Validation of LC-MS/MS High Explosive Analytical Data

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Hazard Class: ☒ Low ☐ Moderate ☐ High/Complex
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The Responsible Manager has determined that the following organizations' review is required for initial procedure release as well as subsequent major revisions. Review documentation is contained in the Document History File.

Technical Leads Quality Assurance

Classification Review: ☒ Unclassified ☐ UCNI ☐ Classified

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REVISION HISTORY

Document No./Revision No.	Issue Date	Action	Description
OIO-TP-5168, Rev. 0.1	4/20/2016	Minor Revision	Periodic Review, changed Document type and Organization. Replacing SOP-5168.
ER-AP-20316, R0	4/24/2017	Major Revision	Revised to reflect the guidance from the National Functional Guidelines for Organic Methods Data Review, January 2017 (EPA-540-R-2017-002) holding time requirements and remove NNSA Model Validation

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1. PURPOSE

This procedure represents the minimum standards for evaluating high-explosives analytical data that were analyzed using liquid chromatography – mass spectrometry/mass spectrometry (LC-MS/MS) methods.

2. SCOPE

This document is intended to assist in the technical review of analytical data generated by environmental laboratories. Qualification of data is the product of data validation, analytical laboratory analysis, and focused validation that describe validation anomalies and their consequences.

3. BACKGROUND

Data qualifiers and reason codes are assigned to analytical results from high explosive organic compound analyses according to the specifications in this method-specific procedure. These guidelines are developed using the EPA method-specific data quality criteria and/or National Functional Guidelines for Organic Data Review.

4. PRECAUTIONS AND LIMITATIONS

Nothing in this procedure precludes the data validator from going beyond the minimum requirements specified within this procedure. If additional directions are required, the data validator shall reference the EPA method-specific guidelines, and/or EPA National Functional Guidelines for Organic Data Review. Implementation of this procedure may be followed by a more focused and data-use−specific evaluation of the data by the project chemist, especially if the implementation of this procedure indicates the data may contain technical deficiencies.

5. PREREQUISITE ACTIONS

Data Validators must:

- Possess a minimum of a bachelor's degree in chemistry or one of the physical sciences and either two (2) years of experience in generating analytical data in an environmental analytical laboratory OR two (2) years of data validation experience.
- Complete Attachment 1, Data Validation Cover Sheet, and Attachment 2, LC-MS/MS High-Explosive Analytical Data Validation Checklist, during data validation.

6. PERFORMANCE

6.1 Validation Process

EIM applies a subset of qualifiers described in this procedure to analytical data using auto-validation subroutines. EIM auto-validation applies qualification to analytical records using tests listed in Attachment 2 that have a Valid Reason Description containing "(AV)". When the project leader requests a focused validation the assigned data validator completes the following steps to assess all potential analytical data qualification:

[1] **REVIEW** the qualifiers assigned during EIM auto-validation to verify that qualifiers were assigned consistently with this procedure. If auto-validation qualification is found to be inconsistent with this procedure then the validator initiates a change request using ER-AP-20304, Change Control for Data in the Environmental Information Management (EIM) Database.

[2] **PRINT** Attachment 1 and **REVIEW** the data package for potential qualification using Attachment 2.

[3] **NOTE** conditions causing recommendation for qualification and options for qualification.

[4] **COMPLETE** Attachment 1 and **FORWARD** to the project leader with conditions and options.

The project leader is the responsible party for making the decision of record if validation qualifiers should be assigned and EIM validation records updated. This record of decision is added to comments section of Attachment 1.

Once the decision of record has been made, Attachment 1 is sent to the Sample Management Office (SMO) staff. The SMO staff re-print the data validation record from EIM and add Attachment 1 that includes the record of decision to the final records package.

6.2 Analyte Quantitation

The assignment of the detection status to analytical measurements is the first step of analytical data validation. Most validation qualifiers and validation reason codes are applied based on the measurement's initial detection status. Results that are less than the report method detection limit (RMDL) are qualified as nondetect with the U validation qualifier. Results greater than or equal to the RMDL and less than the report detection limit (RDL) are qualified as detected and estimated with the J validation qualifier. Results greater than or equal to the RDL are qualified as detected with the NQ validation qualifier.

Criteria	Validation Qualifier	Validation Reason Code
Target analyte result is < RMDL; a nondetect	U	U_LAB
Target analyte result is ≥ RMDL and < RDL; a detect	J	J_LAB
Target analyte result is ≥ RDL; a detect	NQ	NQ

Since a result can have only one validation qualifier and one validation reason code the sequencing of validation steps is important. Analyte quantitation occurs first, then analyte identification, because most other validation functions depend on the correct identification and quantitation of the analytical parameter. When two or more qualifiers can be applied to a record, the qualifier representing the more severe consequence to data usability supersedes the qualifier with less severe consequence. The R validation qualifier has the greatest impact on data usability and supersedes other validation qualifiers.

6.2 Analyte Quantitation (continued)

Order Of Severity	Validation Qualifier	Description
1	R	The reported sample result is classified as rejected due to serious noncompliance regarding quality control acceptance criteria. The presence or absence of the analyte cannot be verified.
2	UJ	The analyte is classified as not detected, with an expectation that the reported result is more uncertain than usual.
3	U	The analyte is classified as not detected.
4	J	The analyte is classified as detected but the reported concentration value is expected to be more uncertain than usual.
5	NQ	No validation qualifier flag is associated with this result, and the analyte is classified as detected.

LANL project chemists may identify quality deficiencies in analytical results affecting analyte quantitation. These deficiencies can include analytical results with detection limits elevated above project data-quality objectives, concentrations above the calibration range of the instrument or method, results exhibiting carryover or detector contamination, large relative percent difference between dual-column detects, chromatographic interference from another analyte, and other quality deficiencies. The reason codes of HE15 or HE19 are applied to affected records by the project chemist to identify these quality deficiencies when they are identified.

6.3 Analyte Identification

The identification of an analytical parameter is the second step of analytical data validation. Identification of high-explosive organic compounds depends upon the relative retention time of the compound of interest to the known retention time of the compound in the calibration standard, and the relative intensity of the mass spectrum of the compound of interest in a sample to the known intensity of the compound in a calibration standard. When mass spectral analyte identification criteria are not met the HE8 series of reason codes are applied to affected parameters. When relative retention time criteria are not met the HE0 series of reason codes are applied to affected parameters.

6.4 Holding Times and Sample Preservation

Sample handling requirements are specified to ensure integrity and defensibility of analytical measurements. Samples are to be prepared and analyzed within specified time limits. Samples are also preserved chemically and physically by controlling temperature and light. When sample handling requirements are not met the HE9 series of reason codes are applied to affected samples.

6.5 Initial and Continuing Calibration

Calibration is performed to set the operating range of the instrument and to ensure that the instrument is performing within specifications. The initial calibration and verification is performed prior to the start of analyses. Continuing calibration checks and instrument performance samples are performed periodically during analysis to ensure the instrument is providing accurate results. When initial calibration criteria are not met the HE7 series of reason codes are applied to affected analytes in all samples analyzed after the unacceptable initial calibration to the next acceptable initial calibration for that instrument. When continuing calibration criteria or are not met the HE7 series of reason codes are applied to affected analytes in all samples analyzed after the unacceptable continuing calibration to the next acceptable continuing calibration for that instrument. When instrument performance checks do not meet criteria the HE16 series of qualifiers are applied to affected analytes in all samples analyzed after the unacceptable instrument performance check to the next acceptable instrument performance check for that instrument.

6.6 Surrogates

Surrogates are compounds not normally found in the environment, but which have quantitation limits and retention times similar to the analytes of interest in a sample. Surrogates are added to samples, standards, and QC samples to determine the effectiveness of analyte quantitation. Sample results are not adjusted based on surrogate recoveries. When surrogate recovery criteria are not met the HE3 series of reason codes are applied to affected samples.

6.7 Internal Standards

Internal standards are compounds not normally found in the environment, but which are easily measurable. They are added to samples, standards, and QC samples to compensate for fluctuations in the analytical system. Sample results are quantitated or adjusted by the relative response of associated internal standards. When internal standard criteria are not met the HE1 series of reason codes are applied to the affected sample.

6.8 Blanks

The Method Blank is an analyte-free matrix that is prepared and analyzed in the laboratory with the samples. The method blank determines contamination from the analytical processes. Method blanks are prepared with every preparation batch. If more than one method blank is associated with a given sample, qualification is based upon a comparison with the associated blank having the highest concentration of the parameter. When method blank criteria are not met the HE4 series of reason codes are applied affected samples.

6.9 Matrix Spike and Laboratory Control Samples

The laboratory control sample is created by adding known amounts of parameters of interest to an aliquot of a blank matrix. The laboratory control sample is used to evaluate the effect of the analytical process of the recovery of analytes. When laboratory control sample criteria are not met the HE12 series of reason codes are applied to all associated samples.

The matrix spike is created by adding known amounts of parameters of interest to an aliquot of a sample matrix. The matrix spike is used to evaluate the effect of the sample matrix on the recovery of analytes. When matrix spike criteria are not met the HE12 series of reason codes are applied to all associated samples.

7. RECORDS

Records generated by this procedure will be submitted to the Environmental Protection Records Management Office for document management in accordance with Institutional Records Management Procedure, P1020-1 and EP-AP-10003, Records Management.

- Completed Data Validation Cover Sheets (Attachment 1)
- Completed LC-MS/MS High-Explosive Analytical Data Validation Checklist (Attachment 2)

8. REFERENCES

EP-AP-10003, Records Management

ER-AP-20304, Change Control for Data in the Environmental Information Management (EIM) Database

P1020-1, Laboratory Records Management

9. ATTACHMENTS

Attachment 1: Data Validation Cover Sheet
Attachment 2: LC-MS/MS High-Explosive Analytical Data Validation Checklist

ATTACHMENT 1

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Data Validation Cover Sheet

Section I.

Request Number: _____ Validation Date: _____ Lab Code: _____

Contract Laboratory Name: _____

Validator: _____ Organization: _____

Analytical Suite (Check All That Apply):

☐ **TPH-GRO** ☐ **High Explosives** ☐ **Dioxin Furans** ☐ **LCMSMS Perchlorates**

☐ **TPH-DRO** ☐ **Metals & Cyanide** ☐ **PCB Congeners** ☐ **Organochlorine Pesticides/Polychlorinated Biphenyls**

☐ **General Chemistry** ☐ **Radiochemistry** ☐ **LCMSMS High Explosives**

☐ **Other (Describe):** _____

_____

Section II. Completeness Check

YES	NO	N/A	(check one)	YES	NO	N/A	(check one)
☐	☐	☐	1. Chain-Of-Custody Form(S)	☐	☐	☐	6. Raw/BSS Data
☐	☐	☐	2. Case Narrative	☐	☐	☐	7. Quality Control Forms
☐	☐	☐	3. Sample Result Forms	☐	☐	☐	8. Quantitation Reports
☐	☐	☐	4. Sample Chromatograms	☐	☐	☐	9. TICS Forms
☐	☐	☐	5. Standard Chromatograms	☐	☐	☐	10. TICS Mass Spectra

Comments/problems noted (include information about requests for further information submitted to the contract laboratory and agreed-upon date of resolution and contract laboratory point of contact):

Validator's Signature: _____ Date: _____

ER-AP-20316, R0	Los Alamos Environmental Safety & Health
	(Attach additional comment sheets as necessary)

ATTACHMENT 2

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LC-MS/MS High-Explosive Analytical Data Validation Checklist

(Check One)				Assign Qualifier Listed Below If Criterion = Yes	
Yes	No	N/A		Nondetected Analyte	Detected Analyte
Holding Time and Sample Preservation					
☐	☐	☐	1. The preserved aqueous sample was extracted > 7-day holding time and ≤ 14-days. (AV)	UJ, HE9	J-, HE9
			2. The preserved non-aqueous sample was extracted > 14-day holding time and ≤ 28-days. (AV)	UJ, HE9	J-, HE9
			3. The sample extract was analyzed > 40-day holding time and ≤ 80-days. (AV)	UJ, HE9	J-, HE9
			4. The sample was extracted or the extract was analyzed > 2x holding time. (AV)	R, HE9a	J-, HE9a
Calibration – Initial and Continuing					
☐	☐	☐	5. The affected results were not analyzed with a valid 5-point calibration curve and/or a standard at the reporting limit.	UJ, HE7	J, HE7
☐	☐	☐	6. The affected analytes were analyzed with an initial calibration curve that exceeded the percent relative standard deviation (%RSD) criteria, and/or the associated multipoint calibration correlation coefficient is less than 0.99.	UJ, R, HE7a	J, HE7a
☐	☐	☐	7. The affected analytes were analyzed with a relative response factor (RRF) of <0.05 in the initial calibration and/or continuing calibration verification (CCV).	UJ, R, HE7b	J, HE7b
☐	☐	☐	8. The initial calibration verification (ICV) and/or CCV were recovered outside the method limits.	UJ, R, HE7c	J, HE7c
☐	☐	☐	9. The ICV and/or CCV were not analyzed at the appropriate method frequency.	UJ, R, HE7d	J, HE7d
☐	☐	☐	10. Required calibration information is missing, or samples were analyzed on an expired calibration. Contact the SMO or external laboratory for information.	R, HE7f	R, HE7f
☐	☐	☐	11. The contract-required detection limit check standard (CRI) sample did not pass method acceptance criteria.	UJ, R, HE16	J, HE16
☐	☐	☐	12. The required CRI sample information is missing. Contact the SMO or external laboratory for information.	R, HE16c	R, HE16c

ATTACHMENT 2

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(Check One)				Assign Qualifier Listed Below If Criterion = Yes	
Yes	**No**	**N/A**		**Nondetected Analyte**	**Detected Analyte**
Blanks					
☐	☐	☐	13. The sample result is ≤5 times the concentration of the related analyte in the method blank. (AV)	N/A	U, HE4
☐	☐	☐	14. The affected analytes are considered estimated and biased high because this analyte was identified in the method blank but was >5 times the concentration in the method blank. (AV)	N/A	J+, HE4a
☐	☐	☐	15. The sample result is ≤5 times the concentration of the related analyte in the trip blank, rinsate blank, and/or equipment blank. (AV)	N/A	U, HE4d
☐	☐	☐	16. Required method-blank information is missing. Data may not be acceptable for use. Contact the SMO or external laboratory for information.	R, HE4e	R, HE4e
☐	☐	☐	17. The absence of sample carryover must be determined and verified.	N/A	R, HE4f
Analyte Identification					
☐	☐	☐	18. The internal standard (IS) retention time has shifted by more than 30 seconds.	R, UJ, HE0	J, HE0
☐	☐	☐	19. Required IS retention time documentation is missing. Data may not be acceptable for use. Contact the Sample Management Office (SMO) or external laboratory for information.	R, HE0b	R, HE0b
☐	☐	☐	20. The affected analyte is considered not detected because mass spectrum did not meet specifications.	N/A	U, HE8
☐	☐	☐	21. The mass spectrum column documentation is missing. Data may not be acceptable for use. Contact the SMO or external laboratory for information.	R, HE8a	R, HE8a

ATTACHMENT 2

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(Check One)				Assign Qualifier Listed Below If Criterion = Yes	
Yes	**No**	**N/A**		**Nondetected Analyte**	**Detected Analyte**
Internal Standards					
☐	☐	☐	22. The quantitating IS area count is <25% of the expected value, which indicates increased potential for false negative results and other possible problems with sample quantitation. Follow the method-specific windows.	R, HE1a	J, HE1a
☐	☐	☐	23. The IS area count for the quantitating IS is <70% but >25% of the average of that obtained from the calibration standards.	UJ, HE1b	J+, HE1b
☐	☐	☐	24. The IS area count for the quantitating IS is >130% of the average of that obtained from the calibration standards.	UJ, HE1c	J-, HE1c
☐	☐	☐	25. Required IS information is missing. Data may not be acceptable for use. Contact the SMO or external laboratory for information.	R, HE1d	R, HE1d
Surrogates					
☐	☐	☐	26. The surrogate is <10 percent recovery (%R). Follow the external laboratory limits.	R, HE3	J-, HE3
☐	☐	☐	27. The surrogate is less than the lower acceptance limit but ≥10%R. Follow the external laboratory limits.	UJ, HE3a	J-, HE3a
☐	☐	☐	28. The surrogate %R value is greater than the upper acceptance limit. Follow the external laboratory limits.	N/A	J+, HE3b
☐	☐	☐	29. At least one surrogate is greater than the upper acceptance limit, and one surrogate is less than the lower acceptance limit. Follow the external laboratory limits.	UJ, HE3c	J, HE3c
☐	☐	☐	30. Required surrogate information is missing. Data may not be acceptable for use. Contact the SMO or external laboratory for information.	R, HE3d	R, HE3d

ATTACHMENT 2

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(Check One)				Assign Qualifier Listed Below If Criterion = Yes	
Yes	No	N/A		Nondetected Analyte	Detected Analyte
Laboratory Control Samples					
☐	☐	☐	31. The laboratory control sample (LCS) %R was <10%. Follow the external laboratory limits. (AV)	R, HE12	J-, HE12
☐	☐	☐	32. The LCS %R was less than the lower acceptance limit but >10%. Follow the external laboratory limits. (AV)	UJ, HE12a	J-, HE12a
☐	☐	☐	33. The LCS %R was greater than the upper acceptance limit. Follow the external laboratory limits. (AV)	N/A	J+, HE12b
☐	☐	☐	34. The LCS documentation is missing. Data may not be acceptable for use. Contact the SMO or external laboratory for information.	R, HE12c	R, HE12c
Matrix Spikes					
☐	☐	☐	35. The matrix spike / matrix spike duplicate (MS/MSD) %R was <10%. (AV)	R, HE12d	R, HE12d
☐	☐	☐	36. The MS/MSD %R was >10% but <70%. (AV)	UJ, HE12e	J, HE12e
☐	☐	☐	37. The MS/MSD %R was >130%. (AV)	N/A	J+, HE12f
☐	☐	☐	38. The MS/MSD relative percent difference was >30%.	UJ, HE12g	J, HE12g
Analyte Quantitation					
☐	☐	☐	39. The non-detected analytes have elevated detection limits and may not meet project data-quality objectives because the sample was diluted without any target analytes identified as a result of matrix interference. Reject non-detected results if the analytical laboratory cannot provide proof for matrix interference.	UJ, R, HE15	NA
☐	☐	☐	40. The sample was diluted because target analytes were greater than the initial verification calibration.	UJ, HE15a	J, HE15a
☐	☐	☐	41. The Los Alamos National Laboratory (LANL) project chemist identified quality deficiencies in the reported data that require further qualification. This code can ONLY be used under advisement of the LANL project chemist.	UJ, R, HE19	J, R, HE19
☐	☐	☐	42. Qualification of data via data validation did occur, however no data quality control requirements in this procedure were applicable. Adhere to the external laboratory qualifiers found within the Form 1 analytical data summary sheets generated by the external laboratory. (AV)	U, U_LAB	J, J_LAB NQ, NQ (No qualification)