THE NELAC INSTITUTE

2015 TNI Standard

Chemistry

Updates

- Calibration requirements 1.7.1
- LOD requirements 1.5.2.1
- LOQ requirements 1.5.2.2

Current (2009) Calibration Requirements

- Quant from initial not continuing
- Range
  - Low standard at or below LOQ
  - High standard defines working range
- Acceptance Criteria
  - Use something, probably correlation coefficient or RSD
- Number of standards
  - At least 3 unless single standard method
- Document what you do

Weaknesses

- Correlation coefficient is either useless or worse than useless
- Three standards is inadequate
- Nothing regarding removal of calibration levels or points from a curve

Correlation coefficient

- For most applications, and calibration curves in particular, the correlation coefficient must be regarded as a relic of the past
  - Meier and Zund, Statistical Methods in Analytical Chemistry, 2000
- "The correlation coefficient in the context of linearity testing is potentially misleading and should be avoided"
  - Royal Society of Chemistry, Technical brief
- "The author has seen cases where a correlation coefficient of 0.997 was believed to be a better fit than 0.996 of a 5 point calibration curve. One can even find requirements in quality assurance plans to recalibrate if the correlation coefficient is less than 0.995!"
  - Taylor, Statistical Techniques for Data Analysis, 1990
- "One practice that should be discouraged is the use of the correlation coefficient as a means of evaluating goodness of fit of linear models"
  - Van Arendonk and Skogerboe, Anal. Chem. 53, 1981, 2349-2350

One calibration, processed three different ways

GC/MS			
	Avg RRF	Unweighted	$1/X^2$ weighted
	%RSD	r^2	r^2
bis(2-chloroethyl)ether	4.68	0.998	0.996
bis(2-chloroisopropyl)ether	4.26	0.999	0.996
n-nitroso-di-N-propylamine	6.35	0.998	0.995
nitrobenzene	6.15	0.999	0.998
bis(2-chloroethoxy)methane	5.14	0.999	0.997
2,4-dichlorophenol	11.54	0.999	0.997
hexachlorobutadiene	3.46	0.999	0.998
2,4-dinitrotoluene	25.72	0.996	0.998
4-chlorophenyl phenyl ether	5.69	0.999	0.998
4-bromophenyl phenyl ether	5.42	0.999	0.998
hexachlorobenzene	2.4	0.999	0.998
bis(2-ethylhexyl)phthalate	22.24	0.999	0.998

Three different results

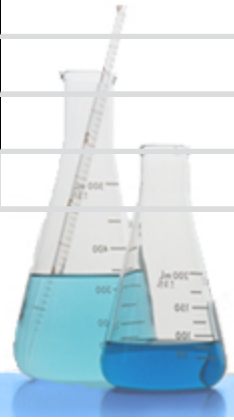
GC/MS

0.5ppm standrd

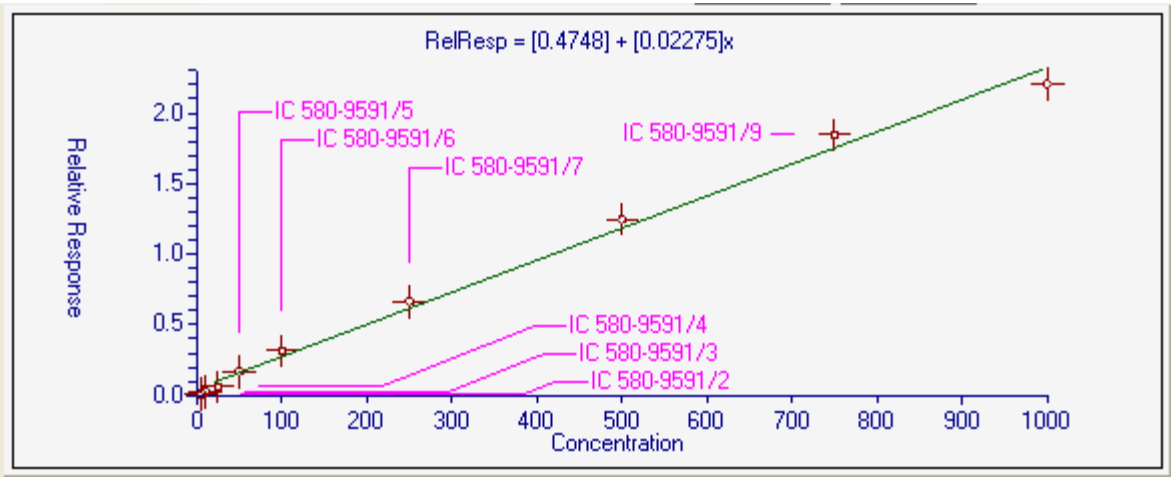
	Avg RRF	unweighted	$1/X^2$ weighted
bis(2-chloroethyl)ether	0.5		0.5
bis(2-chloroisopropyl)ether	0.5		0.5
n-nitroso-di-N-propylamine	0.5		0.5
nitrobenzene	0.5		0.5
bis(2-chloroethoxy)methane	0.5		0.5
2,4-dichlorophenol	0.4		0.5
hexachlorobutadiene	0.5		0.5
2,4-dinitrotoluene	0.2		0.5
4-chlorophenyl phenyl ether	0.5		0.5
4-bromophenyl phenyl ether	0.5		0.5
hexachlorobenzene	0.5		0.5
bis(2-ethylhexyl)phthalate	0.3		0.5

>20% Error

>20% Error



Calibration issues



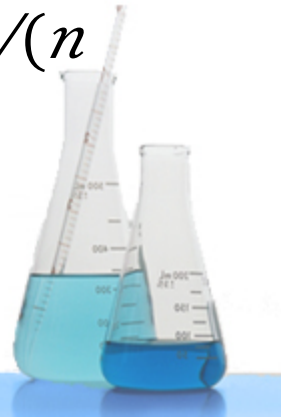
$r = 0.997$, $r^2 = 0.994$

Calibration Standard Levels

Level	Used	Amount	Area	ISArea	%Error
IC 580-9591/2	☑	5	1348	618332	421.63
IC 580-9591/3	☑	10	3250	647316	198.43
IC 580-9591/4	☑	25	7697	646400	78.87
IC 580-9591/5	☑	50	23729	700099	7.13
IC 580-9591/6	☑	100	47131	748204	17.47
IC 580-9591/7	☑	250	111297	833662	8.93
IC 580-9591/8	☑	500	229185	917698	5.52
IC 580-9591/9	☑	750	371628	1005615	5.43
IC 580-9591/10	☑	1000	499631	1131444	5.11

Added requirement for Relative error measurement

- Two options
  - Relative error at the low and mid points
    - Mid point is the CCV
    - Low point $RE = True - Measured/True \; X \; 100\%$
  - Relative Standard Error
    - One number to compare all curve types
    - $\% \; RSE = 100 \times \sqrt{\sum i=1 \uparrow n \blacksquare [x \downarrow i \uparrow ' - x \downarrow i / x \downarrow i \;] \uparrow 2 \;} / (n - p)$



Additions to Calibration

- Specifications for when calibration levels and points may be removed from a curve
- Minimum number of points rationalized so that all curve types require at least 3 degrees of freedom
- Additional details for Aroclors
- Clarification of linear range option for some methods
- Clarification of second source requirements

Current (2009) Detection limit requirements

- Run 1 sample spikes 1-4 X LOD and detect
  - On each instrument
  - Annually
- Not required if not reporting below LOQ

Weaknesses

- Does not protect against false positives
- The verification does not verify that the detection limit is at the correct level to protect against false positives

Addition to detection limit requirements

- Renamed TNI LOD as MDL
- Added several requirements
  - Samples used to determine MDL must be prepped and analyzed over several days
  - Evaluation of routine method blanks must be included
  - Added details for MDLV
  - Specifications for ongoing verification of MDL

Made consistent with revised 40 CFR Part 136 MDL

Current (2009) Quantitation limit requirements

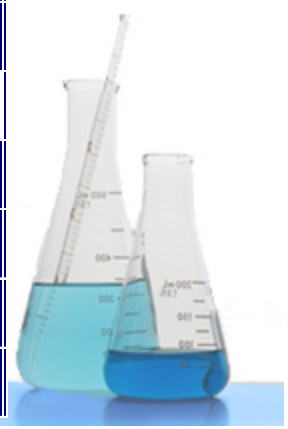
- Successful analysis of 1 sample spiked at 1-2X LOQ
  - Successful defined by lab
- Not required per instrument
- Not required if detection limit study is performed

Weaknesses

- Inadequate to define precision and bias of the method
- Does not protect from false negatives
- Does not protect from false positives
- Can be just marginally above detection limit (if detection limit has been defined)

Chromium, Episode 6000

	Spike Level	STD	N	Mean	Recovery %
	0.007	0.03261	8	**0.900**	12860
	0.01	0.02191	8	**0.901**	9013
	0.015	0.02406	8	**0.903**	6021
	0.02	0.04697	8	**0.840**	4201
	0.03	0.25555	8	**0.734**	2448
	0.04	0.23866	8	**0.943**	2357
MDL	0.07	0.03795	8	0.950	**1357**
	0.1	0.07147	8	**1.01**	1007
	0.15	0.16215	8	**1.04**	695
	0.2	0.24956	8	**1.16**	582
ML	0.3	0.05539	8	1.26	**418**
	0.4	0.02806	8	**1.08**	270
	0.7	0.02448	8	**1.40**	200
	1	0.19004	8	**1.79**	179
	1.5	0.03847	8	**2.24**	149



Additions to Quantitation limit requirements

- Minimum of 7 spikes at or below LOQ
- Details requirements if multiple instruments will have same LOQ
- LOQ is the spiking level, unless < 3X MDL in which case LOQ is 3X MDL
- Allows determination of precision and bias at the LOQ
- Consistent with revised MDL, EPA MRL and EPA LLOQ

Detection / Quantitation

- Detection requirements and quantitation requirements work effectively together
  - Detection limit is calculated, quantitation limit is spiking level
- Detection and quantitation requirements work effectively with existing EPA concepts
  - MRL, LLOQ, MDL

THE NELAC INSTITUTE

Questions?