Guidelines on Validation of Non-Regulatory Chemical and Radiochemical Methods

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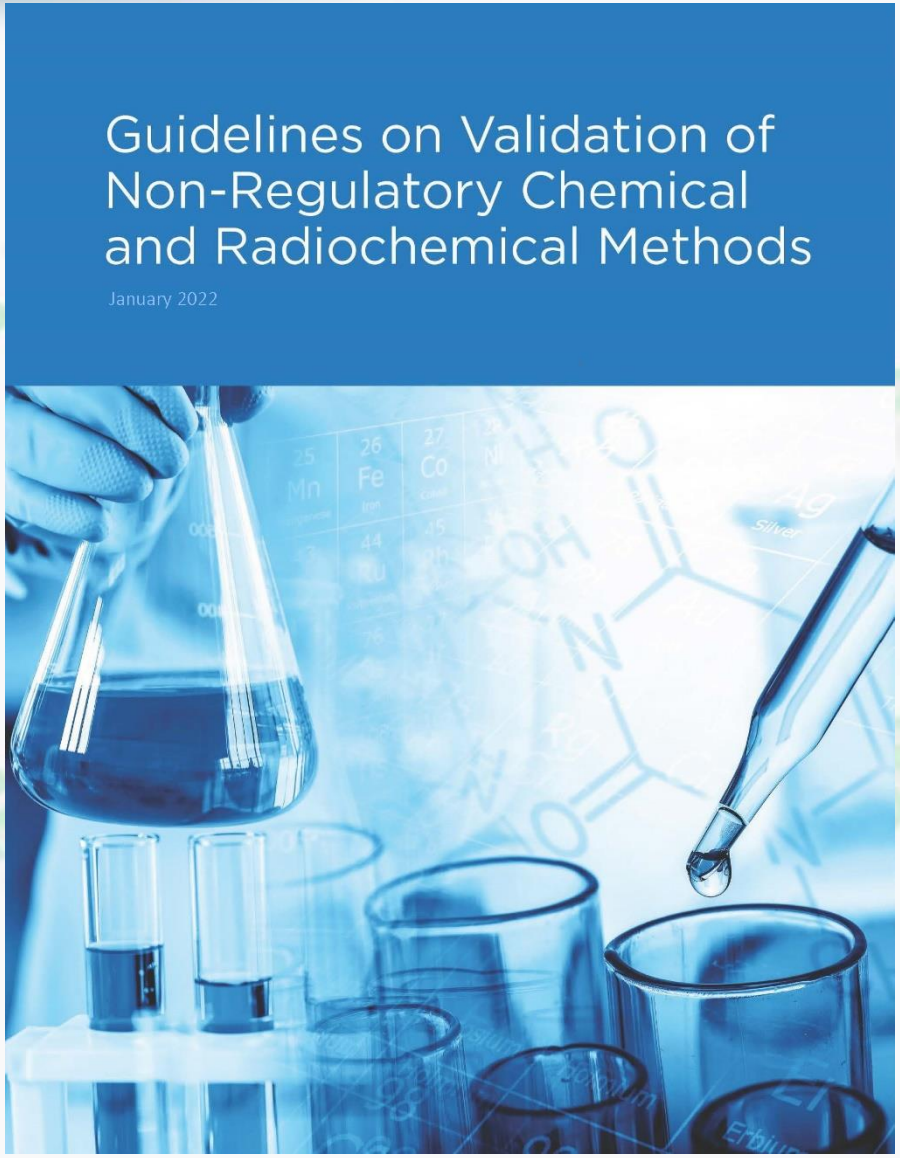
Background

- EPA develops methods for both regulatory and non-regulatory purposes
  - Regulatory method validation follows program/statutory-specific requirements and guidance
- Non-regulatory method development and validation is generally done to meet current and evolving Agency needs (e.g., emerging contaminants)

Issue

There was a lack of Agency-wide guidance for consistent non-regulatory method validation

Solution


Guidelines on Validation of Non-Regulatory Chemical and Radiochemical Methods
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Guidelines Overview

- Addresses newly developed, adopted, or modified chemical and radiochemical methods
- Document provides:
  - An overview of the general principles and important areas of consideration for method validation including method performance characteristics
  - Lists and links to more detailed method validation resources (e.g., Agency documents, international standards, other guidance documents, etc.)
  - Build on concepts developed by the EPA Regional Laboratories and other parts of the Agency
  - Introduces 3 new concepts

Guidelines Overview

- Developed by an internal cross-Agency workgroup, with representatives from the following offices:
  - OAR, OCSPP, OLEM, ORD, OW, Region 7, Region 10

- Document does NOT provide prescriptive or step-by-step guidance on conducting method validation studies

New Concepts

- Document introduces 3 new concepts to promote consistent method development and communication of validation results:
  - Method Life Cycle
  - Validation Descriptor
  - Method Validation Summary

New Concept #1: Method Lifecycle

- Illustrates the steps and processes involved with a method, from its beginning to its retirement
  - Initiates with the need, purpose, and method development
  - Validation is central to determination of method performance
  - Post-release, modifications made outside accepted method flexibilities may require “re-validation”

New Concept #2: Validation Design

- Standardized descriptor to concisely convey extent of validation performed
- Based on number of participating laboratories and different matrices
  - Noted as **[aL,bM]** where "**a**" is number of laboratories (**L**) and "**b**" is the number of different matrices (**M**)
  - For example, Validation Design [3L,2M] conveys that 3 laboratories and 2 matrices were included in the method validation

New Concept #3: Method Validation Summary

- Purpose
  - Concise overview of method validation presented in a consistent format
  - Easy access to pertinent and important information
  - Convenient comparison of similar validation studies
  - Facilitates sharing across the Agency

Document Content

- Reviews major Method Performance Characteristics
- Provides Additional Information on other Method Validation considerations

Method Performance Characteristics

- Guidelines cover typical method performance characteristics:
  - Bias/Trueness, Detection and Quantification Capability, Instrument Calibration, Measurement Uncertainty, Precision, Range, Ruggedness, and Selectivity

- For each characteristic, the document provides:
  - Definition(s)*
  - Short descriptions on its use
  - Useful resources/references

* Generally based on consensus standards

Method Performance Characteristics

- **Bias/Trueness:** *Bias is the difference between the expectation of the test result, and an accepted reference value.* (ASTM E177-20)

$$b(\%) = \frac{\bar{x} - x_{ref}}{x_{ref}} \times 100$$

- **Detection and Quantification Capability:** Addresses terms, and calculational procedures related to detection capability and quantification capability; limit of detection, method detection limits, limits of quantification, minimum reporting levels, etc.

Method Performance Characteristics

- **Instrument Calibration:** Procedures used for correlating instrument response to an amount of analyte (concentration or other quantity) using measurements of suitable reference materials

There are three options for suitable RMs for instrument calibration: 1) Certified Reference Materials (CRMs); 2) RMs with traceability to CRMs; and 3) RMs from other sources.

- **Measurement Uncertainty:** *A parameter associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand (JCGM GUM)*

Method Performance Characteristics

- **Precision:** *closeness of agreement between independent test results under stipulated conditions (ASTM E177-20);* Method Repeatability (between measurements) and Reproducibility (between laboratories) are covered.
- **Range:** interval of analyte concentrations for which there is a meaningful response from the analytical system; quantitation range and calibration range are described and characterized.

Method Performance Characteristics

- **Ruggedness:** *extent to which an analytical method remains unaffected by minor variations in operating conditions (EPA FEM Report);* discusses approaches to validation and statistical analysis
- **Selectivity in the Presence of Interferences:** *selectivity of a method is its ability to produce a result that is not subject to change in the presence of interfering constituents. (ASTM E2857-11)*

Additional Information Included

- In main document:
  - Guidance on interlaboratory validation study designs
  - Suggested resources for use in understanding and implementing statistical assessment of method validation results

Additional Information Included

- In appendices:
  - Discussion of method validation matrix variability considerations, with examples of matrices used/suggested from individual EPA offices
  - Compilation of detection and quantitation limit definitions

Method Validation Summary Overview

Method Validation Summary

- Designed to be placed at the front/introduction to the full Method Validation Report

- Does **NOT** replace the full Method Validation Report, which should be prepared in accordance with expectations and guidelines/protocols of individual offices and/or programs

Method Validation Summary

- Approximately 2-pages with 4 sections
  - Validation Design
  - Method Validation Overview
  - Method Development Considerations
  - Method Performance Characteristics

A	Validation Design	Description
1	Number of Laboratories	
2	Number of Matrices	
3	Types of Matrices Tested (water, soil, sediment, etc.)	
B	**Method Validation Overview**	**Description**
1	Method title	
2	Author(s) list	
3	Date	
4	Purpose	
5	Qualitative or Quantitative	
6	Target Analytes/Parameters	
NOTES		
C	**Method Development Considerations**	**Description and/or Results**
1	Sample Cost	
2	Sample Holding Times	
3	Sample Preservation	
4	Waste Generation	
NOTES		
D	**Method Performance Characteristic**	**Description and/or Results**
1	Bias/Trueness	
2	Detection Capability and Quantification Capability	
3	Instrument Calibration	
4	Measurement Uncertainty	
5	Precision	
6	Range	
7	Ruggedness	
8	Selectivity in the Presence of Interferences	
NOTES		

Benefits to Using the New Concepts

- Method Lifecycle – Promotes a consistent approach to link and integrate method activities from identifying needs to revision/retirement
- Validation Descriptor [aL,bM] – Provides “one glance” overview of the extent of validation
- Method Validation Summary – Concisely communicates Validation Study information in a consistent format

Guidelines: Where to find them

On the EPA website at:

- EPA National Program Manager for Regional Laboratories

  (click the link to follow)

Direct Link to Document at:

- Guidelines on Validation of Non-Regulatory Chemical and Radiochemical Methods

  (click the link to follow)

Next Steps/ Implementation

- Communicate document to internal and external audiences
  - Conduct more training
  - Present at conferences

What we need from You

- Develop Method Validation Summaries for your Validation Studies using the template in the document
- Place the Summary as an introduction of the standard reports required or used for the Validation Studies

Acknowledgements

Workgroup Members:

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Questions?

Example Method Validation Summary

A. Section for Validation Design

- Descriptions include enough detail for a “quick glance” summary of validation
- Number and types of matrices are the focus

Example Method Validation Summary

A	Validation Design	Description
1	Number of Laboratories	1
2	Number of Matrices	1 (surface water)
3	Types of Matrices Tested (water, soil, sediment, etc.)	Surface water in the Kansas City Urban area; Tested three locations on 12 different streams in the Kansas City area. Noted that 1-2 streams had high chlorine which impacted IS results.

Example Method Validation Summary

B. Section for Method Validation Overview

- Title, authors, date
- Purpose including analytes

Example Method Validation Summary

B	Method Validation Overview	Description
1	Method title	Stir Bar Sorptive Extraction (SBSE or Twister)
2	Author(s) list	Lorraine Iverson (Kimball), EPA Region 7 Science and Technology Center
3	Date	January 8, 2010 (Final Internal Report with Attachments—Region 7)
4	Purpose	Test new sorptive extraction technique that reduces the use of methylene chloride while providing better sample results. Develop alternative test procedure for polycyclic aromatic hydrocarbons.
5	Qualitative or Quantitative	Quantitative
6	Target Analytes/Parameters	66 (45) semi-volatile organic compounds including PAHs (18), 17 (14) pesticides, 4 pharmaceutical and personal care products, 5 brominated flame retardants
NOTES Have expanded the list to include selected herbicides. Evaluating in-situ sample collection.		

Example Method Validation Summary

C. Section for Method Development Considerations

- Practical findings and details considered during development that will be important during implementation

Example Method Validation Summary

C	Method Development Considerations	Description and/or Results
1	Sample Cost	Significant reduction in costs for sample shipment, waste disposal, and solvent purchases; Annualized savings over traditional techniques of up to $2162 in solvent and glassware costs and 75% reduction in shipping costs
2	Sample Holding Times	Tested for holding time—results good for 14 days without preservation
3	Sample Preservation	Tested for holding time—results good for 14 days without preservation
4	Waste Generation	Significant reduction in solvent usage and corresponding waste disposal; Annualized savings of up to 32 gallons of solvent, hundreds of glassware
NOTES		

Example Method Validation Summary

D. Sections for Method Performance Characteristics and Results

- Provides the guidance used to validate specific method parameters
- Briefly summarizes results and data findings
- Notes section available in each section for any additional comments or items of note

Example Method Validation Summary

D	Method Performance Characteristic	Description and/or Results
1	Bias/Trueness	Met SW846 8270 and EPA 625 criteria
2	Detection Capability and Quantification Capability	Detection limit is 10-100 times lower than SW-846 8270 and EPA 625, pesticide results are comparable to 608 by gas chromatography/electron capture detection
3	Instrument Calibration	For polycyclic aromatic hydrocarbons: Linearity of the calibration curves was excellent for the range of 0.2 ug/L to 8 ug/L – a factor of 40. Overall Summary: Linear range varied from 40-fold to only 4-fold
4	Measurement Uncertainty	Excellent internal standard area reproducibility, at <10% with no interferents
5	Precision	Met SW846 8270 and EPA 625 criteria
6	Range	0.1-20 µg/L
7	Ruggedness	Eight extraction parameters were tested: liners, split flow rates, range of sample volumes and stir times, temperature for desorption, extraction additives (methanol or salt), immediate removal or wait time, reanalysis of stir bar for removal rates
8	Selectivity in the Presence of Interferences	Consistent with traditional semi-volatile organic compound and pesticide methods on gas chromatography/mass spectrometry
NOTES This method has also been tested on three water sources as part of a multi-laboratory study and is one of the accepted solid phase extraction techniques in the updated EPA Method 625.		