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# INTERIM STANDARD

## VOLUME 1 MODULE 4

### QUALITY SYSTEMS FOR CHEMICAL TESTING

#### SECTIONS 1.5.1 AND 1.5.2

September 2015

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#### **Description**

The Voting Draft Standard, dated May 2015, has been voted on and subsequently modified as a result of persuasive comments received from the voting members. This resulting Interim Standard is now presented for voting.

The changes from the Voting Draft Standard, in response to persuasive comments, are shown through tracking.

A preamble is included that is NOT part of the standard.

**NOTE: Only those changes, or voters' comments that were made on the changes (shown through tracking) are subject to Interim Standard voting. The remaining text, having received no comments at the Voting Draft Standard stage, is final.**

### **Preamble to revised language for LOD and LOQ**

The following is not part of the standard, but instead explains the Chemistry Committee's rationale for the changes to the standard.

1. Why is a change to the current LOD language needed?  
The definition for LOD in the TNI standard is "The minimum result which can be reliably discriminated from a blank with a predetermined confidence level."  
The current requirements for LOD are that all sample processing steps be included in the determination of the LOD, and that the LOD shall be verified using a single standard at 1-3 or 1-4X the LOD on each instrument annually. These requirements are clearly inadequate to meet the LOD definition, since they do nothing to determine the typical levels of blanks, or whether a sample result can be adequately distinguished from a blank result.
2. Why is a change to the LOQ language needed?  
The definition for LOQ in the TNI standards is "The minimum levels, concentrations, or quantities of a target variable (e.g., target analyte) that can be reported with a specified degree of confidence."  
The current requirements for LOQ are that (i) the LOQ shall be above the LOD (ii) the LOQ shall be verified by analysis of a single standard at 1-2X the LOQ (iii) the LOQ verification shall take place annually unless a LOD was determined, in which case there is no requirement.  
There is no way to determine a specified degree of confidence from a single LOQ verification standard, so the current requirements are inadequate to meet the definition.

#### Changes to the LOD standard language

The committee observed that if an environmental laboratory is determining detection limits, the 40 CFR Part 136 MDL procedure is almost always used. We also noted that EPA is updating the 40CFR procedure (a considerable improvement) and that the Office of Drinking Water has indicated that the revised MDL should be used for their methods once it is promulgated.

For these reasons, we determined that it was important that the TNI procedure be compatible with the EPA MDL (otherwise labs would have to determine two detection limits) and that we should consider making the EPA MDL a TNI requirement, in the absence of regulatory requirements to the contrary.

The committee published a Working Draft Standard and received considerable input, and more input at the January 2015 TNI meeting.

The following questions were raised by many commenters:

1. Should the 40CFR Part 136 MDL procedure be mandatory for determining the TNI LOD (in the absence of regulatory constraints to the contrary)?  
There were commenters both in favor and opposed to requiring the MDL procedure. We determined that it would be best to avoid requiring the MDL but ensuring that the MDL, if performed, would meet the TNI requirements for LOD.
2. Should the name of the TNI detection limit be changed from LOD to something else (DL or MDL)?  
The term LOD commonly refers to Currie's  $L_d$ , while environmental labs are typically determining a MDL, which is equivalent to Currie's  $L_c$ . For example, the DOD QAPP defines LOD as a Currie  $L_d$  this way. As a result, considerable confusion is generated. There was a strong consensus that the term should be changed, and we decided that the term MDL should be used for the TNI detection limit. The definitions language will be updated accordingly.
3. Should LOD determination and verification be required if the laboratory does not report below the LOQ?  
We received comments on both sides of this question. The main reason for requiring a LOD is that without it, there is really no guarantee that results close to the LOQ are free from unreasonable levels of false positives. The committee agreed to the compromise of requiring an initial LOD evaluation to establish performance of the method, but not requiring ongoing verification if results are not being reported below the LOQ.

4. Additional clarification of methods for which LOD is not required is needed  
The committee agreed with this comment and has added some language accordingly.

**Changes to the LOQ standard language**

In order to reduce unnecessary workload on laboratories, the committee determined that the LOQ procedure should be as compatible as possible with the LOD (MDL) procedure, while retaining collection of sufficient data to meet the LOQ definition of ability to determine an ability to report with a defined degree of confidence (requiring that precision and bias be known). The LOQ specifications were written such that standards used for the calculation of LOD (MDL) could also be used for verification of LOQ. A couple of examples of how this would work:

**MDL Determination from Spikes**

<b>Spike</b>	1	2	3	4	5	6	7
10	9.5	9.8	10.2	10.6	9.4	9.7	9.9
	<b>MEAN</b>	<b>STD. DEV</b>	<b>MDL S</b>				
	9.9	0.4	1.3				
<b>Blanks</b>	ND	ND	ND	ND	ND	ND	ND
	<b>MEAN</b>	<b>STD. DEV</b>	<b>MDL B</b>				
	0.0	0.0	0.0				
	<b>MDL</b>	<b>3X MDL</b>	<b>Lab LOQ</b>				
	1.3	3.9	10.0				

The primary requirement for the LOQ is that the laboratory collects data from spikes at or below the LOQ so that the precision and bias for analysis at this level is known. In this example, the laboratory is verifying the LOQ of 10 with spikes at 10 and determines a mean recovery of 9.9 and a standard deviation of 1.3. This data is sufficient to both describe performance at the LOQ and to calculate a MDL (LOD) of 1.3  
The second example is for an analyte with poorer recovery – the combination of LOQ and LOD (MDL) still works effectively – in this case the LOQ (spiking level is 10, and the MDL is 3.2

<b>Spike</b>	1	2	3	4	5	6	7
10	6	7.3	7.6	5.7	7.2	7.9	5.3
	<b>MEAN</b>	<b>STD. DEV</b>	<b>MDL S</b>				
	6.7	1.0	3.2				
<b>Blanks</b>	ND	ND	ND	ND	ND	ND	ND
	<b>MEAN</b>	<b>STD. DEV</b>	<b>MDL B</b>				
	0.0	0.0	0.0				
	<b>MDL</b>	<b>3X MDL</b>	<b>Lab LOQ</b>				
	3.2	9.7	10.0				

**Minimum Requirements for LOQ**

The committee received considerable input regarding what the minimum requirements for the LOQ should be, but the input was not consistent.

On one side, some suggested that the TNI standard should set minimum requirements for precision and accuracy for the LOQ. The committee decided that this was not possible or desirable because of the very wide range of precision and accuracy observed for different analytes and methods, and different data quality objectives for different uses. If limits were set wide enough for poor performing analytes, they would be meaningless for well performing analytes. Setting individual limits for specific method analyte combinations would be contrary to the general approach of the TNI standards and would be extremely challenging given the thousands of method analyte combinations.

On the other side, some suggested that the requirements for the LOQ should be minimal, such as “equal to or greater than the low calibration standard” or “greater than the LOD”. The committee did not agree that these minimal requirements were sufficient to meet the definition of LOQ, since they do not allow determination of the degree of confidence in the data, allow quantitation error of over 100% in some cases, and do not control either false positives or false negatives. The committee did agree that having the LOQ at or above the low calibration standard is valuable as one component of LOQ requirements, and has included the low calibration standard in the LOQ language.

The main requirement for the LOQ is that the laboratory collects spike data at or below the LOQ to allow for determination of precision and bias. However, that requirement alone is insufficient for very poor performing analytes since protection from false negatives will not be ensured. Therefore, the committee added an additional requirement that the LOQ be at least 3X the MDL (LOD). The following example shows how this would work, for an analyte with both poor recovery and poor precision. In this example, average recovery is 51% and relative standard deviation is 37% of the mean. Without the 3X MDL requirement many results from a true concentration at the LOQ would be below the MDL, and therefore non-detect by definition. These are false negatives. When the LOQ is raised to 3X the calculated MDL of 6.1 the LOQ is high enough that true concentrations at that level can reasonably be expected to provide results above the MDL.

<b>Spike</b>	1	2	3	4	5	6	7
10	5	7.1	3.2	6.5	7.4	3	3.3
	<b>MEAN</b>	<b>STD. DEV</b>	<b>MDL S</b>				
	5.1	1.9	6.1				
<b>Blanks</b>	ND	ND	ND	ND	ND	ND	ND
	<b>MEAN</b>	<b>STD. DEV</b>	<b>MDL B</b>				
	0.0	0.0	0.0				
	<b>MDL</b>	<b>3X MDL</b>	<b>LOQ</b>				
	6.1	18.2	18.0				

#### Consistency with other Quantitation limit requirements

In order to avoid unnecessary work, the committee desired that the TNI LOQ be compatible with other currently used quantitation limit concepts, including the EPA Office of Drinking Water MRL (Minimum Reporting Level) and the Office of Resource, Conservation and Recovery LLOQ (Lower Limit of Quantitation). We were able to achieve this goal – data collected for the TNI LOQ will be sufficient to allow evaluation of MRL and LLOQ. The 3X MDL requirement is also consistent with Office of Water ML (Minimum Level) specifications.

## VOLUME 1, MODULE 4

### Quality Systems for Chemical Testing

#### 1.5.2 Limit of Detection and Limit of Quantitation (However Named)

Procedures used for determining limits of detection and quantitation shall be documented. Documentation shall include the quality system matrix type. All supporting data shall be retained.

##### 1.5.2.1 Method Detection Limit (MDL)

If a mandated test method or applicable regulation includes protocols for determining detection limits, they shall be followed. The laboratory shall document the procedure used for determining the MDL. If the method or regulation does not contain specific directions for determination of the detection limit, the following requirements shall apply. MDL determinations are not required for methods / analytes for which a detection limit is not applicable such as pH, color, odor, temperature, titrimetric or dissolved oxygen. MDL determinations based on spikes are not required for analytes for which no spiking solutions are available such as total suspended solids. If results are not reported below the LOQ, an initial MDL determination is required, but ongoing verification is not.

##### 1.5.2.1.1 Initial Determination of the MDL

If a mandated test method or applicable regulation includes protocols for determining detection limits, they shall be followed. The laboratory shall document the procedure used for determining the MDL. One option is to follow EPA's MDL procedure specified at 40 CFR Part 136 Appendix B. MDL determinations are not required for those analytes for which no spiking solutions are available or a detection limit is not appropriate, such as pH, color, odor, temperature or dissolved oxygen. MDL determinations are also not required for titrimetric methods. If results are not reported below the LOQ, an initial MDL determination is required, but ongoing verification is not.

The ~~determination~~laboratory MDL procedure, unless following a mandated test method or procedure, at a minimum, shall incorporate language addressing the following requirements:

- a) The MDL must shall reflect current operating conditions:
- b) The MDL determination shall must incorporate the entire analytical process, including sample preservations.
- c) The MDL determination shall include data from low level spikes and routine method blanks  
Samples used to determine the MDL must be prepared and analyzed over multiple days.
- d) Results from spiked samples used in the MDL determination must shall meet qualitative identification criteria in the method, and shall be above zero.

- e) The MDL ~~procedure determination shall~~ must include criteria for and evaluation of false positive rates in routine method blanks.-
- f) The MDL shall be ~~initially~~ determined for the analytes of interest in each test method in ~~a~~ the quality system matrix of interest in which there are neither target analytes nor interferences at a concentration that would impact the results or the MDL shall be performed in the sample matrix of interest.
- ~~g) If the method is altered in a way that can be reasonably expected to change the detection limit, then prepare and analyze a spike at the LOQ concentration and a blank. If the spike at the LOQ concentration gives a result meeting qualitative identification criteria above zero and the blank gives a result below the MDL then the MDL is verified. If not, re-determine the MDL.~~

NOTE: One option is to follow EPA's MDL procedure specified at 40 CFR Part 136 Appendix B.

#### 1.5.2.1.2 Ongoing verification of the MDL

At a minimum, ongoing verification of the MDL shall include assessments of spikes at or below the LOQ and of method blanks. A minimum of one verification spike and one blank ~~shall~~ must be analyzed on each instrument during each quarter in which samples are being analyzed and results are being reported below the LOQ. The criteria listed in section 1.5.2.1.1 ~~a-g~~ must shall be met for ongoing verification over the course of a year.-

If the method is altered in a way other than routine maintenance and the change can be expected to elevate the detection limit, then a spike at or below the LOQ concentration and a blank shall be prepared and analyzed. If the spike at the LOQ concentration gives a result meeting qualitative identification criteria above zero and the blank gives a result below the MDL then the MDL is verified. If not, the MDL shall be re-determined.

In the event that verification fails, the laboratory shall perform a new MDL study.

#### 1.5.2.1.3 When a new MDL is determined, the laboratory shall verify that the LOQ value is at least 3 times the MDL. If it is not, the laboratory shall raise the LOQ value to at least 3 times the MDL.

#### 1.5.2.2 Limit of Quantitation (LOQ)

If a mandated test method or applicable regulation includes protocols for determining quantitation limits, they shall be followed. The procedure used for determining the LOQ shall be documented by the laboratory. The laboratory shall select an LOQ for each analyte, consistent with the needs of their clients, and at least three times the MDL. An LOQ is required for each quality system matrix of interest, technology, method, and analyte, except for any component or property for which spiking solutions are not available or a quantitation limit is not appropriate, such as pH, color, odor, temperature, dissolved oxygen or turbidity.

- a) Each selected LOQ shall be verified through analysis of initial verification samples. An initial verification sample consists of a spiked matrix blank at or below the selected LOQ.
- b) All sample preservation, processing and analysis steps performed for routine sample analysis shall be included in the LOQ verification testing.
- c) The LOQ must be at or above the lowest corresponding calibration standard concentration with the exception of methods using a single point calibration.
- d) The laboratory shall establish acceptance criteria for accuracy for the LOQ verification spikes.

#### 1.5.2.2.1 Initial Verification of the LOQ

When first establishing an LOQ or when an LOQ concentration has been selected that is lower than the concentration of the LOQ verification spikes previously performed, an initial verification shall be performed as follows:

- a) ~~Process a~~ minimum of 7 blanks spiked at or below the LOQ concentration shall be processed through all steps of the method, including any required sample preservation. Both preparation and analysis of these samples ~~must shall~~ include at least 3 batches on 3 separate days.

Note: Spiking slightly below the LOQ may help ensure that the results are also suitable for MDL determination.

Note: If spiked blanks have been analyzed in order to generate a MDL, the results may be used to perform the initial verification of the LOQ.

- i) If there are multiple instruments that will be assigned the same LOQ, then these spiked blanks shall must be distributed across all of the instruments.
  - ii) A minimum of two spiked blanks prepared and analyzed on different days shall be tested on each instrument.
- b) Existing data may be used if compliant with the requirements for at least 3 batches, generated within the last 2 years and representative of current operations.
  - c) The LOQ is verified if the following criteria are met:

- i) All results are quantitative (above zero and meet the qualitative identification criteria of the method ~~under routine operating conditions~~ (e.g., recognizable spectra, signal to noise requirements, and presence of qualifier ions).

If a result from an LOQ verification sample is not above zero and/or does not meet the qualitative identification criteria in the method, the problem ~~must shall~~ be corrected and the verification repeated, or the LOQ verification and LOQ spikes must shall be repeated at a higher concentration.

- ii) Recovery of each analyte is within the laboratory established accuracy acceptance criteria.

- iii) The LOQ ~~must be~~ is at least 3X the established MDL and at or above the spiking concentration

If the LOQ is less than 3 times the MDL, the LOQ shall be raised to at least 3 times the MDL.

Note: It is not necessary to repeat the LOQ verification at a higher concentration when it is necessary to raise the LOQ to 3 times the MDL.

- d) The laboratory shall document the results of the initial LOQ verification as described in section 1.5.2. ~~42-3~~

#### 1.5.2.2.2 Ongoing verification of the LOQ

The laboratory shall prepare and analyze a minimum of one LOQ verification sample spiked at the same concentration as the initial LOQ verification on each instrument during each quarter in which samples are being analyzed for each quality system matrix, method, and analyte.

- a) Results of each LOQ verification sample analysis ~~must~~ shall be evaluated at the time of the testing and ~~must~~ shall meet the qualitative identification criteria in the method and laboratory SOP and the quantitated result ~~must~~ shall be greater than zero.

If a continuing LOQ verification test does not meet this requirement, the laboratory ~~must~~ shall take corrective action. Corrective action shall be either (i) raising the spiking level (and the quantitation limit if the spiking level is above it) and repeating the initial verification study, or (ii) correcting method or instrument performance and repeating the verification test one time. In the event of second failure of a quarterly verification sample, the quantitation limit ~~must~~ shall be raised and the initial study repeated.

- ~~b) At least once per year tabulate all results of the ongoing verification sample testing. Use all data representative of the current operations, if generated within the last two years. A minimum of 7 samples is required.~~

~~The LOQ value must be at least 3 times the MDL. If it is not, raise the LOQ value to at least 3 times the MDL.~~

- ~~e) Document the results of the continuing LOQ verification as described in section 1.5.2.2.3.~~

1.5.2.3 If no analysis was performed in a given year the verification of the MDL/LOQ is not required, but a new initial MDL/LOQ verification shall be performed prior to analysis of client samples

~~1.5.2.2.3~~ 1.5.2.4 Documentation

At least once per year the laboratory shall tabulate all results of the ongoing verification sample testing. All data representative of the current operations shall be used, if generated within the last two years. A minimum of 7 samples is required.

- ~~a) Include~~ The laboratory shall record the analytical and preparation methods used, dates of preparation and testing, the batch identifiers, the testing instrument, quality system matrix, technology, analyte, concentration in the spiked sample with units, and the test result (if any) for each LOQ and/or MDL verification test.
- b) For each ~~result~~ analyte, the laboratory shall record the percent recovery, the number of results (n), the mean and standard deviation of the percent recovery, and the spiking concentration of the spiked samples with units. These data shall be provided to clients upon request.