Protocol for the Evaluation of Alternate Test Procedures for Organic and Inorganic Analytes in Drinking Water

Office of Water (MS-140)

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Foreword

This document provides guidelines for the evaluation of organic and inorganic contaminant analytical methods under EPA's Drinking Water Alternate Test Procedure (ATP) Program. The Drinking Water ATP Program only evaluates alternate methods for analytes regulated under the Safe Drinking Water Act (SDWA), the program will not evaluate methods for unregulated or secondary contaminants. Additionally, devices and equipment will only be evaluated as part of a complete method and not evaluated alone. This drinking water ATP protocol provides guidance for the modification or development of drinking water methods for compliance monitoring. It incorporates current recommendations for method validation that have been developed by the Forum on Environmental Measurements. Under the Drinking Water ATP Program, applicants are required to demonstrate that the alternate method being proposed is an equally effective procedure, relative to an existing EPA-approved method. That demonstration then provides basis for EPA's Office of Ground Water and Drinking Water to consider, independent of the ATP *evaluation*, the *approval* a particular method.

This protocol provides basic information on the criteria the Agency generally uses in deciding whether a method is suitable for evaluation under the Drinking Water ATP Program and the analyses that are generally needed to demonstrate method equivalency. In this protocol, applicants are also directed to demonstrate adequate ruggedness of the drinking water ATP through sufficient multi-laboratory validation to support EPA's consideration of their use at a national level.

EPA anticipates that the standardized procedures described herein will expedite the processing of drinking water ATP reviews, encourage the development of innovative technologies, and enhance the overall utility of the EPA- approved methods for compliance monitoring under the National Primary Drinking Water Regulations.

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1 Introduction

1.1 Background and Objectives

Pursuant to the Safe Drinking Water Act, EPA promulgates, via publication in the *Federal Register*, test procedures (analytical methods) for data gathering and compliance monitoring under National Primary Drinking Water Regulations.

Under the Agency's Drinking Water Alternate Test Procedure (ATP) Program, an organization may request evaluation of a method as an alternate test procedure to a method already approved in the drinking water regulations. These alternate drinking water methods, or ATPs, will be referred to as "candidate" methods through the remainder of this document. Devices and equipment will only be evaluated as part of a complete method and not evaluated alone. The organization or entity seeking the candidate method evaluation is responsible for validating the candidate method. EPA evaluates test methods used to measure regulated contaminants in drinking water and considers them for nationwide approval. Accordingly, EPA assesses any candidate method in such a manner that its interlaboratory range in accuracy, precision and detection capability can be compared to EPA approved test methods measuring the same target analyte(s). To be considered for approval, the candidate method must be an equally effective procedure, relative to the approved method (see Safe Drinking Water Act §1401(1)); that is, the method's performance characteristics in general must be equivalent to, or better than, those of existing approved methods for the contaminant of interest. This allows EPA to ensure that data gathered under the Safe Drinking Water Act are comparable on a nationwide basis. Those methods that demonstrate acceptable performance through their ATP evaluation, become candidates for an EPA approval action.

1.2 Scope of Organic and Inorganic Drinking Water ATP Process

The drinking water ATP evaluation process is based on demonstrating ruggedness of a method (that is the method yields reliable, accurate results over the range of field and lab conditions specified in the method) and establishing equivalency of ATPs to approved methods through a comparison of designated quality control acceptance criteria and method performance.

2 Overview of the Drinking Water ATP Process

Agency staff review the application, including justification for the candidate method provided by the applicant, and determine whether a drinking water ATP evaluation is warranted. If the candidate method application is accepted for consideration, the applicant then develops a validation study plan in consultation with EPA's drinking water ATP staff. Once the study plan is approved, the applicant performs the validation study (working with an independent laboratory(ies)) and submits a validation study report and candidate method to the Drinking Water ATP Program. If laboratory validation demonstrates performance equivalent to or better than that obtained with an approved method, EPA Drinking Water ATP Program representatives will generally recommend approval by EPA senior leadership using one of two options: 1) approval through the conventional "notice and comment" rulemaking process, or 2) approval through the expedited method approval process. Find additional information on EPA's drinking water analytical methods web page. A general checklist of the drinking water ATP process can be found in Appendix A.

2.1 Submission (initial application and subsequent documentation)

Applicants should submit drinking water ATP applications (see Appendix B) to the Drinking Water ATP Coordinator. Upon receipt and acknowledgment of the application, EPA staff will assign an identification number or name to the application. The applicant should use the identification number or name and Appendix B as a cover sheet for all future communications and any supplemental documentation

concerning the application.

2.2 Application Information

Information required on the drinking water ATP application includes: the name and address of the applicant; the date of submission of the application; the title of the proposed candidate method including a shortened method name or number to use in the regulation and for reference; the analyte(s) for which the ATP is proposed; a brief summary of the proposed method and the justification for proposing the ATP. All required application information and any associated attachments should be submitted for the application to be considered complete.

2.2.1 Justification for Drinking Water ATP

The applicant should provide a brief justification for why the drinking water ATP is being proposed. Because EPA review and evaluation of proposed ATPs can entail considerable effort, EPA does not expect to entertain evaluation of impractical methods or method modifications that fall within the scope of flexibility already allowed in an approved method or in EPA's "Technical Notes on Drinking Water Methods" (EPA Document No. EPA-600-R-94-173, October 1994). Examples of appropriate justifications include but are not limited to: the candidate method successfully overcomes some or all of the interferences associated with the approved method; the candidate method reduces the amount of hazardous wastes generated by the laboratory; the cost of analyses or the time required for analysis is reduced; or, the quality of the data is improved. It is highly recommended that the method developer consult with drinking water ATP staff concerning the proposed candidate method and its justification prior to extensive method development.

2.3 Confidential Information in Applications

When submitting information with the proposed drinking water ATP application, the applicant may assert a business confidentiality claim covering part or all of the information. The method for submitting a claim is described in the Code of Federal Regulations (CFR) at 40 CFR 2.203(b). EPA staff will handle such information according to the regulations in subparts A and B of 40 CFR Part 2. Information covered by such a claim will be disclosed by EPA only to the extent, and by means of the procedures, set forth in 40 CFR Part 2, Subpart B. If no such claim accompanies the information when received by EPA, it may be made available to the public by EPA without further notice to the business.

Specifically, in accordance with 40 CFR §2.203(b), a business may assert a business confidentiality claim covering the information by placing on (or attaching to) the information at the time it is submitted to EPA, a cover sheet, stamped or typed legend, or other suitable form of notice employing language such as *trade secret, proprietary* or *company confidential*. Confidential portions of otherwise non-confidential documents should be clearly identified and may be submitted separately to facilitate identification and handling by EPA. If confidential treatment is only required until a certain date, the notice should state so accordingly. It should be noted, however, that any analytical method being considered for approval in the Federal Register cannot itself be claimed as confidential business information; the method developer must be prepared for the method to be published and made widely available.

If a claim of business confidentiality is later received after the information is initially conveyed as part of an ATP application, EPA will make such efforts as are administratively practicable to associate the late claim with copies of the previously submitted information in EPA files. However, EPA cannot ensure that such efforts will be effective considering the possibility of prior disclosure or widespread prior dissemination of the information, See §2.203(c).

3 Method Development and Validation Study

3.1 Introduction

Method development and validation are the processes by which a laboratory substantiates the performance of a method by demonstrating that the method can meet EPA's acceptance criteria and that the method is rugged, that is, yields acceptable method performance and data quality over the range of drinking water sample types and laboratory conditions specified in the method. In order to produce a method that is rugged and meets quality control acceptance criteria, the method developer needs to have a firm understanding of the chemistry involved in the method. Because methods vary widely in their chemistry and procedures, no definitive global guidance can be provided on how to develop a rugged method. In general, though, all candidate methods should: (a) identify critical points of each step in the procedure, (b) demonstrate that these critical points are satisfactorily addressed or controlled in the method and (c) demonstrate that acceptable method performance is attained using all procedural options specified in the method. Generally, there is an expectation that multiple, independent laboratories or sites be used in the validation process to ensure method ruggedness.

Critical points of a method can take a variety of forms depending on the method. For example, certain methods may require extraction of an analyte at a specific pH or narrow pH range. Thus, for the method to be truly rugged, pH control (for example, use of buffers) may be required to ensure that other samples, laboratory conditions or chemists obtain satisfactory results using the method. For candidate methods intended to be used in the field, ambient temperature may be a critical factor affecting performance of the method. The applicant should examine and control such factors or specify the limited conditions under which the method can be used. Other examples of critical steps requiring ruggedness demonstration are:

- Determination of the breakthrough volume in solid phase extraction.
- Effect of laboratory temperature on a purge and trap method.
- Determination of a critical solvent-to-sample ratio in liquid-liquid extraction.

Many methods have procedural options in certain steps, for example, a choice of two sample preservation agents. If more than one preservation option is specified in a candidate method, the applicant must demonstrate acceptable method performance using both preservation options. Similarly, if a candidate method specifies two different solid phase sorbents for extraction, the applicant must demonstrate acceptable performance using both sorbents.

Once an application has been accepted by the Drinking Water ATP Program, the applicant should discuss their plans to address method ruggedness with drinking water ATP staff prior to formulating the validation study plan. Such consultation will help avoid both inadequate study plans (for example, not enough analyses addressing critical points of the method) and study plans with unnecessary analyses. The following sections summarize the major components of the validation study plan.

3.2 Development of a Validation Study Plan

Prior to conducting the candidate method validation study, the applicant should prepare and submit a detailed study plan for EPA approval. Guidelines describing the parameters that should be addressed in a method validation study are provided in Appendix C. In general, the validation study plan will consist of the following sections:

3.2.1 Background

The Background section of the validation study plan should:

- Identify the candidate method.
- Describe the reasons for development, the logic behind the technical approach and the advantages of the method in comparison to existing technology or methodology.
- Include a summary of the candidate method.

- List the analytes measured by the candidate method including corresponding Chemical Abstracts Service Registry identification.

3.2.2 Study Management

The Study Management section of the validation study plan should:

- Identify the organization responsible for managing the study.
- Identify the certified (if applicable), independent laboratories, facilities, and other organizations that will participate in the study.
- Delineate the study schedule.

3.2.3 Technical Approach

The Technical Approach section of the validation study plan should:

- Describe how participating laboratories will be selected.
- Explain who will prepare the test matrix and how it will be distributed.
- Specify the numbers and types of analyses to be performed by the participating laboratories in accordance with this protocol.
- Identify specific reagents, materials, instrumentation, or software required.

3.2.4 Identification of Critical Steps and Plans for Addressing Critical Steps

As mentioned previously, a properly developed and validated method recognizes and controls critical steps in terms of the chemistry or ruggedness, or both, of the method. The applicant should identify those parts of the procedures that could be vulnerable to technician expertise or result in poorer performance with foreseeable departures from ideal conditions. The Plan should identify the steps that will be taken to control these critical steps.

3.2.5 Potential Interferences and Plans to Address Them

Many chemical methods are subject to chemical or physical interferences or both which, if left uncontrolled, result in inaccurate monitoring results. Through an understanding of the chemistry of the method, the applicant should identify potential interferences to the candidate method and plans to address and control these interferences.

3.2.6 Sample Holding Time and Preservation

In general, candidate methods are expected to use the sample holding times, extract holding times (if applicable) and preservation agents specified in approved EPA methods for the analyte, unless these parameters are being explicitly modified in the candidate method. If no changes to holding times or preservation are proposed in a given candidate method and no additional analytes are being added to a method, then this part of the validation study plan is likely to require little discussion. However, if the proposed candidate method alters, or could affect holding times or the preservation of the sample, a holding time or preservation study or both will be required.

3.2.7 Demonstration Data

In this section, the applicant will specify the data to be collected using the candidate method and the approved reference method. Generally, all candidate methods will determine precision and accuracy of the method using both fortified reagent (laboratory) water and different real or synthetic drinking water matrices. Synthetic drinking water matrices should be prepared to provide objective evidence of method capabilities in a “worst case” situation (for example, high hardness or elevated ionic strength and high total organic carbon.)

3.2.8 Fortified Reagent Water Analyses

Generally, candidate methods are required to determine precision, accuracy and sensitivity in reagent

water fortified with the contaminant(s) of interest at relevant concentrations. Accordingly, multiple replicates at the relevant concentration levels will be needed. Concentration levels evaluated in the precision and accuracy studies are expected to extend both above and below the published regulatory Maximum Contaminant Level effectively demonstrating the candidate method will satisfy all regulatory measurement requirements. Sensitivity may be evaluated through any number of quantitation limit and detection limit determinations. More detailed aspects of these parameters are presented in Appendix C.

Fortified reagent water samples should incorporate the preservation agent(s) specified in the method and any other reagents or treatments specified in the method. Fortified reagent water samples should be prepared and analyzed for every option specified in the method. For example, if two or more preservation agents are specified as options in the method, reagent water analyses should be independently performed using each preservation agent given in the method.

3.2.9 Matrix Analyses

For candidate methods, precision and accuracy should be examined using different drinking water matrices that may be encountered during routine sample analysis. These drinking water matrices may be actual or synthetic and the exact number and type needed will be determined when the validation study plan is constructed. Generally, the matrices are a combination of the following types: (1) finished drinking water drawn from a hard ground water source (hardness > 250 mg/L as CaCO3), (2) finished drinking water drawn from a surface water source and containing elevated total organic carbon (TOC ≥2 mg/L), (3) artificial drinking water matrix high in ionic strength and (4) artificial drinking water matrix high in organic content. Additional matrices may need to be examined to document adequate performance of the method as appropriate. For example, if chloride is known or suspected to interfere with a given method, the validation study plan may need to include a public water supply sample or artificial matrix having the maximum, tolerable chloride concentration that the applicant has determined for the candidate method. If a method is designed to measure a particular disinfection byproduct, it may be necessary to examine various finished drinking waters to adequately test the method. Drinking water ATP staff will work with the applicant to determine appropriate matrices to include in the validation study plan.

Analysts should review an applicable approved or published method for indications of matrix effects that are unique to the analyte separation and measurement technologies used in the ATP. Water quality characteristics that can affect analysis of drinking water samples include, but are not limited to, pH, total organic carbon content, turbidity, total organic halogen content, ionic strength, sulfate, metal contamination and trihalomethane contamination of the drinking water sample.

For each drinking water matrix specified in the validation study plan, replicates are fortified at a concentration sufficiently below the Maximum Contaminant Level, along with a mid-level and a high-level spike. Precision and accuracy are determined for each set of replicates. As noted above for reagent water analyses, additional replicates or fortified concentration levels may be required depending on the method. Also, as noted previously, each sample is tested using any and all options specified in the candidate method.

3.2.10 Quality Control

Quality control is an important aspect of method performance. Quality control needs to be incorporated within each candidate method and the applicant should address the quality control specified in the method. Common quality control parameters include:

- Initial calibration and calibration verification.
- Blanks.
- Ongoing precision and accuracy.

- Surrogate recovery.
- Internal standard response.
- Fortified matrix precision and accuracy.

Appendix C, Table 1 summarizes the above quality control parameters as they are addressed for organic and inorganic contaminants in EPA drinking water methods.

3.2.11 Draft Candidate Method

A draft of the candidate method should be included as a separate attachment to the validation study plan. The draft details the step-by-step procedures of the candidate method. This includes all equipment, reagents and materials required and data evaluation or calculation procedures. Unless the applicant is a consensus standards organization or government organization that has their own method format requirements, all applicants should submit the candidate method written in the standard EPA method format (Appendix D). Applicants from organizations having their own format requirements should compare their specific method format with the EPA method format to ensure that all sections of the EPA method format are addressed. The 17 sections listed in Appendix D of this document should be included for all candidate methods. Recent drinking water methods published by EPA (for example, Methods 150.3, 533, 546) may also be consulted for format and the level of detail required.

3.3 Approval of Validation Study Plan

Once EPA is satisfied that the written method and the proposed study plan meet the criteria described in this document, the applicant will be instructed to proceed with the method validation study.

3.4 Method Validation Study Report

The applicant should document the results of the validation study in a formal validation study report containing the elements described in this section. In all cases, a copy of all required validation data should be maintained at the laboratory or other organization responsible for developing the method. The information and supporting data in the validation study report must be sufficient to enable EPA to determine whether the candidate method performs as well as or better than the approved reference method.

The validation study report should contain background information and describe the study design. In addition, the validation study report should detail the process and results of the study, provide an analysis and discussion of the results, and present study conclusions. The approved validation study plan should be appended to the validation study report and referenced as appropriate.

The validation study report should identify and discuss any deviations from the validation study plan that were made in implementing the study along with problems encountered and corrective actions. To the extent possible, deviations should be discussed with EPA in advance of being implemented to ensure that the deviations are appropriate.

See Appendix E for the validation study report template.

3.4.1 Background

The Background section of the validation study report describes the candidate method. The Background section of the validation study report should:

- Include a method summary.
- Summarize the justification for the ATP evaluation and the proposed benefits the candidate method offers to drinking water monitoring.
- List the analytes measured by the candidate method, including corresponding Chemical Abstracts Service Registry identification.

3.4.2 Study Implementation

The Study Implementation section of the validation study report describes the methodology and approach undertaken in the study. This section should:

- Identify the laboratories or other organizations or both that participated in the study.
- Delineate the study schedule that was followed.
- Explain how samples were collected and handled.
- Specify the numbers and types of analyses performed by the laboratory.
- Identify any problems encountered or deviations from the study plan and their resolution or impact on study performance or results or both.

3.4.3 Demonstration Data

This section of the validation study report should include the demonstration data for the analyzed samples. For each sample, the report should compare method performance data obtained with the candidate method to the approved reference method performance data. Demonstration data should be provided for samples using all procedural options specified in the method.

3.4.4 Calculations, Data Analysis and Discussion

This section of the validation study report should provide sufficient documentation of the data obtained with the candidate method to permit an independent reviewer to verify the study results. Example calculations are required as part of the results and should be included in the validation study report. The test data and calculations should be electronically reported in a format compatible with Microsoft© Office applications. The discussion should address any discrepancies between the results and the quality control acceptance criteria.

3.4.5 Conclusions

The Conclusions section of the validation study report describes the conclusions drawn from the study based on the data analysis discussion. The Conclusions section should contain a statement(s) regarding achievement of the study objective(s).

3.4.6 Candidate Method

The candidate method should be appended to the validation study report. Format should follow that specified in Appendix D.

3.4.7 Validation Study Plan

The validation study plan should be appended to the validation study report.

4 EPA Review and Approval

4.1 EPA Review of Candidate Method

EPA's Drinking Water ATP Program reviews the candidate methods and the validation data. If a candidate method is determined to provide equivalent method performance relative to the reference method, it becomes a candidate for approval by EPA senior leadership.

4.2 Approval Recommendation

EPA will complete its review and notify the applicant of EPA's recommendation. If the candidate method is recommended for approval, EPA will pursue formal approval using one of two options: 1) approval via the conventional "notice and comment" rulemaking process or 2) approval via the expedited method approval process. Find additional information on EPA's drinking water analytical methods web page .

4.3 Joint Drinking Water Wastewater Applications

Candidate methods can be submitted for ATP evaluation used for both drinking water and wastewater

applications. However, the requirements for compliance monitoring under the National Primary Drinking Water Regulations differ from those under the National Pollutant Discharge Elimination System permit program. Review and evaluation of ATP candidate methods that are submitted for dual applications are thus handled by both the Drinking Water ATP Program and the Wastewater ATP Program.

Appendix A: Drinking Water ATP Applicant Process: General Checklist

Step 1: Initial Inquiry	Y	N	N/A	Notes
The application includes name, address, date, and title of the proposed method.				
The proposed method is for drinking water and the analysis of regulated contaminants or water quality parameters.				
The EPA has assigned a unique identifier to the submitted method.				
The applicant has included method data with their request (optional).				
The EPA has determined the request is allowed within the method-specified flexibility.				
The EPA has determined an evaluation of the proposed method as an ATP candidate method is warranted.				

Step 2: ATP Initial Application	Y	N	N/A	Notes
The applicant has provided the Application and Document Submission Form with all requested information.				
The application includes the analyte to be studied.				
The application lists the approved EPA reference method(s) used for comparison with the candidate method.				
The applicant has submitted justification for the candidate method to the Drinking Water ATP Coordinator.				
The applicant is asserting a claim the candidate method contains confidential business information (CBI).				
The applicant has attached paperwork pursuant to 40 CFR 2.203(b) regarding CBI.				
The applicant has submitted and separated the CBI and indicated with an appropriate coversheet marked "confidential."				
The EPA has handled CBI pursuant to subparts A and B of 40 CFR Part 2.				

Step 3: Submission of Study Plan	Y	N	N/A	Notes
The study plan cover sheet includes name, address, date, case number, and title of the proposed method.				
A draft of the candidate method has been provided.				
The applicant has identified the critical points of the study proposal.				
The applicant has discussed methods to control the critical points of the proposal.				
The applicant has included experiments to verify all procedural options specified in the method.				
The applicant has included in their validation study plan a discussion to address method ruggedness.				
The applicant has submitted a complete validation study plan to EPA for review following the ATP protocol guidelines.				

Step 3: Submission of Study Plan	Y	N	N/A	Notes
The background of the study plan includes a summary of the candidate method.				
The background of the validation study plan includes a list of the analytes and corresponding Chemical Abstracts Service (CAS) Registry identifications.				
The validation study plan identifies the organization responsible for managing the study.				
The validation study plan identifies the laboratories/organizations that will participate in the study.				
The validation study plan contains and assigns a study schedule to the laboratories/organizations participating in the study.				
The validation study plan uses the same holding times, extract holding times, and preservation agents specified in the candidate method.				
The validation study plan lists all the equipment that will be used in the candidate method.				
The validation study plan lists all the reagents that will be used in the candidate method.				
The validation study plan includes all 17 sections of the EPA method format.				
The validation study plan identifies critical steps and the plan to monitor and account for departures from method performance.				
The validation study plan identifies interferences (chemical, physical) that may affect the results and the plans to mitigate the interferences.				
The validation study plan includes a method to determine precision and accuracy using fortified reagent water.				
The validation study plan includes a method to determine effectiveness above and below the Maximum Contaminant Level (MCL).				
The validation study plan includes a method to incorporate the preservative agent(s) into fortified reagent water as identified in the method.				
The validation study plan includes analysis of drinking water from a hard water source. (Optional)				
The validation study plan includes analysis of drinking water from a source that contains total organic carbon ≥ 2mg/L. (Optional)				
The validation study plan includes analysis of artificial drinking water with a high ionic strength. (Optional)				
The validation study plan includes analysis of artificial drinking water with a high organic content. (Optional)				
The validation study plan includes analysis of artificial drinking water with a high chloride content. (Optional)				
The validation study plan includes analysis of artificial drinking water with a disinfection byproduct. (Optional)				
The validation study plan includes an analysis of the Quality Control Targets used in the candidate method.				

Step 4: Submission and Review of Method Validation Study Report (MVSR)	Y	N	N/A	Notes
The background of the MVSR contains a method summary, justification for the ATP evaluation, and a list of the analytes.				
The MVSR study implementation section identifies the laboratories/organizations that participated in the study.				
The MVSR implementation report lists the study schedule that was followed.				
The MVSR study implementation section explains how the samples were collected and handled.				
The MVSR implementation section specifies the types and numbers of analyses to be performed in the lab.				
The MVSR implementation report identifies and describes any deviations or problems that impacted the study performance.				
The MVSR presents a sufficiently detailed version of the candidate method in the correct EMMC format.				
The MVSR contains sample calculations.				
The test data is reported in a format compatible with Microsoft© Office applications.				
The MVSR contains a discussion of discrepancies between results and quality control acceptance criteria.				
The MVSR contains a conclusion section discussing achievement of the study objective(s).				
The MVSR contains the approved validation study plan in the appendix.				
Developed in collaboration with EPA, the MVSR contains data from multiple matrices to identify interferences or matrix effects.				

Step 5: Data Review of MVSR by EPA	Y	N	N/A	Notes
Applicant has completed the Application and Document Submission Form.				
The applicant has submitted evidence of instrument calibration.				
The applicant has submitted a rigorous evaluation of bias in their analytical method.				
The applicant has submitted an evaluation of precision, using the extremes of the quantitation range, regulatory levels, and multiple matrices.				
The method blank meets the minimum reporting level (MRL) described in the reference method (if applicable).				
The results from the initial demonstration of capability (IDC) passes the Quality Control Targets used in the candidate method.				
The method demonstrates chemical and microbiological storage and stability.				
The method has utilized a minimum number of sites/laboratories for data collection, as determined by the EPA.				

Step 6: Final Evaluation by EPA	Y	N	N/A	Notes
The applicant has demonstrated through design, experiment, and data collection that their candidate method is rugged.				

Step 6: Final Evaluation by EPA	Y	N	N/A	Notes
The applicant has submitted any additional paperwork and data requested by the EPA.				
The EPA has satisfactorily protected the CBI of the applicant.				
The EPA has determined the candidate method as ab ATP submission is equally effective as the reference method.				

Appendix B: Application and Document Submission Form

EPA Office of Ground Water and Drinking Water Alternate Test Procedure Candidate Method Application

☐ Initial Application
☐ Supplemental Documentation
☐ Final Application

Applicant Information
Applicant Name:
Address:
State:
Zip Code:
Contact name:
Phone number:
Email address:
Submission Date:
Candidate method:
Analyte(s):
Candidate method title:
Reference method number or name or both:

Attachments

☐ Justification for Candidate Method
☐ Candidate Method
☐ Validation Study Plan
☐ Validation Study Report
☐ Raw Data Package (spreadsheets, calibrations, etc.)
☐ Data Collection Certification
☐ Other Documentation:

EPA use only Case number:

Appendix C: Method Validation

1 Introduction

Method validation is the process of demonstrating that an analytical method is suitable for its intended use and involves conducting a variety of studies to evaluate method performance under defined conditions. Method validation studies may involve a single laboratory (intralaboratory) or multiple laboratories (interlaboratory). The goal is to demonstrate that analytical results produced by the application of a particular method are fit for an intended purpose. Properly designed and successful method validation studies create confidence in the reliability of a test method. Method validation is one of several important quality system components that are designed to ensure the production of scientifically valid and useful analytical data.

The information in this appendix is intended to serve as a guideline only. Because methods vary significantly in chemistry and technology, it is not possible to define a single set of performance criteria that can be applied to all methods. This is due to the severe problems in translation of a complex domain of knowledge such as analytical chemistry into a mathematical statement. This appendix lists critical elements of the general method validation process that may not apply in all cases. The actual validation components that will be necessary will be determined during the creation of the method validation study plan.

2 Storage Stability

Before validating an analytical method, it is necessary to ensure that proper sample preservation and storage stability studies were performed during method development. Storage stability should investigate the stability of the analyte(s) from the time of sampling through the time of analysis. If an extraction is performed, the extract stability should also be investigated. Analytes may be lost through volatilization, sorption, chemical degradation (abiotic reactions) and microbial degradation (microorganisms have the potential to degrade target analytes and represent a significant pathway for the fate and destruction of organic compounds).

3 Instrument Calibration

Instrument calibration refers to the procedures used for correlating instrument response to an amount of analyte (concentration or other quantity). The characteristics of a calibration function and justification for a selected calibration model should be demonstrated during a method validation study.

The performance of a calibration technique and the choice of calibration model (for example, first order, second order, weighting, etc.) are critical for minimizing sources of instrument bias and optimizing precision. The parameters of the model are usually estimated from the responses of known, pure analytes. Calibration errors can result from failure to identify the best calibration model; inaccurate estimates of the parameters of the model; or inadequately studied, systematic effects from matrix components.

During method development and validation, calibration models are typically evaluated by analyzing multiple levels of calibration standards over a selected working range. After a calibration curve is constructed from the responses, the concentrations of the standards are calculated from the curve. These values are then compared to the appropriate quality control criteria to determine the curve's adequacy. The calibration study results should be included in a method validation report. Access to information about calibration performance characteristics assists the user in implementing new methods and verifying that a laboratory's instrument performance is acceptable.

4 Accuracy (Bias)

Bias refers to the overall magnitude of known systematic (determinate) errors associated with the use of an analytical method. The presence of systematic errors can only be determined 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 or by analyzing fortified materials.

Rigorous evaluations of bias should be included in method validation studies. Minimally, bias should be evaluated at the extremes of the quantitation range, at regulatory levels and in representative matrices. The most common measure of bias is the calculation of a percent recovery.

5 Precision

The general term “precision” is used to describe the magnitude of random (indeterminate) errors associated with the use of an analytical method. The sources of random error evaluated depend upon the range of conditions over which the data are collected.

Precision should be evaluated at the extremes of the quantitation range, at regulatory levels and in representative matrices. Common measures of dispersion are the standard deviation and the percent relative standard deviation of repeated measurements. The repeatability and reproducibility conditions should be clearly stated so that the measures of dispersion can be properly interpreted and evaluated.

6 Quantitation Limits and Range

The term “quantitation range” is used to describe the span of analyte levels, as contained in a sample matrix, for which method performance has been tested and data quality is deemed acceptable for its intended use. For compliance, a quantitation range includes either a regulatory or other type of action level for the compound being analyzed.

A lower limit and an upper limit bound a quantitation range. A quantitation range may be wider than an instrument’s calibration range because of dilution or concentration steps performed during sample preparation. Dilution factors or concentration factors are used to relate the calibration range to the quantitation range. Analyte concentration will influence most method performance characteristics, including accuracy and precision. At a minimum, method accuracy and precision should be evaluated at the extremes of the quantitation range.

The lower limit of the quantitation range is commonly referred to as the “limit of quantitation.” The minimum reporting level (MRL), or the minimum concentration that can be reported by a laboratory as a quantified value for the method analyte in a sample following analysis, should always be above the “limit of quantitation” and both should be at or above the lowest calibration standard.

7 Detection Limit(s)

The term “detection limit” is used to describe the lowest concentration at which the presence of an analyte can be confidently determined. There are many specific definitions for this term, and it is used to describe the detection capabilities of detectors, instruments, and analytical methods. In lieu of detection limits, analysts have also used MRLs and performed MRL confirmations (that may be included in the methodology) as a demonstration of their capability to achieve a required MRL. In those cases where Method detection limits (MDLs) are specified in regulation, the procedure associated with that specification (e.g., 40 CFR, Part 136, Appendix B) must be used to determine them.

8 Ruggedness Testing

Ruggedness refers to the extent to which an analytical method remains unaffected by minor variations in operating conditions. Ruggedness testing involves experimental designs for examining method performance when minor changes are made in operating or environmental conditions. The changes should reflect expected, reasonable variations that are likely to be encountered in different laboratories.

Ruggedness testing is generally conducted at the end of method development but before an interlaboratory method validation study.

9 Quality Control Targets for Method Development

As previously mentioned, the necessary validation components will be determined during the creation of the method validation study plan. This includes the numeric limits for specific quality control parameters. These values will depend on the regulation, intended data use, the quality control parameters for existing reference methods and the individual technology that is being applied. Table 1 provides reference values that are generally used by Office of Ground Water and Drinking Water for method development.

Table 1. Reference Values generally used for Drinking Water Method Development

Parameter	**Organic Methods**	**Inorganic Methods (Ion Chromatography or wet)**	**Metals or Inductively Coupled Plasma**
Method Blank	<1/3 MRL	<1/3 MRL	<1/3 MRL
Initial Demonstration of Capability Accuracy or bias, Continuing calibration checks and Calibration curve checks (as %recovery)	>2 x MRL ± 30%, ≤2x MRL ± 50%	>2 x MRL ± 15%, ≤2x MRL ± 20%	>2 x MRL ± 10%, ≤2x MRL ± 20%
Surrogate Recovery	± 30%	± 15%	Not Applicable
Initial Demonstration of Capability Precision and Duplicate Samples (% Relative Standard Deviation)	± 30%	± 20%	± 15%
Internal Standard	≥50% of the Internal Standard area or response in the active calibration	Same	60%–125%

Additionally, the typical validation study would involve the method being evaluated by three laboratories, at least two of which are independent (i.e., free of conflict of interest) and, if applicable, certified (i.e., certified by the primacy agency [typically the state] for the analysis of compliance monitoring samples for the analytes of interest).

Appendix D: Standard EPA Method Format

[Note: Each method should be a free-standing document, providing all information necessary for the method user to perform the analysis. References within a method should be restricted to associated or source material. Procedural steps or instructions should not be referenced as being found elsewhere but should be included in totality within the method. The following section numbering scheme is typical with the Environmental Monitoring Management Council (EMMC) format.]

1 Scope and Application

[This section outlines the purpose, range, limitations, and intended use of the method and identifies target analytes.]

2 Summary of Method

[This section provides an overview of the method procedure and quality assurance.]

3 Definitions

[This section includes definitions of terms, acronyms and abbreviations used in the method. If preferred, definitions may be provided in a glossary at the end of the method or manual. In this case, the definitions section should still appear in the method, with a notation that definitions are provided in a glossary (refer to the specific section number of the glossary) at the end of the method.]

4 Interferences

[This section identifies known or potential interferences that may occur during use of the method and describes ways to reduce or eliminate these interferences.]

5 Safety

[This section describes special precautions needed to ensure personnel safety during the performance of the method. Procedures described here should be limited to those which are above and beyond good laboratory practices. The section should contain information regarding specific toxicity of analytes or reagents.]

6 Equipment and Supplies

[This section lists and describes all non-consumable supplies and equipment needed to perform the method.]

7 Reagents and Standards

[This section lists and describes all reagents and standards required to perform the method and provides preparation instructions or suggested suppliers or both as appropriate.]

8 Sample Collection, Preservation and Storage

[This section provides requirements and instructions for collecting, preserving, and storing samples.]

9 Quality Control

[This section cites the procedures and analyses required to fully document the quality of data generated by the method. The required components of the laboratory's quality assurance program and specific quality control analyses appropriate to the method are described in this section. It should at least address the quality control specifications listed in Appendix C, Table 1 of this document.]

10 Calibration and Standardization

[This section describes the method or instrument calibration and standardization process and the required calibration verification. Corrective actions are described for cases when performance specifications are not met.]

11 Procedure

[This section describes the sample processing and instrumental analysis steps of the method and provides detailed instructions to analysts.]

12 Data Analysis and Calculations

[This section provides instructions for analyzing data, equations, and definitions of constants used to calculate final sample analysis results and their uncertainties.]

13 Method Performance

[This section provides method performance criteria for the method, including precision or bias statements regarding detection limits and sources or limitations of data produced using the method.]

14 Pollution Prevention

[This section describes aspects of the method that minimize or prevent pollution known to be or potentially attributable to the method.]

15 Waste Management

[This section describes minimization and proper disposal of waste and samples.]

16 References

[This section lists references for source documents and publications that contain ancillary information.]

17 Tables, Diagrams, Forms, Flowcharts and Validation Data

[This section contains all the method, tables, figures, diagrams, example forms for data recording and flowcharts. This section may also contain validation data referenced in the body of the method.]

Appendix E: Validation Report Template

Microsoft© Word

This template is to be used to prepare final validation study reports for ATPs. The template sets up the primary validation study report sections along with brief instructions for each section. The template is prepared using an Adobe®-supported font for proper .pdf conversion. Please do not make any changes to fonts or styles.

If the alternate test method demonstrates equivalency to an approved method, EPA may subsequently approve the method for compliance monitoring through either conventional notice-and-comment rulemaking or through the expedited methods approval process. In either case, this validation report will be incorporated in the public docket associated with the approval action.

If typing the validation study report directly into the template, replace the text of the template and begin typing your report (that is, select the Title section and replace it with your title). This page of instructions can be deleted upon completion of the validation study report.

Insert graphics within the text in TIFF, JPEG or Microsoft© Office compatible file format (*.wmf or *.emf).

Save the file with the graphics in place as a document file (.doc).

Alternate Test Procedure (ATP) Validation Study Report

Title

[The title should clearly and concisely specify the name of the method, the scope of the measurement (for example, “measurement of turbidity”, “nitrate analysis”, etc.) and the instrumentation (if applicable). The title should also include a shortened method name or number to use in the regulation and for reference]

Date

Name and address of organization

Author name(s)

[Include individual(s) with responsibility for overseeing development of the alternate test method and verifying accuracy of the data presented in the validation study report. Designate the appropriate point of contact in the event questions arise after review of the report.]

Phone number and email address

[Author or point of contact phone number and email address.]

1 Background

[Provide a method summary discussing the experimental technique.]

1.1 Method Justification

[Specifically cite the approved method (including revision/version) that the candidate method is being compared to, the organization where the approved method originated (for example, ASTM, Standard Methods, EPA, etc.), and the method number. Summarize justification for the candidate method and describe the advantages relative to the approved method, especially in terms of improved sample throughput, reduction of hazardous waste, cost reduction, elimination of interferences, etc.]

1.2 Method Equivalency

[Summarize the quality control acceptance criteria as defined in the approved method and describe how the candidate method meets these specifications. Clearly indicate in the final sentence whether the candidate method is "equally effective" in meeting quality acceptance criteria as the approved method.]

1.3 Analytes

[Identify the analytes that are determined using the candidate method and list the corresponding Chemical Abstracts Service registry numbers.]

2 Study Implementation

[Clearly identify the managing organization responsible for development of the candidate method validation study plan and all of the laboratories participating in the study. Explain why specific laboratories were selected to participate and address any potential for conflict of interest. Identify whether the study involved the use of different types of instrumentation (for example, gas chromatography–mass spectrometry analyses using ion trap detectors and triple quadrupole detectors).]

2.1 Study Schedule

[Delineate the study schedule.]

2.2 Sample Collection

[Describe how samples were collected and handled. Specify whether required holding times were met.]

2.3 Types of Analyses Performed

[Describe the number and types of analyses performed by each laboratory (for example, specify how many replicate analytical runs were performed to evaluate precision and accuracy in each drinking water matrix, incorporation of blanks, etc.]

2.4 Study Plan Deviations

[Fully describe any problems encountered or deviations from the study plan and the resolution or impact of these issues on the study plan performance results.]

3 Method Procedure and Data

[The candidate method should be prepared in standard EPA EMMC-method format and submitted with the initial validation study plan. In this final validation report, the method should be attached as an addendum and referenced as such in this section. Compare and contrast procedural differences between the candidate method and the approved method.]

3.1 Validation Study Demonstration Data

[Submit complete demonstration data for both reagent water and drinking water matrix analyses in tables, graphs, or figures, as appropriate. The data should clearly present the candidate method data in comparison with the required reference method quality control criteria. Address the items in the following subsections, as appropriate.]

3.1.1 Calibration

[Demonstrate acceptable calibration performance as defined in the validation study plan. Include calibration verification through incorporation of calibration checks.]

3.1.2 Initial Demonstration of Capability

[Demonstrate acceptable low system background, precision and accuracy and detection limit or minimum reporting level confirmation (as specified in the validation study plan).]

3.1.3 Quality Controls

[Include verification of method performance using blanks, surrogates, internal standards, and other quality controls as specified in the validation study plan.]

3.1.4 Precision and Accuracy

[Include all precision and accuracy data for reagent water and drinking water matrix samples.]

3.2 Holding Time or Storage Stability

[If specified in the validation study plan, submit storage stability data. Otherwise, indicate that a holding time study was not required.]

4 Data Analysis and Discussion

[Provide a comparison of the candidate method data to the approved method to confirm equivalency of performance. Discuss in detail any discrepancies between the results and quality control acceptance criteria. Discuss method ruggedness based on overall performance as specified in the validation study plan (for example, multi-laboratory studies, analyses performed on multiple instruments, assessments of various drinking water matrices, etc.)]

5 Conclusions

[Discuss achievement of validation study objectives.]

Validation Report Appendix A: Validation Study Plan

[Append the approved validation study plan.]

Validation Report Appendix B: Supporting Data

Raw Data

[Submit raw data in an excel spreadsheet. Identify instruments used and operating conditions, chromatographic column specifications, high-performance liquid chromatography gradients, gas chromatography temperature programs, detectors, injection volumes, solid phase extraction media and extraction procedures.]

Example Calculations

[Provide sample calculations to verify that the laboratory has used the raw data to correctly arrive at the final results.]

Validation Report Data Collection Certification

It is the expectation of the ATP program that all data will be collected as outlined in the validation study plan. Applicants must attest on the application that the data collection was performed as outlined in the validation study plan.

The applicant hereby certifies that the data included with this application were collected as outlined in the validation study plan.

_____

Applicant (print name)

_____

Applicant (signature) and (Date)

[Questions, comments, or applications should be directed to:

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