WORKING WITH THE EPA TO IMPROVE DETECTION AND QUANTITATION

Richard Burrows

PQL

QOL

ES

DL

Lo

MRL

PAL

AML

MDL

QL

LC

MCL

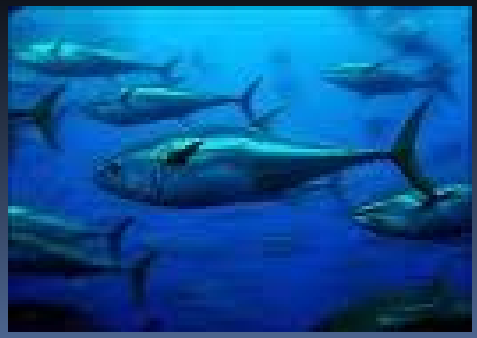
ML

LOD

RL

First, a little history

- Lead in Albacore: Guide to Lead Pollution in Americans
  - Science, Vol 207, March 1980 p1167
  - Typical results for fresh albacore muscle were around 400 ng/g Pb
  - Typical results for albacore muscle from lead soldered cans were around 700-1000 ng/g
- Therefore, the canning process approximately doubles the concentration of lead in tuna?



- Actually, when analyzed using clean preparation techniques and isotope dilution ICPMS the concentration of lead in fresh albacore muscle was found to be approx 0.3 ng/g

	Lab 1	Lab 2
Pb in albacore muscle	400	0.3
Pb in albacore muscle from lead soldered can	700	1400
Factor	1.75	4700

  - Highly regarded government and commercial laboratories at the time were overestimating the concentration of lead in fresh tuna by over 1000 X.

Trace analyses for wastewaters

Method detection limit, a new performance criterion for chemical analysis, is defined as that concentration of the analyte that can be detected at a specific confidence level. Both theory and applications are discussed for reliable wastewater analyses of priority pollutants

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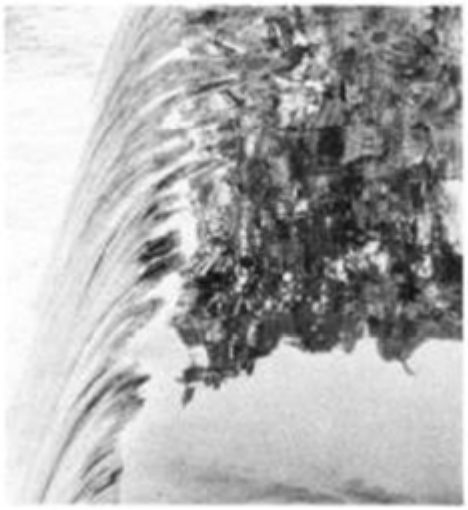
The development of trace analysis methodology brought with it a series of questions about method performance at low concentration levels of analyte (*1*, *2*, *3*). Under Section 304(h) of the Clean Water Act, as amended in 1977, (*4*) the Environmental Monitoring and



ority pollutants, it was incumbent on EMSL to develop method perfor-

detection limit should be related to the standard deviation of the measured values at or near zero concentration of the analyte (*11*).

There is no doubt that the detection limit is one of the most important performance characteristics of an analytical procedure. In most cases, a detection limit must be viewed as a temporary limit to current methodology.

Complete analytical system

Ostensibly, analysts do not directly observe concentrations of analyte. The measurements of the transducer signal, which are related to the analyte concentration, are actually observed. In any analytical system, information

ES&T, 1981, pp1426-1435

Further developments

- 1984 USEPA the MDL procedure is promulgated in 40 CFR, Part 136, Appendix B for use in the wastewater program and defined as 3.14 times the standard deviation of seven low level spiked blanks. The ML is also promulgated at this time.
- 1985 The MDL is widely adopted by other programs within EPA and written into many state and federal regulations.
- 1994 USEPA publishes draft guidance for WQBE:s below analytical detection/quantitation levels. EPA refined the definition of the ML, relating it to the ACS LOQ, which is defined as 10 times the standard deviation of replicate blanks, thus 3.18 times the MDL.

Further developments

- 1999 USEPA published Method 1631B for analysis of mercury using the old MDL approach and modified ML definition, which provided an opportunity for a legal challenge of the MDL and ML.
- 2000 USEPA entered into a settlement agreement with the Alliance of Automobile Manufactures, Chemical Manufacturer's Association, Utility Water Act Group and AFPA.

Yet More

- 2002 USEPA issues a Technical Support Document of Detection and Quantitation Regulations under the Clean Water Act (TSD).
- 2003 Draft revised MDL published
- 2003 Consensus letter submitted to Assistant Administrator of Office of Water signed by 31 parties urging EPA to consider a scientifically sound approach to the detection and quantification issue.

And even more….

- 2005 Federal Advisory Committee on Detection and Quantification (FACDQ) formed by USEPA Office of Water as a result of the 2000 Settlement Agreement
- 2007 FACDQ completes their work issuing a final report with recommendations, with Office of Water to complete a Post FACDQ pilot study based on FACDQ recommendations.
- 2010 TNI forms Environmental Methods Measurement Expert Committee based on a USEPA grant to address Calibration, Detection, Quantification and other measurement issues.
- 2011 Final report on Post FACDQ pilot study issued, recommending further evaluation with additional methods and analytes.
- 2012 USEPA Office of Water issues Methods Update Rule for 40 CFR Part 136 methods, based on traditional MDL approach.

Current Office of Water Position

- Resources are very limited
- Pursuing changes to the MDL/ML would not be a high priority even if resources were available
- EPA would be interested in reviewing a plan for how alternatives to the MDL/ML could be pursued

MDL

MDL = ts

MDL = 3.14 x s for 7 replicates

Where s = the standard deviation of replicate spikes close to the MDL

The lowest concentration at which a sample can be distinguished from a blank

The concentration at which the sample is determined to be greater than zero

Theoretical Basis for the MDL

- Currie L_c = ts
  - Where s is the standard deviation of the blanks

Note that the MDL does not say anything about the minimum quantity of an analyte that will be reliable detected

Curie's L_D does that – L_D is the lowest amount in a sample that will reliably give a result above the MDL

Does the MDL Work?

Examples

- "Episode 6000" data set
  - 7 or 8 spikes blanks at several concentrations above and below the expected MDL
  - MDLs and MLs calculated and included in the TSD

TSD: EPA Technical Support Document for the Assessment of Detection and Quantitation Concepts. Appendix C

"Episode 6000" Examples

- Ammonia by 350.3
  - MDL is 0.01
  - Spikes at 0.001 give results up to 0.35

True value 10X less than MDL gives a result 35 times higher than the MDL

"Episode 6000" Examples

- TSS by 160.2
  - MDL is 1.17
  - Spikes at 0.2 give results up to 2.0

True value 6X less than MDL gives a result 2 times higher than the MDL

"Episode 6000" Examples

- Cobalt by 200.8
  - MDL is 0.001 ML is 0.005
  - 7 spikes at 0.2 (200 x MDL and 40 x ML) all give negative results

True value 200 X the MDL
gives a non-detect

"Episode 6000" Method 502.2

- 1,1 dichloroethene MDL 0.01
  - Blanks have results up to 0.085 (85 times the MDL)and 11 of 23 blanks are > 0.07
- Dibromomethane MDL 0.007
  - 4 of 7 replicates spikes at 0.07 (10 times the MDL) are ND
- Dichlorodifluoromethane MDL 0.009
  - Mean of blank results is 0.77 (85 times MDL) and 22 of 23 blanks are > 0.4

Episode 6000 data, Method 524.2

- 72 of 81 analytes have all 7 replicates not detected when spiked at or above the calculated MDL
- Some have 7 replicates not detected when spiked at > 3.18 times the MDL. (the quantitation limit is below the limit of detection.)

Why does the MDL not work?

ASSUMPTIONS

Assumptions

- There is no blank bias
- The short term variance measured (7 replicates one batch) properly models the long term variance of the method, and instrument sensitivity does not vary

Further assumptions

- Variance in the range of zero concentration to the spiking concentration is constant
- Qualitative identification requirements in the method can be met at the calculated MDL

What can (should) we do?

- We have been doing it this way for 30 years, perhaps it is OK?
- Or are things getting worse?

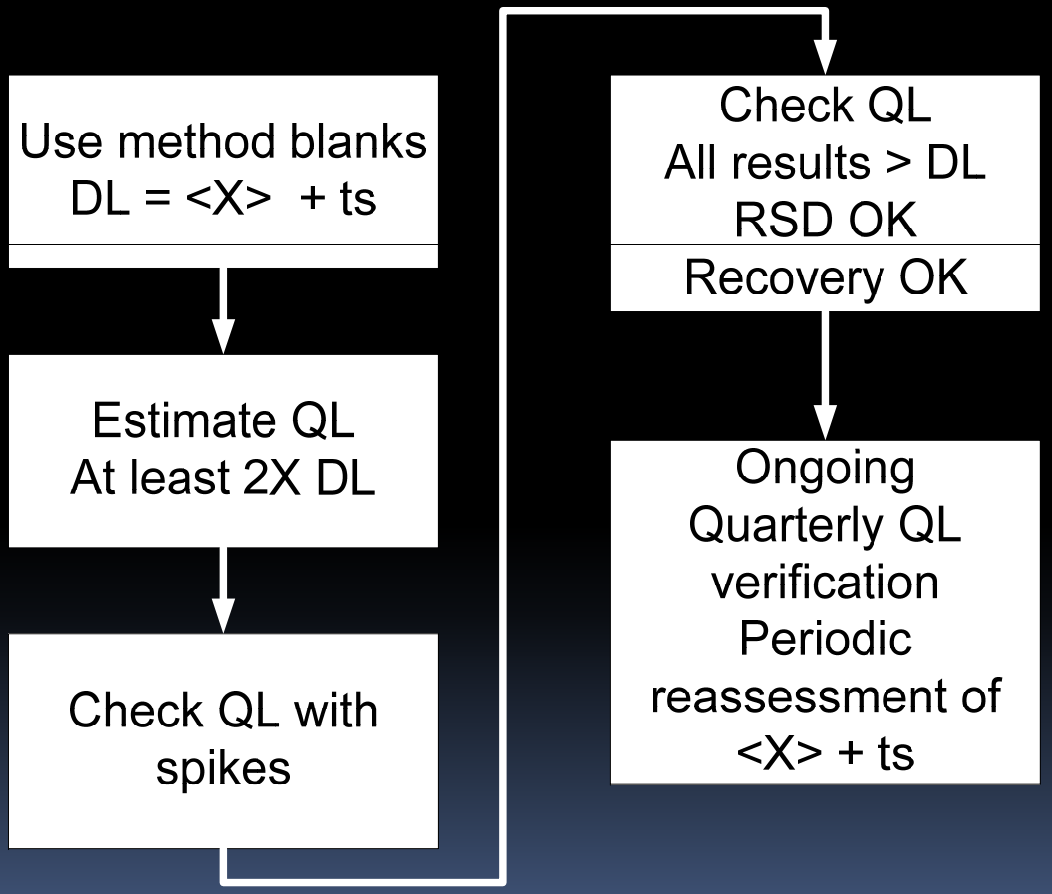
What are our options?

- Replace the MDL
  - DQFAC procedure
  - ASTM IDE/WDE
- Stop reporting below the quantitation limit
- Leave the MDL alone
  - Improve things for TNI labs at least, through development of a standard by the EMMEC
- Modify the MDL
  - Based on principles from the DQFAC and learning from the Pilots

DQFAC DL/QL PROCEDURE

- The procedure was developed from the ACIL procedure which was piloted for 5 methods by at least 8 labs per method.
- Modifications to the ACIL procedure were designed to address shortcomings noted during the pilot study

A Better MDL



Detection/Quantitation Federal Advisory Committee Procedure

Summary of the DQFAC procedure

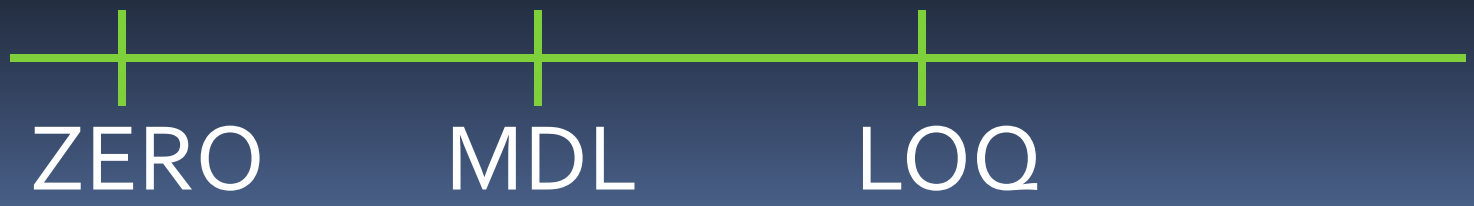
- Uses long term data
- Takes account of blank bias
- Considers qualitative identification
- Checks actual performance against the calculated limits to accommodate non-normal data
- Develops precision/accuracy information at the QL

Whatever the DL/QL procedure, careful selection of the appropriate calibration model is vital to achieve accurate quantitation at low levels

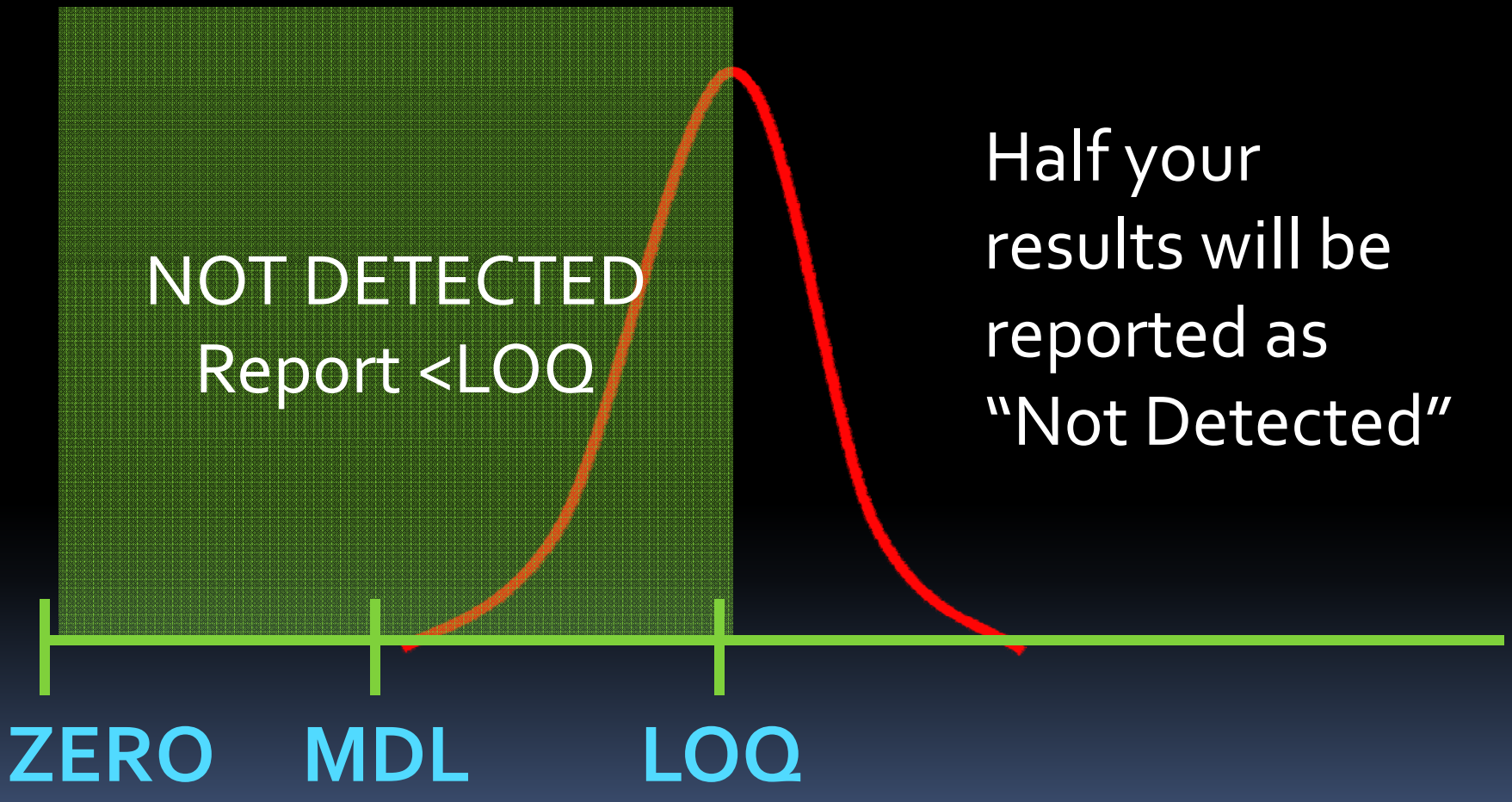
Stop Reporting below LOQ?

But then what is the False **Negative** rate for a true concentration at the LOQ?

Let's assume the best case scenario of 100% recovery



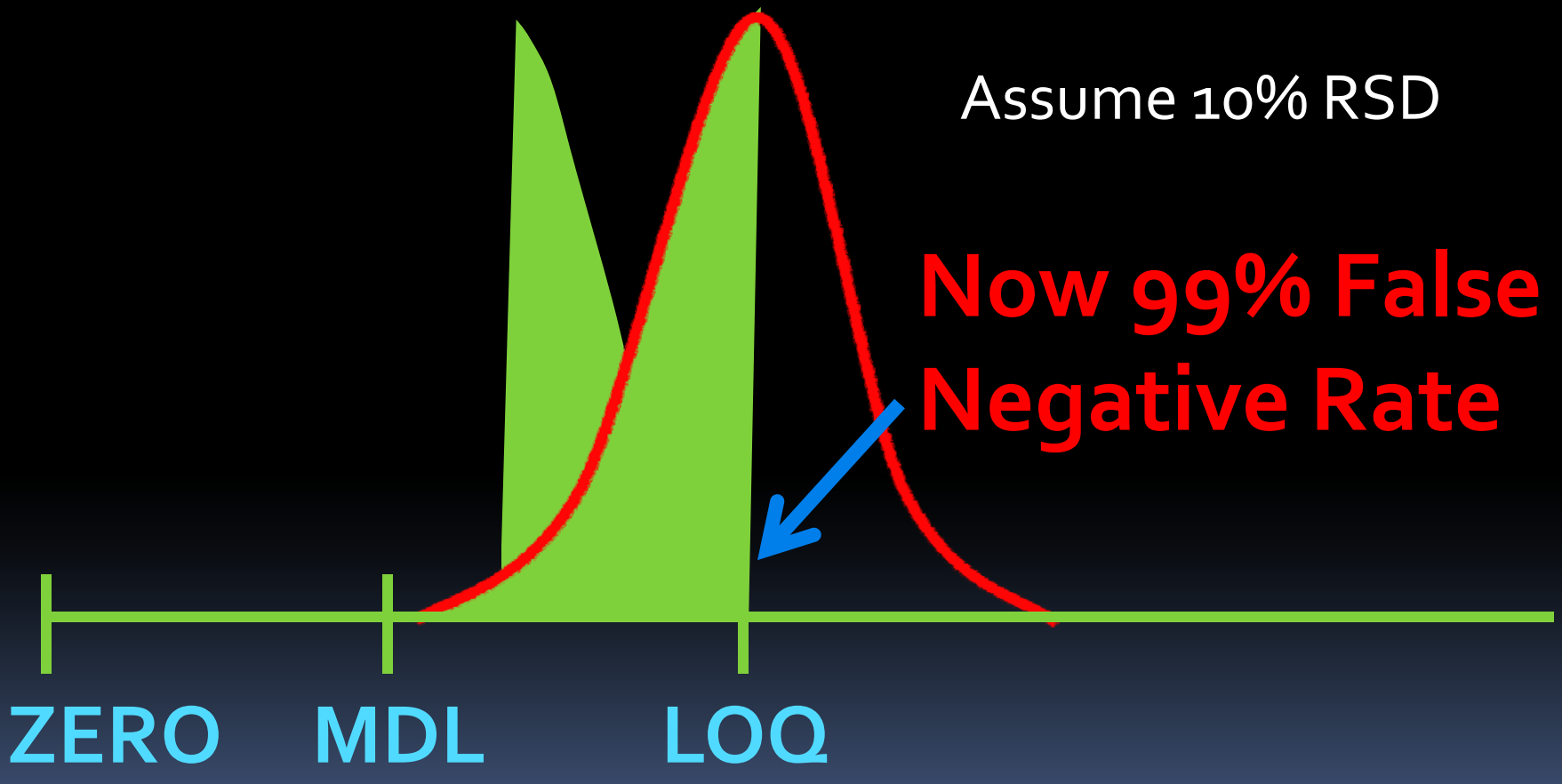
If you run 100 spikes at LOQ…



Half your results will be reported as "Not Detected"

If you run 100 spikes at LOQ…

What if you have 70% average recovery?



Leave the MDL alone and fix things with a standard generated by the EMMEC

- We will give it our best shot, but…..
- Whatever we come up with, we have to be able to call it a MDL

Modify the MDL based on information from the DQFAC and pilots

Although the Committee did not reach consensus on a procedure,
we recommend that EPA act to develop an alternative to the current 40 CFR Part 136 Appendix B procedure.
The results of the Pilot Study, and our evaluation of the DQ FAC Single Laboratory Procedure v2.4, indicate that there are deficiencies in the current 40 CFR Part 136 Appendix B procedure that can and should be corrected.
The DQ FAC Single Laboratory Procedure v2.4 submitted contains elements that would be valuable to the agency in developing a new procedure.

Vote: 20 Agree, 0 Not Opposed, 0 Disagree
Approved By Consensus
Meeting #10, Decision 10.A

Modify the MDL based on information from the DQFAC and pilots

Assumptions

- There is no blank bias
- The short term variance measured (7 replicates one batch) properly models the long term variance of the method

Further assumptions

- Variance in the range of zero concentration to the spiking concentration is constant
- Qualitative identification requirements in the method can be met at the calculated MDL

Appendix B to Part 136—Definition and Procedure for the Determination of the Method Detection Limit—Revision 1.11

Definition

The method detection limit (MDL) is defined as the minimum measured concentration that can be reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.

Scope and application

This procedure is designed for applicability to a wide variety of sample types ranging from reagent (blank) water containing analyte to wastewater containing analyte. The MDL derived by this procedure may vary as a function of sample type. The procedure requires a sample, spiked at a level close to the MDL, and that the sample contain all of the preservatives and be carried through all of the steps of the analytical method. It is essential that all samples processed in the laboratory, including field samples, that are subject to a specific MDL be handled in exactly the same manner.

The MDL is dependent on the analyte, the instrument, the sample matrix, the preparation technique, and the data analysis technique. It is important that the MDL determination be performed in a manner consistent with the procedure and that all relevant factors affecting the MDL be addressed.

The MDL should not be confused with the practical quantitation limit (PQL) or the level of quantitation. The PQL is usually 2 to 5 times the MDL and represents a concentration that can be reliably measured within specified limits of precision and bias during routine laboratory operating conditions. The PQL may be set by a regulatory agency.

Procedure

1. Make an estimate of the detection limit using one of the following:
   a. The concentration value that corresponds to an instrument signal/noise ratio in the range of 2.5 to 5.
   b. The concentration equivalent of three times the standard deviation of replicate instrumental measurements of the analyte in reagent water.
   c. That region of the calibration curve where there is a significant change in sensitivity, i.e., a break in the curve from a steep slope to a shallow slope.
   d. Instrument detection limit.

2. It is suggested that the concentration of the analyte be between one to five times the estimated detection limit as determined in the first iteration of Step 1 above, but not less than the calculated MDL.

3. Prepare seven replicate samples. The replicates must be carried through all steps of the sampling and analytical method, including preservation and pH adjustment. These samples should be analyzed on a day or days commensurate with the anticipated routine use of the method. Do not analyze a calibration standard or blank immediately before or after analysis of the replicates.

4. (a) Calculate the variance (S^2) and standard deviation (S) of the seven replicate measurements.

   (b) If the MDL is to be determined for reagent (blank) water, proceed to Step 5.

   (c) If the MDL is to be determined for matrices other than reagent water, the variance may be substantially greater than that of reagent water. In this case, the sample should be analyzed and if results indicate that the analyte is present at greater than 1 to 5 times the calculated MDL, the concentration should be adjusted and seven new samples analyzed.

5. (a) If the MDL is to be determined for reagent (blank) water, proceed to Step 6.

   (b) If the MDL is to be determined for matrices other than reagent water, the MDL is defined as the greater of the calculated MDL from Step 4 or the concentration at which all seven replicates were recovered.

6. (a) Compute the MDL as follows:

$$MDL = t_{(n-1,1-\alpha=0.99)} \times S$$

Where:

MDL = the method detection limit

$t_{(n-1,1-\alpha=0.99)}$ = the Student's t value appropriate for a 99% confidence level and a standard deviation estimate with $n-1$ degrees of freedom. See Table 1.

S = standard deviation of the replicate analyses.

(b) The 3.14 in Step 4 is equivalent to the one-sided Student's t-statistic appropriate for the MDL definition (see Step 7) for seven samples and a 99% confidence level. The value 3.14 assumes that the number of samples used to calculate S is seven. If the number of samples is other than seven, the appropriate Student's t-statistic value must be substituted. Table 1 gives one-sided Student's t-statistic values for 6 to 60 degrees of freedom.

Table 1. Student's t-Values at the 99% Confidence Level

Number of replicates	Degrees of freedom (n-1)	$t_{(n-1,1-\alpha=0.99)}$
7	6	3.143
8	7	2.998
9	8	2.896
10	9	2.821
11	10	2.764
16	15	2.602
21	20	2.528
26	25	2.485
31	30	2.457
41	40	2.423
61	60	2.390

Reporting

The analytical method used must be specifically identified by number or title and the MDL for each analyte expressed in the appropriate method reporting units. If the analytical method permits options which affect the method detection limit, these conditions must be specified with the MDL value. The sample matrix used to determine the MDL must also be identified with the MDL value. Report the MDL for each analyte level with the MDL and results of the MDL procedure as mentioned. If a laboratory standard or a sample that contained a known amount of analyte was used for this determination, also report the mean recovery.

If the level of analyte in the sample is too close to the determined MDL or exceeds 10 times the MDL of the analyte in reagent water, the contingent value for the MDL.

[49 FR 43430, Oct. 29, 1984; 50 FR 694, 696, Jan. 4, 1985, as amended at 51 FR 23703, June 30, 1986]

Modification 1

The MDL is performed when the method is initiated, and then verification checks are performed approximately every quarter.
The data from the verification check spikes and method blanks is assessed once per year to ensure that the MDL estimate is still reasonable.

Modification 2

Make an estimate of the detection limit using one of the following:

Three times the standard deviation of a set of method blanks, plus the mean of the method blanks.

If there are multiple instruments that will be assigned the same MDL, then the replicates must be evenly distributed across all of the instruments. A minimum of 2 replicates are required on each instrument.

Modification 3

Required procedure to determine if the MDL provides reasonable protection from false positives

Evaluate the mean and variance of a set of method blanks. A minimum of 7 method blanks are required, more should be used if available, up to a full year of method blank determinations.

Calculate the upper confidence limit for the method blanks.

Set the MDL to the greater of the original MDL estimate from spiked samples and the MDL_b

Verification

Once per quarter, analyze a single spike on each instrument. The spike level should be at 2-3 times the MDL for a single analyte method, and 2-5 times the MDL for multi analyte methods (or at the quantitation limit).

All analytes should be detected, but up to 10% may have results below the calculated MDL.

Verification (continued)

Once per year, recalculate the MDL using the most recent quarterly spike results. At least 8 results must be used. If more than 8 results are available from the most recent year, use only the most recent year.

Also, recalculate the MDL_b using the most recent year set of method blank results. If the calculated MDL / MDL_b is greater than 2X the existing MDL or less than 0.5X the existing MDL, reset the MDL to the new value.

What is not added?

- LOD

Definitions

- Definitions
- LOQ (LLOQ, Lq, QL, ML)
  - Lowest TRUE concentration for which there is an expectation of quantitative accuracy
- LOD (Ld, DL)
  - Lowest TRUE concentration for which there is an expectation of detection
- MDL (Lc)
  - Lowest MEASURED concentration that can be reliably distinguished from the measurement of a blank

Questions?