OELA Oregon Environmental Laboratory Association

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THE LEADER IN ENVIRONMENTAL TESTING

EPAs New MDL Procedure
What it Means, Why it Works, and How to Comply

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A Revision to the Method Detection Limit

EPA published a revision to the 40 CFR Part 136 MDL procedure in the Federal Register on Thursday February 19th

This is a proposed rule with public comments due by May 20th

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What is the MDL?

Lloyd Currie's original concept

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L_C

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

Equals the MDL equals the TNI LOD

L_D

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

Not routinely used in environmental testing (included in the DOD QAPP)

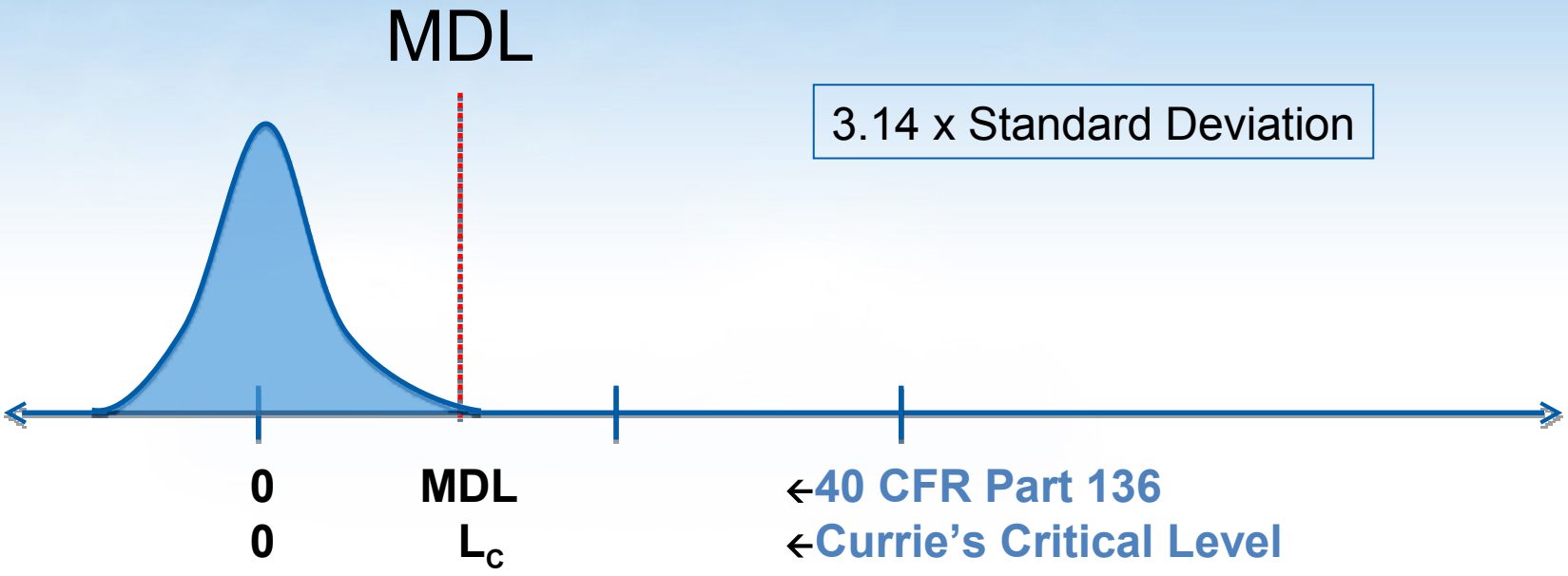
L_Q

- The lowest amount that gives quantitative results

Conceptually, equals TNI LOQ, EPA ML and EPA LLOQ

MDL

MDL The method detection limit (MDL) is defined as the minimum measured concentration of a substance that can be reported with 99% confidence that the measured concentration is distinguishable from method blank results



What the MDL is (and is not):

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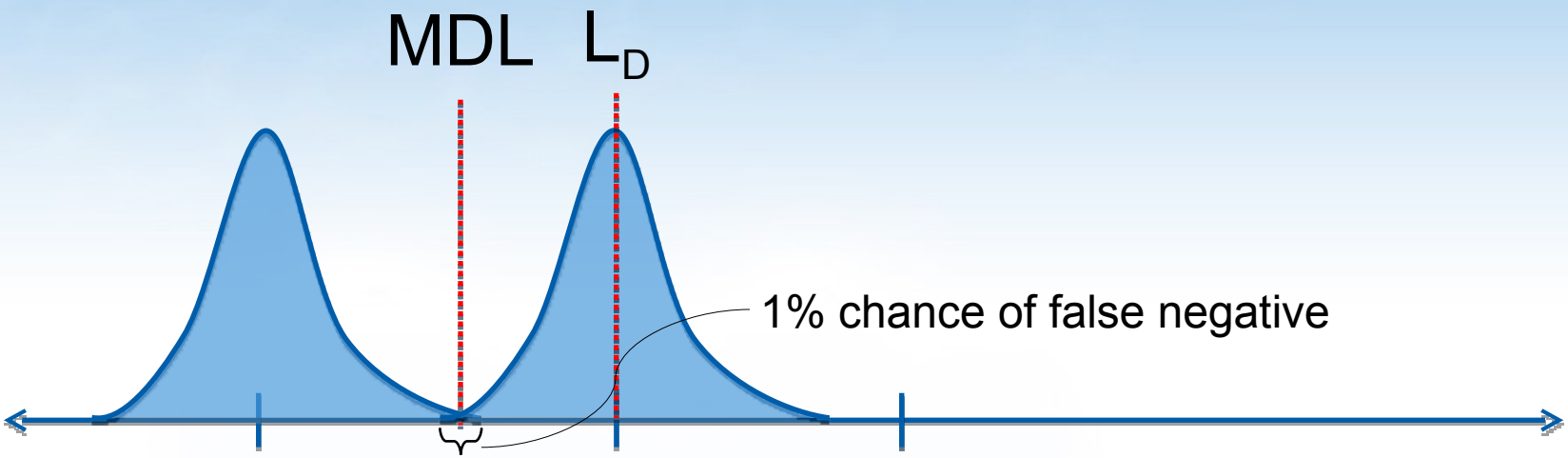
MDL = Lowest result that can be distinguished from blanks

Or, lowest result that means there is actually something in the sample

MDL ≠ Lowest amount in a sample that can be reliably detected

MDL and Currie's L_D

Currie's L_D is the minimum true concentration that is reliably detected (i.e., gives a result above the MDL)



0	MDL	--	←40 CFR Part 136
0	L_C	L_D	←Currie's Detection Level
0	DL	(LOD_{DOD})	← DOD

What does this mean regarding verification?

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- MDL **can** be verified by examining blank results
- MDL **cannot** be verified with spiked samples
  - (Curries L_D could be verified with spiked samples)

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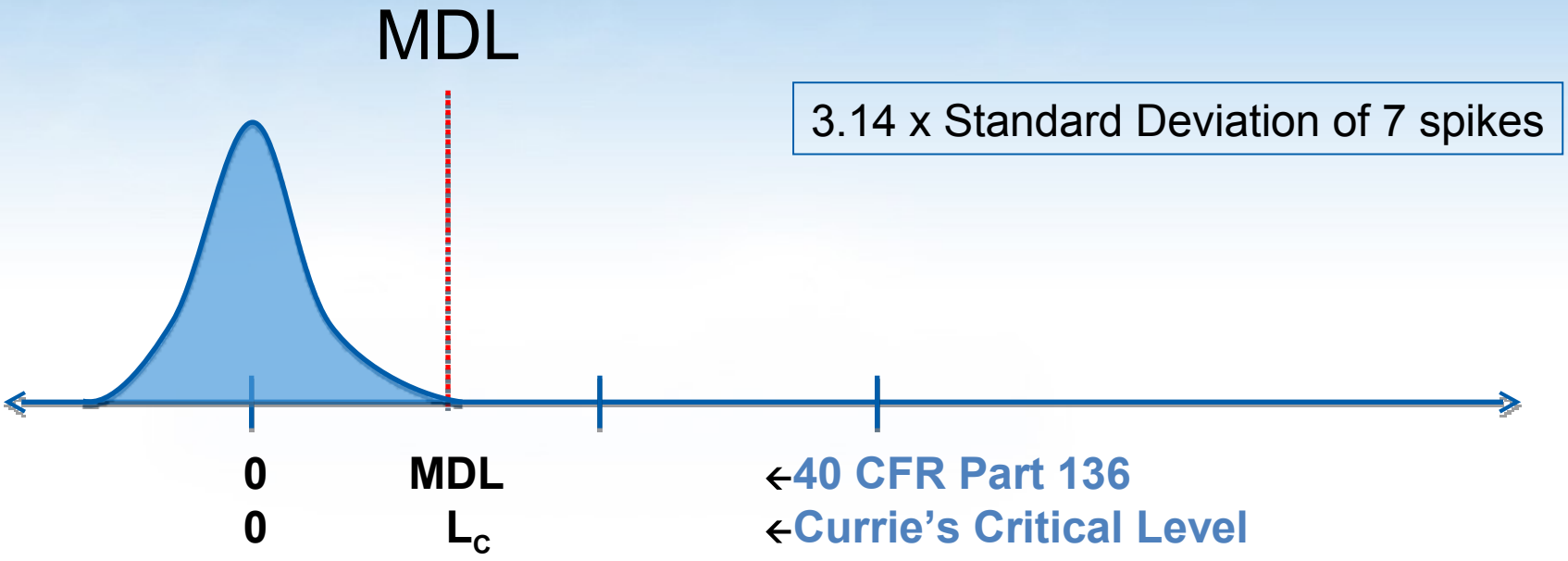
Problems with the Current MDL

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



Lead in Particulate Matter

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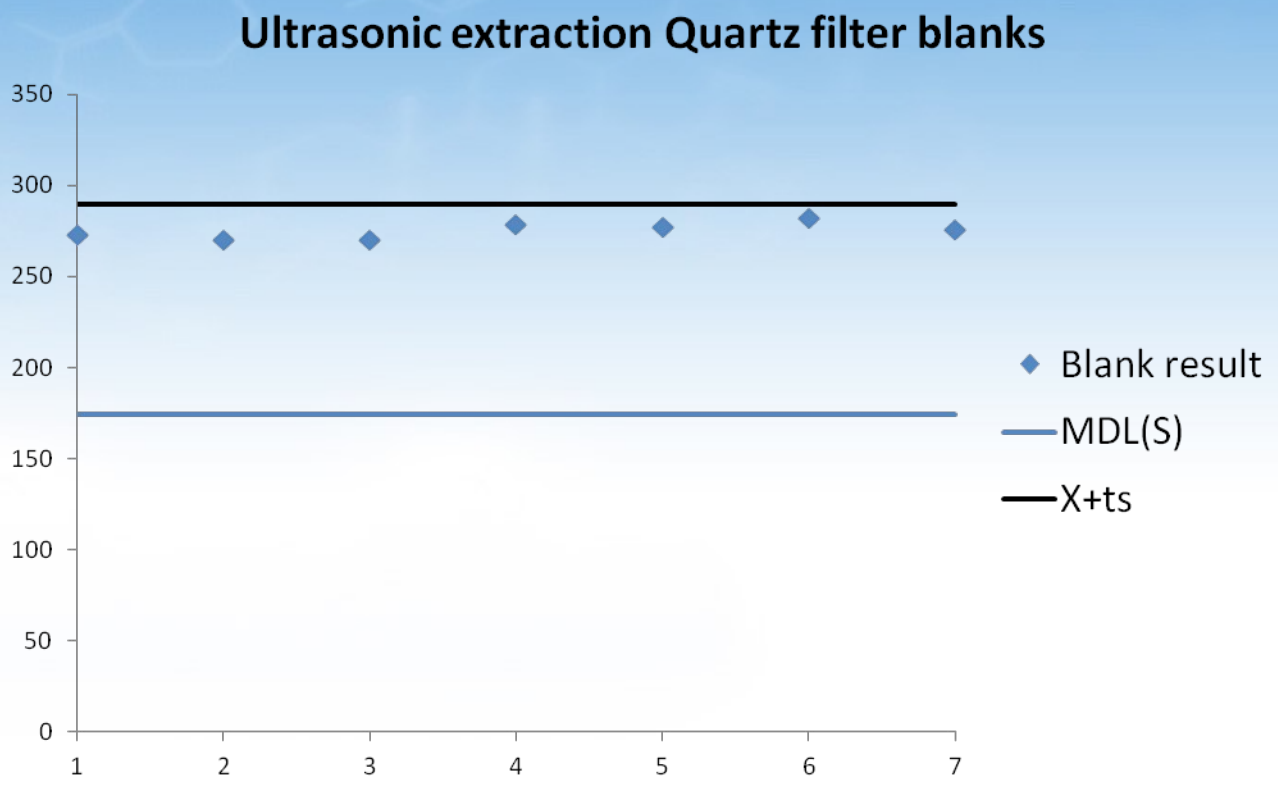

Variance and Verification

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- Current MDL assumes that short term and long term variance are the same
  - Variability of instrument response in one batch is the same as variability of instrument response over the course of a year???
- Current MDL has no verification that results obtained are reasonable

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Why do we need an MDL?

Reason #1 that we need MDLs

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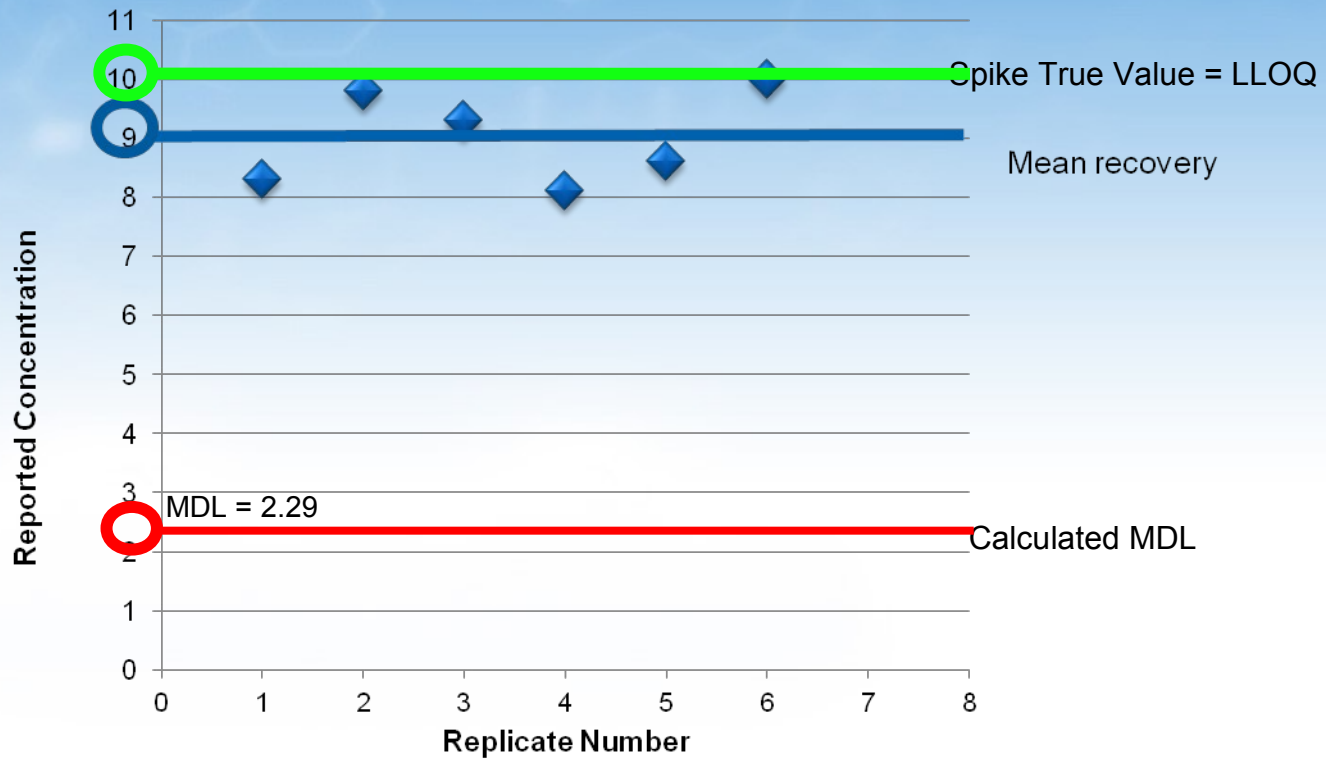
We need to make the Quantitation limit meaningful

- Applies to MRL, LLOQ, or any quantitation limit

90% recovery, 9% RSD

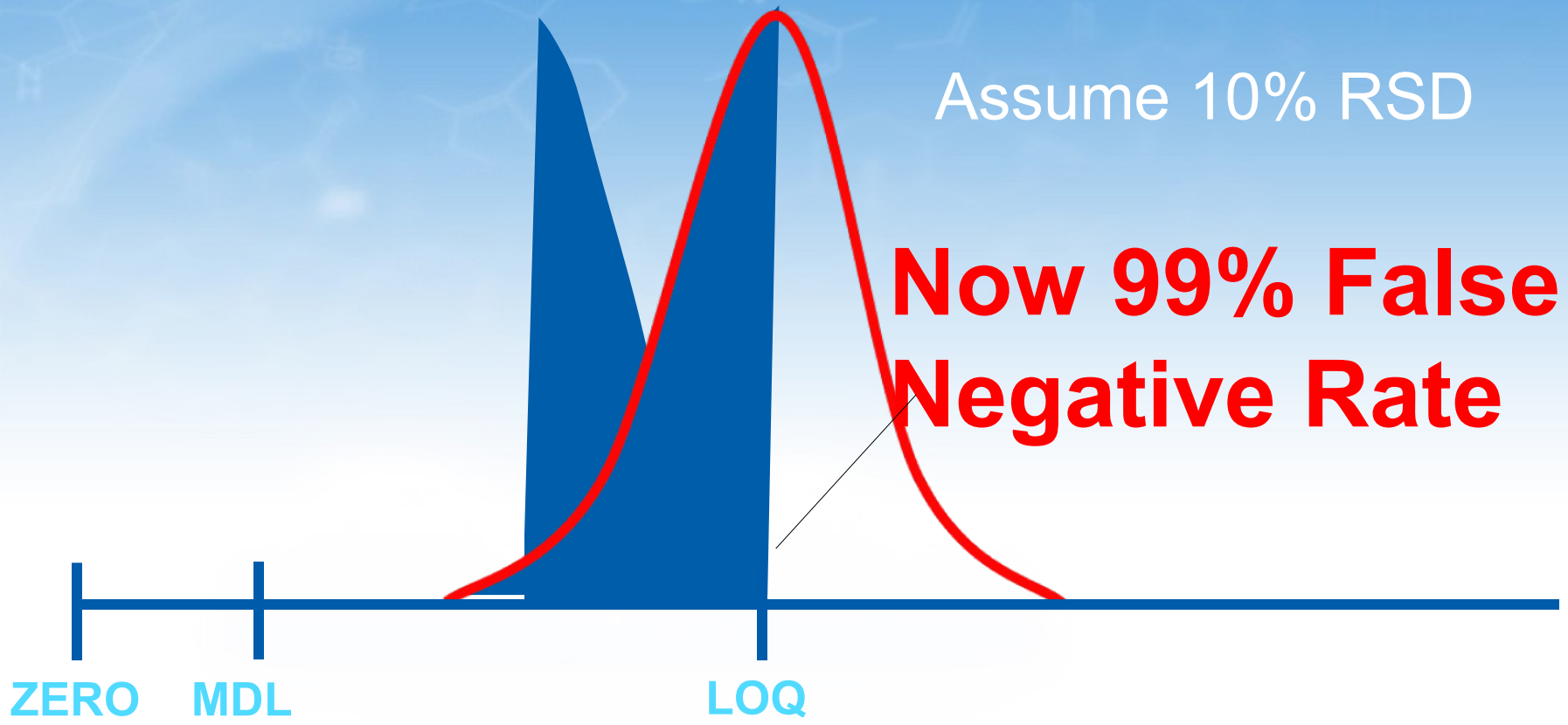
Spike	#1	#2	#3	#4	#5	#6	#7	Mean	MDL
10	9	8.3	9.8	9.3	8.1	8.6	10.0	9.0	2.29



Reported results (without MDL)	ND	ND	ND	ND	ND	ND	10

If you run 100 spikes at LLOQ…

What if you have 70% average recovery?



Bottom Line

If you don't report below the LOQ you have a lot of false negatives

You can't minimize false negatives and false positives at the same level

With the LOQ and the MDL, false negatives are controlled at the LOQ and false positives are controlled at the MDL

Reason #2 that we need MDLs

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MDLs are needed in risk assessment

- Handling non-detects
  - ~ Substitute a value such as ½ detection limit or detection limit
  - ~ More sophisticated methods such as Maximum Likelihood estimation and Regression on Order statistics
    - These still benefit from a detection limit as low as possible

If we do not have a detection limit, the Quantitation limit will become the new Detection limit

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Details of the Modifications

First, what stays the same?

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- Fundamental concept 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?
- Fundamental approach is unchanged
  - Describe the distribution as Student's t times the standard deviation of results

What is different?

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- Requires calculation of a MDL based on blanks as well as a MDL based on spikes (the higher of the two becomes the MDL)
- Incorporates longer term variance
- Includes checks for reasonableness
- Works effectively with various quantitation limit concepts and procedures

Details, details

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- Spiking level
  - 2-10 times estimated MDL
- Run spiked replicates in at least 3 separate preparation and analysis batches
- Multiple instruments
  - At least 2 spike replicates on each instrument
- If blanks give ND, MDL_B does not apply
- Addendum for MDL determined on a specific matrix
- No 10X rule
- Use all method blanks unless batch was rejected

How the modifications improve the procedure

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- 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%
    - ~ 8021B 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

How the modifications improve the procedure

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- 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 to the MDL
- Ongoing verification
- Very consistent with EPA office of Water MRL, EPA ORCR LLOQ and the proposed TNI LOQ

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Conformity with TNI Standards

TNI proposed Quantitation Limit (LOQ) Requirements

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- Select a Quantitation Limit (at least 3 times MDL)
- At or above low calibration standard
- Initial Verification
- Process 7 samples through all steps of the method, spiked at of below LOQ
- At least 3 batches on 3 separate days
- Must be at least 3X MDL, if not raise to at least 3X MDL but do not repeat spikes at higher level
- Measure precision and accuracy of LOQ spikes

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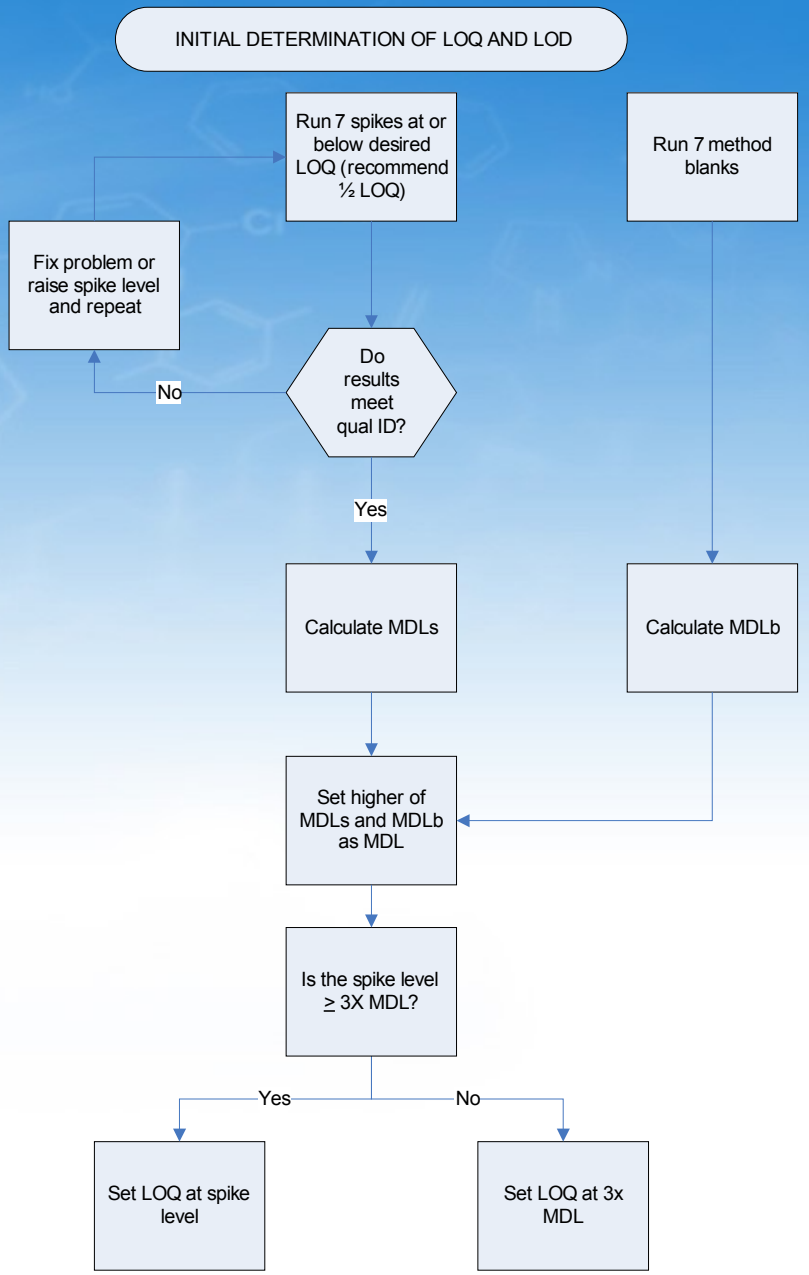
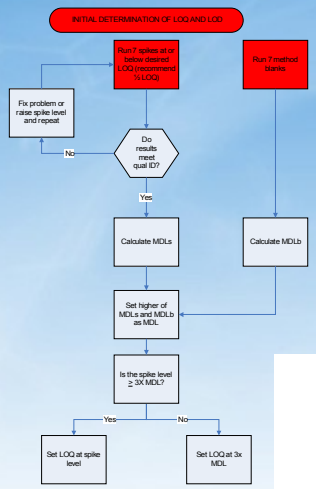
How to do a LOQ / MDL study

LOD/LOQ Process flow chart



Initial LOQ



Select LOQ

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- Choose your LOQ
  - Must be at or above low calibration standard
- Run 7 spikes through the whole method in the range 0.5 – 1X LOQ
  - At least 3 separate batches
  - At least 2 replicates on each instrument
- Run 7 method blanks
  - At least 3 separate batches
  - At least 2 replicates on each instrument

Can use existing data

LOQ – Key Components

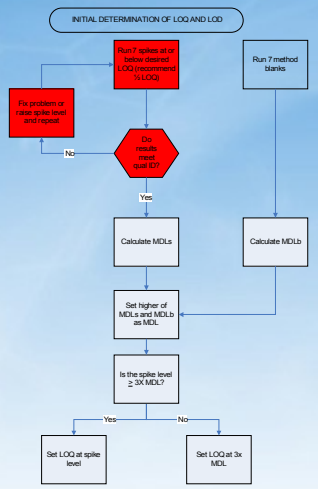
- Spike at or below LOQ
- Results must be > LOD
- Statement of precision and accuracy
- Ongoing verification

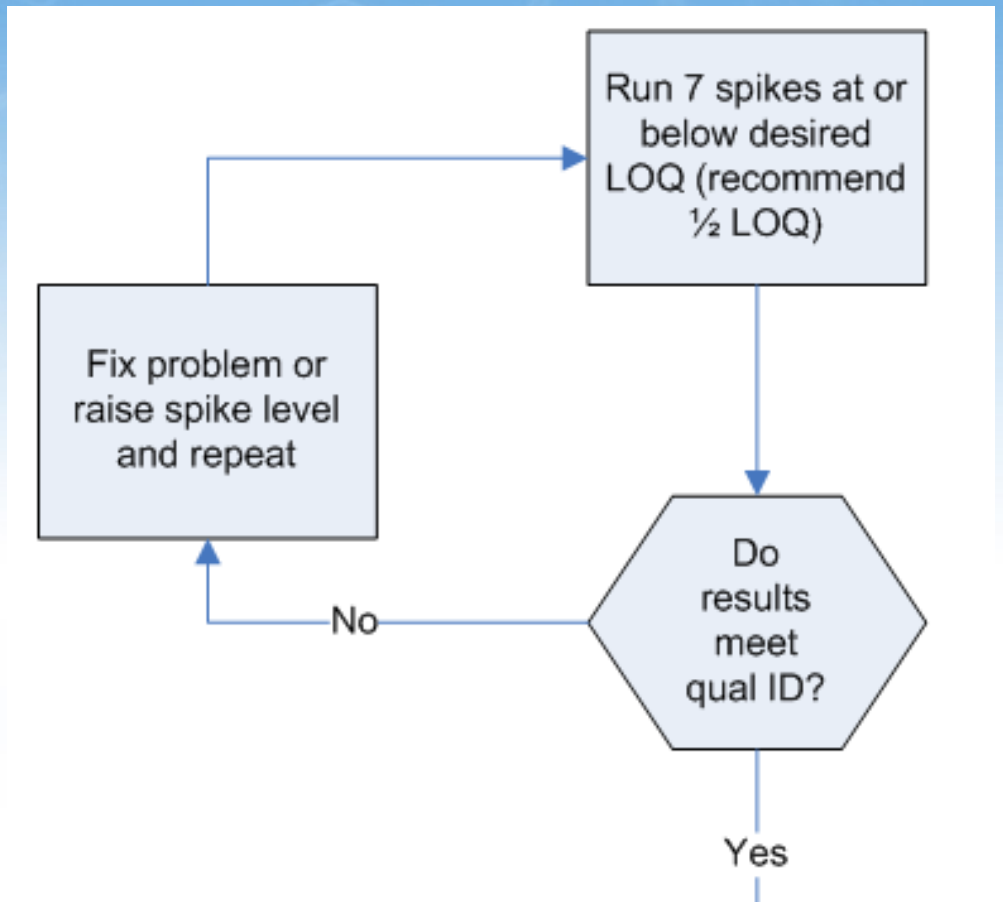
Multiple instruments

i) If there are multiple instruments that will be assigned the same LOQ, then the initial verification samples must be distributed across all of the instruments

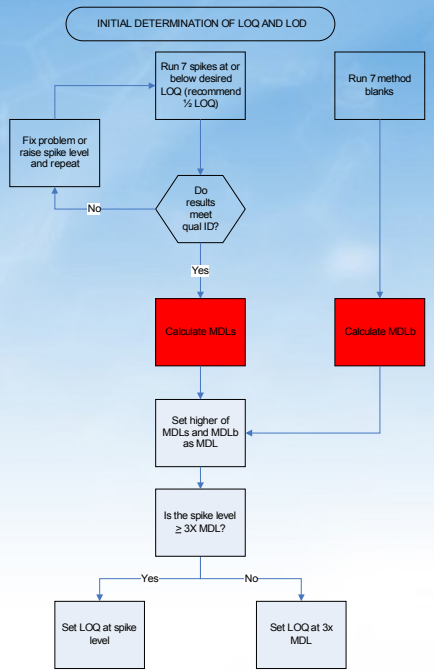
ii) A minimum of two initial verification samples prepared and analyzed on different days is required for each instrument

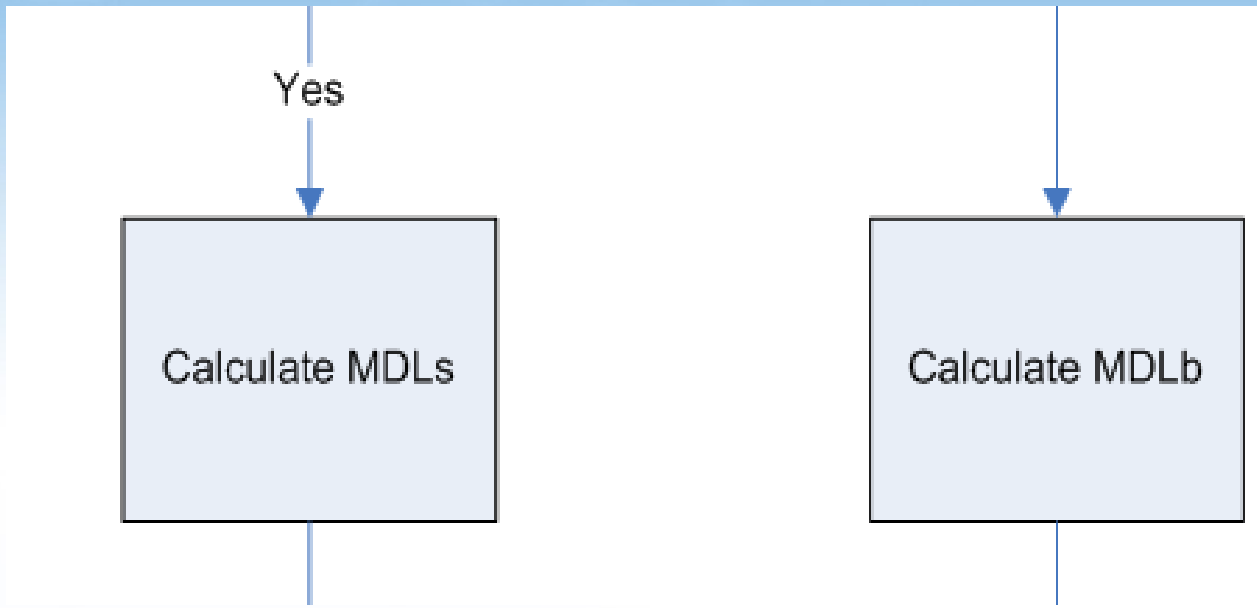
Verify meeting Qualitative ID criteria





Calculation of MDL (LOD)





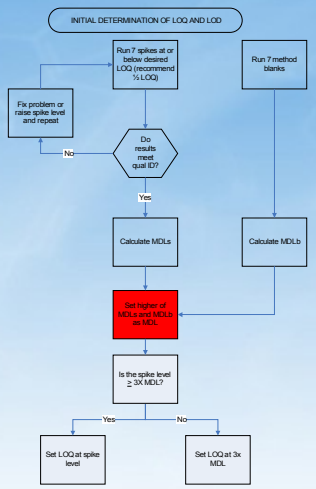
Evaluation of Blanks

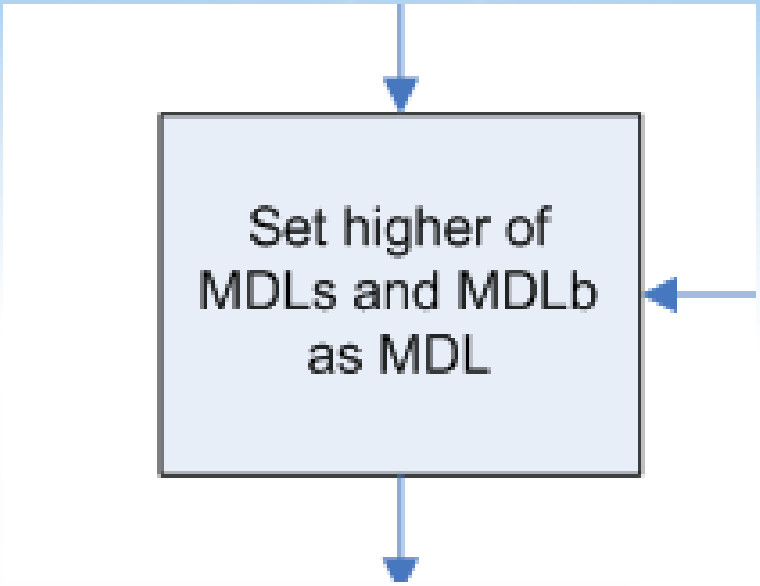
If all blanks are ND	MDL_B = Zero
If all blanks have numerical results	MDL_B = X +ts
If some blanks have numerical results	Use 99 percentile

Eg: There are 164 blank results
Highest results are 10, 5, 1.9, 1.7
164 x 0.99 = 162.36, rounds to 162
Use the 162nd highest blank, which is 1.9

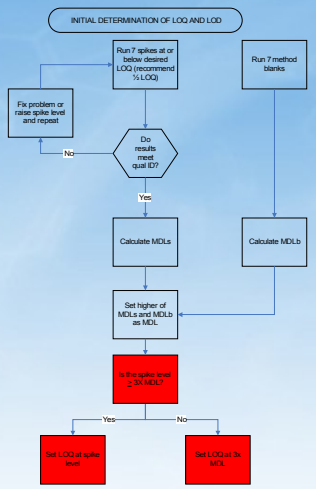
The percentile approach may also be used when there are > 100 blank results and all blanks have numerical results

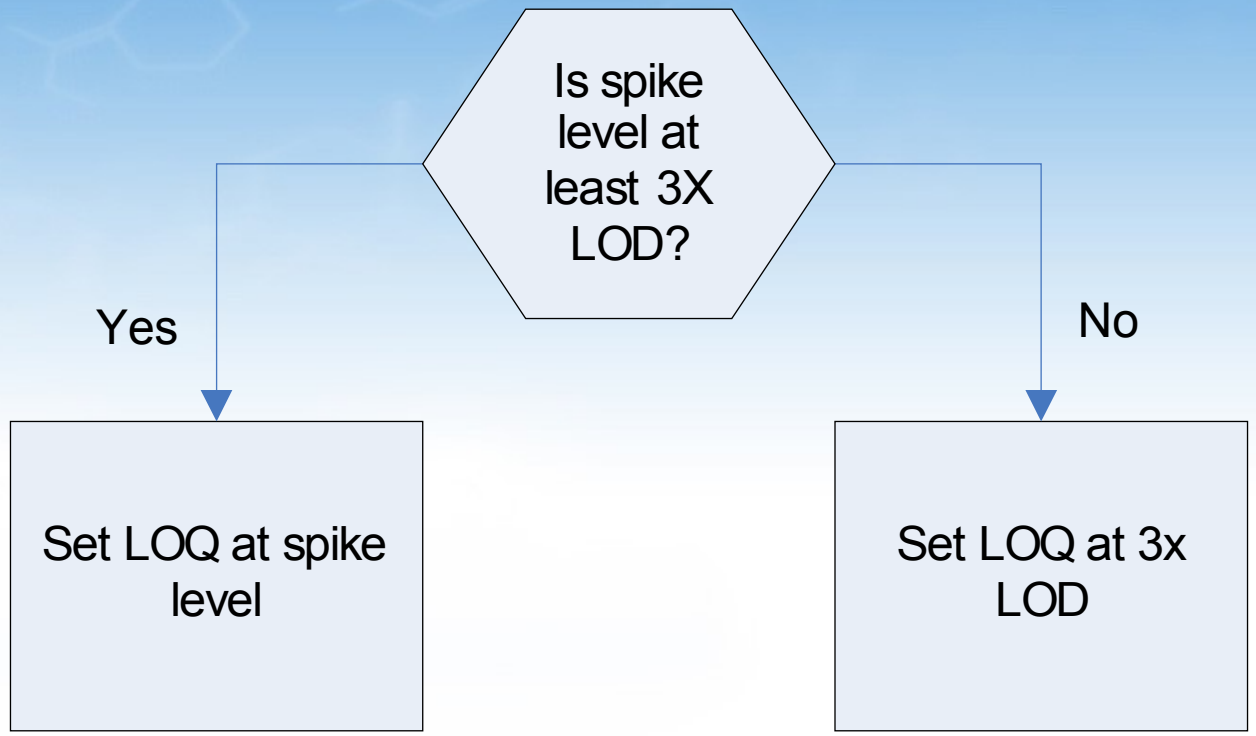
Finalize MDL (LOD)





Assess LOQ relative to LOD





Good precision, good recovery

Spike	1	2	3	4	5	6	7
10	9.5	9.8	10.2	10.6	9.4	9.7	9.9

MEAN	STD. DEV	MDL S
9.9	0.4	1.3

Blanks	ND	ND	ND	ND	ND	ND	ND

MEAN	STD. DEV	MDL B
0.0	0.0	0.0

MDL	3X MDL	LOQ
1.3	3.9	10.0

Good precision, moderate recovery

Spike	1	2	3	4	5	6	7
10	7	7.3	6.9	8.1	7.7	7.3	7.9

MEAN	STD. DEV	MDL S
7.5	**0.5**	**1.4**

Blanks	ND	ND	ND	ND	ND	ND	ND

MEAN	STD. DEV	MDL B
0.0	0.0	0.0

MDL	3X MDL	LOQ
1.4	**4.3**	**10.0**

Poor/Moderate precision and recovery

Spike	1	2	3	4	5	6	7
10	6	7.3	7.6	5.7	7.2	7.9	5.3

MEAN	STD. DEV	MDL S
6.7	1.0	3.2

Blanks	ND	ND	ND	ND	ND	ND	ND

MEAN	STD. DEV	MDL B
0.0	0.0	0.0

MDL	3X MDL	LOQ
3.2	9.7	10.0

Poor precision, poor recovery

Spike	1	2	3	4	5	6	7
10	5	7.1	3.2	6.5	7.4	3	3.3

MEAN	STD. DEV	MDL S
5.1	**1.9**	**6.1**

Blanks	ND	ND	ND	ND	ND	ND	ND

MEAN	STD. DEV	MDL B
0.0	**0.0**	**0.0**

MDL	3X MDL	LOQ
6.1	**18.2**	**18.0**

Good precision, elevated blanks

Spike	1	2	3	4	5	6	7
10	13.5	12.8	14.2	14.6	13.4	13.7	13.9

MEAN	STD. DEV	MDL S
13.7	**0.6**	**1.8**

Blanks	3.1	4.2	3.9	4.4	3.8	3.2	4

MEAN	STD. DEV	MDL B
3.8	**0.5**	**5.3**

MDL	3X MDL	LOQ
5.3	**16.0**	**16.0**

Determine the LOQ – with 10% RSD

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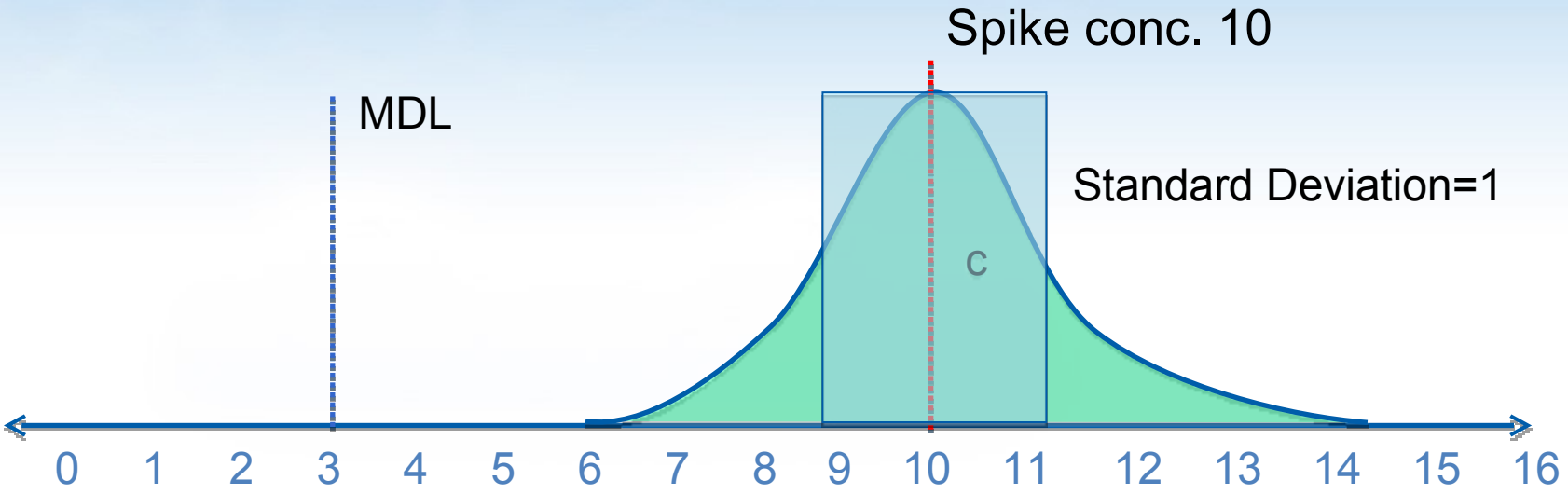
1. Spike at: **10**
2. If RSD is 10%, the standard deviation is: **1**
3. So MDL would be about: **3**
4. CHECK: Is spike concentration at least 3x MDL?
5. YES: MDL (3) x3 = 9, and 10 is greater than 9.



Determine the LOQ – with 20% RSD

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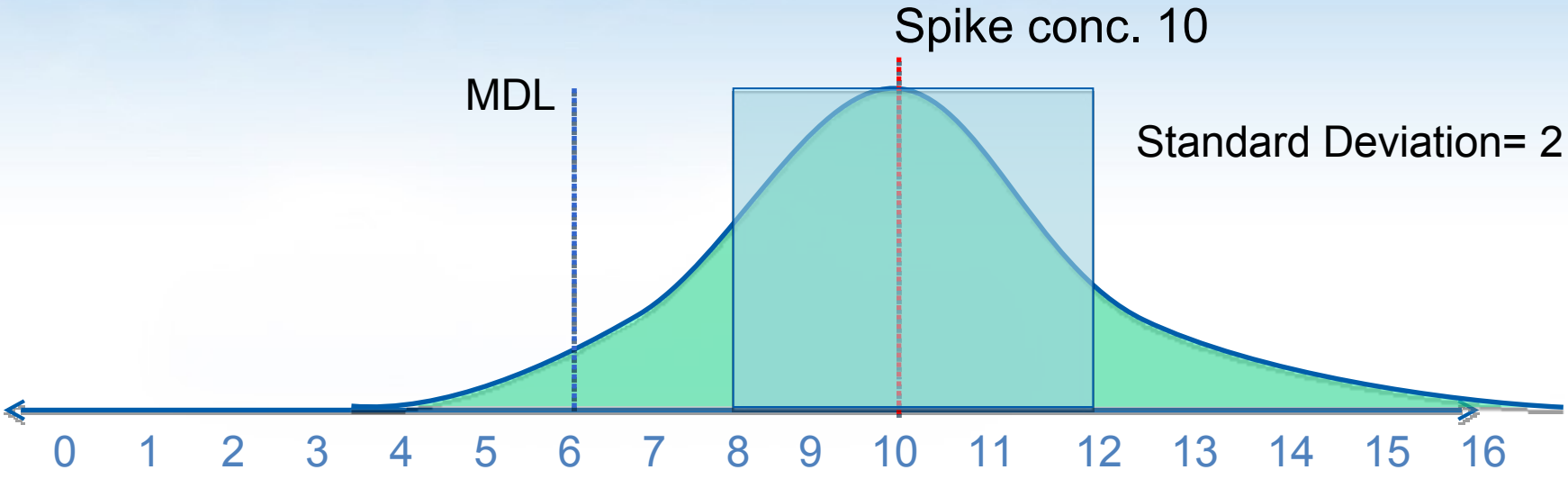
1. Spike at: 10
2. If RSD is 20%, the standard deviation is: 2
3. So MDL would be about: 6
4. CHECK: Is spike concentration at least 3x MDL?
5. NO: MDL (6) x3 = 18. Ten is not greater than 18. LOQ needs to be at least 18.



4,6-Dinitro-2-methylphenol

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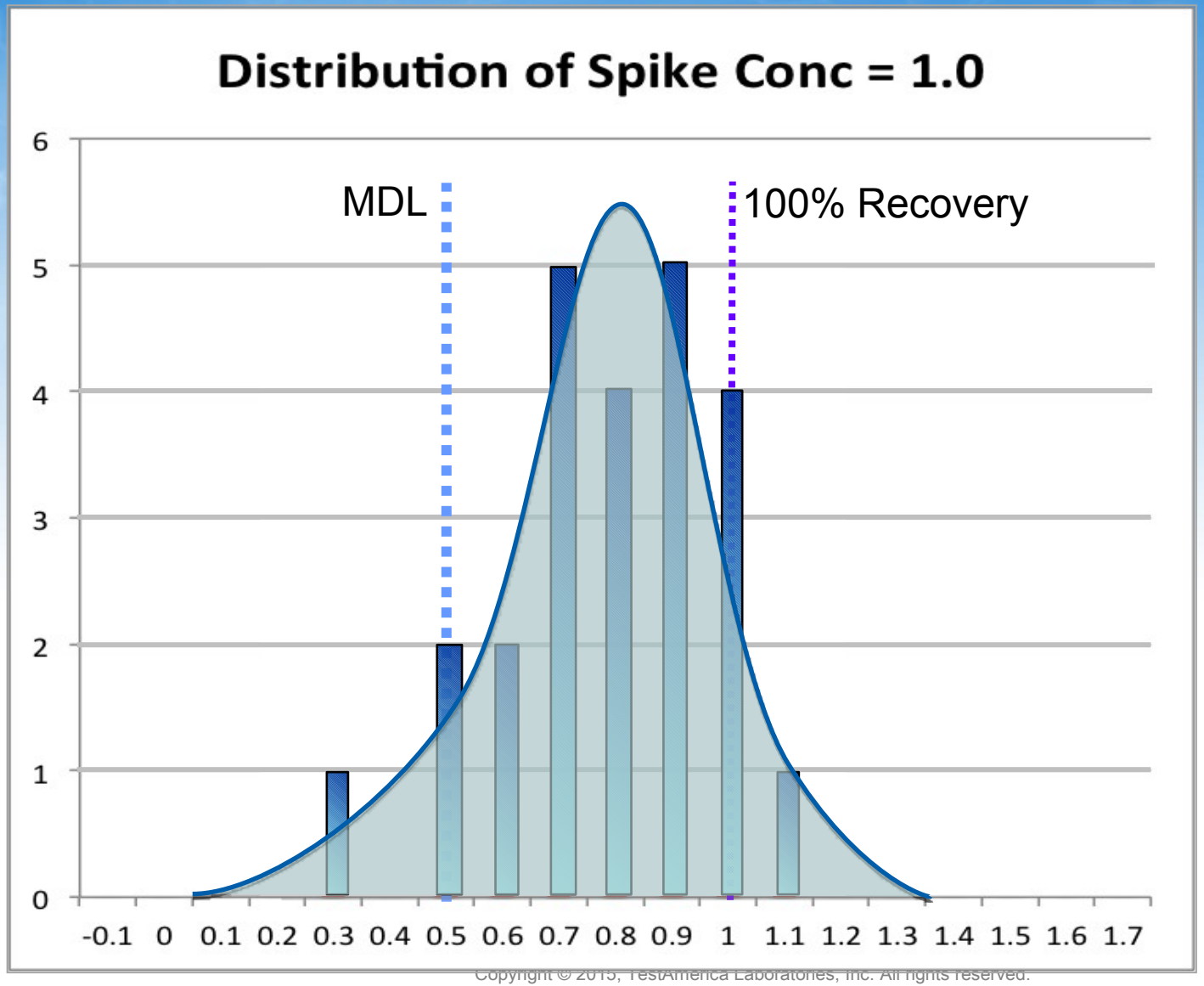

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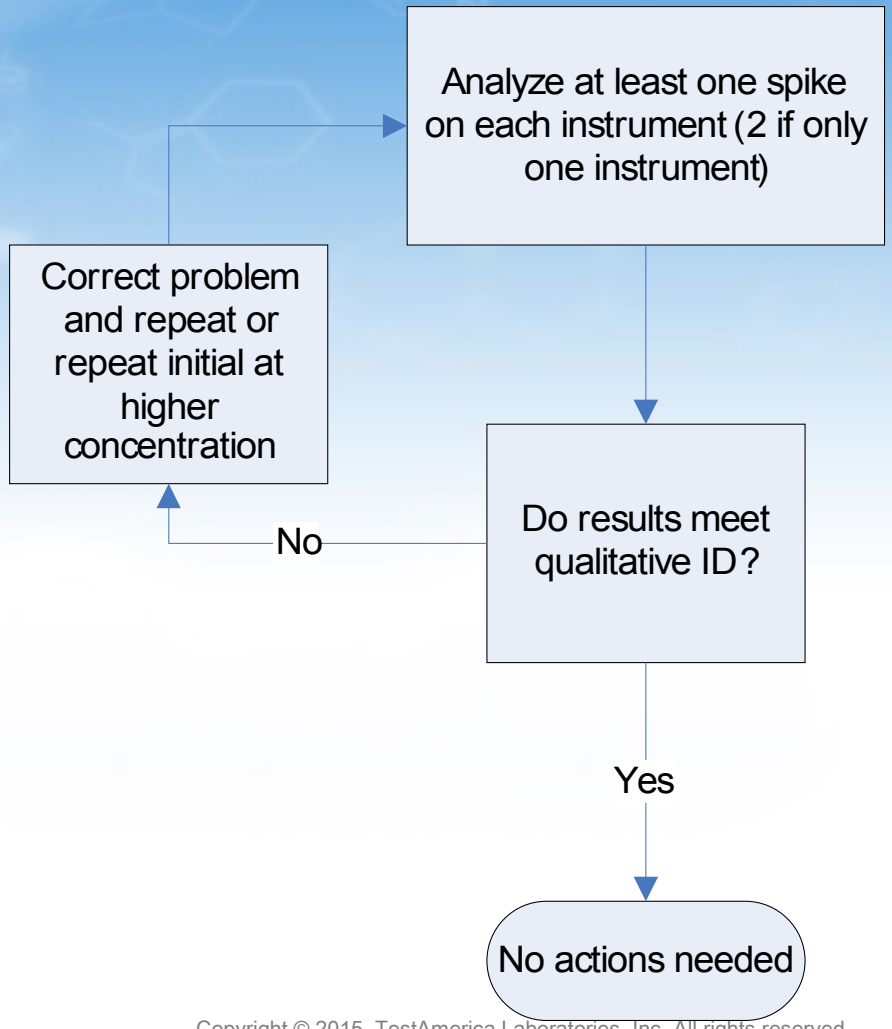
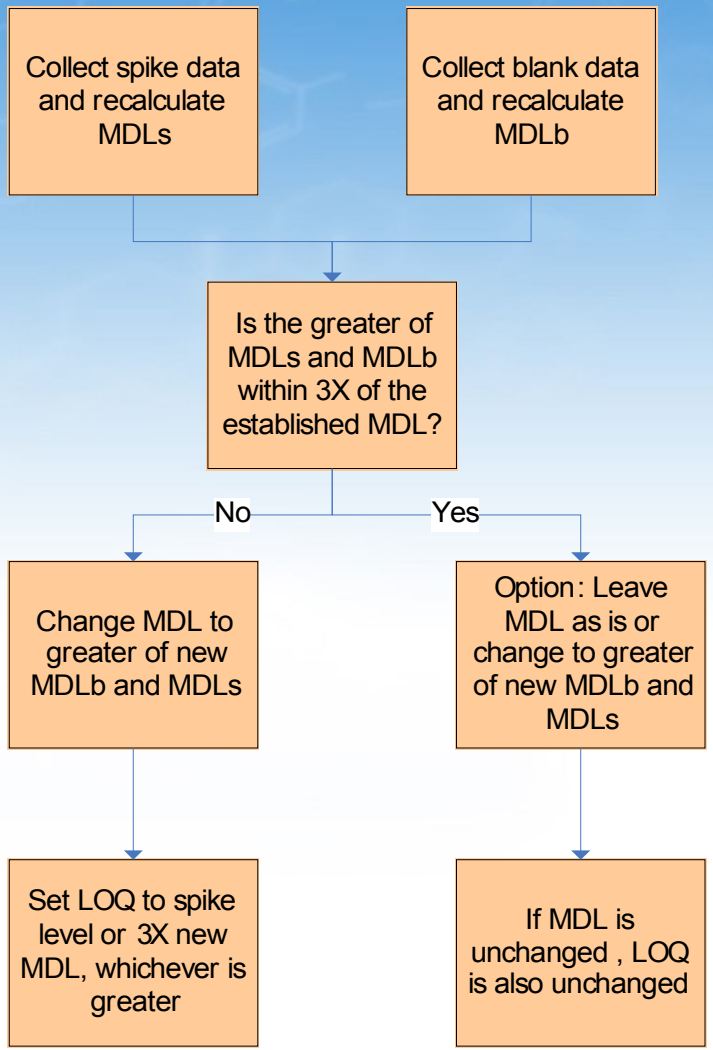
Ongoing verification

Quarterly verification



Annual verification - If using MDL as MDL



What do we expect from a LOQ?

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Known precision? 

Known accuracy? 

Ability to detect and report? 

- Freedom from false negatives? 

Freedom from False positives? 

What do we expect from a MDL?

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Freedom from false positives (99%)? 

Known accuracy? 

Ability to detect and report? 

Freedom from false negatives? 

What does this mean to labs?

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- Clear requirements
- Sensible MDLs
- Level playing field
- Low transition costs since existing data can be used
  - Note – labs should start complying with 3 batch rule right now
- Some additional organizational requirements

What does this mean to data users?

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- MDLs that make sense
- Much lower rate of false positives, especially for ICP, ICPMS and some general chemistry tests
- Easier to compare labs
- In general, more reliable data = better decision making

How much will MDLs change?

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- Analytes with minimal or no detects in blanks, eg most GC/MS analytes at normal levels:

Not Much

- Analytes with frequent detects in blanks, eg, metals, very low level PAH, some general chemistry tests:

Depends

  - If the lab is currently adjusting MDLs to avoid excessive false positives, not much
  - If the lab has been pushing MDLs below levels justified by the blanks, potentially quite a bit

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Questions?