



**Data Review and Validation Guidelines for Perfluoroalkyl
Substances (PFASs) Analyzed Using EPA Method 537**

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NOTICE

The procedures set forth here are intended as guidance to the United States Environmental Protection Agency and other governmental employees. They do not constitute rule-making by the EPA and may not be relied upon to create a substantive or procedural right enforceable by any other person. The government may take action that is at a variance with the procedures in the manual.

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Table of Contents

ACRONYMS AND ABBREVIATIONS	vi
INTRODUCTION	1
I. Purpose of this Document.....	1
II. Limitations of Use	1
III. References	1
GENERAL DATA REVIEW	2
I. Initial Demonstration of Capability	2
II. Preliminary Review	4
III. Data Qualifies Definitions	5
IV. Data Review Narrative	6
METHOD SPECIFIC DATA REVIEW	7
I. Preservation and Holding Times	7
II. Liquid Chromatograph/Mass Spectrometer Instrument Performance Check	8
III. Initial Calibration.....	9
IV. Quality Control of Sample (QCS)	13
V. Continuing Calibration Check (CCC)	15
VI. Blanks	18
VII. Surrogate (SUR) Analyte Standards.....	20
VIII. Laboratory Fortified Blank (LFB).....	22
IX. Lab Fortified Sample Matrix (LFSM) (aka: Matrix Spike/Matrix Spike Duplicate)	23
X. Internal Standard.....	25
XI. Target Analyte Identification.....	27
XII. Target Analyte Quantitation	29
XIII. System Performance	30
XIV. Performance Evaluation Sample.....	31
XV. Regional Quality Assurance and Quality Control	32
XVI. Overall Assessment of Data.....	34
APPENDIX A: GLOSSARY	36
APPENDIX B: Table 18. Compounds analyzed by EPA Method 537.....	39

Table of Tables

Table 1. Method 537 Initial Demonstration of Capability Quality Control Requirements.....	3
Table 2. Data Qualifiers and Definitions	5
Table 3. Preservation and Holding Time Actions for PFAS Analysis.....	8
Table 4. Concentration and Recent Recovery (%R), Acceptance Criteria in ICAL and CCC for PFAS Analysis.....	12
Table 5. Initial Calibration Actions for PFAS Analysis	12
Table 6. Initial Calibration Actions for Associated Target Analytes of Internal Standards in PFAS Analysis.....	13
Table 7. QCS Actions for PFAS Analysis	14
Table 8. CCC Actions for PFAS Analysis.....	17
Table 9. Blank Actions for PFAS Analysis	20
Table 10. EPA Method 537 PFAS SUR Recovery Limits (Water)	22
Table 11. SUR Actions for PFAS Analysis	22
Table 12. LFB Actions for PFAS Analysis.....	23
Table 13. MS/MSD %R and RPD Limits for PFAS Analysis.....	25
Table 14. MS/MSD Actions for PFAS Analysis	25
Table 15. Internal Standards and Associated Target Analytes	27
Table 16. Internal Standard Actions for PFAS Analysis	27
Table 17. PE Sample Actions for PFAS Analysis	32
Table 18. Compounds analyzed by EPA Method 537	39

ACRONYMS AND ABBREVIATIONS

The following acronyms and abbreviations may be found throughout this document. For definitions, see Appendix A: Glossary at the end of the document.

CASRN	Chemical Abstracts Service Registry Number
CCV	Continuing Calibration Verification
CF	Calibration Factor
CS3	Mid-point Calibration Standard
DQA	Data Quality Assessment
DQO	Data Quality Objective
EPA	United States Environmental Protection Agency
LC/MS/MS	Liquid Chromatograph/Mass Spectrometer/Mass Spectrometer or Liquid Chromatography/Mass Spectrometer /Mass Spectrometry
ICAL	Initial Calibration
IDC	Initial Demonstration of Capability
IS	Internal Standard
IUPAC	International Union of Pure and Applied Chemistry
LFB	Laboratory Fortified Blank
LRB	Laboratory Reagent Blank
LCS	Laboratory Control Sample
MRL	Minimum Reporting Level
MS	Matrix Spike
MSD	Matrix Spike Duplicate
NFG	National Functional Guidelines
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
OSRTI	Office of Superfund Remediation and Technology Innovation
%Breakdown	Percent Breakdown
%D	Percent Difference
%R	Percent Recovery
%Resolution	Percent Resolution
%RSD	Percent Relative Standard Deviation
%Solids	Percent Solids
PFAS	Perfluoroalkyl Substances
PIR	Prediction Interval of Result
QA	Quality Assurance
QAPP	Quality Assurance Project Plan
QC	Quality Control
QCS	Quality Control Sample
RFQ	Request for Quote

RIC	Reconstructed Ion Chromatogram
RPD	Relative Percent Difference
RRT	Relative Retention Time
RT	Retention Time
SAP	Sampling and Analysis Plan
SDG	Sample Delivery Group
SRM	Single Reaction Monitoring
SOP	Standard Operating Procedure
SUR	Surrogate Analyte Standards
TAL	Target Analyte List
TR/COC	Traffic Report/Chain of Custody Record

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INTRODUCTION

I. Purpose of this Document

This document contains guidance to aid the data reviewer in determining the usability of analytical data generated for perfluoroalkyl substances (PFAS). It is primarily based on EPA Method 537 and the general validation approach developed under EPA's Contract Laboratory Program. This document is intended to be applicable to data gathered using EPA Method 537 for investigative purposes. Data users evaluating drinking water sample results, assessing potential human exposure relative to published drinking water health advisory levels, should not qualify or use analytical result data that fail Method 537 quality control criteria.

The guidelines presented in this document are designed to assist the data reviewer in evaluating: (a) whether the analytical data meet the technical and Quality Control (QC) criteria specified in project plans for programs, and (b) the usability and extent of bias of any data not meeting these criteria. This document contains definitive guidance in areas such as blanks, calibration standards, QC audit samples, and instrument performance checks, in which performance is fully under a laboratory's control. General guidance is provided to aid the reviewer in making subjective judgments regarding the use of data that are affected by site conditions (e.g., sample matrix effects) and do not meet specific project requirements.

II. Limitations of Use

To use this document effectively, the reviewer should have an understanding of the analytical methods and a general overview of the data generated.

While this document is a valuable aid in the data review process, other sources of guidance and information, along with professional judgment, are useful in determining the ultimate usability of the data. This is particularly critical in those cases where all data do not meet project or method specific technical and QC criteria. To make the appropriate judgments, the reviewer needs to gain a complete understanding of the intended use of the data and is strongly encouraged to establish a dialogue with the data user prior to and following the data review, to discuss usability issues and resolve questions regarding the review.

III. References

EPA Method 537, Determination of Selected Perfluorinated Alkyl Acids in Drinking Water by Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS), Revision 1.1, September 2009.

USEPA Contract Laboratory Program National Functional Guidelines for Organic Data Review, OLEM 9355.0-136, EPA 540/R-2017-002, January 2017.

Technical Advisory - Laboratory Analysis of Drinking Water Samples for Perfluorooctanoic Acid (PFOA) Using EPA Method 537 Rev. 1.1,

<https://www.epa.gov/sites/production/files/2016-09/documents/pfoa-technical-advisory.pdf>

GENERAL DATA REVIEW

I. Initial Demonstration of Capability

- A. Verify that the laboratory has successfully performed Initial Demonstration of Capability (IDC) analyses that meets the needs of the project. Table 1 lists requirements associated with EPA Method 537 for drinking water analyses and can be considered for other matrices and procedures. Verification can be accomplished through review of associated IDC results and data using the guidance in this document. A review of IDC results should be performed before considering use of the laboratory for analyses. If the lab cannot provide all of the required IDC information in Table 1, use professional judgment to qualify data as appropriate.
- B. METHOD MODIFICATIONS – The analyst is permitted to modify LC columns, LC conditions, evaporation techniques, internal standards or surrogate standards, and MS and MS/MS conditions. Each time such method modifications are made, the analyst must repeat the procedures of the IDC. Modifications to LC conditions should still produce conditions such that co-elution of the method analytes is minimized to reduce the probability of suppression/enhancement effects
- C. However, extraction procedures must be consistent with EPA Method 537 for both the IDC and for samples. If extraction procedures are not properly performed, use professional judgment to qualify data as an estimate (J, UJ) or unusable (R).
1. Since some of the PFASs adsorb to surfaces, the sample volume may NOT be transferred to a graduated cylinder for volume measurement. Verify that the lab has determined sample volume by either:
 - a) Marking the level of the sample on the bottle and determining the bottle volume after extraction, or
 - b) Weighing the sample and bottle to the nearest 10 g.
 2. Verify that sample processing was by solid phase extraction (SPE) following the specific method procedures; cartridge conditioning; sample elution at ~ 10-15 mL/min and bottle/transfer tube rinsing - all with the proper volumes of methanol and then reagent water; nitrogen concentration followed by addition of 96:4% (vol/vol) methanol:water solution.
 3. Verify that all sample containers, centrifuge tubes, extract storage vials, autosampler vials, graduated cylinders, and pipettes used were polypropylene, or of polyethylene that meets all QC criteria.

Table 1. . Method 537 Initial Demonstration of Capability Quality Control Requirements

Method 537 Reference	Requirement	Specification and Frequency	Acceptance Criteria
Sect. 9.2.1	Demonstration of Low System Background	Analyze LRB prior to any other IDC steps.	Demonstrate that all method analytes are below 1/3 the MRL and that possible interferences from extraction media do not prevent the identification and quantification of method analytes.
Sect. 9.2.2	Initial Demonstration of Precision (IDP)	Analyze four to seven replicate LFBs fortified near the midrange calibration concentration.	%RSD must be < 20%
Sect. 9.2.3	Initial Demonstration of Accuracy (IDA)	Calculate average recovery for replicates used in IDP.	Mean recovery \pm 30% of true value
Sect. 9.2.4	Initial Demonstration of Peak Asymmetry Factor	Calculate the peak asymmetry factor using the equation in Section 9.3.9 for the first two eluting chromatographic peaks in a mid-level CAL standard.	Peak asymmetry factor of 0.8 - 1.5
Sect. 9.2.5	Minimum Reporting Level (MRL) Confirmation	Fortify, extract and analyze seven replicate LFBs at the proposed MRL concentration. Calculate the Mean and the Half Range (HR). Confirm that the upper and lower limits for the Prediction Interval of Result (Upper PIR, and Lower PIR, Sect.9.2.5.2) meet the recovery criteria.	Upper PIR \leq 150% Lower PIR \geq 50%
Sect. 9.2.6 and 9.3.10	Quality Control Sample (QCS)	Analyze a standard from a second source, as part of IDC.	Results must be within 70-130% of true value.
Sect. 9.2.7	Detection Limit (DL) Determination (optional)	Over a period of three days, prepare a minimum of seven replicate LFBs fortified at a concentration estimated to be near the DL. Analyze the replicates through all steps of the analysis. Calculate the DL using the equation in Sect. 9.2.7.1.	Data from DL replicates are <u>not required</u> to meet method precision and accuracy criteria. If the DL replicates are fortified at a low enough concentration, it is likely that they will not meet precision and accuracy criteria.

II. Preliminary Review

Preliminary review should be performed on the data, prior to embarking on the data validation. During this process, the reviewer should compile the necessary data package elements to ensure that all of the information needed to determine data usability is available.

- A. The reviewer should verify that the following information is identified in the sampling records (e.g., TR/COCs and field logs). Verify the complete list of samples is present with information on:
1. Sample matrix
 2. Field reagent blanks (and trip blanks of applicable)
 3. Field duplicates (if applicable)
 4. Field spikes (if applicable)
 5. Performance Evaluation (PE) samples (if applicable)
 6. Sampling dates
 7. Sampling times
 8. Shipping dates
 9. Preservatives
 10. Laboratory
 11. Signatures and dates for all transfer of custody
- B. The Laboratory Narrative is another source of general information, which includes notable problems with matrices; insufficient sample volume for analysis or reanalysis; samples received in broken containers; preservation information; and unusual events. The reviewer should also inspect any email or telephone/communication logs in the data package detailing any discussion of sample logistics, preparation, and/or analysis issues between the laboratory and the EPA.
- C. The reviewer should also have a copy of the Quality Assurance Project Plan (QAPP), lab specific Standard Operating Procedure (SOP), or similar documents, for the project for which samples were analyzed, to assist in the determination of final usability of the analytical data.
- D. In recognition of technological advances in analytical systems and techniques, the laboratory is permitted to modify the evaporation technique, separation technique, LC column, mobile phase composition, LC conditions and MS and MS/MS conditions. Changes may not be made to sample collection and preservation, the sample extraction steps, or to the quality control requirements. Method modifications should be considered only to improve method performance. Modifications that are introduced in the interest of reducing cost or sample processing time, but result in poorer method performance, should not be used. Analytes must be adequately resolved chromatographically in order to permit the mass spectrometer to dwell on a minimum number of compounds eluting within a retention time window. Instrumental sensitivity (or signal-to-noise)

will decrease if too many compounds are permitted to elute within a retention time window. In all cases where method modifications are proposed, the analyst must perform the procedures outlined in the initial demonstration of capability described in Sections 9.2 and 9.3 of Method 537, verify that all Quality Control acceptance criteria in this method are met, and that acceptable method performance can be verified in a real sample matrix.

- E. Extraction procedures must be consistent with EPA Method 537. Verify the SOP(s) for proper sample preparation such as the following:
1. Determined sample volume by marking the level of the sample on the bottle or by weighing the sample and bottle to the nearest 10 g.
 2. Performed solid phase extraction (SPE); cartridge conditioning; sample elution at ~ 10-15 mL/min; and bottle/transfer tube rinsing - all with the proper volumes of methanol and then reagent water; nitrogen concentration followed by addition of 96:4% (vol/vol) methanol:water solution, etc.
 3. Verify that all sample containers, centrifuge tubes, extract storage vials, and autosampler vials, graduated cylinders, and pipettes used were polypropylene, or of polyethylene that meets all QC criteria.
 4. Procedures for transferring of samples and extracts is as described in the method.
 5. If extraction procedures are not properly performed, use professional judgment on whether to qualify data as an estimate (J) or unusable (R).

III. Data Qualifies Definitions

The following definitions (Table 2) provide brief explanations of the national qualifiers assigned to results during the data review process. The reviewer should use these qualifiers as applicable. If the reviewer chooses to use additional qualifiers, a complete explanation of those qualifiers should accompany the data review, and they must be documented in the associated EPA-approved planning document.

Table 2. Data Qualifiers and Definitions

Data Qualifi	Definition
U	The analyte was analyzed for, but was not detected above the level of the reported sample quantitation limit.
J	The result is an estimated quantity. The associated numerical value is the approximate concentration of the analyte in the sample.
J+	The result is an estimated quantity. The associated numerical value is expected to have a positive or high bias.
J-	The result is an estimated quantity. The associated numerical value is expected to have a negative or low bias.
NJ	The analyte has been “tentatively identified” or “presumptively” as present and the associated numerical value is the estimated concentration in the sample.

UJ	The analyte was analyzed for, but was not detected. The reported quantitation limit is approximate and may be inaccurate or imprecise.
R	The data are unusable. The sample results are rejected due to serious deficiencies in meeting QC criteria. The analyte may or may not be present in the sample

IV. Data Review Narrative

The reviewer should complete a Data Review Narrative that includes comments that address the problems identified during the review process and state the limitations of the data. The sample numbers, analytical methods, extent of the problem(s), and assigned qualifiers should also be listed in the document.

METHOD SPECIFIC DATA REVIEW

I. Preservation and Holding Times

A. Review Items

Traffic Report/Chain of Custody (TR/COC) documentation, raw data, sample extraction sheets, and the Laboratory Narrative checking for: pH, preservatives, shipping container temperature, holding time, and other sample conditions.

B. Objective

The objective is to determine the validity of the analytical results based on the sample conditions and the holding time of the sample.

C. Criteria

1. The extraction technical holding time is determined from the date of sample collection to the date of sample extraction
2. Samples should be in proper condition with shipping container temperatures at ≤ 10 °C upon receipt at the laboratory. All samples shall be preserved prior to collection with TRIZMA to maintain a pH of 7.0. These preservative acts also to dechlorinate and as an anti-microbial agent, and maximizes the efficiency of the extraction. All samples shall be protected from light and refrigerated at ≤ 6 °C (but not frozen) from the time of receipt at the laboratory. Sample extracts shall be stored at room temperature from the time of the extraction completion until analysis.
3. The extraction technical holding time criteria for samples that are properly preserved is 14 days.
4. The analysis technical holding time criteria for extracts is 28 days and is determined from the date of sample extraction to the date of extract analysis.

D. Evaluation

1. Review the Laboratory Narrative and the TR/COC documentation to determine if the samples are received intact and iced. If there is an indication of problems with the samples, the sample integrity may be compromised.
2. Verify that the extraction dates and the analysis dates for samples on the reports match the respective extraction sheets and analytical run logs/analytical batch sheet.
3. Establish extraction technical holding times for samples by comparing the sample collection dates on the TR/COC documentation with the dates of extraction on the sample extraction sheets.
4. Determine the analysis technical holding times for samples after the completion of extraction by comparing the dates of extraction with the dates of analysis from the analytical run logs.

E. Action

1. If a sample is not properly preserved, extraction is performed outside the 14-day technical holding time, and/or the extract is analyzed outside the 28-day technical holding time, qualify detects and non-detects as estimated (J and UJ).
2. If technical holding times are grossly exceeded (greater than 28 days to extraction, or greater than 56 days to analysis), qualify detects as estimated (J) and qualify non-detects as unusable (R).
3. If a sample is not properly preserved, and if holding time is exceeded, analysts should consider qualifying the non-detects as unusable (R).

Table 3. Preservation and Holding Time Actions for PFAS Analysis

Preserved	Criteria	Action	
		Detect	Non-detect
No	≤ 14 days (for extraction) and ≤ 28 days (for analysis)	J	UJ
No	> 14 days (for extraction) and/or > 28 days (for analysis)	J	UJ
Yes	> 14 days (for extraction) and/or > 28 days (for analysis)	J	UJ
Yes/No	Holding time grossly exceeded > 28 days (for extraction) and/or > 56 days (for analysis)	J	R

II. Liquid Chromatograph/Mass Spectrometer Instrument Performance Check

A. Review Items

Chromatograms and calculations.

B. Objective

The objective of performing Liquid Chromatograph/Mass Spectrometer/Mass Spectrometer (LC/MS/MS) instrument peak symmetry factor check is to ensure adequate chromatography prior to analyzing any sequence of standards or samples.

C. Criteria

1. Run time, peak elution times, and injection volume must be consistent with method 537.
2. A minimum of 10 scans across the chromatographic peak in a mid-level CAL standard under optimized LC/MS/MS conditions is required to ensure adequate precision.

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3. When acquiring MS/MS data, LC operating conditions must be carefully reproduced for each analysis to provide reproducible retention times. If this is not done, the correct ions will not be monitored at the appropriate times. As a precautionary measure, the chromatographic peaks in each window must not elute too close to the edge of the segment time window.
 4. The peak symmetry factor check is performed on a mid-level calibration standard analysis and first two eluting peaks. A peak asymmetry factor must be calculated using the equation specified in Method 537 every time a calibration curve is generated.
 - a) If broad, split or fronting peaks are observed for the first two eluting chromatographic peaks (if only two analytes are being analyzed, both must be evaluated), the laboratory must change the initial mobile phase conditions to higher aqueous content until the peak asymmetry ratio for each peak is 0.8 – 1.5. Modifying the standard or extract composition to more aqueous content to prevent poor shape is not permitted.
 - b) The peak asymmetry ratio for each peak must be 0.8 – 1.5.

D. Evaluation

1. Verify run time, peak elution times, injection volume, and scans are consistent with Method 537.
2. Verify the peak symmetry factor check has been performed and meets criteria.
3. Evaluate peaks and calculations.

E. Action

1. If the peak symmetry factors have not been performed or do not meet criteria, use professional judgment to qualify detects and non-detects NJ/UJ/R.

III. Initial Calibration

A. Review Items

Quantitation reports and chromatograms.

B. Objective

The objective of initial calibration (ICAL) is to ensure that the instrument is capable of producing acceptable qualitative and quantitative data.

C. Criteria

1. ICAL shall be performed at the method specified frequency and sequence.
2. Each LC/MS/MS system must be calibrated to determine instrument sensitivity and the linearity of LC/MS/MS response for the target analytes and surrogates (SURs). At least five calibration concentrations are required to prepare the initial calibration curve spanning a 20-fold concentration range. Larger concentration ranges will require more calibration points.

Quadratic curves require 6 points. This curve must always be forced through zero and may be concentration weighted, if necessary.

3. ICAL standards must be analyzed prior to any analysis of the QCS, samples, and required blanks, and at the beginning of each analytical sequence, or as necessary if the continuing calibration check (CCC) acceptance criteria are not met.
4. When each calibration standard is calculated as an unknown using the calibration curve, the analyte results should be 70-130% of the true value for all except the lowest standard, which should be 50-150% of the true value.
5. The peak area counts for all internal standards (IS) in all injections must be within $\pm 50\%$ of the average peak area calculated during the initial calibration and 70-140% from the most recent CCC.
6. The relative percent difference (RPD) between the high and low areas for each IS must be $\leq 20\%$.
7. PFHxS, PFOS, NMeFOSAA, and NEtFOSAA may have multiple chromatographic peaks. All the chromatographic peaks observed in the standard must be integrated and the areas totaled.

D. Evaluation

1. Verify that the ICAL is performed at the specified frequency and sequence.
2. Verify the calculated target analyte and surrogate results are 50-150% of the true value for the lowest standard, and 70-130% of the true value for all other standards, when calculated back against the curve.
3. Verify that peak area counts for all ISs in all injections are within $\pm 50\%$ of the average peak area calculated during the initial calibration and 70-140% from the most recent CCC.
4. Verify that the RPD calculated between the high and low areas for each IS are $\leq 20\%$.
5. PFHxS, PFOS, NMeFOSAA, and NEtFOSAA may have multiple chromatographic peaks. All the chromatographic peaks observed in the standard must be integrated and the areas totaled.

E. Action

1. If the specified frequency and/or sequence is not met, check to see if it's still viable for the laboratory to reanalyze extracts that are still within holding time maximums.
2. If the %RPD is $>$ Maximum %RPD value in Table 4 for any IS, qualify detects in the associated samples as estimated (J). Use professional judgment to qualify non-detects in the associated samples.
3. No qualification of the data is necessary based on the SUR data alone. Use professional judgment to evaluate the SUR data in conjunction with the SUR recoveries to determine the need for data qualification.

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4. Based on the project-specific Data Quality Objectives (DQOs), a more in-depth review may be necessary. The following guidelines are recommended:
 - a) If the low-point of the ICAL curve is outside 50-150% of the true value:
 - (1) Qualify detects in the associated samples with analyte concentrations in the range between the lowest and second calibration standard as estimated (J).
 - (2) Detects in the associated samples with analyte concentrations within the calibration range should not be qualified.
 - (3) For low-point ICAL values below 50%, qualify non-detects as estimated (UJ), or use the next lowest point of the ICAL curve to determine the new quantitation limit.
 - (4) For low-point ICAL values above 150%, non-detects should not be qualified.
 - b) If any other point is outside 70-130% of the true value:
 - (1) Qualify detects in the associated samples with analyte concentrations in the non-linear range as estimated (J).
 - (2) Detects in the associated samples with analyte concentrations within the calibration range should not be qualified.
 - (3) Non-detects should not be qualified.
 - c) IS area counts for all ISs in all injections must be within $\pm 50\%$ of the average peak area calculated during the initial calibration and 70-140% from the most recent CCC.
 - d) If the RPD for any internal standard is $> 20\%$, qualify all associated data as estimated (J).
 5. PFHxS, PFOS, NMeFOSAA, and NEtFOSAA may have multiple chromatographic peaks. If not all of the chromatographic peaks observed in the standard are integrated and the areas totaled, qualify detects in the associated samples as estimated (J).
 6. Annotate the potential effects on the reported data due to exceeding the ICAL criteria in the Data Review Narrative.

Table 4. Concentration and Recent Recovery (%R), Acceptance Criteria in ICAL and CCC for PFAS Analysis

	Maximum %RPD (ICAL) peak counts	Opening/Closing CCC %R of true value¹
Target Analytes in ICAL/CCC (except low point)		70-130%
Low ICAL standard/Low CCC		50-150%
Internal Standards	20%	70-140% of the most recent CCC and within 50-150% from the average responses of the initial calibration
Surrogate Analyte Standards		70-130%

¹If a closing CCC is used as an opening CCC, all target analytes must meet the requirements for an opening CCC

Table 5. Initial Calibration Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-detect
Recalculated ICAL values > 130% of true value (except low-point)	J	No qualification
Recalculated ICAL values < 70% of true value (except low-point)	J	UJ
Recalculated low-point ICAL values > 150% of true value	J	No qualification
Recalculated low-point ICAL values < 50% of true value	J	UJ

Table 6. Initial Calibration Actions for Associated Target Analytes of Internal Standards in PFAS Analysis

Criteria	Action	
	Detect	Non-detect
Internal standard < 70% of the most recent CCC	J	UJ
Internal standard > 150% of the most recent CCC	J	No qualification
Internal Standard < 50% of the average responses of the initial calibration	J	UJ
Internal Standard > 150% of the average responses of the initial calibration	J	No qualification
RPD > 20% for Internal Standard	J	UJ

IV. Quality Control of Sample (QCS)

A. Review Items

Quantitation reports and chromatograms.

B. Objective

The objective is to ensure that the instrument is calibrated accurately to produce acceptable qualitative and quantitative data throughout each analytical sequence by the use of a second-source check standard.

C. Criteria

1. The QCS needs to be analyzed as part of the IDC, each time an analyte Primary Dilution Standard (PDS) is prepared, and at least quarterly or when preparing new standards as well as during the IDC.
2. The QCS standard must contain all required target analytes and surrogates, from an alternate source or a different lot than that used for the ICAL standards, at or near the mid-point concentration of the ICAL. SURs do not need to be from an alternate source.
3. Results must be within 70-130% of true value.

D. Evaluation

1. Verify that the QCS standard is analyzed at the specified frequency and sequence, and that it is associated with the correct ICAL. Also, verify that the correct ICAL is represented in the data package and meets criteria, as described in Section III.

2. Verify that the concentrations of the target analytes and the SURs in the QCS are at or near the mid-point standard from the ICAL.
3. Verify that the % recoveries (%R) for each target analyte and SUR are reported. Recalculate the % recoveries for at least one target analyte and SUR associated with each internal standard and verify that the recalculated values agree with the laboratory reported values.
4. Verify that the % recoveries are within the QCS %R limits in Table 7 for each target analyte and SUR.

E. Action

1. If the QCS is not performed at the specified frequency, use professional judgment to qualify detects and non-detects. The laboratory could repeat the analysis, if holding times have not expired and there are remaining sample vials. If reanalysis is not possible, carefully evaluate all other available information, including the quality of analyte peak shapes and mass spectral matches, the stability of internal standard Retention Times (RTs) and areas in each affected sample, and compare to the most recent calibration performed on the same instrument under the same conditions. Using this information and professional judgment, the reviewer may be able to justify unqualified acceptance of qualitative results.
2. If the QCS is not performed at the specified concentration, use professional judgment to qualify detects and non-detects. Special consideration should be given to sample results at the opposite extreme of the calibration range if this defect is noted.
3. If errors are detected in the calculations of the %R, perform a more comprehensive recalculation.
4. If the %R in an QCS is outside the limits in Table 7 for any target analyte, qualify detects as estimated (J) and non-detects as estimated (UJ).
5. No qualification of the data is necessary based on the SUR recovery alone. Use professional judgment to evaluate the SUR %R data in conjunction with the SUR recoveries to determine the need for data qualification.
6. Note the potential effects on the data due to QCS criteria exceedance in the Data Review Narrative.

Table 7. QCS Actions for PFAS Analysis

Criteria for QCS	Action	
	Detect	Non-detect
QCS not performed at the specified frequency and sequence	Use professional judgment	Use professional judgment
QCS not performed at the specified concentration	Use professional judgment	Use professional judgment
%R < 70%	J	UJ
%R < 10%	J	R

%R > 130%	J	No qualification
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V. Continuing Calibration Check (CCC)

A. Review Items

Quantitation reports and chromatograms.

B. Objective

The objective is to ensure that the instrument continues to meet the sensitivity and linearity criteria to produce acceptable qualitative and quantitative data throughout C

C. Criteria

1. The calibration for each LC/MS/MS system used for analysis must be verified at the beginning, after every 10 samples, and after the last sample. The beginning CCC of each analysis batch must be at or below the MRL in order to verify instrument sensitivity prior to any analyses. Subsequent CCCs should alternate between a medium and high concentration CAL standard. After the injection of all samples and required QC, but no more than 10 total injections of field samples, injection of the closing CCC is required. (Blanks, CCCs, LFBs, field duplicates, and matrix spikes are not counted as samples.) The closing CCC used to bracket the end of an analytical sequence may be used as the opening CCC for a new analytical sequence, provided that all technical acceptance criteria are met for an opening CCC.
2. The CCC standards must contain all required target analytes and SURs.
3. Recovery for each analyte and SUR must be within 70-130% of the true value for all but the lowest level of calibration. Recovery for each analyte in the lowest CAL level (beginning) CCC must be within 50-150% of the true value and the SUR must be within 70-130% of the true value.
4. No qualification of the data is necessary based on the SUR data alone. Use professional judgment to evaluate the SUR data in conjunction with the SUR recoveries to determine the need for data qualification.
5. Internal standard responses must be within 70-140% of the most recent CCC or within 50-150% from the average areas of the initial calibration.

D. Evaluation

1. Verify that the CCC is analyzed at the specified concentration and frequency (opening and closing and every 10 field samples), and that it is associated with the correct ICAL. Also, verify that the correct ICAL is represented in the data package and meets criteria, as described in Section III.
2. Verify that the appropriate concentration standards from the ICAL are used as an opening or a closing CCC, (low for opening; mid and high for subsequent CCCs).

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3. Verify that the concentration and %R for each target analyte and SUR are reported. Recalculate the concentration and recovery for at least one target analyte and SUR associated with each internal standard, and verify that the recalculated values agree with the laboratory reported values.
 4. For an opening CCC, verify that the concentrations are within the Opening CCC %R limits in Table 8 for each target analyte and SUR.
 5. For a closing CCC, verify that the concentrations are within the Closing CCC %R limits in Table 8 for each target analyte and SUR.
 6. Verify internal standard responses are reported and are within 70-140% of the most recent CCC and within 50-150% from the average responses of the initial calibration.

E. Action

1. If the CCC is not performed at the specified frequency, the laboratory could repeat the analysis if holding times have not expired. If reanalysis is not possible, carefully evaluate all other available information, including the quality of analyte peak shapes and mass spectral matches, the stability of internal standard RTs and areas in each affected sample, and compare to the most recent calibration performed on the same instrument under the same conditions. Using this information and professional judgment, the reviewer may be able to justify unqualified acceptance of qualitative results and qualification of all quantitative results as estimated (J). Otherwise, qualify all detects and non-detects as unusable (R).
2. If the CCC is not performed at the specified concentration, use professional judgment to qualify detects and non-detects.
3. If errors are detected in the calculations of the concentrations, perform a more comprehensive recalculation.
4. For a CCC outside the limits in Table 8 for any target analyte, qualify detects as estimated (J) and non-detects as estimated (UJ). If the %R is > 130%, do not qualify non-detects. If the %R is < 10%, qualify non-detects as unusable (R).
5. For internal standard responses that are not within the limits in Table 8 qualify detects as estimated (J) and non-detects as estimated (UJ). For internal standards that exceed the range, non-detects should not be qualified. If the %R is < 10%, qualify non-detects as unusable (R).
6. Note the potential effects on the data due to CCC criteria exceedance in the Data Review Narrative.

Table 8. CCC Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-detect
CCC not performed at the specified frequency and sequence	Use professional judgment J or R	Use professional judgment UJ or R
CCC not performed at the specified concentration	Use professional judgment	Use professional judgment
%R < 50% for target analyte, %R < 70% for SUR	J	UJ
%R < 70% %R < 50% for low CCC	J	UJ
%R < 10% for any CCC	J	R
%R > 130% %R > 150% for low CCC	J	No qualification
Internal standard responses < 70% of CCC or < 50% of ICAL average	J	UJ
Internal standard responses > 140% of CCC or > 150% of ICAL average	J	No qualification
Surrogates %R < 70%	Use professional judgment, J	Use professional judgment, UJ
Surrogates %R > 130%	Use professional judgment, J	No qualification

VI. Blanks

A. Review Items

Chromatograms and quantitation reports.

B. Objective

The objective of a blank analysis results assessment is to determine the existence and magnitude of contamination resulting from laboratory (or field) activities.

C. Criteria

The criteria for evaluation of blanks should apply to any blank associated with the samples (e.g., method or laboratory reagent blanks, field reagent blanks, etc.). If problems exist with any blank, all associated data must be carefully evaluated to determine whether or not there is an inherent variability in the data or if the problem is an isolated occurrence not affecting other data.

1. Laboratory Reagent blanks (LRB) must be performed at the specified frequency. An LRB must be extracted each time samples are extracted. The number of samples extracted with each LRB shall not exceed 20 field samples. The LRB must be extracted by the same procedure used to extract samples and analyzed on each LC/MS/MS system under the same conditions used to analyze associated samples.
2. Analysis of a field reagent blank is required if any field sample contains target analytes \geq MRL.
3. All blanks must meet the technical acceptance criteria for sample analysis.
4. The concentration of a target analyte in any blank must not exceed 1/3 the MRL, (Blank results $<$ MRL are determined by extrapolation from the curve.) If targets exceed 1/3 the MRL or if interferences are present, results for the subject analytes in the extraction batch are qualified.

D. Evaluation

1. Verify that LRBs are extracted at the specified frequency.
2. Verify that LRBs are extracted at the specified frequency.
3. Review the results of all associated blanks on the forms and raw data (chromatograms and quantitation reports) to evaluate the presence of target analytes and non-target compounds in the blanks.

E. Action

1. If the appropriate blanks are not extracted at the correct frequency, use professional judgment to determine if the associated sample data should be qualified. Obtain additional information from the laboratory, if necessary.

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2. Action regarding unsuitable blank results depends on the circumstances and origin of the blank. Verify that the data qualification decisions based on field QC are supported by the EPA approved QAPP, sampling plan, or EPA Regional SOP. At a minimum, contamination found in field blanks should be documented in the Data Review Narrative. In instances where more than one blank is associated with a given sample, qualification should be based upon a comparison with the associated blank having the highest concentration of a contaminant. Do not correct the results by subtracting any blank value.
 3. For any blank (including laboratory reagent blank), if a target analyte is detected, but it is not detected in the sample, non-detects should not be qualified (Table 9).

The following are examples of applying the blank qualification guidelines. Certain circumstances may warrant deviations from these guidelines.

Example 1: Sample result is greater than the MRL but is less than 10x multiple of the blank result.

Blank Result - 7
MRL - 10
Sample Result - 20
Final Sample Result - 20U

In this example the sample result is less than 70 (or 10 x 7) and would be qualified as not detected.

Example 2: Sample result is less than the MRL and is also less than the 10x multiple of the blank result.

Blank Result - 10
MRL - 5
Sample Result - 4J
Final Sample Result - 5U

Note that data are not reported as 4U, as this would be reported as a detection limit below the MRL. Also: Method 537 states that extrapolation below the curve for samples is not allowed (except for estimating blank contamination).

Example 3: Sample result is greater than the 10x multiple of the blank result.

Blank Result - 10
MRL - 5
Sample Result - 120
Final Sample Result – 120

The sample result exceeded the adjusted blank results of 100 (or 10 x10) and therefore are not qualified.

Table 9. Blank Actions for PFAS Analysis

Blank Result	Sample Result	Action
Detect	Non-detect	No qualification
< MRL	< MRL	Report at MRL and qualify as non-detect (U)
	$\geq 10x$ Blank Result	No qualification
\geq MRL	< MRL	Report at MRL and qualify as non-detect (U)
	\geq MRL and $\leq 10x$ Blank Result	Report at sample result and qualify as non-detect (U)
Gross contamination	Detect	Qualify as unusable (R)

VII. Surrogate (SUR) Analyte Standards

A. Review Items

Quantitation reports and chromatograms.

B. Objective

The objective is to evaluate SUR percent recovery (%R) to ensure that the analytical method is efficient.

C. Criteria

1. All samples and blanks are spiked with isotopically labeled SURs listed in Table 10 prior to the sample extraction procedure, to measure SUR %R. Although alternate SUR standards may be used provided they are isotopically labeled compounds with similar functional groups as the method analytes, the analyst must have documented reasons for using alternate SUR standards. The alternate SUR standards chosen must still span the water solubility range of the method analytes.
2. The %R for each SUR shall be calculated correctly according to the method.
3. The %R for each SUR in samples and blanks must be within the limits in Table 10.

D. Evaluation

1. Check the raw data (e.g., chromatograms and quantitation reports) to verify the recoveries of the surrogates.
2. Check for any calculation or transcription errors. Verify that the SUR recoveries were calculated correctly using the equation in the method and that the recalculated values agree with the laboratory reported values.

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3. Whenever there are two or more analyses for a particular sample, use professional judgment to determine which analysis has the most acceptable data to report. Considerations include, but are not limited to:
 - a) SUR recovery (marginal versus gross deviation).
 - b) Technical holding times.
 - c) Comparison of the target analyte results reported in each sample analysis.
 - d) Other QC information, such as performance of internal standards.
 - e) Surrogate recovery should be reported from the undiluted analysis.

E. Action

1. If a SUR was not added to the samples and blanks or the concentrations of SURs in the samples and blanks are not as specified, use professional judgment to qualify detects and non-detects.
2. If errors are detected in the calculations of %R, perform a more comprehensive recalculation. It may be necessary to have the laboratory resubmit the data after making corrections.
3. If any SUR %R is outside the method limits (Table 10) in samples, qualify all target analytes, considering the existence of interference in the raw data as indicated below and summarized in Table 11. Considerations include, but are not limited to:
 - a) If the SUR %R in the undiluted sample analysis is $< 10\%$, qualify detects as estimated (J) and non-detects as unusable (R).
 - b) If the SUR %R in the undiluted sample analysis is $\geq 10\%$ and $< 70\%$, qualify detects as estimated (J) and non-detects as estimated (UJ).
 - c) If the SUR %R in the diluted sample analysis is $< 70\%$, use professional judgment to qualify the detected analytes reported from the dilution analysis as estimates (J). (Non-detects should be reported from the undiluted analysis.)
 - d) If the SUR %R is $> 130\%$, qualify detects as estimated (J). Non-detects should not be qualified.
4. If any SUR %R is outside the method limits (Table 10) in a blank, special consideration should be taken to determine the validity of the associated sample data. The basic concern is whether the blank problems represent an isolated problem with the blank alone, or whether there is a fundamental problem with the analytical process.

For example, if one or more samples in the analytical sequence show acceptable SUR %R, the blank problem may be considered as an isolated occurrence.

Table 10. EPA Method 537 PFAS SUR Recovery Limits (Water)

Surrogates	Acronym	%R for Samples
Perfluoro-n-[1,2- ¹³ C ₂]hexanoic acid	¹³ C-PFHxA	70-130%
Perfluoro-n-[1,2- ¹³ C ₂]decanoic acid	¹³ C-PFDA	70-130%
N-deuterioethylperfluoro-1-octanesulfonamidoacetic acid	d5-NEtFOSAA	70-130%

Table 11. SUR Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-detect
% R < 10%	J	R
10% ≤ %R < Lower Acceptance Limit	J	UJ
%R < Lower Acceptance Limit (diluted sample analysis)	Use professional judgment	Not applicable*
%R > Upper Acceptance Limit	J	No qualification

* Non-detects should be reported from the undiluted analysis.

VIII. Laboratory Fortified Blank (LFB)

A. Review Items

Laboratory Narrative, QC results summaries, chromatograms and quantitation reports.

B. Objective

The objective of the LFB analysis is to evaluate whether the preparation and analysis procedures are being performed according to the method and to evaluate the accuracy of the analytical method and laboratory performance.

C. Criteria

1. An LFB shall be analyzed at least daily or one for each extraction batch of up to 20 samples.
2. The fortified concentration of the LFB must be rotated between low, medium, and high concentrations from batch to batch. The low concentration LFB must be as near as practical to, but no more than two times, the MRL. Similarly, the high concentration LFB should be near the high end of the calibration range established during the initial calibration.

3. Results of the low-level LFB analyses must be 50-150% of the true value. Results of the medium and high-level LFB analyses must be 70-130% of the true value.

D. Evaluation

1. Verify that LFB samples were analyzed at the required frequency.
2. Verify that the recalculated LFB %R values agree with the laboratory reported values.
3. Inspect the LFB %R and verify that they are within the limits listed in C. 3. above.

E. Action

1. If LFB samples were not analyzed at the specified frequency, use professional judgment to determine the impact on sample data, if any. Obtain additional information from the laboratory, if necessary. Record the situation in the Data Review Narrative. It is not likely that data qualification will be warranted if the frequency requirements are not met. Carefully consider all factors, known and unknown, about method performance on the matrix at hand, in lieu of LFB data.
2. If errors are detected in the calculations of the LFB %R, perform a more comprehensive recalculation.
3. If the LFB %R is outside the acceptance limits in C. 3. above, qualify the detects and non-detects in the associated samples as summarized in Table 12.

Table 12. LFB Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-detect
LFB not performed at the specified frequency or concentration	Use professional judgment	Use professional judgment
%R > 150% for low LFB, or >130% for medium or high LFB	J	No qualification
%R < 50% for low LFB, or <70% for medium or high LFB	J	UJ
%R < 10%	J	R

IX. Lab Fortified Sample Matrix (LFSM) (aka: Matrix Spike/Matrix Spike Duplicate)

A. Review Items

Laboratory Narrative, QC results summaries, chromatograms and quantitation reports.

B. Objective

The objective of the Matrix Spike (MS)/Matrix Spike Duplicate (MSD) analysis is to evaluate the effect of each sample matrix on the sample preparation procedures and the measurement methodology.

C. Criteria

1. One pair of MS/MSD samples should be analyzed per matrix or per batch. If an MSD is not analyzed, then a field duplicate sample (in a separate container) may be analyzed.
2. Samples identified as field blanks or QC samples cannot be used for spiked sample analysis.
3. The spike level for an analyte needs to be at least equal to or greater than the native amount in the sample for the measured recovery to be used to evaluate data quality.
4. The MS/MSD %R and the Relative Percent Difference (RPD) between MS and MSD results must be calculated according to the method.
5. The MS/MSD %R and RPD shall be within the acceptance limits in Table 13.

D. Evaluation

1. Verify that requested MS/MSD samples (or MS and duplicate sample) were analyzed at the required frequency.
2. Verify that a field blank or QC sample was not used for MS/MSD analysis.
3. Verify whether the spike level for an analyte is at least equal to or greater than the native amount in the sample. For analytes that have spike levels too low, the recovery is not used to assess data quality. Describe in the data validation narrative.
4. Verify that the recalculated MS/MSD %R and RPD values agree with the laboratory reported values.
5. Inspect the MS/MSD %R and RPD and verify that they are within the limits listed in Table 13.

E. Action

1. If MS/MSD samples (or MS and duplicate sample) were not analyzed at the specified frequency, use professional judgment to determine the impact on sample data, if any. Obtain additional information from the laboratory, if necessary. Record the situation in the Data Review Narrative. Carefully consider all factors, known and unknown, about method performance on the matrix at hand, in lieu of MS/MSD data.
2. If the spike level for an analyte is not at least equal to or greater than the native amount in the sample, do not use the recovery to assess data quality. Describe this fact in the Data Review Narrative.

3. If the MS/MSD %R or RPD is outside the acceptance limits in Table 13, qualify the detects and non-detects in the original source sample only to include the consideration of the existence of interference in the raw data. (In lieu of MS/MSD data, evaluate the sample and sample duplicate RPD in the same way MS/MSD RPDs are evaluated.) Considerations include, but are not limited to:
 - a) If MS/MSD %R is < 10%, qualify detects as estimated (J) and non-detects as unusable (R).
 - b) If the MS/MSD %R is $\geq 10\%$ and < the lower acceptance limit, qualify detects as estimated (J) and non-detects as estimated (UJ).
 - c) If the MS/MSD %R or RPD is > upper acceptance limit, qualify detects as estimated (J). Non-detects should not be qualified.
 - d) If the RPD of any analyte falls outside the designated range, and the laboratory performance for that analyte is shown to be in control in the CCC, the recovery is judged to be matrix biased. The result for that analyte in the unfortified sample is labeled suspect/matrix to inform the data user that the results are suspect due to matrix effects.

Table 13. MS/MSD %R and RPD Limits for PFAS Analysis

%R for high or medium level spike	%R for low level spike	RPD for high or medium level spike	RPD for low level spike
70 – 130%	50-150%	30%	50%

Table 14. MS/MSD Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-detect
%R < 10%	J	R
$10\% \leq \%R < \text{Lower Acceptance Limit}$	J	UJ
%R > Upper Acceptance Limit	J	No qualification
RPD > Upper Acceptance Limit	J	No qualification

X. Internal Standard

A. Review Items

Quantitation reports and chromatograms.

B. Objective

The objective is to evaluate the internal standard performance to ensure that LC/MS/MS sensitivity and response are stable during each analysis.

C. Criteria

1. The internal standard solution must be added to all samples and blanks at the specified concentration. The internal standard solution must contain all internal standard compounds specified in the method.
2. Peak area counts for quantitation ions of all ISs in all injections must be within $\pm 50\%$ of the average peak area calculated during the initial calibration and 70-140% from the most recent CCC.

D. Evaluation

1. Verify that all required internal standard compounds were added to sample and blank analyses at the specified concentrations.
2. Check the raw data (e.g., chromatograms and quantitation reports) to verify that the RT and area response of each internal standard compound in a sample or blank are reported.
3. Verify that the RTs and area responses for all internal standard compounds are within the specified criteria. If internal standard RTs are significantly different from the associated CCC or ICAL midpoint (i.e., more than 30 seconds), the internal standard peak may have been misidentified, but most likely a change in the chromatographic system should be suspected. This could be an improper injection, a leak in the LC system, or the effect of a highly contaminated matrix. Normally, the area counts will also suffer in this situation, but even if they appear unaffected, both quantitative and qualitative results should be considered highly suspect.
4. If there is a reanalysis for a particular sample, determine which analysis is the best data to report. Considerations include, but are not limited to:
 - a) Magnitude and direction of the internal standard area response shift.
 - b) Magnitude and direction of the internal standard RT shift.
 - c) Technical holding times.
 - d) Comparison of the values of the target analytes reported in each analytical run.
 - e) Other QC information.

E. Action

NOTE: Apply the action to the target analytes in samples or blanks that are associated to the noncompliant internal standard compound. The internal standards and the associated target analytes are in Table 15. (Verify these associations with the laboratory.)

1. If the required internal standard compounds were not added to a sample or blank, qualify detects and non-detects as unusable (R).
2. If the required internal standard compound was not analyzed at the specified concentration in a sample or blank, use professional judgment to qualify detects and non-detects.

3. If the area response of an internal standard compound in a sample or blank is < 70% of the area response of the same internal standard compound in the associated opening CCC and/or less than 50% of the average peak area calculated from the associated ICAL, qualify detects as estimated (J) and non-detects as UJ.
4. If the area response of an internal standard compound in a sample or blank is > 140% of the area response of the same internal standard compound in the associated opening CCC and/or greater than 150% of the average peak area calculated from the associated ICAL, qualify detects as estimated (J). Non-detects should not be qualified.
5. If the internal standard performance criteria are grossly exceeded, annotate the potential effects on the data in the Data Review Narrative.

Table 15. Internal Standards and Associated Target Analytes

Internal Standard (IS)	Acronym	Conc. of IS in sample (ng/μL)	Associated analytes and surrogates
Perfluoro-[1,2- ¹³ C ₂]octanoic acid	¹³ C-PFOA	1.0	PFOA, PFHxA, PFHpA, PFNA, PFDA, PFUnA, PFDoA, PFTrDA, PFTA, ¹³ C-PFHxA, ¹³ C-PFDA
Sodium perfluoro-1-[1,2,3,4- ¹³ C ₄]octanesulfonate	¹³ C-PFOS	3.0	PFOS, PFBS, PFHxS
N-deuteriomethylperfluoro-1-octanesulfonamidoacetic acid	d ₃ -NMeFOSAA	4.0	NMeFOSAA, NEtFOSAA, d ₅ -NEtFOSAA

Table 16. Internal Standard Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-detect
Area response < 70% of the most recent CCC and/or less than 50% of the average area calculated from the ICAL	J	UJ
Area response > 140% of the most recent CCC <i>or</i> > 150% average area calculated from the ICAL	J	No qualification

XI. Target Analyte Identification

A. Review Items

Quantitation reports, mass spectra, and chromatograms.

B. Objective

The objective is to provide acceptable LC/MS/MS qualitative analysis to minimize the number of erroneous analyte identifications.

C. Criteria

1. The precursor and product mass ions of the analyte from the sample analysis must match that of the same analyte in the associated opening CCC or mid-point standard from the associated ICAL according to the following criteria:
2. The Retention Time Window for a positively identified target analyte must be within the criteria established by the analyst. A value of plus or minus three times the standard deviation of the (RT obtained while establishing the initial calibration and completing the initial demonstration of capability can be used to calculate a suggested window size. However, the experience of the analyst should weigh heavily on the determination of the appropriate retention window size.

D. Evaluation

1. Verify that the positively identified target analyte precursor and product mass ions meets the specified criteria. Check peak shape and resolution. Although the presence of a co-eluting interferent may preclude positive identification of the analyte, the presumptive evidence of its presence may be useful information to include in the Data Review Narrative.
2. Verify that the RT of the positively identified target analyte meets the applied criteria.
3. Verify that peaks are correctly identified as target analytes, SURs, or internal standards on the chromatogram for samples and blanks.
4. Verify that there is no erroneous analyte identification, either false positive or false negative, for each target analyte. The positively identified target analyte can be more easily detected for false positives than false negatives. More information is available for false positives due to the requirement for submittal of data supporting positive identifications. Non-detected target analytes, on the other hand, are more difficult to assess.

E. Action

1. If the positively identified target analyte mass spectrum does not meet the specified criteria, use judgment to determine if target is present and should be qualified as an estimate (e.g., failure is caused by interference). Otherwise, qualify as non-detect (U) at the MRL or detected concentration, whichever is higher.
2. If the RT for a positively identified target analyte is outside the specified criteria, use judgment to determine if target is present and should be qualified as an estimate. Otherwise, qualify as non-detect (U) at the MRL or detected concentration, whichever is higher.
3. If it is determined that cross-contamination has occurred, use professional judgment to qualify detects. Annotate any changes made to the reported analytes due to either false positive or negative identifications or concerns regarding target analyte identifications in the Data Review Narrative.

XII. Target Analyte Quantitation

A. Review Items

Sample preparation sheets, initial calibration, QC summaries, quantitation reports, and chromatograms.

B. Objective

The objective is to ensure that the reported results and MRLs for target analytes are accurate.

C. Criteria

1. Target analyte results and the sample-specific MRLs must be calculated according to the method equations
2. Quantitation must be based on the quantitation ion (m/z) specified in the method for both the internal standards and target analytes. Target analyte results must be calculated using the linear or quadratic regression curves from the associated ICAL. Estimation of sample concentration below the lowest standard by curve extrapolation is not allowed by the method.
3. To account for linear and branched isomers, integration and quantitation of samples include peaks that represent both linear and branched isomers. Since there are currently no certified quantitative standards containing both linear and branched isomers that can be used to quantitate in the traditional manner, laboratories must use the following approach:
 - a) Calibrate instrumentation using a certified quantitative standard containing only the linear isomer.
 - b) Identify the branched isomers by analyzing a “qualitative/semi-quantitative” PFAS mixed standard that includes both linear and branched isomers and compare retention times and tandem mass spectrometry transitions.
 - c) Quantitate PFAS by integrating the total response (i.e., accounting for peaks that are identified as linear and branched isomers) and relying on the initial calibration with the linear-isomer quantitative standard.
4. PFHxS, PFOS, NMeFOSAA, and NEtFOSAA may have multiple chromatographic peaks. All the chromatographic peaks observed in the standard must be integrated and the areas totaled. Chromatographic peaks in a sample must be integrated in the same way as the standard.

D. Evaluation

1. Verify that the results for all positively identified analytes are calculated and reported by the laboratory.
2. Verify that reported results are within calibration ranges.

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3. Verify that the correct internal standard, quantitation ion, and initial calibration are used to calculate the reported results.
 4. Verify that the same internal standard, quantitation ion, and initial calibration are used consistently.
 5. Verify that the sample-specific MRLs and detected analyte results have been calculated and adjusted to reflect Percent Solids (%Solids), original sample mass/volume, and any applicable dilutions and reported accordingly.
 6. If the phases of a sample were separated and processed separately, no particular qualification on the grounds of matrix distribution is warranted.

E. Action

1. If errors are detected in results and MRL calculations, perform a more comprehensive recalculation.
2. It may be necessary to have the laboratory resubmit the data deliverable or portions thereof with corrections.
3. If a detected sample result is reported from an analysis with the response above the calibration range, qualify this result as estimated (J). The laboratory should have reanalyzed the extract or sample with further dilution. Check the data deliverable to see if this was done.
4. Sample results should not be reported < MRLs. Qualify as non-detect (U) at the MRL.

XIII. System Performance

A. Review Items

Chromatograms.

B. Objective

The objective is to ensure that the system is stable during the analytical sequence to produce quality data.

C. Criteria

There are no specific criteria for system performance

D. Evaluation

1. Abrupt discrete shifts in the baseline may indicate a change in the instrument sensitivity. A baseline “shift” could indicate a decrease in sensitivity in the instrument, possibly causing target compounds at or near the detection limit to miss detection. A baseline “rise” could indicate problems such as a leak or degradation of instrument components.
2. Poor chromatographic performance affects both qualitative and quantitative results. Indications of substandard performance include:

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- a) High background levels or shifts in absolute RTs of internal standards.
 - b) Excessive baseline rise.
 - c) Extraneous peaks.
 - d) Loss of resolution.
 - e) Poor peak shapes, e.g., tailing or widening, that may result in inaccurate quantitation.
3. A drift in instrument sensitivity may occur during a sequence and may be an indication of possible internal standard spiking problems. This could be discerned by examination of the internal standard area for trends such as a continuous or near-continuous increase or decrease in the internal standard area over time.

E. Action

1. Use professional judgment to qualify the data if it is determined that system performance has degraded during sample analyses.
2. Note any degradation of system performance which significantly affect the data.
3. If feasible, contact the laboratory for more information if needed.

XIV. Performance Evaluation Sample

A. Review Items

TR/COC documentation, preparation logs, instrument printouts, and raw data.

B. Objective

The objective is to determine the validity of the analytical results based on the recovery of the performance evaluation (PE) sample(s). The expected PE sample results are kept blind to the laboratory and is an external check of the laboratory's performance.

C. Criteria

Matrix-specific PE samples shall be analyzed utilizing the same analytical methods and Quality Assurance/Quality Control (QA/QC) procedures as employed for the samples, at a frequency to be determined by each EPA Region for each project. PE samples may be analyzed as part of an external laboratory accreditation program and/or with a batch of field samples for the project, using the same procedures, reagents and instrumentation.

D. Evaluation

1. Verify, using preparation logs, and raw data, that the PE samples were analyzed with the field samples and field blanks in the batch.

2. Verify that the PE sample results are within the warning limits (95% confidence interval) and action limits (99% confidence interval).
3. If a significant number (i.e., half or more) of the analytes in the PE samples fall outside of the 95% warning or 99% action criteria, or a number of false positive results are reported, evaluate the overall impact on the data.

E. Action

NOTE: If the PE sample criteria are not met, the laboratory performance and method accuracy are in question. Use professional judgment to determine if the data should be qualified or rejected. The following guidance is suggested for qualifying sample data associated with a PE sample that does not meet the required criteria.

For a PE sample that does not meet the technical criteria, apply the action to all samples in the same preparation batch. If the concentration of any analyte in a PE sample is not comparable to the analyte's concentration in the field samples or field blanks (i.e., it is much higher or much lower than the concentration in these samples), the action may be applied to only those samples in which the analyte's concentration is comparable to the PE sample concentration.

1. If the PE sample was not analyzed with the field samples and field blanks, use professional judgment to determine if the associated sample results should be qualified. Obtain additional information from the laboratory, if necessary. If a laboratory fails to analyze the PE sample(s) provided with field samples and field blanks, or if a laboratory consistently fails to generate acceptable PE sample results, record the situation in the Data Review Narrative.
2. If the PE sample results are outside the lower action limits, qualify detects and non-detects as estimated (J/UJ).
3. If the PE sample results are outside the upper action limits, qualify detects as estimated (J). Non-detects should not be qualified.
4. Annotate the potential effects on the data due to out-of-control PE sample results in the Data Review Narrative.

Table 17. PE Sample Actions for PFAS Analysis

Criteria	Action	
	Detect	Non-Detect
PE sample results outside lower action limits	J	UJ
PE sample results outside upper action limits	J	No qualification

XV. Regional Quality Assurance and Quality Control

A. Review Items

Chromatograms, TR/COC documentation, quantitation reports, and other raw data from QA/QC samples.

B. Objective

The objective is to use results from the analysis of EPA Regional QA/QC samples such as field duplicates, blind spikes, and blind blanks to determine the validity of the analytical results.

C. Criteria

Regional requirements are in addition to those described in the cited method. Criteria are determined by each EPA Region.

1. The frequency of EPA Regional QA/QC samples should be defined in the project QAPP.
2. Performance criteria for EPA Regional QA/QC samples should also be defined in the project QAPP.
3. The EPA Region may provide the laboratory with PE samples to be analyzed with each set of samples. These samples may include blind spikes and/or blind blanks. The laboratory must analyze a PE sample when provided by the EPA Region. Refer to Section VI, above, for blanks criteria. Refer to Section XIV, above, for PE samples criteria.
4. The RPD between field duplicates shall fall with the specific limits in the EPA Region's SOP or project QAPP.

D. Evaluation

1. Evaluation procedures must follow the EPA Region's SOP for data review.
2. Determine whether the results of EPA Regional QA/QC samples impact all samples in the project or only those directly associated (i.e., in the same batch, collected on the same day, prepared together, or contained in the same analytical sequence).
3. Calculate the RPD between field duplicates and provide this information in the Data Review Narrative. Also verify that the value falls within the specific limits in the EPA Region's SOP or project QAPP.
4. Determine whether poor precision is the fault of the laboratory, or a result of sample non-homogeneity in the field. Laboratory observations of sample appearance may become important in these situations.

E. Action

1. Any action must be in accordance with EPA Regional specifications and the criteria for acceptable field duplicate sample results.
2. In general, for EPA Regional QA/QC performance not within project plan specification, qualify detects as estimated (J) and non-detects as estimated (UJ). The impact on overall data quality should be assessed after consultation with the data user and/or field personnel.

XVI. Overall Assessment of Data

A. Review Items

Entire data package, data review results, project plans such as QAPPs and Sampling and Analysis Plan (SAP).

B. Objective

The objective is to provide the overall assessment on data quality and usability.

C. Criteria

1. Review all available materials to assess the overall quality of the data, keeping in mind the additive nature of analytical problems.
2. Reported analyte concentrations must be quantitated according to the appropriate equations, as listed in the method. All sample results must be within the linear calibration ranges per the cited method(s).

D. Evaluation

Examine the raw data to verify that the correct calculation of the sample results was reported by the laboratory. Analysis logs, instrument printouts, etc., should be compared to the reported sample results.

1. Evaluate any technical problems which have not been previously addressed.
2. Examine the raw data for any anomalies (e.g., baseline shift).
3. Verify that the appropriate method is used in sample analysis.
4. Verify that there are no transcription or reduction errors.
5. Verify that target analyte results fall within the calibrated ranges.
6. If the lab shortened the analytical run time, chromatography, resolution, coelution, scans per peak etc., may be impacted. Determine whether analyte identification or quantitation have been affected.
7. If appropriate information is available, use professional judgment to assess the usability of the data in order to assist the data user in avoiding inappropriate use of the data. Review all available information, including the QAPP (specifically the acceptance and performance criteria), SAP, and communication with the data user that concerns the intended use and desired quality of these data.

E. Action

1. Use professional judgment to determine if there is any need to qualify data which were not qualified based on the QC criteria previously discussed.

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2. If a sample is not diluted properly when sample results exceed the upper limit of the calibration range, qualify sample results as estimated (J).
 3. Use professional judgement on whether the reported results qualified as estimates from this review should be reported with positive/negative bias qualifiers as well (J+/J-).
 4. Write a Data Review Narrative to give the user an indication of the limitations of the analytical data.
 5. Note any inconsistency of the data with the Laboratory Narrative. If sufficient information on the intended use and required quality of the data is available, include an assessment of the usability of the data within the given context.

APPENDIX A: GLOSSARY

Analysis Date/Time – The date and military time (24-hour clock) of the injection of the sample, standard, or blank into the Liquid Chromatograph/Mass Spectrometer/Mass Spectrometer (LC/MS/MS) system.

Blank – An analytical sample that has negligible or unmeasurable amounts of a substance of interest. The blank is designed to assess specific sources of contamination. Types of blanks may include calibration blanks, instrument blanks, laboratory reagent blanks, and field blanks. See the individual definitions for types of blanks.

Calibration Factor (CF) – A measure of the Liquid Chromatographic response of a target analyte to the mass injected.

Case – A finite, usually predetermined number of samples collected over a given time period from a particular site.

Contamination – A component of a sample or an extract that is not representative of the environmental source of the sample. Contamination may stem from other samples, sampling equipment, while in transit, from laboratory reagents, laboratory environment, or analytical instruments.

Continuing Calibration Check (CCC) – A single parameter or multi-parameter standard solution prepared by the analyst and used to verify the stability of the instrument calibration with time, and the instrument performance during the analysis of samples. The CCC can be one of the calibration standards.

Surrogate Analyte Standards (SUR) – Compound added to every calibration standard, blank, and sample used to evaluate the efficiency of the extraction/purge-and-trap procedures, and the performance of the Liquid Chromatograph/Mass Spectrometer/Mass Spectrometer (LC/MS/MS) systems. SURs are isotopically labeled analogs of native target analytes. SURs are not expected to be naturally detected in the environmental media.

Field Blank – A blank used to provide information about contaminants that may be introduced during sample collection, sample shipment, and in the laboratory. A field blank includes trip blanks, rinsate blanks, bottle blanks, equipment blanks, preservative blanks, decontamination blanks, etc.

Field Reagent Blank – A blank used to provide information about contaminants that may be introduced during sample collection, sample shipment, and in the laboratory. Reagent water is poured from one pre-cleaned sample bottle to a second re-cleaned bottle while in the field, and delivered with the field samples from that site.

Field Sample – A portion of material to be analyzed that is contained in single or multiple containers and identified by a unique EPA sample number.

Initial Calibration – Analysis of analytical standards for a series of different concentrations; used to define the quantitative response, linearity, and dynamic range of the instrument to target analytes.

Instrument Blank – A blank designed to determine the level of contamination either associated with the analytical instruments, or resulting from carryover.

Internal Standards – Compounds added to every standard, blank, sample, or sample extract aliquot, at a known concentration, prior to analysis. Internal standards are used to monitor instrument performance and quantitation of target compounds.

Laboratory Control Sample (LCS) – A reference matrix spiked with target analytes at known concentrations. LCSs are analyzed using the same sample preparation, reagents, and analytical methods employed for the EPA samples received.

Laboratory Narrative – Portion of the data package which includes laboratory, contract and sample number identification, and descriptive documentation of any problems encountered in processing the samples, along with corrective action taken and problem resolution.

Laboratory Fortified Blank (LFB) - A volume of reagent water or other blank matrix to which known quantities of the method analytes and all the preservation compounds are added in the laboratory. The LFB is analyzed exactly like a sample, and its purpose is to determine whether the methodology is in control, and whether the laboratory is capable of making accurate and precise measurements.

Laboratory Reagent Blank (LRB) - An aliquot of reagent water or other blank matrix that is treated exactly as a sample including exposure to all glassware, equipment, solvents and reagents, sample preservatives, internal standard, and surrogates that are used in the analysis batch. The LRB is used to determine if method analytes or other interferences are present in the laboratory environment, the reagents, or the apparatus.

m/z – Mass-to-charge ratio; synonymous with “m/e”.

Matrix – The predominant material of which the sample to be analyzed is composed. For the purpose of this document, the sample matrix is either aqueous or non-aqueous.

Matrix Effect – In general, the effect of a particular matrix on the constituents under study. Matrix effects may affect purging/extraction efficiencies, and consequently affect Surrogate Analyte Standards (SUR) recoveries and cause interference for the qualitative and quantitative analyses of the target analytes.

Matrix Spike (MS) – Aliquot of the sample (aqueous/water or soil/sediment) fortified (spiked) with known quantities of specific compounds and subjected to the entire analytical procedure to indicate the appropriateness of the method for the matrix by measuring recovery.

Matrix Spike Duplicate (MSD) – A second aliquot of the same sample as the Matrix Spike (MS) (above) that is spiked in order to determine the precision of the method.

Minimum Reporting Level (MRL) – The minimum concentration that can be reported as a quantitated value for a method analyte in a sample following analysis. This defined concentration can be no lower than the concentration of the lowest calibration standard for that analyte and can only be used if acceptable QC criteria for this standard are met.

Percent Difference (%D) – The difference between two values calculated as a percentage of one of the values.

Percent Relative Standard Deviation (%RSD) – The Percent Relative Standard Deviation is calculated from the standard deviation and mean measurement of either Relative Response Factors (RRFs) or Calibration Factors (CFs) from initial calibration standards. Percent Relative Standard Deviation indicates the precision of a set of measurements.

Precursor Ion – For the purpose of this method, the precursor ion is the deprotonated molecule ($[M-H]^-$) of the method analyte. In MS/MS, the precursor ion is mass selected and fragmented by collisionally activated dissociation to produce distinctive product ions of smaller m/z .

Primary Dilution Standard (PDS) – The analyte PDS contains all the method analytes of interest at various concentrations in methanol containing 4% water. The ESI and MS/MS response varies by compound; therefore, a mix of concentrations may be needed in the analyte PDS. The analyte PDS is prepared by dilution of the combined Analyte Stock Standard Solutions and is used to prepare the CAL standards, and fortify the LFBs, the LFSMs, the LFSMDs and FDs with the method analytes.

Product Ion - For the purpose of this method, a product ion is one of the fragment ions produced in MS/MS by collisionally activated dissociation of the precursor ion.

Quality Control Sample (QCS) – Analysis of the calibration standard from an alternate source or a different lot than that used for the initial calibration (ICAL) standards at the mid-point CS3 concentration of the ICAL standards to ensure the instrument is calibrated accurately.

Reconstructed Ion Chromatogram (RIC) – A mass spectral graphical representation of the separation achieved by a Liquid Chromatograph (LC); a plot of total ion current versus Retention Time (RT).

Relative Percent Difference (RPD) – The relative percent difference is based on the mean of the two values, and is reported as an absolute value (i.e., always expressed as a positive number or zero).

Relative Response Factor (RRF) – A measure of the mass spectral response of an analyte relative to its associated internal standard. RRFs are determined by analysis of standards and are used in the calculation of concentrations of analytes in samples.

Relative Retention Time (RRT) – The ratio of the Retention Time (RT) of a compound to that of a standard (such as an internal standard).

Resolution – Also termed *Separation* or *Percent Resolution*, the separation between peaks on a chromatogram, calculated by dividing the depth of the valley between the peaks by the peak height of the smaller peak being resolved, multiplied by 100.

Retention Time (RT) – The time a target analyte is retained on a Liquid Chromatograph (LC) column before elution. The identification of a target analyte is dependent on a target analyte's RT falling within the specified RT window established for that analyte. The RT is dependent on the nature of the column's stationary phase, column diameter, temperature, flow rate, and other parameters.

Sample Delivery Group (SDG) – A group of samples that are delivered together to the laboratory.

Sample Number (EPA Sample Number) – A unique identification number designated by the EPA to each sample. An EPA Sample Number appears on the Traffic Report/Chain of Custody (TR/COC) which documents information on that sample.

Storage Blank – Reagent water (two 40.0 mL aliquots) or clean sand stored with samples in a Sample Delivery Group (SDG). It is analyzed after all samples in an SDG have been analyzed. It is used to determine the level of contamination acquired during storage.

Surrogates (Surrogate Standard) – Compounds added to every blank, sample [including Laboratory Control Sample (LCS)], Matrix Spike/Matrix Spike Duplicate (MS/MSD), and standard. Surrogates are added to the sample and subjected to the entire analytical procedure. Surrogates are used to evaluate analytical efficiency by measuring recovery. Surrogates are not expected to be detected in environmental media.

Target Analyte List (TAL) – A list of analytes designated for analysis.

Technical Holding Time – The maximum length of time that a sample may be held from the collection date until extraction and/or analysis.

Traffic Report/Chain of Custody Record (TR/COC) – An EPA sample identification form completed by the sampler, which accompanies the sample during shipment to the laboratory and is used to document sample identity, sample chain of custody, sample condition, and sample receipt by the laboratory.

Trip Blank – A blank used to provide information about contaminants that may be introduced during sample transport.

APPENDIX B: Table 18. Compounds analyzed by EPA Method 537

Table 18. Compounds analyzed by EPA Method 537

<u>Analyte</u>	<u>Acronym</u>	<u>Chemical Abstract Services Registry Number (CASRN)</u>
N-ethyl perfluorooctanesulfonamidoacetic acid	NEtFOSAA	—
N-methyl perfluorooctanesulfonamidoacetic acid	NMeFOSAA	—
Perfluorobutanesulfonic acid	PFBS	375-73-5
Perfluorodecanoic acid	PFDA	335-76-2
Perfluorododecanoic acid	PFDoA	307-55-1
Perfluoroheptanoic acid	PFHpA	375-85-9
Perfluorohexanesulfonic acid	PFHxS	355-46-4
Perfluorohexanoic acid	PFHxA	307-24-4
Perfluorononanoic acid	PFNA	375-95-1
Perfluorooctanesulfonic acid	PFOS	1763-23-1
Perfluorooctanoic acid	PFOA	335-67-1
Perfluorotetradecanoic acid	PFTA	376-06-7
Perfluorotridecanoic acid	PFTTrDA	72629-94-8
Perfluoroundecanoic acid	PFUnA	2058-94-8