

Limits, Levels and Choices ... Oh My!

Method Detection Limits ... MDLs
Method Reporting Limits ... MRLs
Levels of Quantitation ... LOQs

Northern Pike

Before it came out of the
water ... did you know it was
a pike?



Photo compliments of ND Game
and Fish

Muskie

... or could you have lured this muskie instead?



Photo compliments of
ND Game and Fish

How do you know ... before you know ...?



Or ... Do you know what you know
when you know it?



Its foggy ... and the Mallards are all mixed together ...



How do you know the difference between the drakes and the hens?



Knowledge Tools Experience

... the necessities of a
great hunt ...
Gets Results!



Photo compliments of ND Game
and Fish

Knowledge Tools Experience

Knowledge Tools Experience

We know what to
look for.

We know how low
we can look.

We know how high
we can look.

Defensible
Laboratory Results

So ... I'm getting results from the lab ...

... How do I know it's the right thing ... the right level ... and
... how sure can I be that ... “it is what it is” ?

QC

Great ... another acronym ...

And there are so many Acronyms

QC QUAP **IDL** LOD LFB PT QCS ICP GSMS
PCB FID SOS LRB CAB LFM DUP LFMD SOP
LCR LDR **MLQ** **MDLs** LQ ODLSTW HELP
FIA ISE MS ECD PH EPA **LOL** NDELCP
MRLs **ASAP** DBP THM SOC VOC ASTM
PDQ IRS SDWA CWA **LOQ** ODW **CRM** AOAC
OMG

QC ... Quality Control. It's in the Acronyms!

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Acronyms for limits and levels

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IDL and MDLs

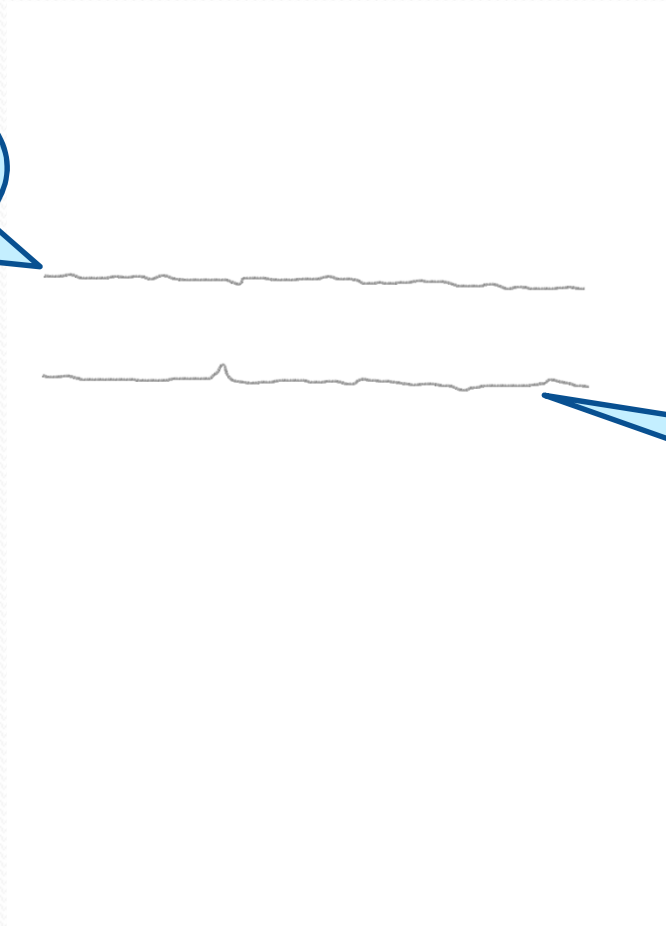
IDL ... Instrument Detection Level

“ ... concentration that produces a signal greater than five times the instrument’s signal:noise ratio ... “ or ...
... “1.645 times the standard deviation of blank analysis”.

*From Standard Methods For the Examination of
Water and Wastewater*

IDL ... observed and/or calculated amount.

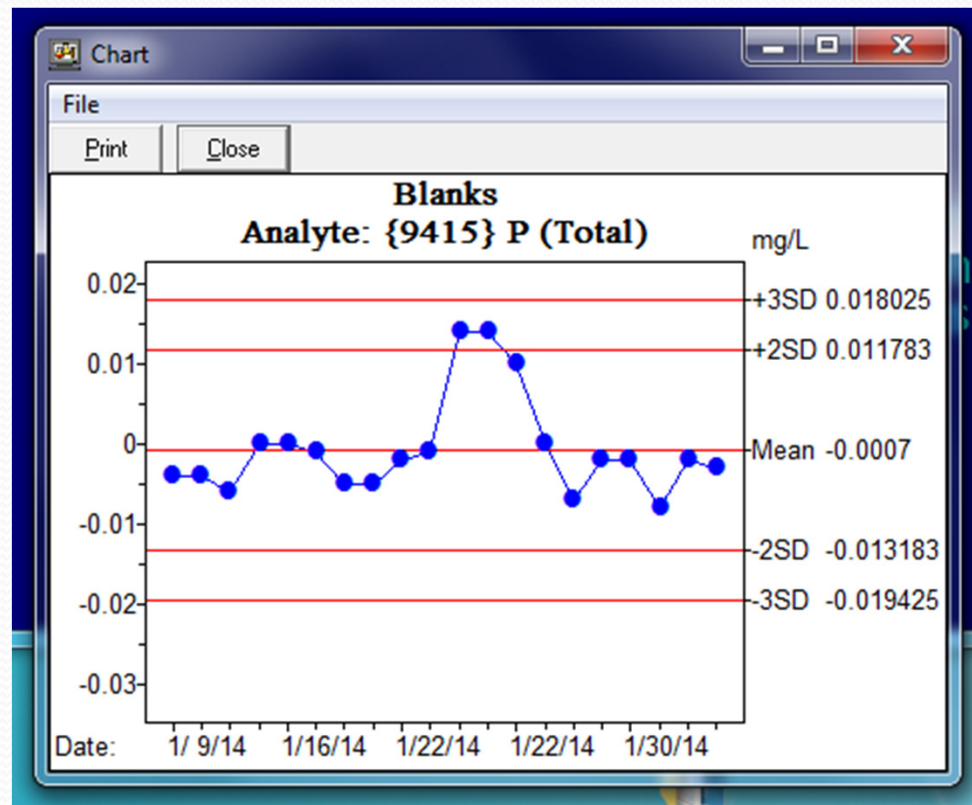
Signal/Noise



2-5X
Signal/Noise

IDL ... observed and/or calculated amount.

IDL is about 0.009 mg/L



MDLs ... Method Detection Limits/Levels

... is defined as the minimum concentration of a substance that can be measured and 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.

40 CFR APPENDIX B TO PART 136

MDLs ... Method Detection Limits/Levels

“ ... the constituent concentration that, when processed through the entire method, produces a signal that has 99% probability of being different from the blank.”

*Standard Method For the Examination of Water
and Wastewater*

Blah ... Blah ... Blah ...





The laboratory limbo ...

“How looooooowwwww can you go?”

Zero < **IDLs** < **MDLs**

Instrument signal < **about 5x signal:noise** < **99%**
certain that the signal = analyte

The **MDL** ...

- Statistically calculated concentration where you would expect to “qualitatively” identify the analyte
- 50% of analyses at this level will fall above the MDL (detected). 50% of analyses at this level will fall below this level (not detected)
- Math applied to a process

MDL ...the math

- $MDL = t_{(n-1, 1-\alpha=0.99)} (S)$
- where:
- MDL = the method detection limit
- $t_{(n-1, 1-\alpha=.99)}$ = the students' t value appropriate for a 99% confidence level and a standard deviation estimate with n-1 degrees of freedom. See Table.
- S = standard deviation of the replicate analyses

<http://www.ecfr.gov/cgi-bin/text-idx?SID=4fo1ee455bc83d7085022ca63dcfoo80&node=40:24.0.1.1.1.0.1.8.2&rgn=div9>

MDLs ... the process

1. Observe instrument signal, method baseline
2. Use the QC chart for Blanks to determine standard deviation.
3. 2-4x the standard deviation = estimated MDL concentration.
4. Spike that concentration into matrix.
5. Process 7 of those matrix spikes and analyze. Must be repeated if 50-150% recovery is not obtained. Ugh!
6. Plug results into mathematical formula and ‘VOILA ... **MDL!**
7. $\text{Spike}/10 < \text{Calculated MDL} < \text{Spike Concentration}$
8. Re-evaluate and re-do if this is not the case.
9. Are we there yet? The process is usually “a study”.

MDL ...the math applied to the process

% recovery : 50-150

Spike/10 < MDL < spike concentration

Successful MDL study!

MDL Calculation Form				
Analyte:	Total Nitrogen			
Method:	SM 4500-PJ			
Instrument:	FIA 8500			
Analyst:				
Date:	2/13/2014			
Replicate	Fortification Level (mg/L)	Result	% Rec	Spike/10
1	0.05	0.0507	101.4	0.005
2	0.05	0.0461	92.2	0.005
3	0.05	0.0464	92.8	0.005
4	0.05	0.0513	102.6	0.005
5	0.05	0.0465	93	0.005
6	0.05	0.0449	89.8	0.005
7	0.05	0.0418	83.6	0.005
Mean		0.046814		
SD		0.003287		
RSD	(SD/Mean) x 100	7.020405		
MDL	SD x 3.14 for 7 replicates	0.01032		

MDLs ... are an estimated, processed and calculated amount.

Required component of each new analyst's demonstration of capability.

Required process each time a major element of the method is changed.

Required as a function of time: annually, semi-annually etc.

- Affected by:
- Method
- Instrumentation and Detectors
- Analyst experience
- Matrix quality
- Environmental conditions of the Laboratory

MRLs

MRLs ... Minimum Report Limits/Levels

“The *Lowest Concentration Minimum Reporting Level* (LCMRL) is defined as the lowest *spiking* concentration at which recovery of between 50 and 150% is expected 99% of the time by a single analyst.” *Definition provided by EPA Office of Groundwater and Drinking Water*

MRLs ... Minimum Report Limits/Levels

“(MRL) – the minimum concentration that can be reported as a quantified value for a target analyte in a sample. Defined concentration is no lower than the concentration of the lowest calibration standard for that analyte and can only be used if acceptable QC criteria for this standard are met.” *Definition provided by Standard Methods for the Examination of Water and Wastewater*

Say what?



MRLs ... are a processed and ... quantitated amount.

If 10 ppm is my MRL:

1. I spike a matrix with 10 ppm
2. If I get a result of 5-15 ppm I am confident that my system and method are working at this lowest level.

What happens if I don't get the expected 50-150% recovery? System out of control ... assess the system from sample preparation through data analysis. Fix the problem and begin anew.

MRLs ... Minimum Report Limits/Levels

- **Required QC** for methods
- **Mandatory Limits** can be defined within CFR and/or within promulgated methods.
- Can be required as part of sample batch QC
- Method may require an MRL to be processed through same extraction as samples. And/or:
- **MRL concentration is the lowest standard in the calibration curve.**

MRLs ... are affected by:

- **Sample dilutions.** A sample diluted at 1:2 will increase the MRL by a factor of 2.
- **Matrix cleanliness.** A sample that needs to be cleaned up may need to be diluted or processed differently. This could result in loss of analyte, loss of method sensitivity and resulting in an increased MRL.
- **Change in Method.** Different detector, eluant, carrier gas, inlet liner, glassware ... and any other number of things used throughout the process.
- **Change in Quantitation.** Calibration curves change with increasing orders of magnitude. If analysis is performed at large orders of magnitude, this can substantially affect the lower end of the curve and thereby “mess with the MRL”.

LOQ

LOQ ... Level of Quantitation

The range of detectable concentration of analyte greater than the detection limit where the accuracy (precision & bias) demonstrated by the laboratory achieves the objectives of the intended purpose.

Oh ... puh ... leeze.

English?

English?

LOQ = Numbers! Results!

The range of detectable concentration of analyte greater than the detection limit where the accuracy (precision & bias) demonstrated by the laboratory achieves the objectives of the intended purpose.

The range is the concentrations of standards used in the calibration curve. From the MRL to a higher defined concentration.

LOQ = Numbers! Results!

The range of detectable concentration of analyte greater than the detection limit where the accuracy (precision & bias) demonstrated by the laboratory achieves the objectives of the intended purpose.

The accuracy objectives are the rest of the QC items within a method : “goodness of fit” of the calibration curve; concentration of measured analyte is bracketed by concentrations above and below the measured analyte; % recovery of analyte is achieved ; etc.

LOQ ...more acronyms ...

- **LDR** : Linear Dynamic Range. The range of analyte concentration where the response to analyte ratio is linear. This linear response is observed past the highest calibration standard
- **LCR**: Linear Calibration Range. The range of calibration standards where the response to analyte ratio is linear.
- **LOQ** : Limit/Level of Quantitation. The entire calibration range where data quality objectives can be met.

Linear Dynamic Range

Linear Dynamic Range

Highest Calibration
Standard

Range past the last
calibration standard
where the analyte
response to
concentration is linear



LOQ ...more acronyms ...


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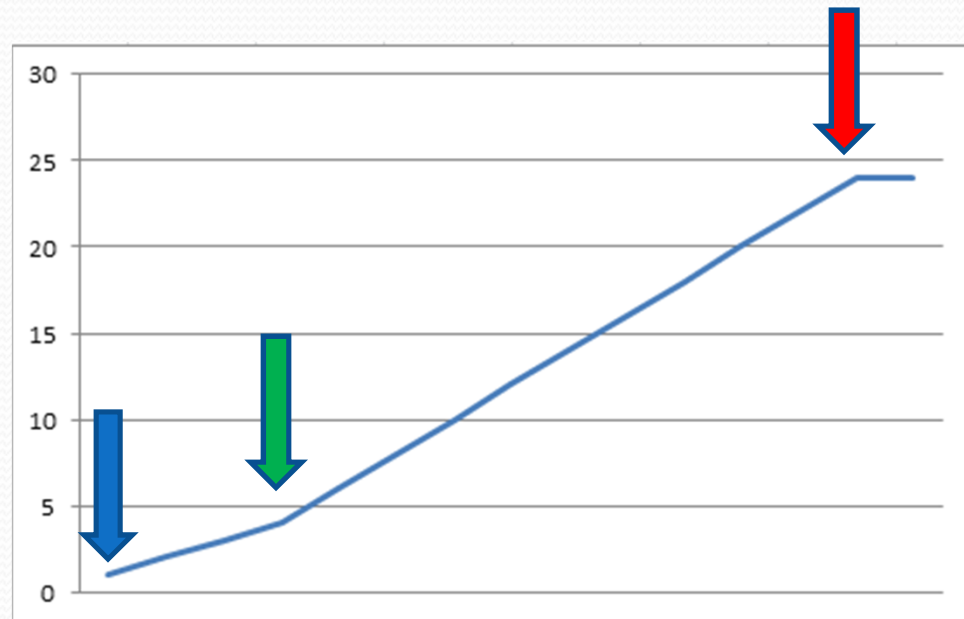
Linear Calibration Range

Three portions of this
“Calibration Curve”

1.  MRL area

2.  Linear portion

3.  Exceeded linearity



LOQ ...more acronyms ...

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- **LCR**: Linear Calibration Range. The range of calibration standards where the response to analyte ratio is linear.
- **LOQ** : Limit/Level of Quantitation. The entire calibration range where data quality objectives can be met. Can also be defined as Operational Range.

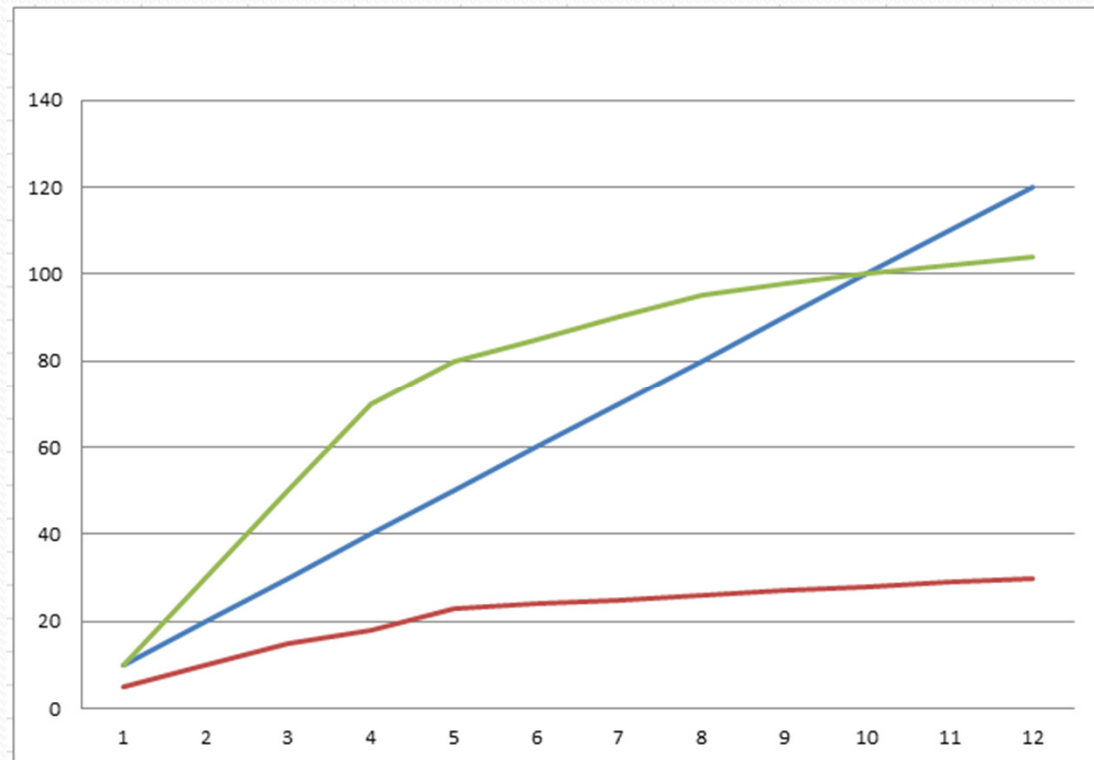
LOQ ... What happened?

Calibration Curves

Linear Curve : proportional response with increasing concentration. An analysts dream!

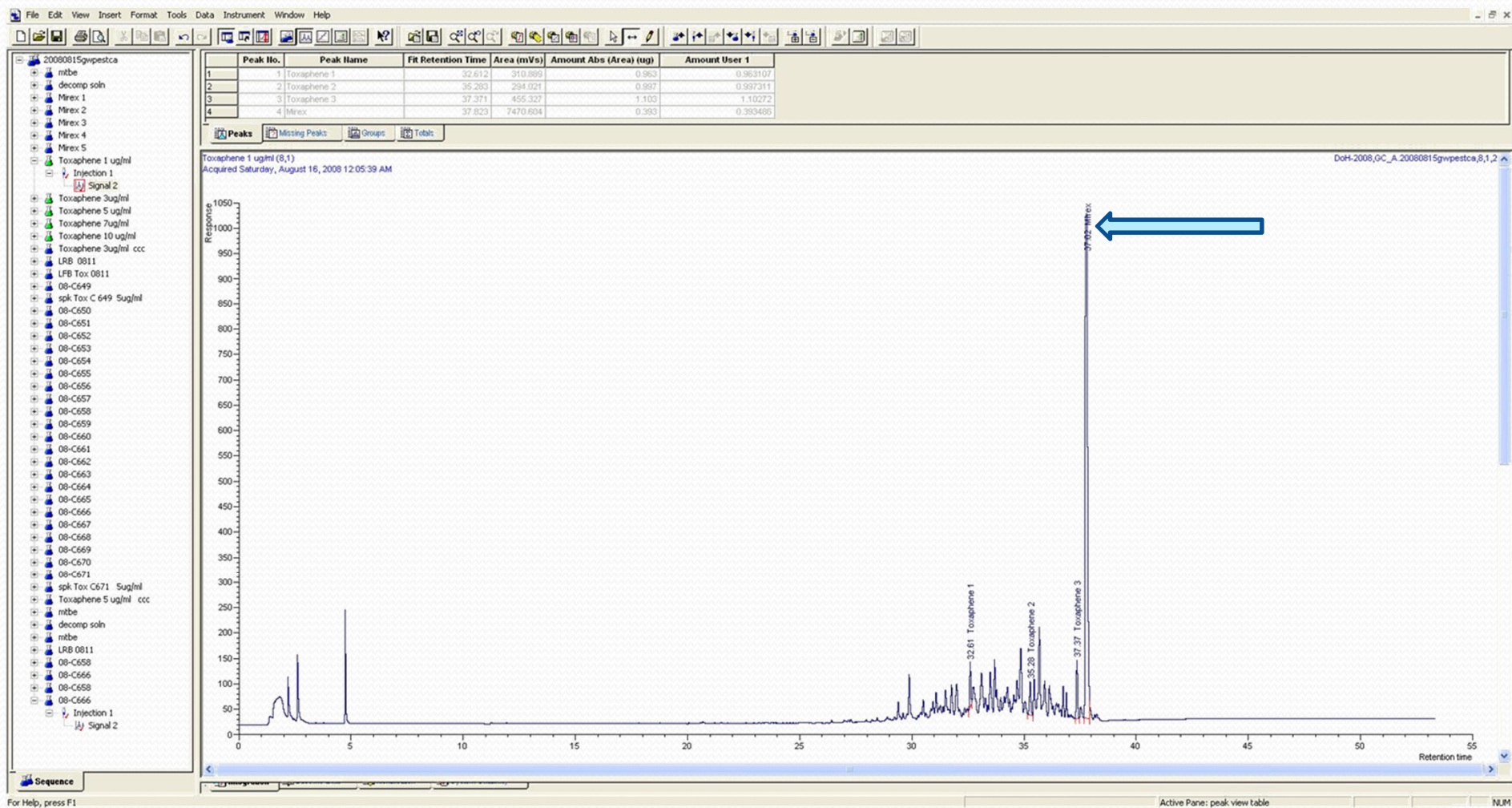
Plateau : shows high end roll-off, indicating saturation. The system has been gob smacked! Too much analyte for the system capabilities!

Poor Response follows a gob smacking ... or ... needs maintenance. To restore instrument response: clean the system; replace system components; etc

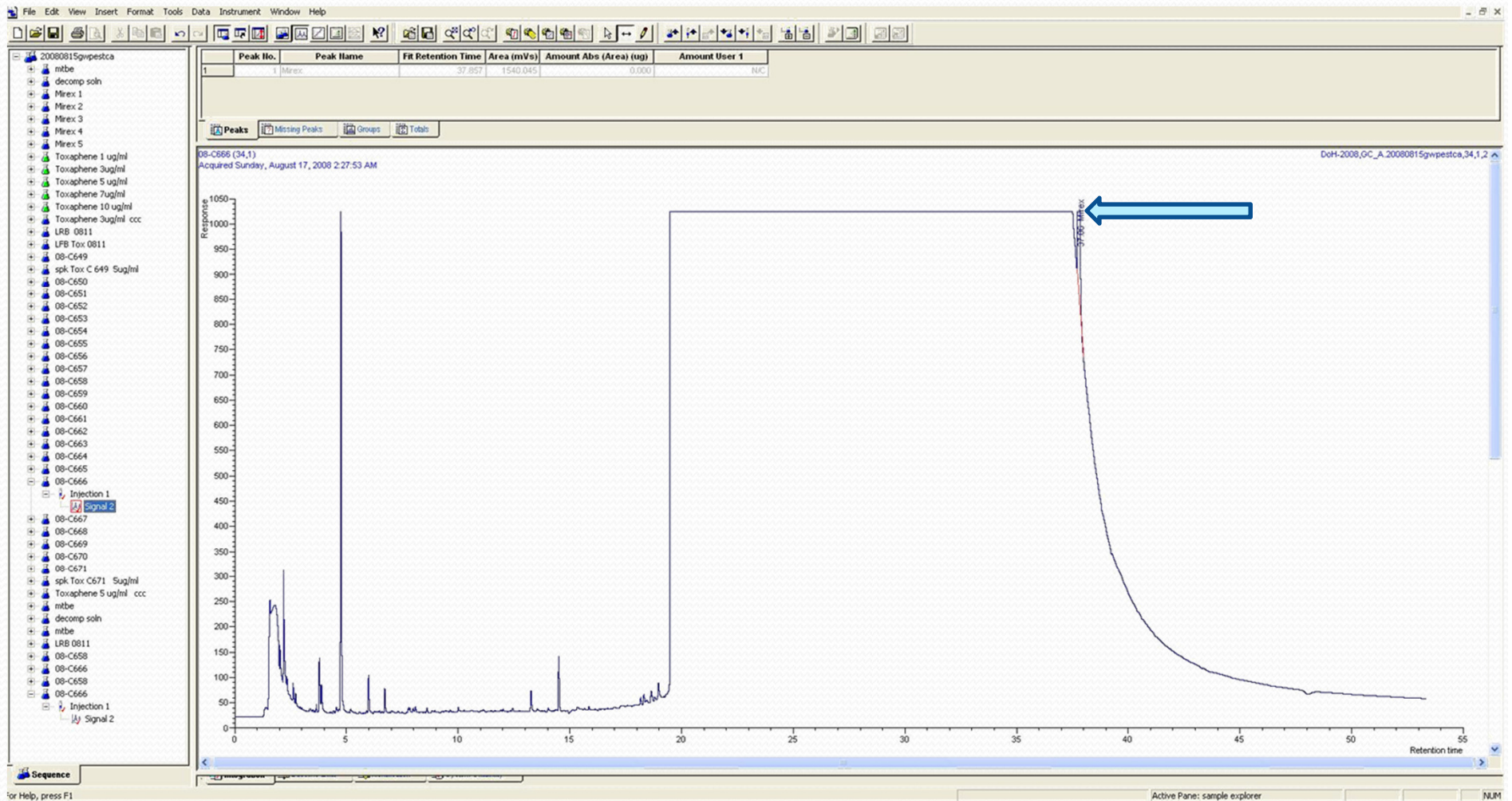


Umm ... Gob Smacked?

Toxaphene Standard @ report level



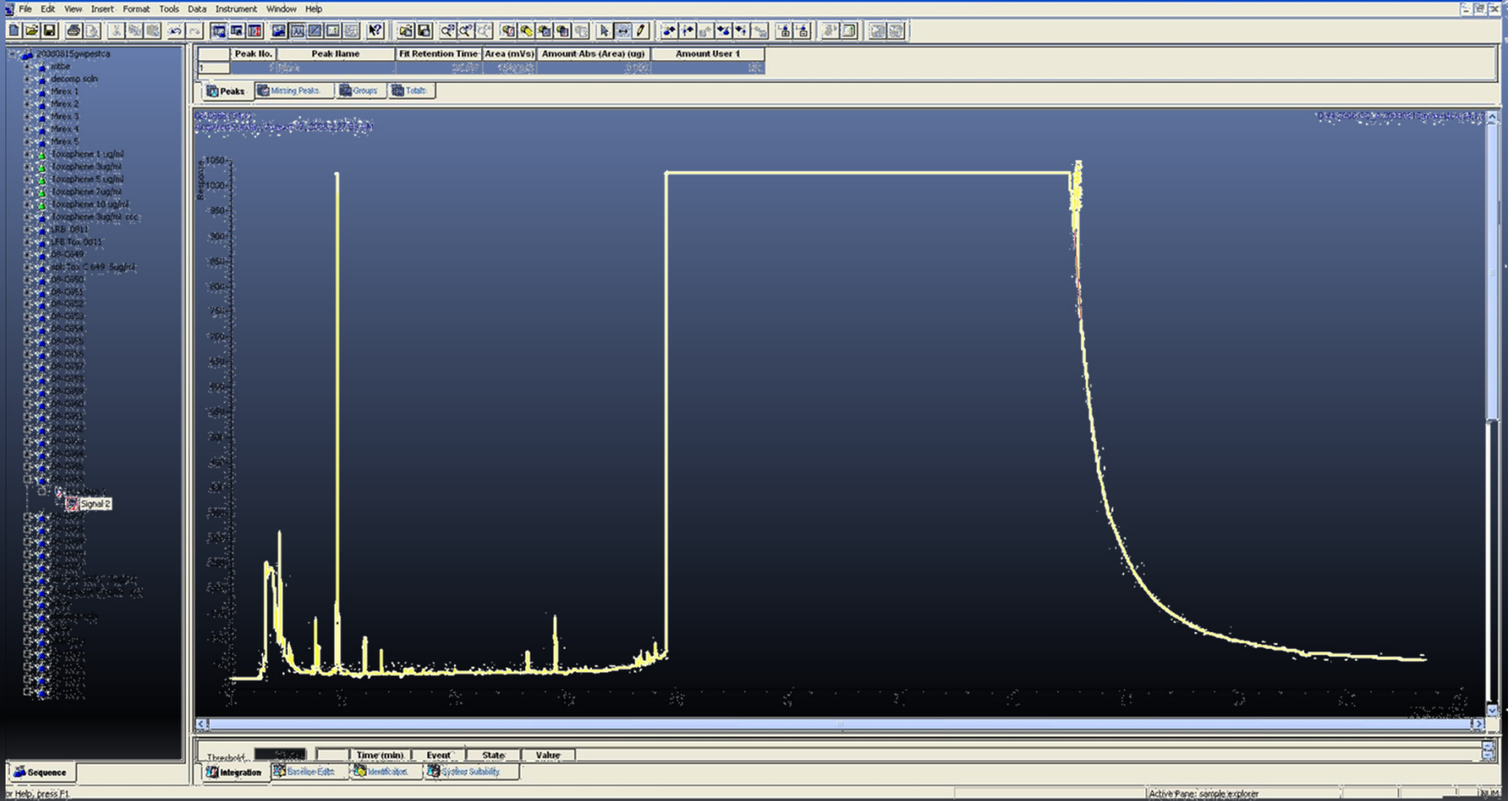
Dahn dahn daaa ... Gob Smacked



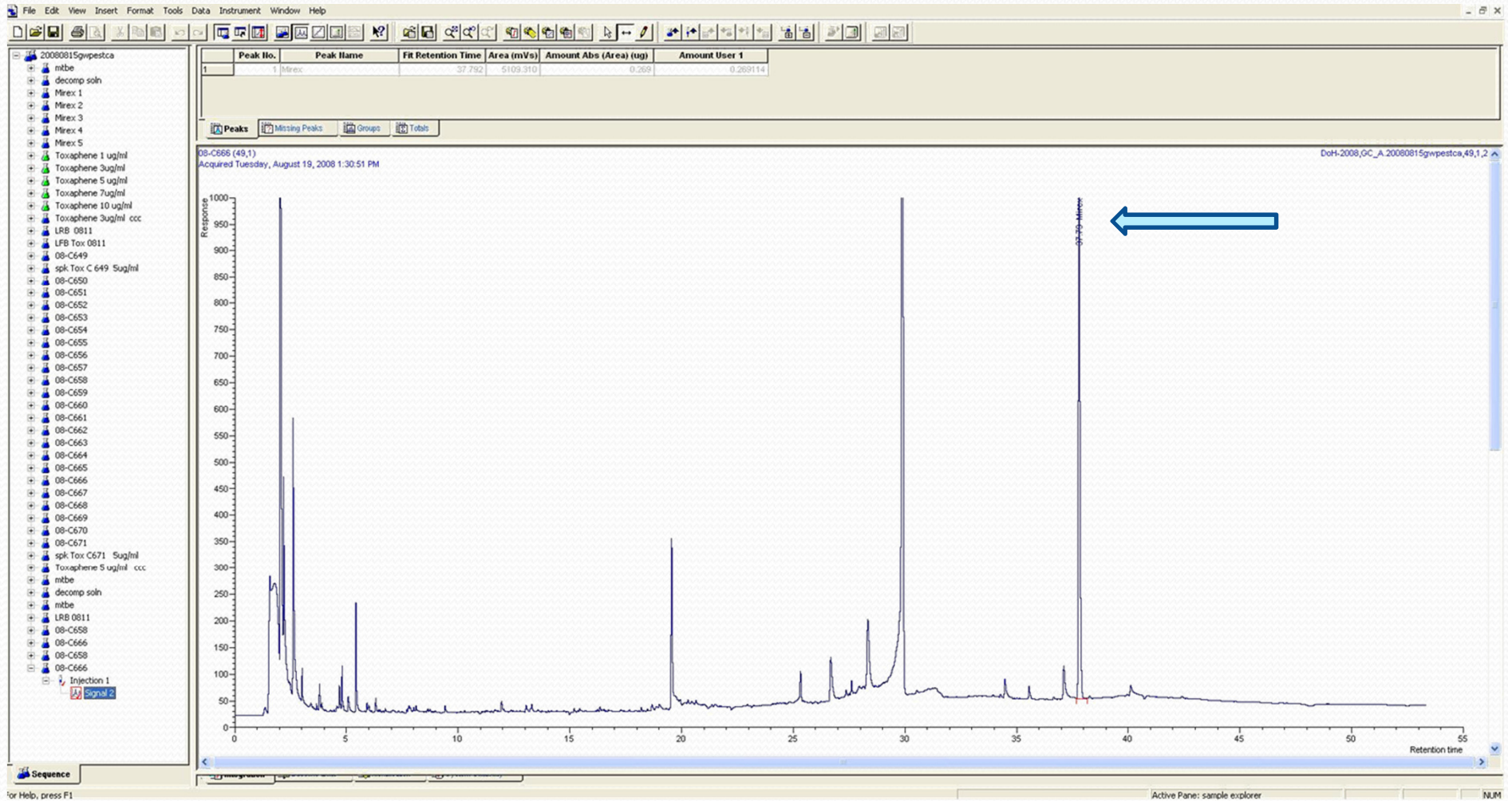
ODLSTW

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OMG

08-C666



Cu++ cleanup = No SULFUR





Gob Smacking isn't limited to instruments ...

NOOOOOOOOOOOOOOOOO ...

No limits ... No levels ... No choices





Hang in there ...
almost done!

From the beginning ...

Instrument is on.

Zero < **IDLs** < **MDLs** ≤ **MRLs** < **LOQ**

A signal is present where you expect analyte. Signal is 5x larger than “instrument on” baseline. **OBSERVATION** and/or **math** from QC charts.

Zero < **IDLS** < **MDLs** ≤ **MRLs** < **LOQ**

Real life sample **Qualitative Process** at low levels + math = 99% sure this signal is from the analyte.

Zero < **IDLs** < **MDLS** ≤ **MRLs** < **LOQ**

I can
QUANTITATE
at this concentration
with
50-150% confidence

Zero < IDLs < MDLs ≤ **MRLS** < LOQ

Results definitely on the radar!

Results! **Defensible** ... take it to the bank **Results!** All data quality objectives are met.

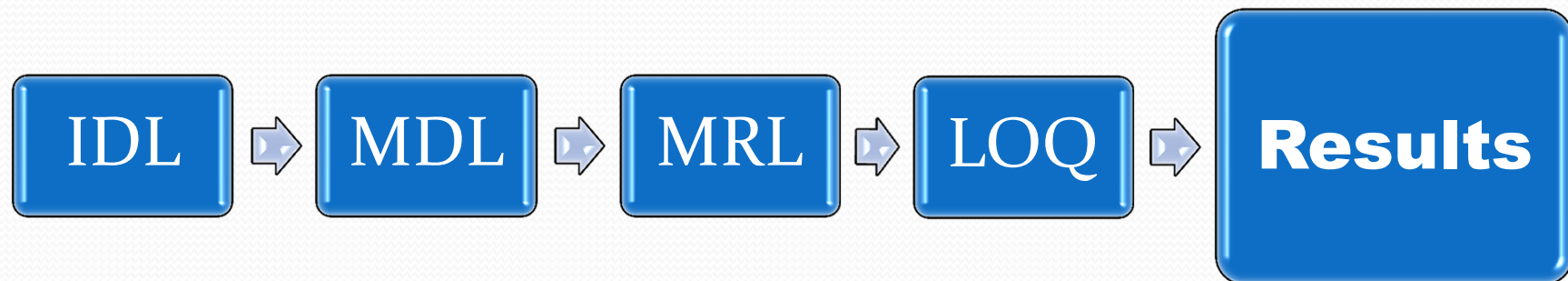
Zero < **IDLs** < **MDLs** ≤ **MRLs** < **LOQ**

Relationships between the limits and levels.

IDLs < **MDLs** ≤ **MRLs** < **LOQ**

1 : 2 : 4 : 10

Knowledge Tools Experience



One more time ... what affects the limits and levels?

- Method of choice
- Instrumentation
- Eluant, carrier gas, columns, detectors
- Matrix quality: clean up or dilute or use another instrument
- Multiple analytes in sample: exceed calibration curve or overwhelm system. DILUTION

Choices ... didn't you say something about choices?

Choices may be available. The lab is your greatest resource for information and available technology. Consult the lab for how best your needs can be met.

BUT ... we are still waiting for that magical instrument that takes anything and gives you everything!





Questions?