the reference value
$u(K)$	is the standard uncertainty of the reference value

3. A relative bias in the measurement process is indicated if

$$|T| > t_{1-\alpha/2}(\nu_{eff}) \tag{8}$$

The number of *effective degrees of freedom* for the *T* statistic is calculated as follows:

$$\nu_{eff} = (N-1)\left(1 + \frac{u^2(K)}{s_X^2 / N}\right)^2 \tag{9}$$

ν_{eff} as calculated by the equation generally is not an integer so ν_{eff} should be truncated (rounded down) to an integer. Then, given the significance level of 0.05, the critical value for $|T|$ is defined to be $t_{1-\alpha/2}(\nu_{eff})$, the $(1-\alpha/2)$-quantile of the *t*-distribution with ν_{eff} degrees of freedom (see MARLAP Appendix G, Table G.2).

5.6.2.2 Test Level Samples with Slightly Different Known Values

When the PT samples for a test level have slightly different concentrations or activities (e.g., independently prepared[7] water samples, air filters, or swipes), the following protocol (paired *t*-test) for testing relative bias for each method validation test level is:

1. Calculate the average difference ($\overline{D}$) between the measured value and the known spiked value using Equation 10:

$$\overline{D} = \frac{1}{N}\sum_{i=1}^{N}(X_i - K_i) \tag{10}$$

where
- X_i is the measured value for the i^{th} sample at a particular test level
- K_i is the known value for the same sample
- N is the number of samples at that test level

2. Calculate the standard deviation of the differences, S_D, as:

$$S_D = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(D_i - \overline{D})^2} \tag{11}$$

where $D_i = X_i - K_i$.

3. Calculate the absolute value of the *t* statistic as:

$$|T| = \frac{|\overline{D}|}{S_D / \sqrt{N}} \tag{12}$$

4. A relative bias in the measurement process for a test level is indicated if

$$|T| > t_{1-\alpha/2}(N-1) \tag{13}$$

6.0 Method Validation Documentation

The information and data to be retained should be specified in the method validation plan for each radionuclide and matrix combination. When the laboratory conducts project method validation for incident response applications, the detailed analytical method and all records, laboratory workbooks, and matrix spike data used to validate the analytical method should be retained on file and be retrievable for a specified length of time after the method has been discontinued. Data evaluations such as comparison of individual results to the validation acceptance criteria and absolute bias in

[7] During the preparation of the proficiency test samples for a test level, the spread in activity deposited on the samples of the test level should be controlled so that the coefficient of variation of the test-sample activities does not exceed 3%.

blanks and, when available, method precision and bias, should be part of the data validation package retained as part of the documentation related to the laboratory's quality system. In addition, for each radionuclide and matrix combination, a synoptic method validation report containing the analytical method identification, method validation acceptance criteria, test levels, validation results and a method acceptability decision should be generated and retained.

7.0 References

American National Standards Institute (ANSI) N42.23. Reapproved 2003. Measurement and Associated Instrumentation Quality Assurance for Radioassay Laboratories.

U.S. Environmental Protection Agency (EPA). 2006. *Validation and Peer Review of U.S. Environmental Protection Agency Radiochemical Methods of Analysis*. FEM Document Number 2006-01, November 8.

U.S. Environmental Protection Agency (EPA). 2008. *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Water*. Revision 0. Office of Air and Radiation, Washington, DC. EPA 402-R-07-007, January. Available at: www.epa.gov/narel/recent_info.html.

U.S. Environmental Protection Agency (EPA). 2009a. *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Air.* Revision 0. Office of Air and Radiation, Washington, DC. EPA 402-R-09-007, June. Available at: www.epa.gov/narel/recent_info.html.

U.S. Environmental Protection Agency (EPA). 2009b. *Radiological Laboratory Sample Screening Analysis Guide for Incidents of National Significance.* Revision 0. Office of Air and Radiation, Washington, DC. EPA 402-R-09-008, June. Available at: www.epa.gov/narel/recent_info.html.

EURACHEM Guide. 1998 *The Fitness for Purpose of Analytical Methods, A Laboratory Guide to Method Validation and Related Topics*. Available at: http://www.eurachem.org/.

International Standard ISO/IEC 17025. 2005. General Requirements for the Competence of Testing and Calibration Laboratories. ISO, Geneva, Switzerland.

International Organization for Standardization (ISO). 1993. *International Vocabulary of Basic and General Terms in Metrology*. 2nd Edition. ISO, Geneva, Switzerland.

Multi-Agency Radiological Laboratory Analytical Protocols Manual (MARLAP). 2004. EPA 402-B-04-001A, July. Volume I, Chapters 6, 7, 20, Glossary; Volume II and Volume III, Appendix G. Available at: www.epa.gov/radiation/marlap.

Multi-Agency Radiation Survey and Site Investigation Manual (MARSSIM)*, Revision 1*. 2000. NUREG-1575 Rev 1, EPA 402-R-97-016 Rev1, DOE/EH-0624 Rev1. August. Available from www.epa.gov/radiation/marssim/.

Appendix A:
Tables Summarizing the Derived Radionuclide Concentrations and Required Method Uncertainties Corresponding to PAGs or Risks for the Water, Air, and Soil Matrices

TABLE A1 – Alpha-Emitting Radionuclide Concentrations and Required Method Uncertainties in Water Corresponding to 500- and 100-mrem AAL Derived Water Concentrations (DWCs)

Radionuclide	pCi/L				
	500 mrem		100 mrem		
	AAL DWC [1][2]	Screening Methods Required Method Uncertainty (u_{MR}) [6]	AAL DWC [1][2][3]	Screening Methods Required Method Uncertainty (u_{MR}) [6]	Nuclide-Specific Required Method Uncertainty (u_{MR}) [6]
Gross α Screen [5]	2.0×10^3	610	400	120	—
Am-241	2.0×10^3	610	400	120	50
Cm-242	1.4×10^4	4.3×10^3	2.8×10^3	850	350
Cm-243	2.5×10^3	760	500	150	63
Cm-244	2.9×10^3	880	580	180	73
Np-237	3.9×10^3	1.2×10^3	780	240	98
Po-210	130	40	26	7.9	3.3
Pu-238	1.8×10^3	550	360	110	45
Pu-239	1.7×10^3	520	340	100	43
Pu-240	1.7×10^3	520	340	100	43
Ra-226 [4]	910	280	180	55	23
Th-228 [4]	2.6×10^3	790	520	160	65
Th-230	1.8×10^3	550	360	110	45
Th-232	1.6×10^3	490	320	97	40
U-234	6.3×10^3	1.9×10^3	1.3×10^3	400	160
U-235	6.6×10^3	2.0×10^3	1.3×10^3	400	160
U-238	7.0×10^3	2.1×10^3	1.4×10^3	430	180

Notes:

[1] Values are based on the dose conversion factors in Federal Guidance Report No.13, CD Supplement, 5-year-old child and the 50th percentile of water consumption.

[2] 365-day intake.

[3] Values obtained by dividing 500-mrem DWC values by 5.

[4] Includes the dose from the decay products originating from the ^{226}Ra or ^{228}Th in the body.

[5] Values for gross alpha screening are based on ^{241}Am.

[6] The required relative method uncertainty (φ_{MR}) for values greater than the AALs in this table is obtained by dividing the u_{MR} value by the corresponding AAL.

TABLE A2 – Beta/Gamma-Emitting Radionuclide Concentrations in Water and Required Method Uncertainties Corresponding to 500- and 100-mrem AAL Derived Water Concentrations (DWCs)

Radionuclide	pCi/L				
	500 mrem		100 mrem		
	AAL DWC [1][2]	Screening Methods Required Method Uncertainty (u_{MR}) [5]	AAL DWC [1][2][3]	Screening Methods Required Method Uncertainty (u_{MR}) [5]	Nuclide-Specific Required Method Uncertainty (u_{MR}) [5]
Gross β/γ Screen[4]	5.8×10^{4}	1.8×10^{4}	1.2×10^{4}	3.6×10^{3}	—
Ac-227DP[6]	1.1×10^{3}	330	220	67	28
Ce-141	2.2×10^{5}	6.7×10^{4}	4.4×10^{4}	1.3×10^{4}	5.5×10^{3}
Ce-144	2.9×10^{4}	8.8×10^{3}	5.8×10^{3}	1.8×10^{3}	730
Co-57	6.3×10^{5}	1.9×10^{5}	1.3×10^{5}	4.0×10^{4}	1.6×10^{4}
Co-60	3.3×10^{4}	1.0×10^{4}	6.6×10^{3}	2.0×10^{3}	830
Cs-134	4.3×10^{4}	1.3×10^{4}	8.6×10^{3}	2.6×10^{3}	1.1×10^{3}
Cs-137	5.8×10^{4}	1.8×10^{4}	1.2×10^{4}	3.6×10^{3}	1.5×10^{3}
H-3	7.7×10^{6}	2.3×10^{6}	1.5×10^{6}	4.6×10^{5}	1.9×10^{5}
I-125	1.3×10^{4}	4.0×10^{3}	2.6×10^{3}	790	320
I-129	3.3×10^{3}	1.0×10^{3}	660	200	83
I-131	5.4×10^{3}	1.6×10^{3}	1.1×10^{3}	330	140
Ir-192	1.2×10^{5}	3.6×10^{4}	2.4×10^{4}	7.3×10^{3}	3.0×10^{3}
Mo-99	3.2×10^{5}	9.7×10^{4}	6.4×10^{4}	1.9×10^{4}	8.1×10^{3}
P-32	5.9×10^{4}	1.8×10^{4}	1.2×10^{4}	3.6×10^{3}	1.5×10^{3}
Pd-103	7.8×10^{5}	2.4×10^{5}	1.6×10^{5}	4.9×10^{4}	2.0×10^{4}
Pu-241	1.0×10^{5}	3.0×10^{4}	2.0×10^{4}	6.1×10^{3}	2.5×10^{3}
Ra-228[6]	160	49	32	9.7	4.0
Ru-103	2.3×10^{5}	7.0×10^{4}	4.6×10^{4}	1.4×10^{4}	5.8×10^{3}
Ru-106	2.2×10^{4}	6.7×10^{3}	4.4×10^{3}	1.3×10^{3}	550
Se-75	6.7×10^{4}	2.0×10^{4}	1.3×10^{4}	4.0×10^{3}	1.6×10^{3}
Sr-89	6.3×10^{4}	1.9×10^{4}	1.3×10^{4}	4.0×10^{3}	1.6×10^{3}
Sr-90	1.2×10^{4}	3.6×10^{3}	2.4×10^{3}	730	300
Tc-99	2.4×10^{5}	7.3×10^{4}	4.8×10^{4}	1.5×10^{4}	6.0×10^{3}

Notes:

[1] Values are based on the dose conversion factors in Federal Guidance Report No.13, CD Supplement, 5-year-old child and the 50th percentile of water consumption.

[2] 365-day intake.

[3] Values obtained by dividing 500-mrem DWC values by 5.

[4] Gross beta screening values are based on ^{137}Cs.

[5] The required relative method uncertainty (φ_{MR}) for values greater than the AALs is obtained by dividing the u_{MR} value in this table by the corresponding AAL value.

[6] Includes the dose from the decay products originating from the ^{228}Ra or ^{227}Ac in the body.

TABLE A3 – Alpha-Emitting Radionuclide Concentrations in Air and Required Method Uncertainties Corresponding to 2-rem and 500-mrem AAL Derived Air Concentrations (DACs)

Radionuclide	pCi/m³					
	2 rem			500 mrem		
	AAL DAC [1]	Screening Method Required Method Uncertainty (u_{MR}) [3]	Nuclide-Specific Required Method Uncertainty (u_{MR}) [3]	AAL DAC [1]	Screening Method Required Method Uncertainty (u_{MR}) [3]	Nuclide-Specific Required Method Uncertainty (u_{MR}) [3]
Gross α Screen[4]	0.70	0.21	—	0.17	0.052	—
Am-241	0.70	0.21	0.088	0.17	0.052	0.021
Cm-242	11	3.3	1.4	2.8	0.85	0.35
Cm-243	0.97	0.29	0.12	0.24	0.073	0.030
Cm-244	1.2	0.36	0.15	0.29	0.088	0.037
Np-237	1.3	0.40	0.16	0.34	0.10	0.043
Po-210	16	4.9	2.0	3.9	1.2	0.49
Pu-238	0.62	0.19	0.081	0.15	0.046	0.020
Pu-239	0.56	0.17	0.071	0.14	0.043	0.018
Pu-240	0.56	0.17	0.071	0.14	0.043	0.018
Ra-226 [2]	7.0	2.1	0.88	1.8	0.55	0.23
Th-228 [2]	1.7	0.52	0.21	0.42	0.13	0.053
Th-230	0.66	0.20	0.083	0.17	0.052	0.021
Th-232	0.61	0.19	0.077	0.15	0.046	0.019
U-234	7.1	2.2	0.89	1.8	0.55	0.23
U-235	7.9	2.4	0.99	2.0	0.61	0.25
U-238	8.3	2.5	1.0	2.1	0.64	0.26

Notes:

[1] Morbidity for long-term inhalation. Child as receptor. Value corresponds to solubility class having lowest value.

[2] Includes the dose from the decay products originating from the ^{226}Ra or ^{228}Th in the body.

[3] Required method uncertainty values are based on a sampled aerosol volume of 68 m³ at the 2 rem or 500-mrem DAC. The required relative method uncertainty (φ_{MR}) for values greater than the AALs in this table is obtained by dividing the u_{MR} value in this table by the corresponding AAL value.

[4] The gross α screening values are not related to a specific radionuclide.

TABLE A4 – Beta/Gamma-Emitting Radionuclide Concentrations in Air and Required Method Uncertainties Corresponding to 2-rem and 500-mrem AAL Derived Air Concentrations (DACs)

Radionuclide	pCi/m³					
	2 rem			500 mrem		
	AAL DAC [1,4]	Screening Method Required Method Uncertainty (u_{MR}) [3]	Nuclide-Specific Required Method Uncertainty (u_{MR}) [3]	AAL DAC [1,4]	Screening Method Required Method Uncertainty (u_{MR}) [3]	Nuclide-Specific Required Method Uncertainty (u_{MR}) [3]
Gross β Screen[5]	420	130	—	110	33	—
Ac-227+DP [2]	0.43	0.13	0.054	0.11	0.033	0.014
Ce-141	1.8×10^4	5.5×10^3	2.3×10^3	4.5×10^3	1.4×10^3	570
Ce-144	1.3×10^3	400	160	320	97	40
Co-57	6.7×10^4	2.0×10^4	8.4×10^3	1.7×10^4	5.2×10^3	2.1×10^3
Co-60	2.2×10^3	670	280	540	170	69
Cs-134	3.3×10^3	1.0×10^3	420	820	250	100
Cs-137	1.7×10^3	520	210	430	130	54
H-3	2.6×10^5	7.9×10^4	3.3×10^4	6.4×10^4	1.9×10^4	8.1×10^3
I-125 [6]	1.3×10^4	4.0×10^3	1.6×10^3	3.2×10^3	970	400
I-129 [6]	1.9×10^3	580	240	470	140	59
I-131 [6]	9.1×10^3	2.8×10^3	1.1×10^3	2.3×10^3	700	290
Ir-192	1.0×10^4	3.0×10^3	1.3×10^3	2.5×10^3	760	310
Mo-99	6.8×10^4	2.1×10^4	8.6×10^3	1.7×10^4	5.2×10^3	2.1×10^3
P-32	1.7×10^4	5.2×10^3	2.1×10^3	4.3×10^3	1.3×10^3	540
Pd-103	1.5×10^5	4.6×10^4	1.9×10^4	3.8×10^4	1.2×10^4	4.8×10^3
Pu-241	29	8.8	3.7	7.3	2.2	0.92
Ra-228 [2]	4.2	1.3	0.53	1.0	0.30	0.13
Ru-103	2.3×10^4	7.0×10^3	2.9×10^3	5.7×10^3	1.7×10^3	720
Ru-106	1.0×10^3	300	130	250	76	31
Se-75	5.0×10^4	1.5×10^4	6.3×10^3	1.3×10^4	4.0×10^3	1.6×10^3
Sr-89	8.4×10^3	2.6×10^3	1.1×10^3	2.1×10^3	640	260
Sr-90	420	130	53	110	33	14
Tc-99	5.0×10^3	1.5×10^3	630	1.3×10^3	400	160

Notes:

[1] Derived air concentration yielding stated committed effective dose assuming a 365-day year. Child as receptor. Value corresponds to solubility class having lowest value.

[2] Includes the dose from the decay products originating from the ^{228}Ra or ^{227}Ac in the body. DP refers to "decay products."

[3] Required method uncertainty values are based on a sampled aerosol volume of 68 m³ at the 2 rem or 500-mrem DAC. The required relative method uncertainty (φ_{MR}) for values greater than the AALs in this table is obtained by dividing the u_{MR} value in this table by the corresponding AAL value.

[4] All nuclides can be collected on a fibrous or membrane air filter media except ^{3}H, ^{125}I, ^{129}I, and ^{131}I in the vapor states.

[5] Gross beta screening values are based on ^{90}Sr.

[6] These values are based on the vapor plus particulate dose rate.

TABLE A5 – Alpha-Emitting Radionuclide Concentrations in Air and Required Method Uncertainties Corresponding to AAL Derived Air Concentrations (DACs)

Radionuclide	pCi/m^3			
	10^{-4} Risk AAL DAC [1]	10^{-4} Risk AAL Required Method Uncertainty (u_{MR}) [3]	10^{-6} Risk AAL DAC [1]	10^{-6} Risk AAL Required Method Uncertainty (u_{MR}) [3]
Gross α Screen [4]	0.33	0.042	3.3×10^{-3}	4.2×10^{-4}
Am-241	0.33	0.042	3.3×10^{-3}	4.2×10^{-4}
Cm-242	0.62	0.078	6.2×10^{-3}	7.8×10^{-4}
Cm-243	0.34	0.043	3.4×10^{-3}	4.3×10^{-4}
Cm-244	0.35	0.044	3.5×10^{-3}	4.4×10^{-4}
Np-237	0.43	0.054	4.3×10^{-3}	5.4×10^{-4}
Po-210	0.86	0.11	8.6×10^{-3}	1.1×10^{-3}
Pu-238	0.24	0.030	2.4×10^{-3}	3.0×10^{-4}
Pu-239	0.22	0.028	2.2×10^{-3}	2.8×10^{-4}
Pu-240	0.22	0.028	2.2×10^{-3}	2.8×10^{-4}
Ra-226 [2]	0.44	0.055	4.4×10^{-3}	5.5×10^{-4}
Th-228 [2]	0.094	0.012	9.4×10^{-4}	1.2×10^{-4}
Th-230	0.36	0.045	3.6×10^{-3}	4.5×10^{-4}
Th-232	0.30	0.038	3.0×10^{-3}	3.8×10^{-4}
U-234	0.45	0.057	4.5×10^{-3}	5.7×10^{-4}
U-235	0.49	0.062	4.9×10^{-3}	6.2×10^{-4}
U-238	0.52	0.065	5.2×10^{-3}	6.5×10^{-4}

Notes:

[1] Morbidity for long-term inhalation. Value corresponds to solubility class having lowest value.

[2] Includes the dose from the decay products originating from the ^{226}Ra or ^{228}Th in the body.

[3] Required method uncertainty values are based on a sampled aerosol volume of 1,600 m^3 at the 10^{-4} and 10^{-6} risk DACs, respectively. The required relative method uncertainty (φ_{MR}) for values greater than the AALs in the table is obtained by dividing the u_{MR} value by the corresponding AAL value.

[4] The gross α screening values are not related to a specific radionuclide.

TABLE A6 – Beta/Gamma-Emitting Radionuclide Concentrations in Air and Required Method Uncertainties Corresponding to AAL-Derived Air Concentrations (DACs)

Radionuclide	pCi/m^3			
	10^{-4} Risk AAL DAC [1,4]	10^{-4} Risk AAL Required Method Uncertainty (u_{MR}) [3]	10^{-6} Risk AAL DAC [1,4]	10^{-6} Risk AAL Required Method Uncertainty (u_{MR}) [3]
Gross β Screen (Sr-90)	29	3.8	0.29	0.038
Ac-227+DP [2]	0.083	0.010	8.3×10^{-4}	1.0×10^{-4}
Ce-141	920	120	9.2	1.2
Ce-144	69	8.7	0.69	0.087
Co-57	3.3×10^{3}	420	33	4.2
Co-60	120	15	1.2	0.15
Cs-134	180	23	1.8	0.23
Cs-137	110	14	1.1	0.14
H-3 Vapor	1.5×10^{4}	1.9×10^{3}	150	19
I-125	1.2×10^{3}	150	12	1.5
I-129	200	25	2	0.25
I-131	640	81	6.4	0.81
Ir-192	510	64	5.1	0.64
Mo-99	2.6×10^{3}	330	26	3.3
P-32	890	110	8.9	1.1
Pd-103	7.0×10^{3}	880	70	8.8
Pu-241	14	1.8	0.14	0.018
Ra-228 [2]	0.28	3.5×10^{-2}	2.8×10^{-3}	3.5×10^{-4}
Ru-103	1.2×10^{3}	150	12	1.5
Ru-106	56	7.1	0.56	0.071
Se-75	2.5×10^{3}	310	25	3.1
Sr-89	410	52	4.1	0.52
Sr-90	29	3.7	0.29	0.037
Tc-99	330	42	3.3	0.42

Notes:

[1] Morbidity for long-term inhalation. Value corresponds to solubility class having lowest value.

[2] Includes the dose from the decay products originating from the ^{228}Ra or ^{227}Ac in the body.

[3] Required method uncertainty values are based on a sampled aerosol volume of 1,600 m^3 at the 10^{-4} and 10^{-6} risk DAC, respectively. The required relative method uncertainty (φ_{MR}) for values greater than the AALs in the table is obtained by dividing the u_{MR} value by the corresponding AAL value.

[4] All nuclides can be collected on a fibrous or membrane air filter media except ^{3}H, ^{125}I, ^{129}I, and ^{131}I in the vapor states.

TABLE A7 – Alpha and Beta/Gamma-Emitting Radionuclide Concentrations in Soil and Required Method Uncertainties Corresponding to Derived Soil Concentrations

Table to be determined following publication of Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Soil.

Appendix B:
Examples of the Method Validation Process for Required Method Uncertainty Specifications

Two examples are provided to demonstrate the method validation process when the MQO involves a required method uncertainty (u_{MR} or φ_{MR}) specification. The first example is when an Incident Commander (IC) specifies a required method uncertainty for a method and an AAL (PAG or risk-based derived radionuclide concentration) for a typical radionuclide and matrix combination as provided in Appendix A. The radionuclide and matrix combination for this first example is ^{241}Am in potable water. Values for the derived radionuclide concentration AAL and required method uncertainty were obtained from the *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance–Radionuclides in Water* (EPA 2008). The three testing level concentrations were determined using the AAL concentration value and the lower, mid and upper test level multipliers in Table 2. Acceptable validation criteria are established in Table 3 for Validation Level D.

The second example is when an Incident Commander specifies a required method uncertainty for a method used to analyze a radionuclide or matrix not provided in Appendix A. For this example, the radionuclide and matrix combination is ^{241}Am in street runoff water. Values for the derived AALs and required method uncertainty were obtained from Tables 1 and 4, respectively. The three testing level concentrations were determined using the AAL concentration value and the lower, mid and upper test level multipliers in Table 2. Acceptable validation criteria are established in Table 3 for validation Level D.

Example 1. Method Validation for Am-241 in Potable Water; Established AALs

Nuclide: ^{241}Am

Matrix: Water

Analytical Action Level: 400 pCi/L (Appendix A, Table A1, 100 mrem)

Proposed Method: Radiochemistry with alpha spectrometry

Required Method Validation Level: D

Required Method Uncertainty[8]: 50 pCi/L at AAL or below; 13% above AAL

Acceptance Criteria (Table 3): Measured value within ±3 u_{MR} (± 150 pCi/L) of known value ≤ AAL and ±3 φ_{MR} (± 39%) of known value > AAL.

Test levels (Table 2): Lower (0.5 × AAL = 200 pCi/L; Mid (AAL) = 400 pCi/L; Upper (3 × AAL) = 1,200 pCi/L

[8] EPA 2008. *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance – Radionuclides in Water*, Table 9A.

Data Evaluation:

TABLE B1 – Required Method Uncertainty for Am-241 in Potable Water

	Lower Test Level Concentration 200 pCi/L Acceptable Range: 50 to 350 pCi/L		Mid Test Level Concentration[1] 400 pCi/L[2] Acceptable Range: 250 to 550 pCi/L		Upper Test Level Concentration 1,200 pCi/L Acceptable Range: 732 to 1,670 pCi/L	
Test Sample	**Measured Value ± 1 CSU[3]**	**Acceptable Value (Y/N)**	**Measured Value ± 1 CSU[3]**	**Acceptable Value (Y/N)**	**Measured Value ± 1 CSU[3]**	**Acceptable Value (Y/N)**
1	221 ± 27	Y	429 ± 40	Y	1,283 ± 87	Y
2	179 ± 24	Y	381 ± 37	Y	1,117 ± 78	Y
3	210 ± 26	Y	405 ± 39	Y	1,241 ± 85	Y
4	190 ± 25	Y	304 ± 32	Y	1,159 ± 80	Y
5	169 ± 25	Y	362 ± 36	Y	1,262 ± 86	Y
6	225 ± 27	Y	458 ± 42	Y	1,138 ± 79	Y
7	213 ± 26	Y	390 ± 38	Y	994 ± 72	Y

Notes:

[1] Mid test level is at the AAL (Table 2)

[2] AAL taken from Table 9A, *Radiological Laboratory Sample Analysis Guide for Incidents of National Significance– Radionuclides in Water* (EPA 2008).

[3] Approximate combined standard uncertainty for a 100-minute count on an alpha detector having a typical detector efficiency plus another 5% uncertainty for other method parameters at the action level. Counting time was estimated so that the required method uncertainty would be met at the AAL. All samples would be counted for the same length of time regardless of the test level.

Example 2. Method Validation for Am-241 in Street Runoff Water - Default AAL and Required Method Uncertainty

Nuclide: ^{241}Am

Matrix: Street runoff water

Default AAL: 40 pCi/sample (Table 1, liquid, specific nuclide)

Proposed Method: Radiochemistry with alpha spectrometry. Specific nuclide measurement.

Required Method Validation Level: D, new matrix

Required Method Uncertainty: 5.2 pCi/test sample at AAL or below; 13% above AAL (Table 4)

Acceptance Criteria (Table 2): Measured Value within ±3 u_{MR} (±15.6 pCi/sample) of known value ≤ AAL and ±3 φ_{MR} (± 39%) of known value > AAL

Method Validation Test Levels (Table 2): Lower (0.5 × AAL) = 20 pCi/sample; Mid (AAL) = 40 pCi/sample; Upper (3 × AAL) = 120 pCi/sample

Data Evaluation:

TABLE B2 – Required Method Uncertainty for Am-241 in Street Runoff Water

	Lower Test Level Concentration 20 pCi/sample Acceptable Range: 4.4 to 35.6 pCi		**Mid Test Level Concentration[1] 40 pCi/sample[2] Acceptable Range: 24.4 to 55.6 pCi**		**Upper Test Level Concentration 120 pCi/sample Acceptable Range: 73.2 to 167 pCi**	
Test Sample	Measured Value ± 1 CSU[3]	Acceptable Value (Y/N)	Measured Value ± 1 CSU[3]	Acceptable Value (Y/N)	Measured Value ± 1 CSU[3]	Acceptable Value (Y/N)
1	22.3 ± 2.3	Y	44.2 ± 3.6	Y	128.6 ± 8.0	Y
2	17.6 ± 2.0	Y	36.7 ± 3.2	Y	112.2 ± 7.2	Y
3	20.9 ± 2.2	Y	42.4 ± 3.5	Y	124.7 ± 7.8	Y
4	23.4 ± 2.4	Y	38.1 ± 3.2	Y	117.0 ± 7.4	Y
5	15.8 ± 1.9	Y	50.5 ± 3.9	Y	140.0 ± 8.6	Y
6	21.7 ± 2.2	Y	41.5 ± 3.4	Y	122.0 ± 7.7	Y
7	18.8 ± 2.1	Y	31.1 ± 2.8	Y	113.4 ± 7.2	Y

Notes:

[1] Mid test level is at the AAL, (Table 2)

[2] Table 1, liquid, specific nuclide

[3] Approximate combined standard uncertainty for a 15-minute count on an alpha detector having a typical detector efficiency plus another 5% uncertainty for other method parameters at the action level. Counting time was estimated so that the required method uncertainty would be met at the AAL. All samples would be counted for the same length of time regardless of the test level. Sample volume ~ 100 mL.

Appendix C:
Example of the Method Validation Process for Verification of the Required MDC Specification

Refer to Section 5.5.2 (page 21) for the protocol to follow for verifying that a method's MDC meets the required MDC specification.

Nuclide: ^{90}Sr

Matrix: Street runoff water

Required MDC = 2 pCi/L (MQO designated by Incident Commander)

Proposed Method: Radiochemistry with beta counting on gas proportional counter. Sample volume = 1 L, counting time = 240 minutes. Analytical result calculations to include detector efficiency, detector background (cpm) and ^{90}Y ingrowth factor.

Number of Blanks: 7

Number of Spiked Test Samples: 10

Testing Level: 2 pCi/L of ^{90}Sr

Calculations:
a) ^{90}Sr concentration and associated combined standard uncertainty for the blanks and test samples.
b) *Critical Net Concentration* = 1.94 × standard deviation of the seven blank results.
c) Number (Y) of sample results at or below the estimated *Critical Net Concentration*

Test: Does the number (Y) of sample results at or below the estimated *Critical Net Concentration* exceed 2?

- If $Y \leq 2$, the method tested at the required MDC passes the test for the required MDC specification.
- If $Y > 2$, the method tested at the required MDC fails the test for the required MDC specification.

TABLE C1 – Results of Blank Sample Analyses

Blank Number	Result (pCi/L)
1	–0.21 ± 0.44
2	0.10 ± 0.45
3	0.44 ± 0.46
4	0.82 ± 0.46
5	–0.40 ± 0.44
6	–0.75 ± 0.44
7	0.61 ± 0.46
Average	**0.09**
Standard Deviation of Results	**0.57**
Critical Net Concentration	**1.11**

TABLE C2 – Results of MDC Test Sample Analyses; Test Concentration = 2.0 pCi/L

Test Sample Number	Result (pCi/L)	Result ≤ Critical Net Concentration (1.11 pCi/L)
1	2.57 ± 0.50	N
2	1.00 ± 0.47	Y
3	2.43 ± 0.50	N
4	1.57 ± 0.48	N
5	2.29 ± 0.50	N
6	1.71 ± 0.48	N
7	2.01 ± 0.49	N
8	3.14 ± 0.52	N
9	0.86 ± 0.46	Y
10	1.43 ± 0.48	N
Average	**1.90**	
Standard Deviation of Results	**0.72**	
Y - Number of Results ≤ Critical Net Concentration		2

Conclusion: *The hypothesis that the true MDC for the method is at or below the required MDC cannot be rejected. Therefore, the method is assumed to be capable of meeting the required MDC specification.*

Appendix D:
Example of the Effect of Bias on the Probability of Failing the Method Validation Acceptance Criteria for Required Method Uncertainty

Suppose one is validating a method for water using Level D acceptance criteria, so tests should be made at three concentration levels with seven samples at each level. Consider that the action level is 100 pCi/L, and that this is one of the test levels. Also suppose that the required method uncertainty at 100 pCi/L is u_{MR} = 10 pCi/L, i.e. the relative required method uncertainty is φ_{MR} = 10%. The acceptance bounds are then 100 ± 30 pCi/L. For the purpose of this illustration, only a positive method bias will be considered (although the same effect would occur for negative biases).

In Figure D1, the area under the curves above 130 pCi/L is the probability that a single sample will fail validation for the given method uncertainty and bias. If the method just meets the criterion and there is no bias, the figure shows that the probability of an individual sample failing is very small (<0.01%). Now suppose there is a bias of +10%. What is the probability of failing a single sample? When the uncertainty is 10 pCi/L it is 2.28%. Of course, if the method uncertainty already exceeds the required 10%, (e.g., 12.5 pCi/L), this probability is even higher, 5.48%. However, if the method uncertainty is less than that required (e.g., 7.5 pCi/L or 5 pCi/L), then this probability becomes lower, 0.38% and 0.13%, respectively.

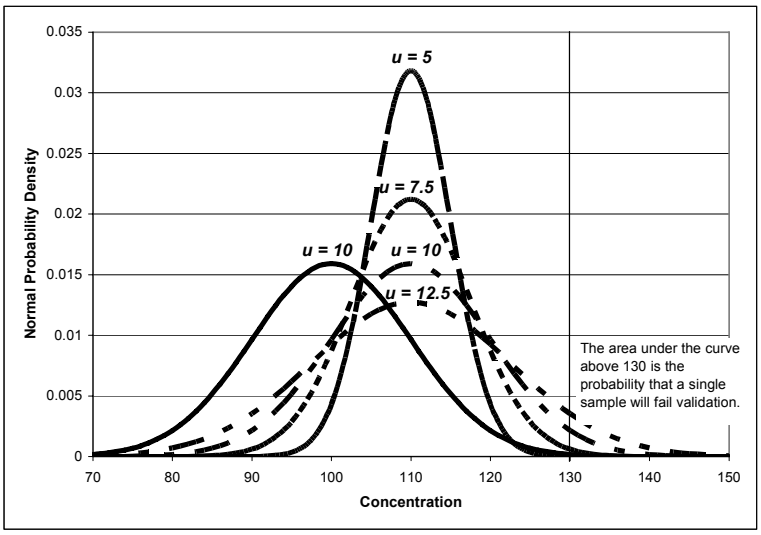


Figure D1 – Probability of a validation sample failing at concentration 100 pCi/L with and without bias at various values of the method standard uncertainty.

The probabilities above are for a single sample. At each level, seven samples must pass. Because there are three levels, there are 21 tests, and if the probability of failure for a single sample is F, then the overall probability of failure is about $1 – (1–F)^{21}$. If F is 2%, $1 – (1–F)^{21} >> 35\%$.

Consider an example of method validation Level D for a water matrix. There are 3 test levels with 7 samples each, or 21 total samples:

- 0.5 ×AAL level = 50 pCi/L; u_{Req} = 10 pCi/L, φ_{Req} = 0.20
- AAL level = 100 pCi/L; u_{Req} = 10 pCi/L, φ_{Req} = 0.10
- 3.0 ×AAL level = 300 pCi/L; u_{Req} = 30 pCi/L, φ_{Req} = 0.10

The acceptance criterion is that each measured value (for all 21 samples) must be within ±3.0 u_{Req} or ±3.0 φ_{Req} of the validation test activity. The probability of passing the acceptance criteria was calculated for four assumed relative method uncertainty values: 5%, 7.5%, 10%, and 12.5%. The range of biases evaluated included 0 to 20% at the AAL.

Figure D2 shows the overall probability of failing the Level D validation as a function of bias and relative method uncertainty. It is clear that if the method just meets the required relative method uncertainty, then there is not much room to accommodate bias. However, when the relative method uncertainty is 7.5%, about an equal amount of bias might be tolerated. If the relative method uncertainty is half that required, three times as much bias can exist without bringing the probability of failure over 5%.

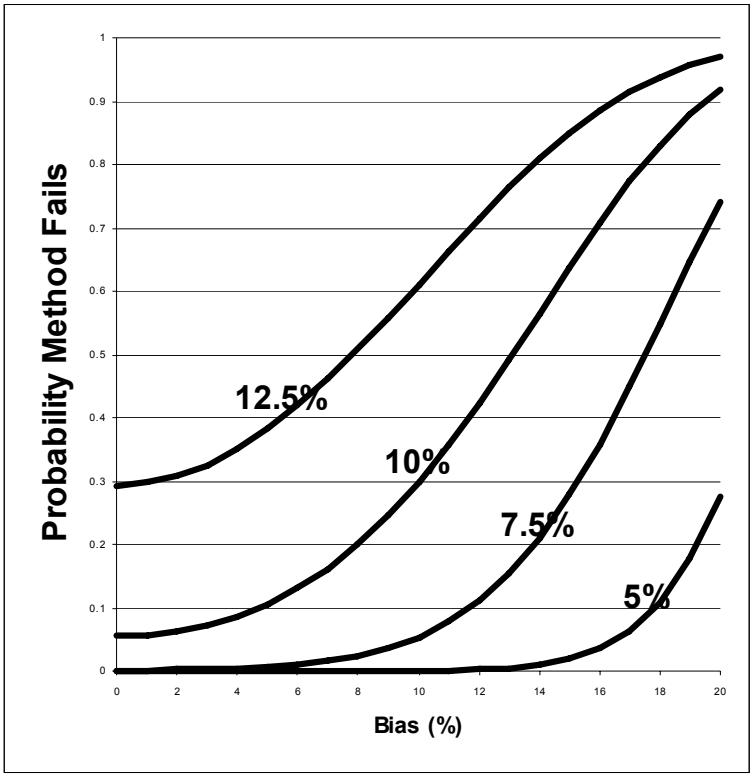


Figure D2 – Level D validation (21 samples) failing at test level as a function of relative method bias for relative method uncertainties of 5%, 7.5%, 10%, and 12.5%.

- When the actual relative method uncertainty is one-half or less than the relative required method uncertainty, biases up to 15% may be tolerated without substantially increasing the probability of failing the acceptance criteria.
- When the actual relative method uncertainty is equal to the relative required method uncertainty, it is best not to have a bias in order to maintain a reasonable probability of passing the acceptance criteria.
- When the actual relative method uncertainty is greater than the relative required method uncertainty, the probability of failing the acceptance criteria is extremely high, regardless of the magnitude of the bias.

Detecting Bias

Testing for a bias smaller than the standard uncertainty is difficult. There must be at least 16 replicate measurements to make the minimum detectable bias (MDB) less than σ, the true method standard deviation, and at least 54 replicate measurements to make the MDB less than $\sigma/2$ (see MARLAP Chapter 6A). This problem seems to be inescapable for absolute bias tests based on method-blank analyses. For relative bias tests based on spiked samples, statistics can be improved if there are high-activity samples whose reference values have small uncertainties.

The mean squared error (MSE) is the sum of the squared differences between the measurements and the true values. The MSE is the sum of the variance, σ^2, and the square of the bias, b^2. The root MSE $= \sqrt{\sigma^2 + b^2}$. If the root mean squared error is kept below the required method uncertainty, the MQOs are likely to be met. If the bias is less than one third the relative method standard uncertainty, bias will only contribute 10% to the MSE.

The validation criteria in MARLAP were developed with the presumption that any known biases in the method will be corrected, and that any remaining bias will be small compared to the method uncertainty. Thus, the primary focus was placed on detecting an unacceptably high method uncertainty. Note that if the reverse is true, namely that the method uncertainty is much smaller than the bias, the method may pass the acceptance criteria while having what might be considered unacceptably high bias. In the extreme case of zero method uncertainty, a method with bias up to 30% might still pass the criteria. In this case different validation criteria may be desirable. Appendix E contains alternative method validation criteria which treat the detection of excessive bias and imprecision more equally using the concept of MSE.

Appendix E:
An Alternative Method Validation Criterion

Introduction

The method validation process and acceptance criteria described in Section 5.4 are based on the criteria recommended in Chapter 6 of the *Multi-Agency Radiological Laboratory Analytical Protocols Manual* (MARLAP). This appendix presents alternative method performance acceptance criteria that may have greater power to detect large imprecision and bias in some situations. However, the number of test levels and replicates for the appropriate method validation level (B, C, D, E) as presented in Section 5.4.2 are still to be used.

Every measurement process involves both bias and imprecision to some degree. The MARLAP method validation criterion is predicated on the assumption that the laboratory has eliminated any substantial bias in the measurement process, so that measurement results are likely to be evenly distributed about the true value. If this assumption is not true, use of the MARLAP test alone may in some cases allow a method with a substantial bias to be accepted for use. Although MARLAP recommends that the candidate method be evaluated for bias, it does not recommend an objective criterion for determining whether a detected bias is tolerable. Furthermore, as noted in MARLAP and in Appendix D of this document, testing for bias tends to be difficult in any case, because of the number of measurements required to detect a bias that is comparable in magnitude to the standard deviation.

The assumption of this appendix is that a measurement process may be considered adequate for its intended use if a certain combination of bias and imprecision, called the "root mean squared error," does not exceed the required uncertainty. According to this view, the fact that bias is hard to quantify is less troublesome, because what one cares about most is not bias alone or imprecision alone but a combination of the two.

Definitions

Suppose $\hat{X}$ is an estimator for some parameter *K*. The *variance* of $\hat{X}$, denoted by $V(\hat{X})$ or $\sigma^2_{\hat{X}}$, is defined as the expected value of the square of the deviation of $\hat{X}$ from its mean.

$$\sigma^2_{\hat{X}} = E[(\hat{X} - E(\hat{X}))^2] \quad \text{(E1)}$$

where $E(\bullet)$ denotes the expected value (mean) of the operand within the brackets or parentheses. The square root of the variance, denoted by $\sigma_{\hat{X}}$, is called the *standard deviation*. The standard deviation of an estimator is commonly used as a measure of its imprecision.

The *error* of $\hat{X}$ (as an estimator for *K*) is defined to be the difference between $\hat{X}$ and *K*.

$$Error(\hat{X}) = \hat{X} - K \quad \text{(E2)}$$

The error $\hat{X} - K$, like $\hat{X}$ itself, is a random variable.

The *bias* of $\hat{X}$ is defined as the difference between the expected value (or mean) of $\hat{X}$ and the value of the parameter *K*. In symbols,

$$Bias(\hat{X}) = E(\hat{X}) - K \tag{E3}$$

The bias of $\hat{X}$ also equals its mean error. So $Bias(\hat{X}) = E(\hat{X} - K)$.

If $\hat{X}$ is an unbiased estimator (i.e., if $E(\hat{X}) = K$), then the standard deviation is a good measure of the overall quality of $\hat{X}$ as an estimator. However, in the context of laboratory analyses, the estimator $\hat{X}$ is typically the result of a measurement made using a specified method and measurement process, and in this situation, $\hat{X}$ is usually biased to some extent. It is common to evaluate a laboratory method or measurement process in terms of both the bias and imprecision (standard deviation) of the estimator $\hat{X}$. During method validation, separate limits may be set for the maximum allowable bias and for the maximum allowable standard deviation; however, since the overall quality of a measurement process is affected by both bias and imprecision, one may instead choose to specify a limit for some combination of the bias and imprecision. If this is done, then a biased but precise method may be considered to be as good as an essentially unbiased but less precise method.

Note that although neither the bias nor the standard deviation is ever known exactly, it is possible to use statistical methods to test hypotheses about their magnitudes or to determine likely bounds for their values. Note also that acknowledging the existence of bias in a measurement process does not mean that one should cease trying to find and eliminate the causes of any significant bias.

The "mean squared error" or the "root mean squared error" of an estimator is often used as a measure of the estimator's overall quality. The *mean squared error* of $\hat{X}$, as the name implies, is the expected value of the squared error of $\hat{X}$. So:

$$MSE(\hat{X}) = E[(\hat{X} - K)^2] \tag{E4}$$

Notice that the definition of $MSE(\hat{X})$ resembles that of the variance $\sigma^2_{\hat{X}}$, but with *K* substituted for the mean $E(\hat{X})$. It can be shown mathematically that the mean squared error of $\hat{X}$ is equal to the sum of its squared bias and its variance.

$$MSE(\hat{X}) = Bias(\hat{X})^2 + \sigma^2_{\hat{X}} \tag{E5}$$

The *root mean squared error* of $\hat{X}$ is simply the positive square root of $MSE(\hat{X})$.

$$\sqrt{MSE(\hat{X})} = \sqrt{E[(\hat{X} - K)^2]} = \sqrt{Bias(\hat{X})^2 + \sigma^2_{\hat{X}}} \tag{E6}$$

So the root mean squared error can be viewed as a mathematical combination of bias and imprecision. For an unbiased estimator, the root mean squared error is exactly equal to the standard deviation, but for a biased estimator, the root mean squared error is always larger than the standard deviation.

The approach to method validation described in this document is based on the concept of a required uncertainty at each activity level. If one interprets this required uncertainty, u, as a required bound for $\sqrt{MSE\left(\hat{X}\right)}$, then an unbiased method can have a standard deviation $\sigma_{\hat{X}}$ as large as u, or a perfectly precise method can have a bias as large as u. In general, both the bias and standard deviation may be nonzero, but in principle, neither the bias nor the standard deviation is allowed to exceed the required uncertainty, u, at any level of activity.

Alternative Method Validation Criterion

The validation procedure of Section 5.4 involves making several measurements of samples spiked at known activity levels. Let L denote the number of activity levels and N the number of measurements made at each level. Then the test described in Section 5.4 compares each result X_{ij} (where i denotes the number of the activity level and j denotes the number of the measurement) to acceptance limits:

$$K_i \pm k u_i \tag{E7}$$

where

K_i = target value at the i^{th} activity level ($1 \le i \le L$)
k = uncertainty multiplier (from Table 3)
u_i = required uncertainty at the i^{th} analyte level

The method is judged acceptable if every result X_{ij} falls within the appropriate acceptance limits for its activity level.

As noted under Table 3, the uncertainty multiplier, k, may be calculated as follows:

$$k = z_{0.5+0.5(1-\alpha)^{1/LN}} \tag{E8}$$

where α is the chosen significance level, or the probability of a false rejection ($\alpha = 0.05$), and for any p, z_p denotes the p-quantile of the standard normal distribution. (Note that k is rounded to two figures in Table 3.) The multiplier k also equals the square root of the $(1-\alpha)^{1/LN}$-quantile of the chi-squared distribution with one degree of freedom, and for purposes of exposition, it will be convenient to use the latter interpretation here.

$$k = \sqrt{\chi^2_{(1-\alpha)^{1/LN}}(1)} \tag{E8'}$$

The required uncertainty, u_i, at each activity level equals the required method uncertainty, u_{MR}, if $K_i \le$ AL, and it equals $\varphi_{MR} K_i$ if $K_i >$ AL.

$$u_i = \begin{cases} u_{MR}, & \text{if } K_i \le AL \\ \varphi_{MR} \times K_i, & \text{if } K_i > AL \end{cases} \tag{E9}$$

A more traditional presentation of the same statistical test would define a test statistic and a critical value for that statistic. For this test, the statistic can be defined as:

$$M = \max_{\substack{1 \le i \le L \\ 1 \le j \le N}} Z_{ij}^2 \tag{E10}$$

where for each i and j, Z_{ij} denotes the "Z-score" for the measurement:

$$Z_{ij} = \frac{X_{ij} - K_i}{u_i} \tag{E11}$$

The corresponding critical value for the statistic M is just the square of the uncertainty multiplier, which equals:

$$m_C = k^2 = \chi^2_{(1-\alpha)^{1/LN}}(1) \tag{E12}$$

So the method's performance is considered acceptable if the value of M does not exceed m_C.[9]

Because the statistic M is derived from only the most extreme value of Z_{ij}, it essentially discards much of the information contained in the measurement data, resulting in reduced power for the test. A different statistic that makes better use of the same data is the following:

$$W = \max_{1 \le i \le L} \sum_{j=1}^{N} Z_{ij}^2 \tag{E13}$$

where all the symbols on the right-hand side are as defined above for M. The critical value of the statistic W is the $(1 - \alpha)^{1/L}$-quantile of the chi-squared distribution with N degrees of freedom:

$$w_c = \chi^2_{(1-\alpha)^{1/L}}(N) \tag{E14}$$

where again $\alpha = 0.05$. This test can also be implemented by calculating a statistic W_i at each activity level:

$$W_i = \sum_{j=1}^{N} Z_{ij}^2 \tag{E15}$$

and comparing W_i to the critical value w_C. If W_i at any activity level exceeds w_C, the method is rejected.[10]

Note that both the MARLAP test and the W test can be viewed as chi-squared tests. The MARLAP test, which is equivalent to the method validation criterion presented in Section 5.4, uses a chi-squared statistic with one degree of freedom for each of the LN measurements, while the W test pools the data for each activity level to obtain fewer statistics (L of them), each of which has more degrees of freedom (N).

[9] The test could also be based on a statistic equal to the maximum of the absolute values $|Z_{ij}|$, using k as a critical value.

[10] The expected value of W_i equals N times the ratio of the mean squared error (MSE) to the square of the required uncertainty (u_i^2) at this activity level.

Under the assumptions that the root MSE of the measurement process at each activity level does not exceed the required uncertainty, and that all the measurement results are independent, either test (MARLAP or *W*) will incorrectly reject a candidate method at most 5 % of the time (because $\alpha = 0.05$). The greatest false rejection rate (5 %) occurs when the bias is zero and the standard deviation at each activity level exactly equals the required uncertainty. The important differences between the two tests are the differences in their power to reject methods with larger bias or imprecision. For example, if a candidate method has negligible imprecision, either test will reject it if the measurement bias at some activity level is larger than a specified multiple of the required uncertainty. However, the associated uncertainty multiplier for the *W* test ($\sqrt{w_c / N}$) is generally smaller than the multiplier (*k* or $\sqrt{m_c}$) for the MARLAP test. Furthermore, the MARLAP test has the undesirable property that it actually loses power to detect such biases as the number of measurements (*N*) as each activity level increases, because the value of *k* increases with *N*. The power of the *W* test, on the other hand, improves, because the value of $\sqrt{w_c / N}$ decreases with *N*, approaching 1 as *N* goes to infinity.

The Holst-Thyregod Test for Mean Squared Error

The *W* test described above was originally derived as a test of variance given a presumed value for the mean, but it can be employed as a test of the MSE or root MSE, as was done above. Holst and Thyregod have also derived a statistical test that explicitly tests hypotheses about the MSE of a measurement process (Holst and Thyregod, 1999). The Holst-Thyregod statistic is slightly more complicated to calculate, and tables of percentiles for the statistic are not widely available. However, the Holst-Thyregod test has an advantage over the *W* test when the MSE is dominated by bias. In some situations where the measurement process has good precision and somewhat large bias, the power of the Holst-Thyregod test far exceeds the power of the *W* test, just as the power of the *W* test in some situations can far exceed the power of the MARLAP test. In other situations, and especially when the MSE is dominated by variance rather than bias, the *W* test outperforms the Holst-Thyregod test. For these reasons, this appendix recommends the *W* test as the best choice for most method validation experiments.

Example

Suppose the action level for a certain project is 100 pCi/L and the required method uncertainty is $u_{MR} = 10.0$ pCi/L at the action level. The relative required method uncertainty (at or above the action level) is $\varphi_{MR} = 0.10$, or 10 %. A Level D validation experiment is performed for a candidate method, with three activity levels ($L = 3$) and seven measurements at each activity level ($N = 7$). Suppose the measurement results are as shown in Table E1.

TABLE E1 – Method Validation Measurement Results

Measurement (j)	Target Value (K_i)		
	50 pCi/L	100 pCi/L	300 pCi/L
1	36.1	83.2	256.1
2	39	83.7	235.2
3	42.2	84.8	249
4	44.4	75.4	258.5
5	47.5	82.3	265.2
6	40.2	94.7	255.7
7	44	88.4	254.5
Average	$\overline{x}$ = 41.91	$\overline{x}$ = 84.64	$\overline{x}$ = 253.46
Standard deviation	s = 3.81	s = 5.90	s = 9.40

The method appears to have good precision, but it also has a relative bias of approximately −16 %, which is larger than the required relative method uncertainty (10 %).[11] If one performs the validation test described in Section 5.4, the acceptance limits for the results are as shown below.

TABLE E2 – Acceptance Limits, MARLAP Test

Target Value K_i/(pCi/L)		Required Uncertainty u_i/(pCi/L)	Acceptance Limits $(K_i \pm ku_i)$/(pCi/L)
50		10	20 – 80
100	(AL)	10	70 – 130
300		30	210 – 390

Note: The "uncertainty multiplier" (k) in this case equals 3.0307, which is rounded to 3.0.

Since all the measured results are within these acceptance limits, the method is judged acceptable in spite of the obvious negative bias.

If the chi-squared test described in this appendix is used instead, then the critical value for the chi-squared statistic is

$$w_c = \chi^2_{(1-\alpha)^{1/L}}(N) = \chi^2_{0.95^{1/3}}(7) = 17.07$$

and the results are shown in Table E3.

[11] Presumably the laboratory was unaware of this bias; otherwise, it would have corrected it.

TABLE E3 – Method Validation Results, Alternative Test (*W* Test)

Measurement (*j*)	Activity Level (*i*)					
	1		2		3	
	K_i = 50 pCi/L u_i = 10.0 pCi/L		K_i = 100 pCi/L u_i = 10.0 pCi/L		K_i = 300 pCi/L u_i = 30.0 pCi/L	
	X_{ij}	$Z_{ij} = \frac{X_{ij} - K_i}{u_i}$	X_{ij}	$Z_{ij} = \frac{X_{ij} - K_i}{u_i}$	X_{ij}	$Z_{ij} = \frac{X_{ij} - K_i}{u_i}$
1	36.1	−1.39	83.2	−1.68	256.1	−1.4633
2	39	−1.10	83.7	−1.63	235.2	−2.1600
3	42.2	−0.78	84.8	−1.52	249	−1.7000
4	44.4	−0.56	75.4	−2.46	258.5	−1.3833
5	47.5	−0.25	82.3	−1.77	265.2	−1.1600
6	40.2	−0.98	94.7	−0.53	255.7	−1.4767
7	44	−0.60	88.4	−1.16	254.5	−1.5167
	$W_i = \sum Z_{ij}^2 =$	5.45	$W_i = \sum Z_{ij}^2 =$	18.6	$W_i = \sum Z_{ij}^2 =$	17.4

Because the statistics W_2 and W_3 both exceed the critical value w_C = 17.1, the method is judged to be unacceptable.

Theoretical Comparison of Statistical Power

The following set of four figures graphically illustrates the power of the MARLAP test and the *W* test for the same conditions assumed in Figure D2 of Appendix D. The power of the Holst-Thyregod (H-T) test is also graphed for comparison. The scenario (as above) involves a Level D validation of a method for a project where the required method uncertainty is 10 pCi/L at an action level of 100 pCi/L. Each of the following figures assumes a different value for the ratio of the relative standard deviation (RSD) to the required uncertainty at each activity level. In Figure E1a, the ratio is 0.5, so that the RSD at the action level equals 5 %. The ratios for Figures E1b, E1c, and E1d are 0.75, 1, and 1.25, respectively. In each graph, the horizontal axis represents possible values for the relative bias of the method ranging from 0 to 20 %. The vertical axis, labeled *P*, represents the probability that a method with the given relative standard deviation and relative bias will be rejected.

In every case, the *W* test outperforms the MARLAP test, although the differences are most noticeable when the precision of the method is good but the bias is large. Also note that the power of the Holst-Thyregod test exceeds that of the *W* test in Figures E1a and E1b but not in E1c and E1d.

Reference

Holst, Erik and Poul Thyregod. 1999. "A statistical test for the mean squared error," *Journal of Statistical Computation and Simulation*, 63:4, 321–347.

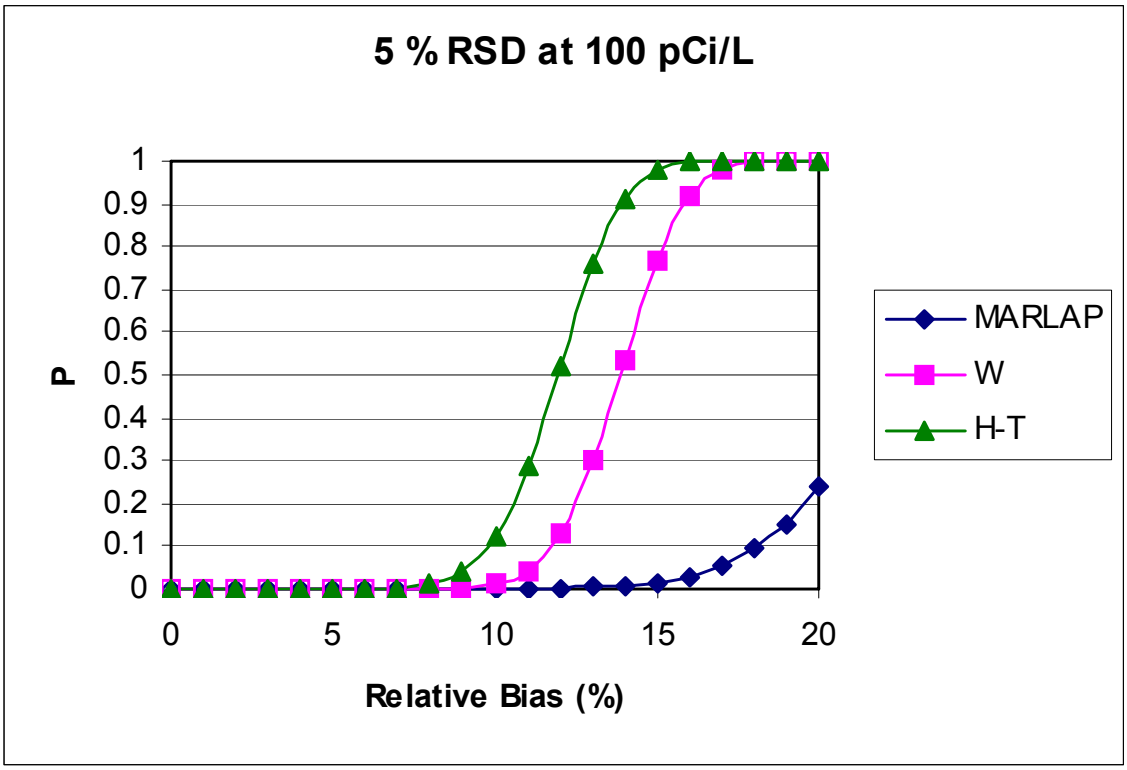


Figure E1a

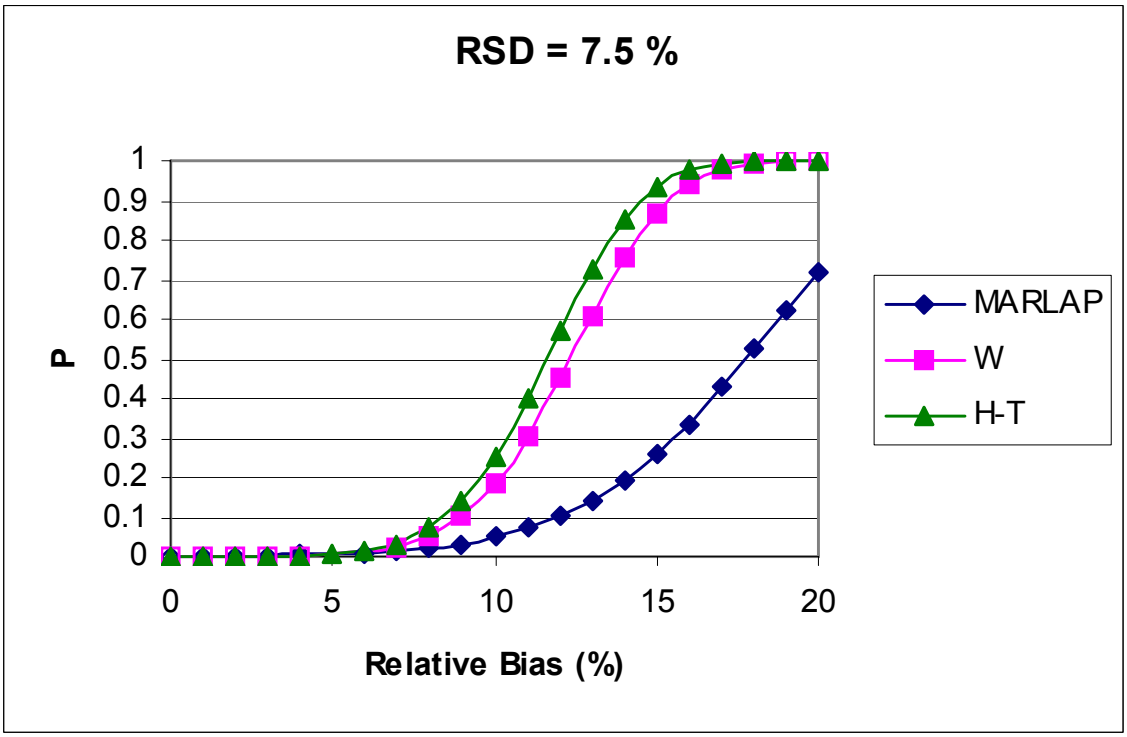


Figure E1b

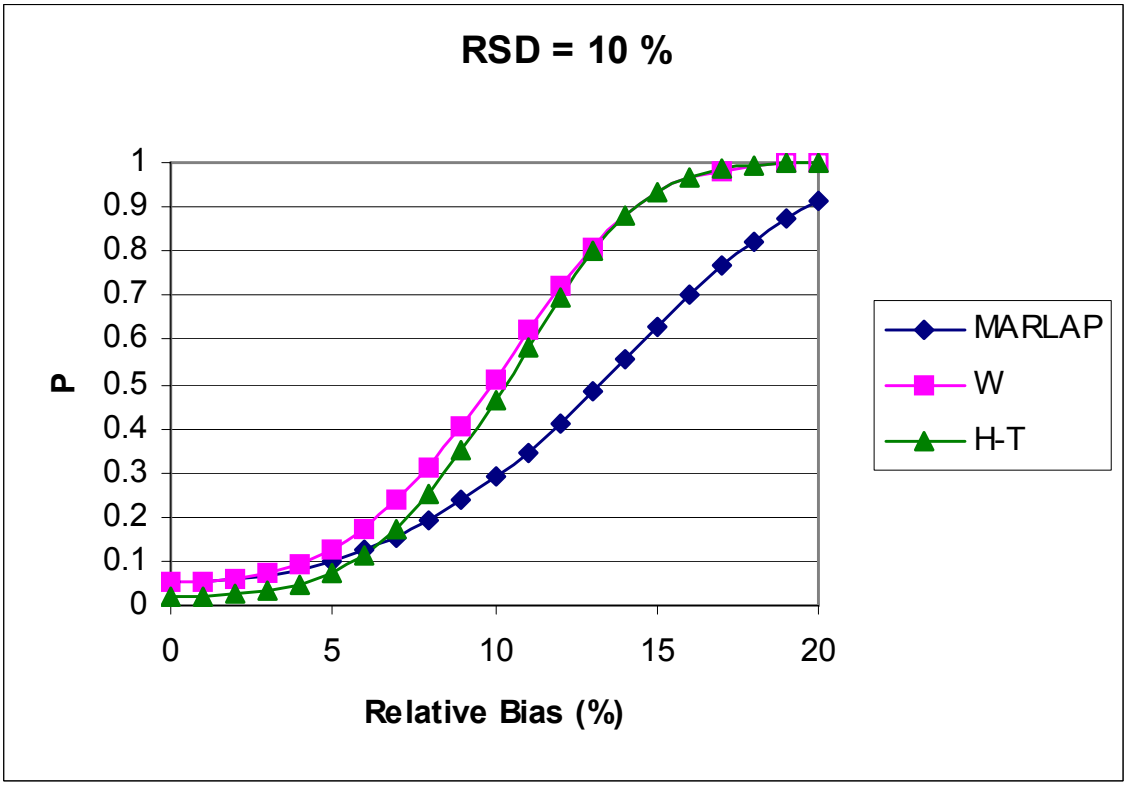


Figure E1c

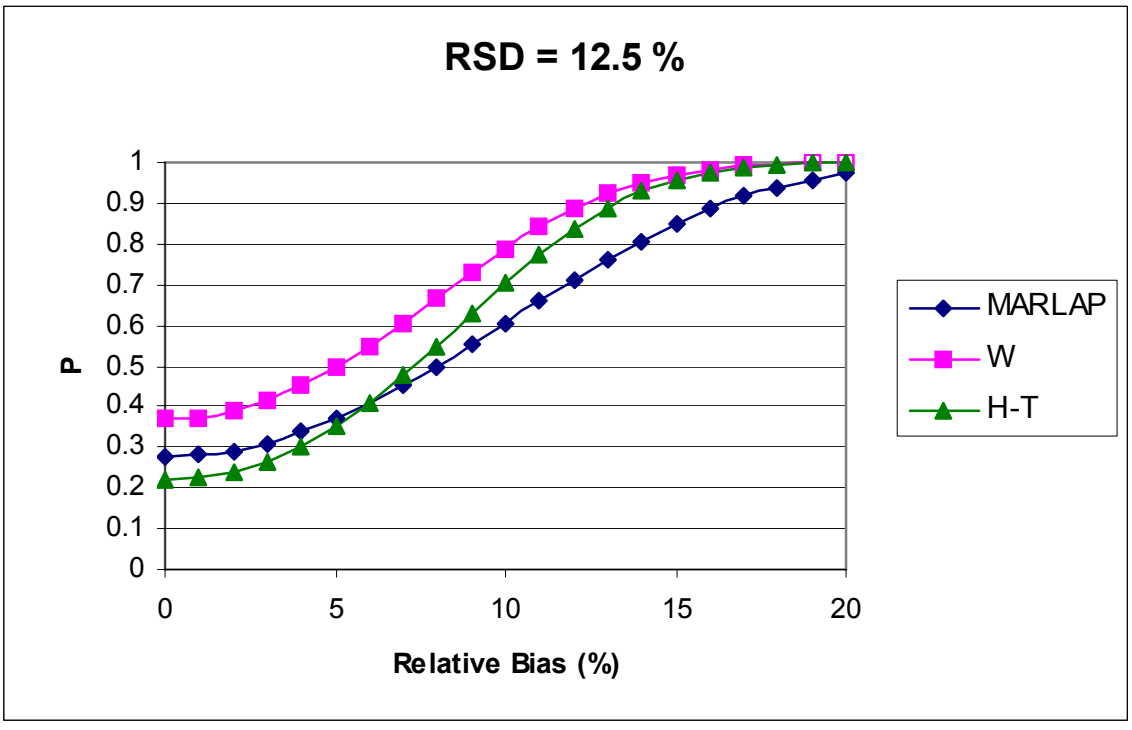


Figure E1d

Appendix F: Glossary

***accuracy*:** The closeness of a measured result to the true value of the quantity being measured. Various recognized authorities have given the word "accuracy" different technical definitions, expressed in terms of bias and imprecision. Following MARLAP, this document avoids all of these technical definitions and uses the term "accuracy" in its common, ordinary sense.

aerosol: A suspension of fine solid or liquid particles within a gaseous matrix (usually air).

***aliquant*:** A representative portion of a homogeneous *sample* removed for the purpose of analysis or other chemical treatment. The quantity removed is not an evenly divisible part of the whole sample. An aliquot, by contrast, is an evenly divisible part of the whole.

***analyte*:** For this document, an analyte is a specific radionuclide or a category of radionuclides that comprise gross alpha or beta analyses. An analyte may be on the list of radionuclides of interest or a radionuclide of concern for a project. See *target analyte*.

***analyte concentration range*:** (1) Method validation definition – the radionuclide concentration range corresponding to three test levels (lower, mid and upper) that are used during method validation. The mid level concentration corresponds to the action level. (2) MQO definition – the expected concentration range (minimum to maximum) of an *analyte* expected to be present in a *sample* for a given project. While most analytical protocols are applicable over a fairly large range of concentration for the *radionuclide of interest*, performance over a required concentration range can serve as a measurement quality objective for the protocol selection process, and some analytical protocols may be eliminated if they cannot accommodate the expected range of concentration.

***analytical action level* (AAL):** The value of a quantity that will cause the decision maker to choose one of the alternative actions. The action level may be a derived concentration level (such as the *derived water concentration* in this document), background level, release criteria, regulatory decision limit, etc. The AAL is often associated with the type of media, *target analyte*, and concentration limit. Some AALs are expressed in terms of a derived radionuclide concentration corresponding to a dose or risk, such as a protective action guide. MARLAP uses the term "action level."

analytical decision level (ADL): The minimum measured value for the radionuclide concentration in a sample that indicates the amount of radionuclide present is equal to or greater than the *analytical action level* at a specified *Type II error* rate. (Assumes that *method uncertainty* requirements have been met.) Any measurement result equal to or greater than the applicable ADL is considered to have exceeded the corresponding *analytical action level*. MARLAP uses the term "*critical level*."

***analytical protocol specification* (*APS*):** The output of a *directed planning process* that contains the project's analytical data needs and requirements in an organized, concise form. The level of

specificity in the APSs should be limited to those requirements that are considered essential to meeting the project's *analytical data requirements* to allow the laboratory the flexibility of selecting the protocols or methods that meet the analytical requirements.

***background (instrument)*:** Radiation detected by an instrument when no *source* is present. The background radiation that is detected may come from radionuclides in the materials of construction of the detector, its housing, its electronics, and the building, as well as the environment and natural radiation.

***background level*:** A term that usually refers to the presence of radioactivity or radiation in the environment. From an analytical perspective, the presence of background radioactivity in samples needs to be considered when clarifying the radioanalytical aspects of the decision or study question. Many radionuclides are present in measurable quantities in the environment.

***bias (of a measurement process)*:** A persistent deviation of the mean measured result from the true or accepted reference value of the quantity being measured, which does not vary if a measurement is repeated.

***blank (analytical or method)*:** A *sample* that is assumed to be essentially free of the *target analyte* (the "unknown"), which is carried through the radiochemical preparation, analysis, mounting, and measurement process in the same manner as a routine sample of a given matrix.

***calibration*:** The set of operations that establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure, and the corresponding known value of a parameter of interest.

***calibration source*:** A prepared *source*, made from a *certified reference material* (standard), that is used for calibrating instruments.

***carrier*:** (1) A stable isotopic form of a tracer element or nonisotopic material added to effectively increase the quantity of a tracer element during radiochemical procedures, ensuring conventional behavior of the element in solution. (2) A substance in appreciable amount that, when associated with a tracer of a specified substance, will carry the tracer with it through a chemical or physical process, or prevent the tracer from undergoing non-specific processes due to its low concentration (IUPAC, 1995). A stable isotope of a *radionuclide* (usually the *analyte*) added to increase the total amount of that element so that a measurable mass of the element is present.

***chain of custody*:** Procedures that provide the means to trace the possession and handling of a sample from collection to data reporting.

***check source*:** A material used to validate the operability of a radiation measurement device, sometimes used for instrument quality control. See *source, radioactive*.

***combined standard uncertainty*:** *Standard uncertainty* of an *output estimate* calculated by combining the standard uncertainties of the *input estimates*. The *combined standard uncertainty* of y is denoted by $u_c(y)$. See *uncertainty (of measurement)*.

critical level: Termed *analytical decision level* in this document in the context of evaluating sample results relative to an *analytical action level*. In the context of analyte detection, *critical level* means the minimum measured value (e.g., of the instrument signal or the radionuclide concentration) that indicates a positive (nonzero) amount of a radionuclide is present in the material within a specified probable error. The critical level is sometimes called the *critical value* or *decision level*.

critical net concentration: Similar in concept as the "critical level."

***data quality objective* (*DQO*)**: Qualitative and quantitative statements that clarify the study objectives, define the most appropriate type of data to collect, determine the most appropriate conditions from which to collect the data, and specify tolerable limits on decision error rates. Because DQOs will be used to establish the quality and quantity of data needed to support decisions, they should encompass the total *uncertainty* resulting from all data collection activities, including analytical and sampling activities.

default AAL test level: Radionuclide test concentration for a given general matrix category to be used in the method validation process in the absences of PAG or risk-based AALs.

derived air concentration (DAC): The concentration of a radionuclide, in pCi/m^3, that would result in exposure to a specified dose level. Generally refers to a *protective action guide* or other specified dose- or risk-based factor related to an *analytical action level*. In this document, for example, the "500-mrem DAC for ^{239}Pu" is the concentration of ^{239}Pu, in pCi/m^3, that would result in an exposure of 500 mrem and would refer to the 500-mrem PAG. The DAC is radionuclide-specific.

derived radionuclide concentration (DRC): General application term used in discussions involving both of the terms DAC and DWC.

derived water concentration (DWC): The concentration of a radionuclide, in pCi/L, that would result in exposure to a specified dose level. Generally refers to a *protective action guide* or other specified dose- or risk-based factor related to an analytical action level.

***detection capability*:** The capability of a *measurement process* to distinguish small amounts of *analyte* from zero.

***detection limit*:** The smallest value of the amount or concentration of *analyte* that ensures a specified high probability of detection. Also called "*minimum detectable value.*"

discrimination limit (DL): The DL is the point where it is important to be able to distinguish expected signal from the *analytical action level*. The boundaries of the *gray region*.

***dose equivalent*:** Quantity that expresses all radiations on a common scale for calculating the effective absorbed dose. This quantity is the product of absorbed dose (*grays* (Gy) or rads) multiplied by a quality factor and any other modifying factors (MARSSIM, 2000). The quality factor adjusts the absorbed dose because not all types of ionizing radiation create the same effect on human tissue. For example, a dose equivalent of one *sievert* (Sv) requires 1 Gy of beta or gamma radiation, but only 0.05 Gy of alpha radiation or 0.1 Gy of neutron radiation. Because the sievert is a large unit, radiation doses often are expressed in millisieverts (mSv). See *total effective dose equivalent* and *roentgen*.

***gray (Gy)*:** The International System of Units (SI) unit for absorbed radiation dose. One gray is 1 joule of energy absorbed per kilogram of matter, equal to 100 *rad*. See *sievert*.

***gray region*:** The range of possible values in which the consequences of decision errors are relatively minor. Specifying a gray region is necessary because variability in the analyte in a population and imprecision in the measurement system combine to produce variability in the data such that the decision may be "too close to call" when the true value is very near the *analytical action level*. The *gray region* establishes the minimum distance from the *analytical action level* where it is most important to control *Type II decision errors*.

***hypothesis testing*:** The use of statistical procedures to decide whether a null hypothesis should be rejected in favor of an *alternative hypothesis* or not rejected.

incident response method validation: Project method validation for incident response applications. See *project method validation* and *method validation*.

***interferences*:** The presence of other chemicals or *radionuclides* in a *sample* that hinder the ability to analyze for the *radionuclide of interest*.

***MARLAP Process*:** A performance-based approach that develops *Analytical Protocol Specifications*, and uses these requirements as criteria for the analytical protocol selection, development, and evaluation processes, and as criteria for the evaluation of the resulting laboratory data. This process, which spans the three phases of the *data life cycle* for a project, is the basis for achieving MARLAP's basic goal of ensuring that radioanalytical data will meet a project's or program's data requirements or needs.

***measurand*:** "Particular quantity subject to measurement" (ISO, 1993a).

***measurement quality objective (MQO)*:** The analytical data requirements of the *data quality objectives*, which are project- or program-specific and can be quantitative or qualitative. These analytical data requirements serve as measurement performance criteria or objectives of the analytical process. MARLAP refers to these performance objectives as MQOs. Examples of quantitative MQOs include statements of required analyte detectability and the *uncertainty* of

the analytical protocol at a specified radionuclide concentration, such as the action level. Examples of qualitative MQOs include statements of the required specificity of the analytical protocol (e.g., the ability to analyze for the radionuclide of interest [or *target analyte*] given the presence of interferences).

***measurement uncertainty*:** See *uncertainty*.

***method blank*:** A *sample* assumed to be essentially *target analyte*-free that is carried through the radiochemical preparation, analysis, mounting and measurement process in the same manner as a routine sample of a given matrix.

***method performance characteristics*:** The characteristics of a specific *analytical method* such as *method uncertainty*, *method range*, *method specificity*, and *method ruggedness*. MARLAP recommends developing *measurement quality objectives* for select *method performance characteristics*, particularly for the *uncertainty (of measurement)* at a specified concentration (typically the *action level*).

***method ruggedness*:** The relative stability of method performance for small variations in method parameter values.

***method specificity*:** The ability of the method to measure the *analyte* of concern in the presence of interferences.

***method uncertainty*:** Refers to the predicted *uncertainty* of the result that would be measured if the method were applied to a hypothetical laboratory *sample* with a specified analyte concentration. Although individual measurement uncertainties will vary from one measured result to another, the *required method uncertainty* is a target value for the individual measurement uncertainties and is an estimate of uncertainty before the sample is actually measured.

***method validation (MV)*:** The demonstration that the method selected for the analysis of a particular analyte in a given matrix is capable of providing analytical results to meet the project's *measurement quality objectives* and any other requirements in the analytical protocol specifications.

***minimum detectable concentration (MDC)*:** An estimate of the smallest true value of the analyte concentration that gives a specified high probability of detection.

***nuclide-specific analysis*:** Radiochemical analysis performed to isolate and measure a specific radionuclide.

***null hypothesis (H_0)*:** One of two mutually exclusive statements tested in a statistical *hypothesis test* (compare with alternative hypothesis). The null hypothesis is presumed to be true unless the test provides sufficient evidence to the contrary, in which case the *null hypothesis* is rejected and the alternative hypothesis (H_1) is accepted.

***performance evaluation (PE) program*:** A laboratory's participation in an internal or external program of analyzing proficiency-testing samples appropriate for the analytes and matrices under consideration (i.e., PE program traceable to a national standards body, such as NIST). Reference-material samples used to evaluate the performance of the laboratory may be called performance-evaluation, performance or proficiency-testing samples or materials. See *proficiency test samples*.

***precision*:** The closeness of agreement between independent test results obtained by applying the experimental procedure under stipulated conditions. Precision may be expressed as the standard deviation. Conversely, imprecision is the variation of the results in a set of replicate measurements.

proficiency test (PT) samples: Samples having a known radionuclide concentration used in a PE program or internally at the laboratory for method validation and for the measurement of bias.

***project method validation*:** The demonstrated method applicability for a particular project.

protective action guide (PAG): The radiation dose to individuals in the general population that warrants protective action following a radiological event. In this document, PAGs limit the projected radiation doses for different exposure periods: not to exceed 2-rem *total effective dose equivalent (TEDE)* during the first year, 500-mrem TEDE during the second year, or 5 rem over the next 50 years (including the first and second years of the incident). See *derived water concentration* and *analytical action level*.

***quality control (QC)*:** The overall system of technical activities that measures the attributes and performance of a process, item, or service against defined standards to verify that they meet the stated requirements established by the project; operational techniques and activities that are used to fulfill requirements for quality. This system of activities and checks is used to ensure that measurement systems are maintained within prescribed limits, providing protection against out-of-control conditions and ensuring that the results are of acceptable quality.

***radiochemical analysis*:** The analysis of a sample matrix for its *radionuclide* content, both qualitatively and quantitatively.

***radionuclide*:** A nuclide that is *radioactive* (capable of undergoing *radioactive decay*).

***relative required method uncertainty* (φ_{MR}):** The *required method uncertainty* divided by the *analytical action level*. The relative required method uncertainty is applied to radionuclide concentrations above the *analytical action level*. A key *measurement quality objective*.

***rem*:** The common unit for the effective or equivalent dose of radiation received by a living organism, equal to the actual dose (in rads) multiplied by a factor representing the danger of the radiation. Rem is an abbreviation for "roentgen equivalent man," meaning that it measures the biological effects of ionizing radiation in humans. One rem is equal to 0.01 Sv. See *sievert*.

***replicates*:** Two or more *aliquants* of a homogeneous *sample* whose independent measurements are used to determine the *precision* of laboratory preparation and analytical procedures.

***required method uncertainty* (u_{MR}):** *Method uncertainty* at a specified concentration. A key *measurement quality objective*. See *relative required method uncertainty*.

***required minimum detectable concentration* (*RMDC*):** An upper limit for the *minimum detectable concentration* required by some projects.

***sample*:** (1) A portion of material selected from a larger quantity of material. (2) A set of individual samples or measurements drawn from a population whose properties are studied to gain information about the entire population.

***screening method*:** An economical gross measurement (alpha, beta, gamma) used in a tiered approach to method selection that can be applied to *analyte* concentrations below an *analyte* level in the *analytical protocol specifications* or below a fraction of the specified *action level.*

***sievert (Sv)*:** The SI unit for the effective dose of radiation received by a living organism. It is the actual dose received (*grays* in SI or rads in traditional units) times a factor that is larger for more dangerous forms of radiation. One Sv is 100 *rem*. Radiation doses are often measured in mSv. An effective dose of 1 Sv requires 1 gray of beta or gamma radiation, but only 0.05 Gy of alpha radiation or 0.1 Gy of neutron radiation.

***swipe*:** A filter pad used to determine the level of general radioactive contamination when it is wiped over a specific area, about 100 cm^2 in area. Also called "smear" or "wipe."

***target analyte*:** A radionuclide on the list of radionuclides of interest or a radionuclide of concern for a project. For incident response applications, typical radionuclides of interest are provided in Appendix A.

***total effective dose equivalent*:** The sum of the effective dose equivalent (for external exposure) and the committed effective dose equivalent (for internal exposure), expressed in units of Sv or rem.

***Type I decision error*:** In a hypothesis test, the error made by rejecting the null hypothesis when it is true. A Type I decision error is sometimes called a "false rejection" or a "false positive."

***Type II decision error*:** In a hypothesis test, the error made by failing to reject the null hypothesis when it is false. A Type II decision error is sometimes called a "false acceptance" or a "false negative."

***uncertainty*:** A parameter, usually associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the *measurand*.