A Few More Demons, Bugbears, and Hobgoblins

- MDLs
- Method Validation data and Lab Performance
- Holding Times

Method Detection Limits

A Demon that has now been conquered!

Hypotheses

- MDLs verify that something was actually in the sample.
- A laboratory's calculated MDL should reflect this.

The Reality

- Most MDLs, in both the methods and calculated by laboratories, do not reflect a true MDL, and in general are much lower than the true MDL

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

Developments Since 1983

- 1984 MDL 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.
- Twenty-six years of controversy culminating in a FACDQ report
- 2010 TNI Chemistry committee begins work on a MDL revision and submits to EPA in 2013
- 2015 **EPA publishes revised MDL as part of a Methods Update Rule**

Lloyd Currie's Original Concepts

- L_C The lowest result that can be reliably distinguished from a blank

EPA: The minimum measured concentration of a substance that can be reported with 99% confidence that the measured concentration is distinguishable from method blank results

- L_D The lowest amount present in a sample that will reliably give a result that is above L_C

- L_Q The lowest amount that gives quantitative results

Analytical Chemistry: 1968

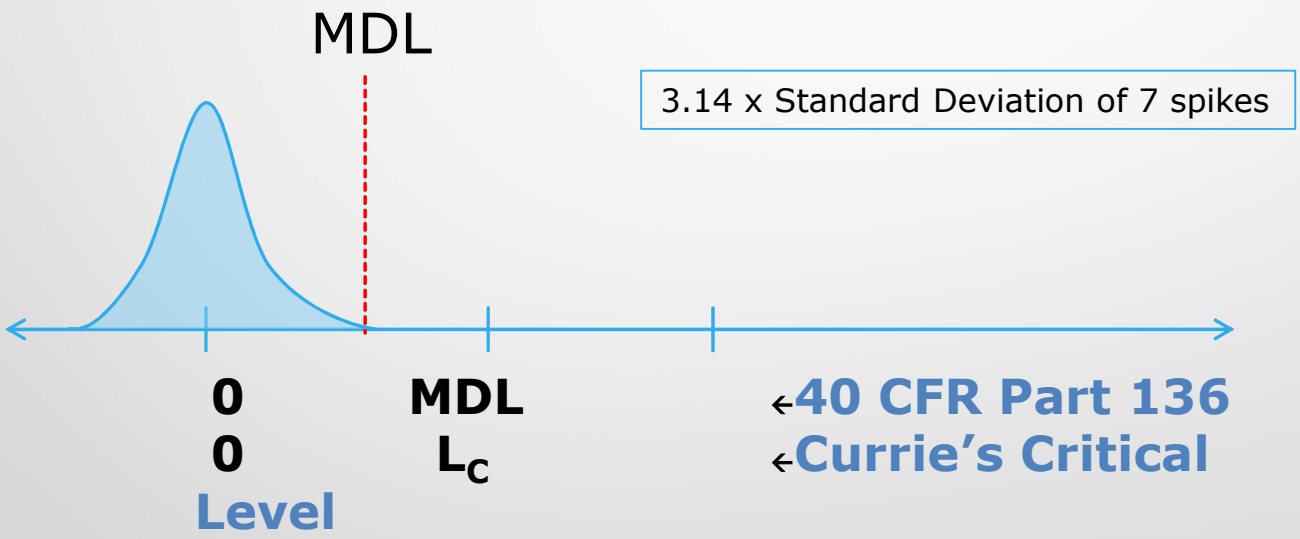
Problems with the Current MDL

Is the Current MDL Procedure a Viable L_C?

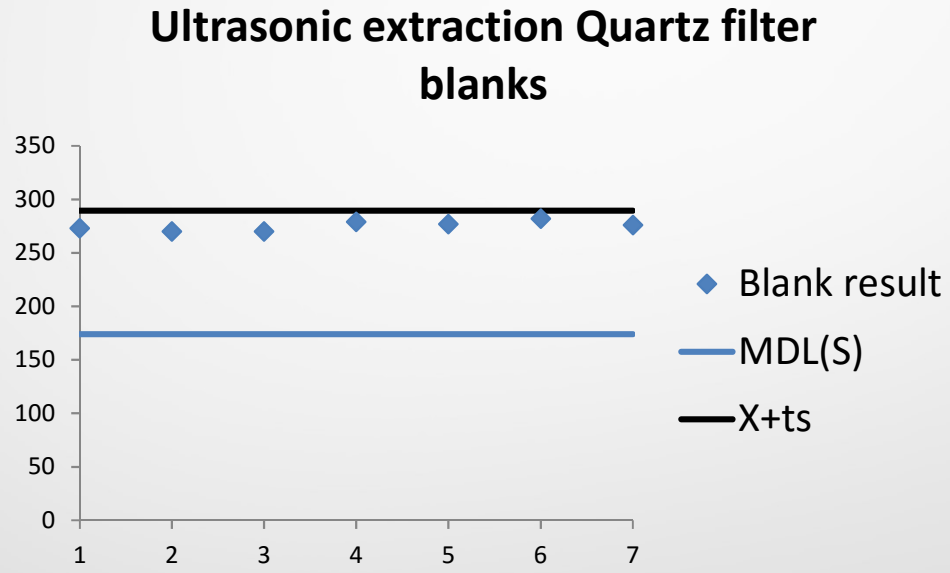
- Assumptions in the MDL
  1. There is no blank contamination
  2. Short term standard deviation is the same as long term standard deviation
  3. A response at the MDL indicates analyte detection

Blank Bias

Current MDL assumes blank results are centered around zero
If blanks are not centered around zero, then the MDL will be too low and many false positives will result.

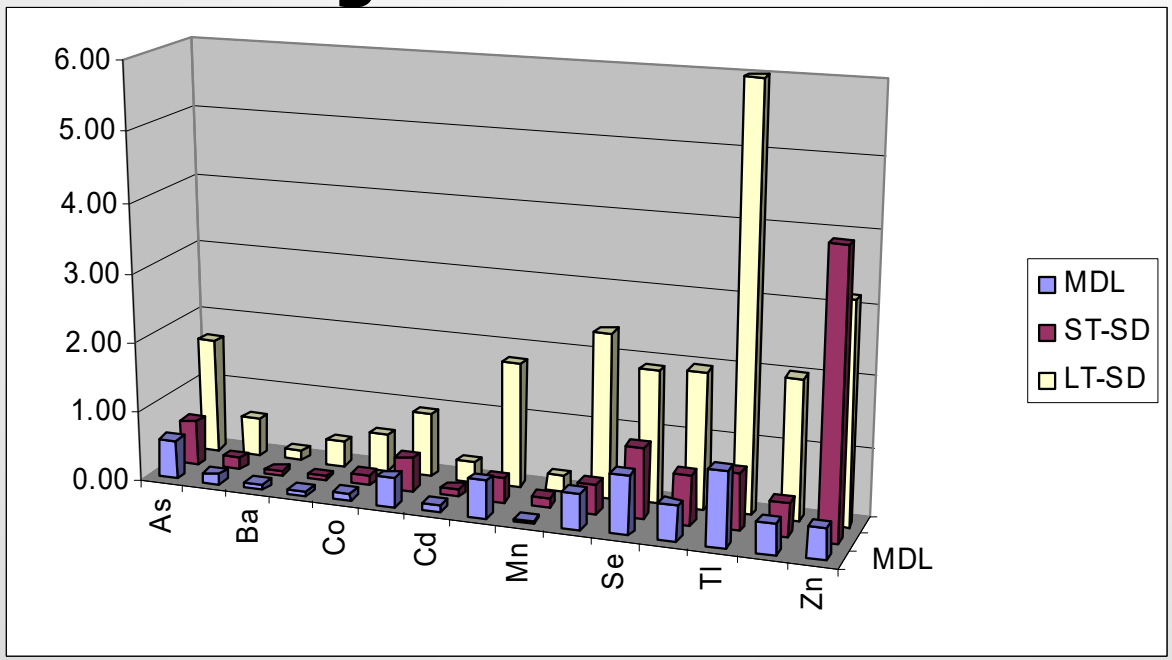


MDLs Calculated Below Blank Levels

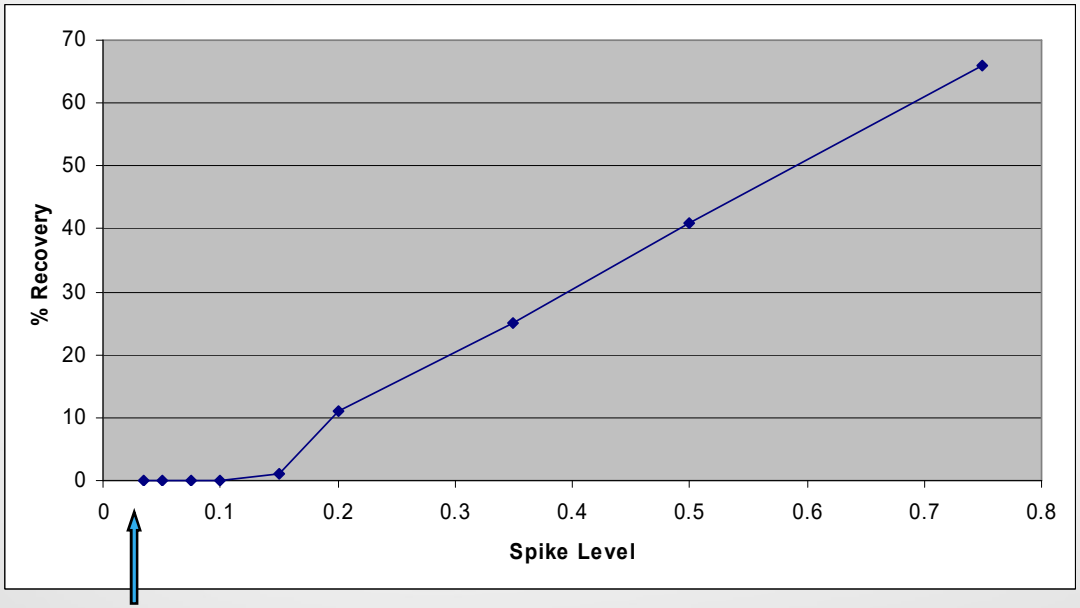


Source: EPA Memo January 3, 2013

Procedure Does Not Reflect Long-Term Variance



Calculated MDLs Below Level of Detection



Calculated MDL
= 0.054

Data from EPA MDL Study of Method 524.2

Fundamentals Stay the Same

- Definition is unchanged
  - What is the lowest result that is qualitatively reliable, i.e., the lowest result that reliably indicates the analyte is in the sample?
- Calculation is unchanged
  - Describe the distribution as Student's t times the standard deviation of results

New Elements of the Procedure

- Include data from low-level spikes and method blanks analyzed over multiple days
- Include criteria for evaluating false positives in blanks
- Include criteria for evaluating qualitative identification
- Include SD of blanks in calculation

An Improved Procedure

- Accounts for Problems in Current Procedure
  - Blank contamination
  - Long-term variance
  - Actual detectability
- Ensures Scientific Reliability
- Benefits Labs and Data Users
- Valid MDLs should not change much

Accounts for Blank Bias

- Sensible MDLs when there is blank bias
  - 1980 Lead in tuna results overstated by 1000X due to blank contamination
  - 2004 EPA Episode 6000 data Chromium by ICPMS, 1400% recovery at the MDL and 600% recovery at the ML due to blank bias
  - 2013 Multi-lab blank detection rates
    - 8270 SIM 6.4%
    - 8921B 16%
    - ICPMS 8%
  - 2014 Lead in particulate matter
    - All blanks in the validation study exceeded the MDL

This problem is getting worse because of the need for low level data and increasing sensitivity of instrumentation

Accounts for Variance

- Long term vs. short term bias
  - The difference varies from method to method and lab to lab, but can be large
  - Long term bias is what matters when it comes performance

Ensures Scientific Reliability

- Low level spikes must meet qualitative criteria for identification
- Low level spikes must be greater than the mean of blank results

Status of the Procedure

- Expected to be final later this year
- Only minimal changes are expected
- New TNI Standard encourages use of this procedure
- Labs could begin implementing now, except where not allowed

For more information, Yesterday at 3:30

Method Validation and Laboratory Performance

A bugbear that has solutions if we have courage

Hypothesis

- Results from method validation study by method developer should represent typical performance in terms of precision, accuracy and sensitivity
- Laboratories should be able to use these data to establish QC limits, at least initially.

Is this hypothesis valid?

Method 3545: Pressurized Fluid Extraction

Analyte	% Recovery*	3541 Recovery
4-Chloroaniline	100.0	0
Hexachlorocyclopentadiene	100.0	0
2-Chloronaphthalene	100.0	0
3,3'-Dichlorobenzidine	100.0	0
Chrysene	100.0	0

*As compared to 3541

So when did 0/0 become 100?

Method 1666:Volatiles for Pharmaceutical Manufacturing Industry

Analyte	Acceptance Limits
N-butyl alcohol	D-199
Tert-butyl alcohol	D-212
Isopropanol	D-441

1666 Method Validation

"This method was developed and validated in a single laboratory."

Validation Study

7 replicates at 50 ppb

Use 1 for Calibration

Use 7 for MDL

Use 4 for IPR

"Look at the results to see if they are reasonable . If discussions with the lab that obtained the data indicate that they screwed up and that they believe that they could do better, adjust sigma downward accordingly. Similarly, if the data appear to be too good based on experience with similar analytes in other labs; adjust sigma upward accordingly. Given 1imited data, there isn't much more that could be done."

Methods 625 and 8270 (water matrix)

Analyte	Acceptance Limit (625)	Acceptance Limit (8270)	DOD/DOE Limit
Naphthalene	21-133	86.8	40-121
Phenol	5-112	81.8	NA

"Conceptual" Analytes

- Analytes published with no performance data, but someone thinks it could be possible to analyze for them
  - e.g., Phthalic Anhydride (8270D)

Phthalic Anhydride and Water

- "Half-life for phthalic anhydride in water is 30.5 seconds at pH 7.24. At pH 6.8 the half-life is prolonged to 61 seconds."
  - So how can this be measured in water?
  - Why do at least 13 labs have this in their scope?
  - Where is their performance data?
  - How did they get accredited for this?

Solutions

- Consider any published performance data to be suspect, especially single-laboratory data
- Use limits established through inter-laboratory studies
- Generate your own limits and be prepared to defend them
- Eliminate analytes from methods that do not work
- Ask EPA to perform rigorous method validation on any new methods, or not publish them

PBMS

Holding Times

"Samples should be analyzed as soon as possible after collection. The times listed are the maximum times that samples may be held before analyses and still be considered valid."

40 CFR Part 136

A hobgoblin that likely cannot be destroyed anytime soon

Hypothesis

- If they are valid, data quality is jeopardized if holding times not met
- If they are not valid:
  - Thousands of data point qualified as less accurate each year.
  - Meeting holding times is a major factor in laboratory fraud

Causes of Analyte Degradation

- Microbiological degradation
- Volatilization
- Reaction with preservative
- Light
- Other????

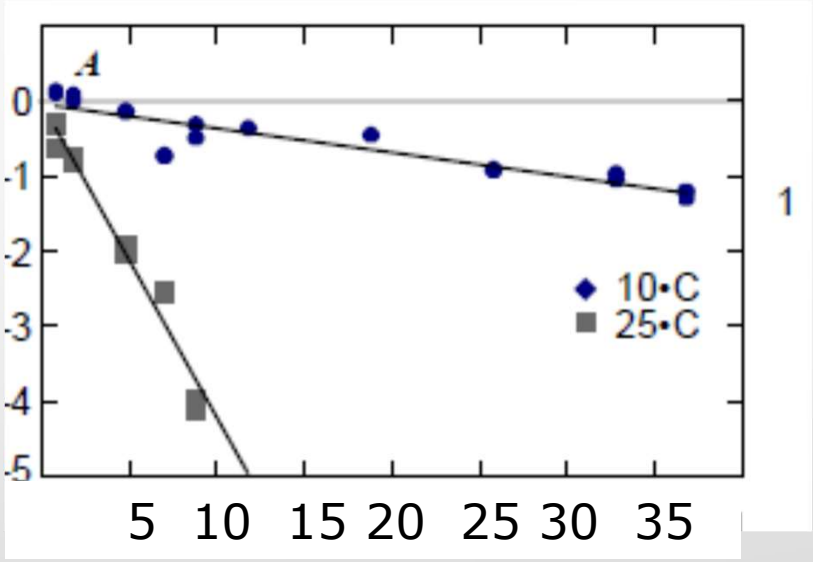
How likely are any of these factors in a zero-headspace vial stored at 4 degrees in the dark and with acid preservation?

Do all organics degrade at 7 days?

Carbaryl

- Do not apply within 3 days of harvest
- Implication: This pesticide degrades in 3 days.

Degradation Rates of Six Pesticides in Water from the Sacramento River, California



PCBs

- Manufacturing ceased in the 1960's
- If they degrade in 7 days, why do we still find them?

"Our results are further evidence that a maximum intrinsic elimination half-life for persistent chemicals such as PCBs exists and is approximately 10-15 **years**."

What about Volatile Organics?

- The results of the studies demonstrate that nearly all target analytes are stable over a 16 week period. Inter-laboratory performance was determined to be a much greater source of variation than holding times, even for unpreserved samples.

Dave Bottrel and Joan Fisk, USEPA

NEMC 1989

Solutions???

- No silver bullet and nothing easy because they have been in place for so long
- Start with the data validation guidelines and get HT removed as a data quality element
- Work with EPA to only publish HTs when data exists to support them
- Work with EPA to revise the footnote to Table II of Part 136 and modify Table II