

Analytical Methods for Emerging Contaminants- the Good, the Bad, and the Ugly!

Presented to SAWPA Workgroup Meeting

7/31/08

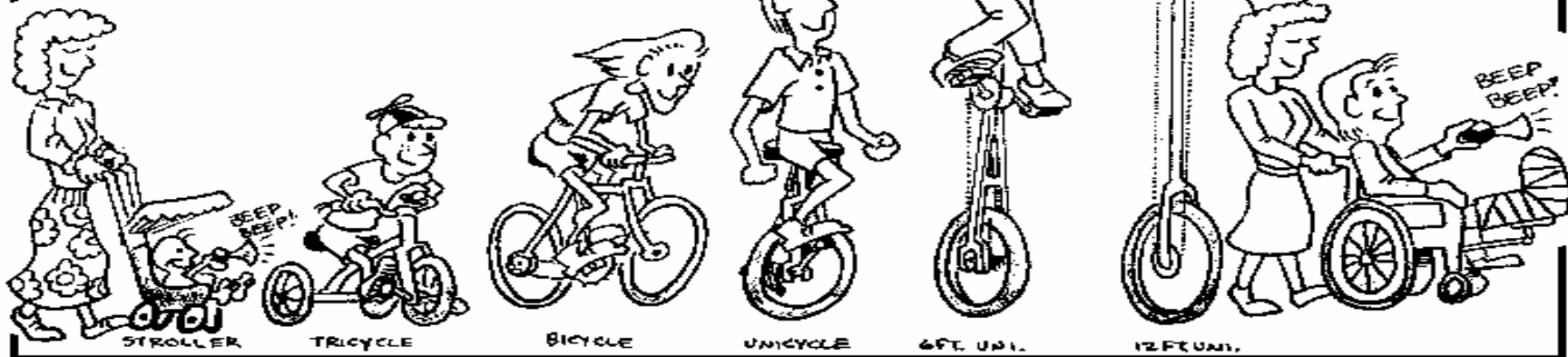


The Evolution from LC-MS-MS Methods Development to LC-MS-MS Production



Expect Continued Evolution in Emerging Contaminant Methods-and a Few Falls

Evolution of a Chemist



RCM - PATH 43
TUF. 8-24-93

Issues Requiring Consideration for Emerging Contaminant Analysis Methods

- Specificity
- Sensitivity
- Ruggedness/matrix effects
- QA/QC
- Target Lists
- Intra-lab variability
- Inter-lab variability
- Cost



Categories of Emerging Contaminants (ECs) by Compound Type

- Disinfection Byproducts
- SOCs
- Pesticides
- Flame Retardants
- Pharmaceuticals and Personal Care Products
 - Hormones (natural and synthetic)
 - Personal care products
 - Pharmaceuticals (prescription and OTCs)
 - Stimulants

Or Does It Make More Sense to Look at ECs by Analytical Method?

- Preparation method
 - Solid Phase Extraction vs Liquid Liquid Extraction
- Analytical Technique
 - GC-MS-EI full scan or Selected Ion Monitoring (SIM)
 - GC-MS-MS (tandem mass spectrometry)
 - LC-MS (liquid chromatography mass spectrometry)
 - LC-MS-MS (tandem mass spectrometry)
 - Electrospray positive (ES+)
 - Electrospray negative (ES-)
 - Atmospheric Pressure Chemical Ionization (APCI)
 - Isotope Dilution Mass Spectrometry (IDMS)

1a. What Methods are Used to Detect ECs?

- Pesticides – GC-MS or LC-MS-MS
- Flame Retardants – GC-MS or LC-MS-MS (some)
- Analgesics – LC-MS-MS based methods
- Hormones – LC-MS-MS (low), GC-MS (high)
- Antibiotics – LC-MS-MS (not all are “good” behaviors)
- Narcotics - LC-MS-MS, but few labs test
- Antihistamines – LC-MS-MS, but few labs test
- Stimulants – LC-MS-MS or GC-MS

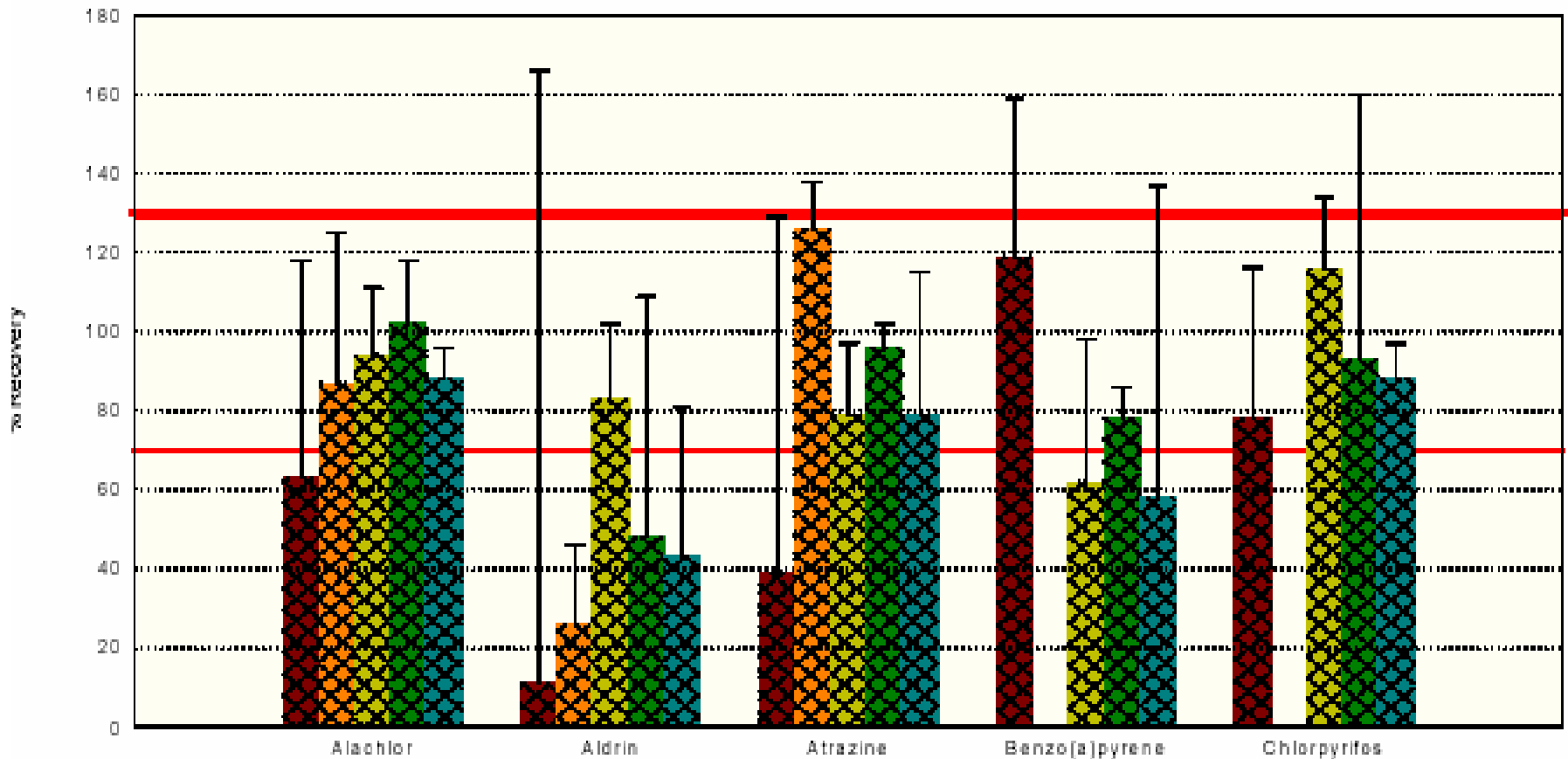
The bigger issue may relate to sample preparation (LLE vs SPE) and even preservation.

1b. Do methods Differ From Priority Pollutant Methods?

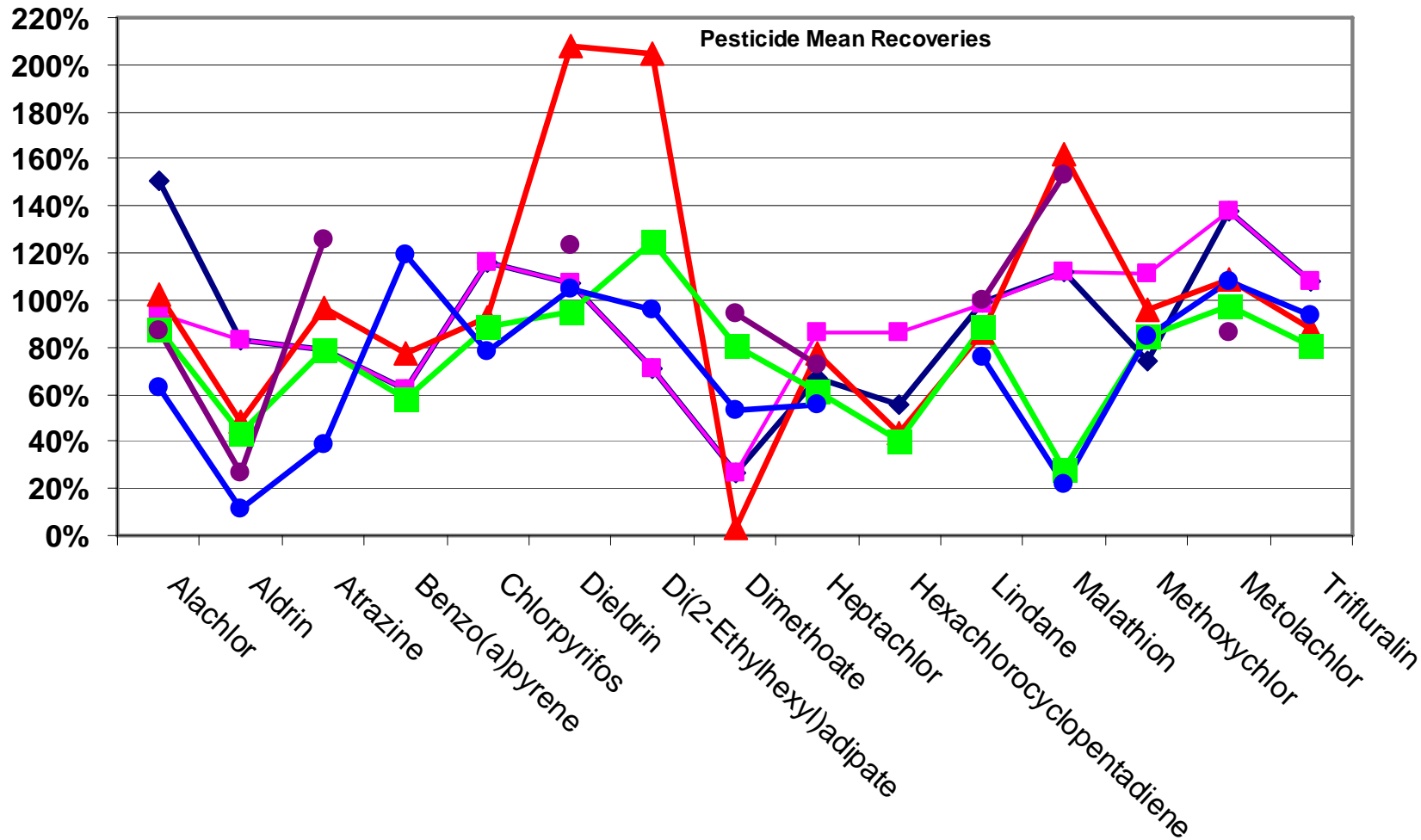
- In a word..... YES
- Newer methods (not as yet proven)
 - e.g. EPA 1694 was only promulgated in December 2007 and has never really been used... (note – several external reviewers “panned” this method as being too broad)
- Looking in general at much lower concentrations
 - The lower you go, the harder it is....
- LC-MS-MS is a \$200-500K instrument vs <\$100K for GCMS now, so not nearly as available

Pesticides – 5 International Labs and Multiple Blind Samples Spiked at Low Levels

Summary Table (Pesticide Residues)



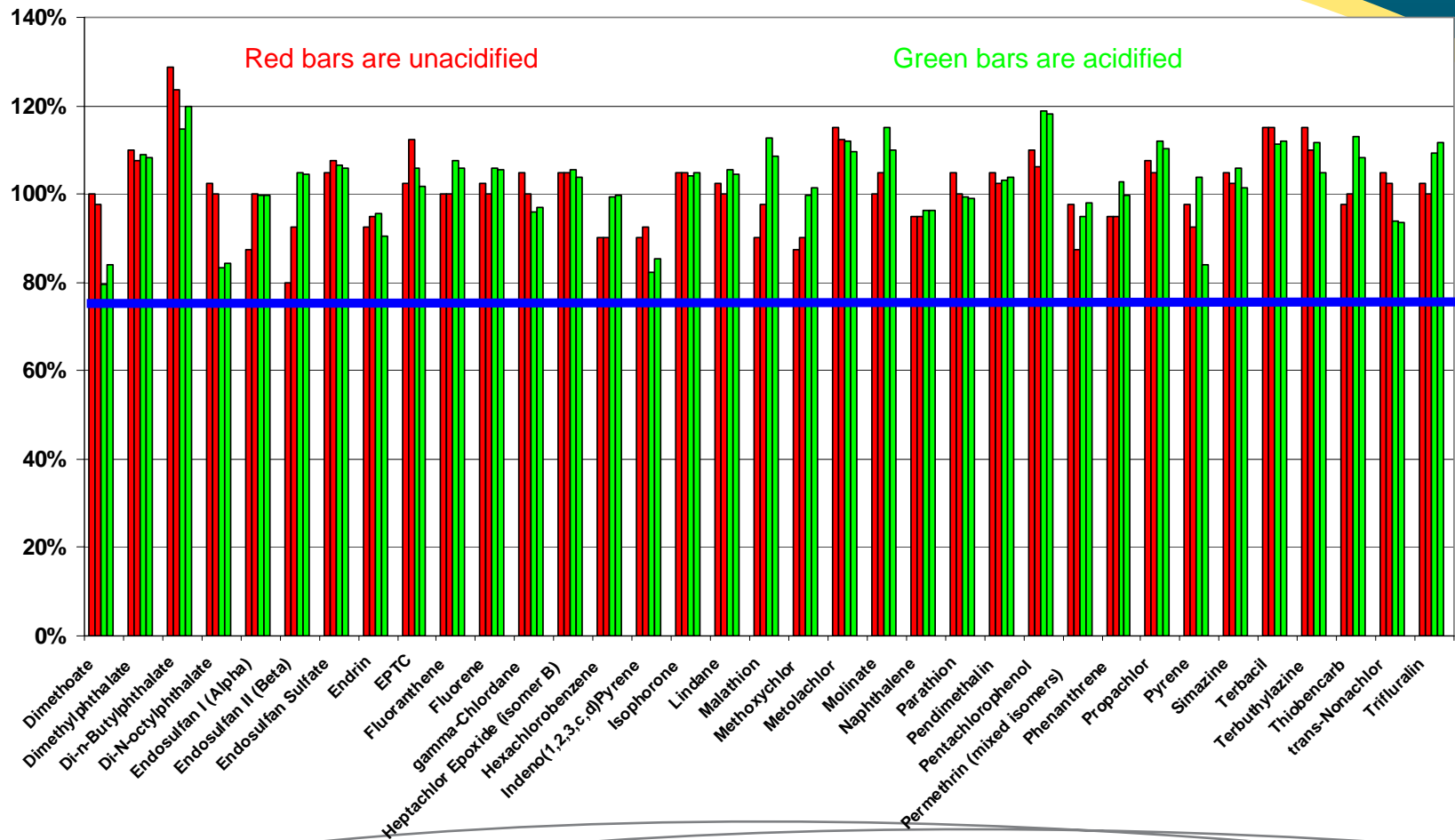
Results of a Global Inter-lab Study for Pesticides at the 0.1 to 1 ppb Level



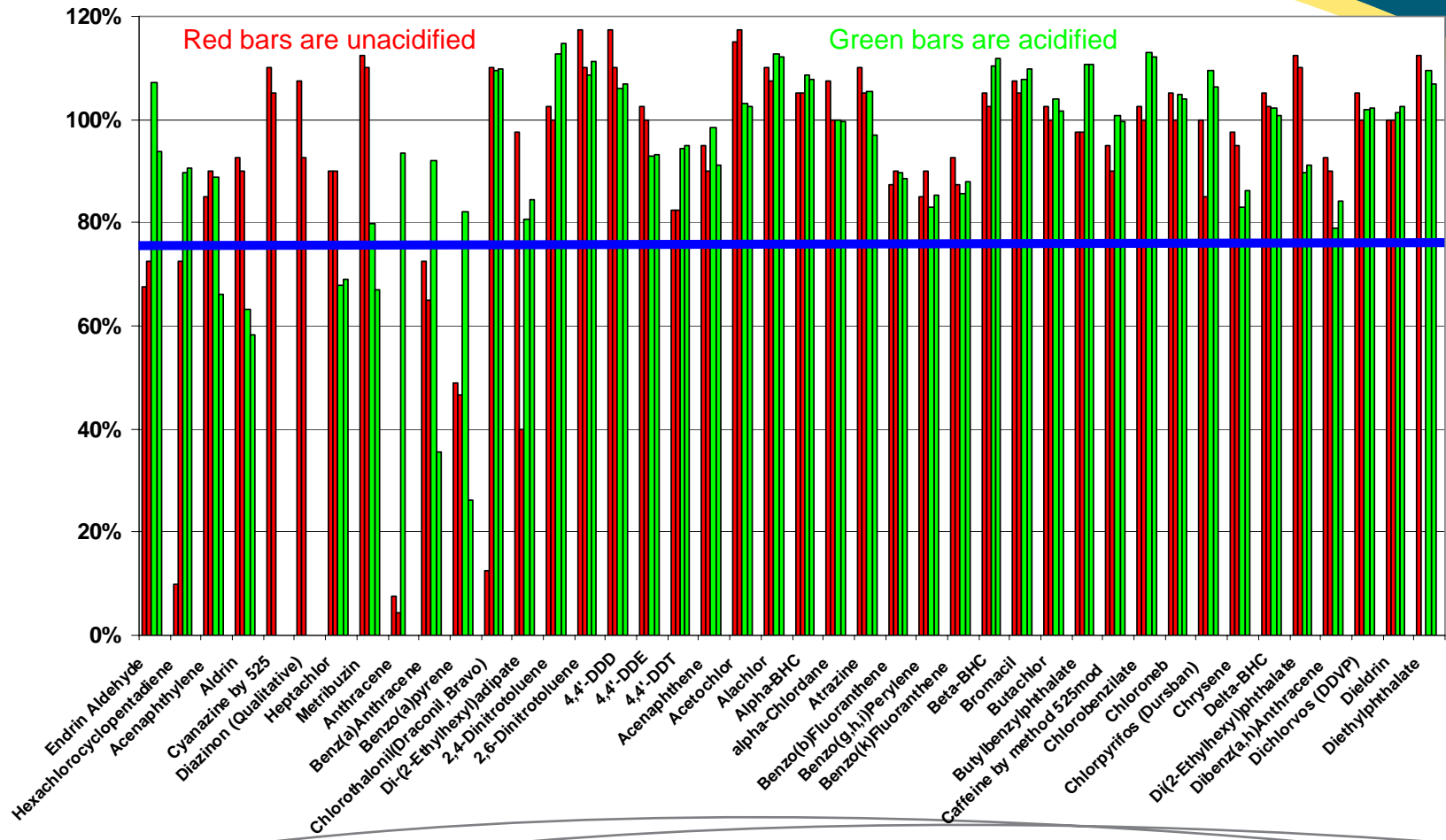
There is Often Little Consistency in Preservation Among EPA Methods for the Same Contaminant

Method	Preservation	Storage Temp	Holding Time	Compound Class
524.2	Ascorbic+ HCl	4 deg C	14 days	VOCs
624	None	4 deg C	14 days	VOCs
525.2	Sulfite+HCl	4 deg C	14 days	Pesticides/SOCs
625	None	4 deg C	7 days	Pesticides/SOCs/ PAHs
507	Thiosulfate	4 deg C	14 days	Pesticides
506	Thiosulfate	4 deg C	14 days	Phthalates/Adipates
550/550.1	Thiosulfate + HCl	4 deg C	7 days	PAHs
505	Thiosulfate	4 deg C	7-14 days	pesticides

For Many Pesticides, Stability is Not Impacted by Preservation Approach



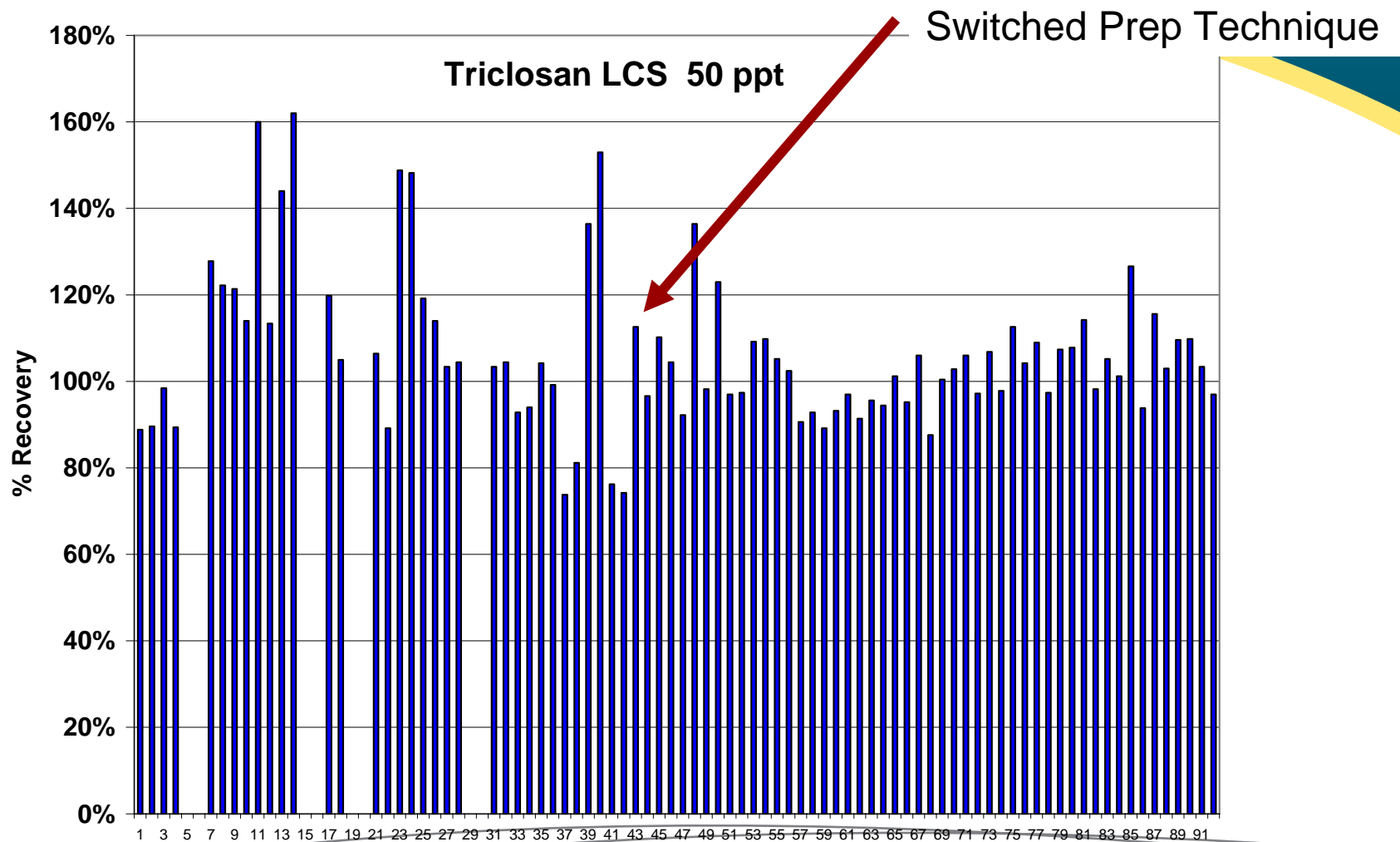
Sometimes Preservation Technique Can Make a Big Difference



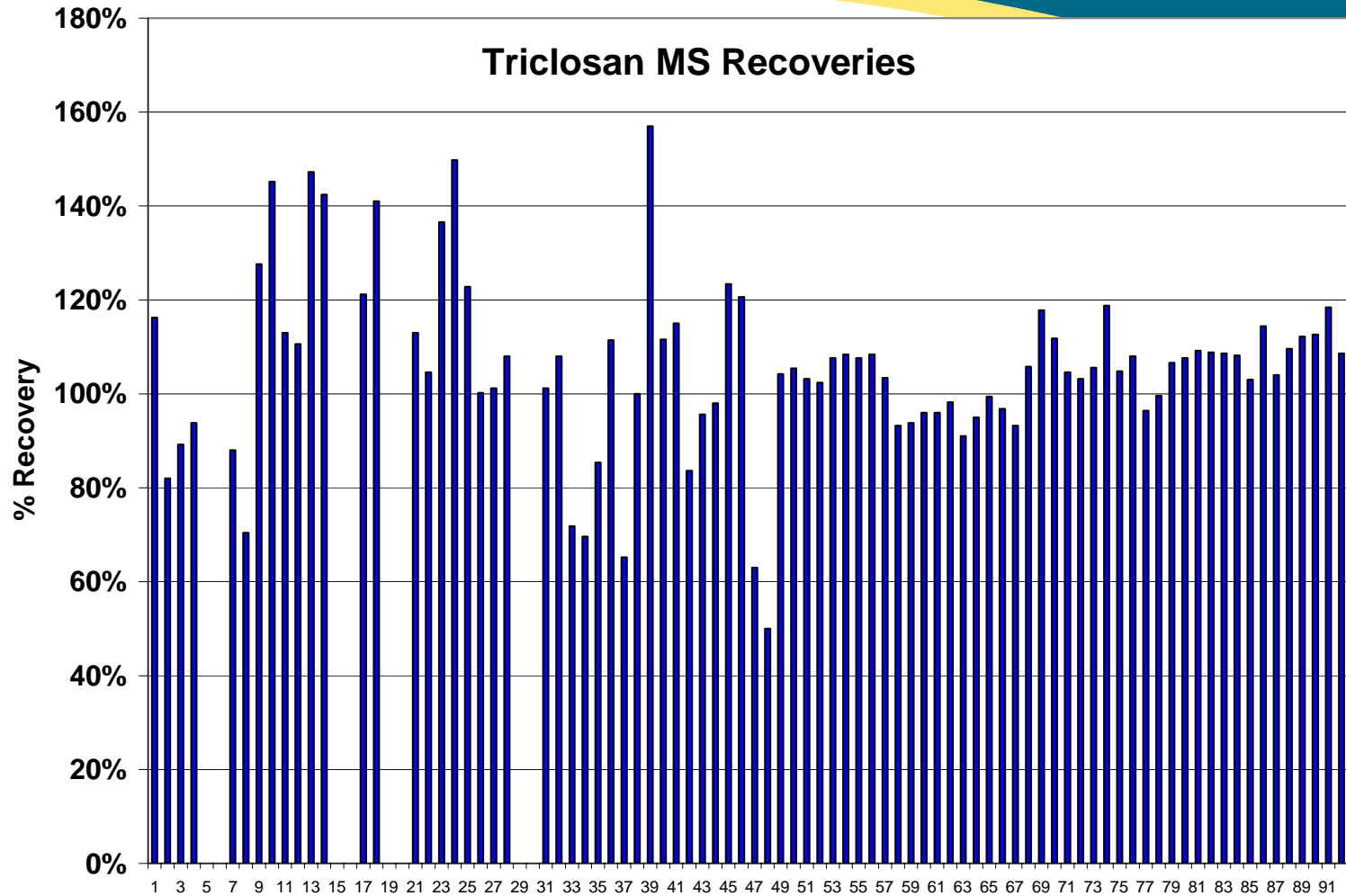
2. What sort of MLs and PQLs Does One See? What is the expected precision?

- MLs/PQLs/RLs are method/matrix dependent.
 - With good technique, the MLs by LC-MS-MS methods are generally 1-10 ppt
 - The MLs for GC-MS methods range from 25-500 ppt
- Intra-lab precision is compound dependent, but is generally <30% RSD
- Inter-lab precision is probably closer to 50-100% RSD, but is compound dependent; when labs use similar methods, results are closer.

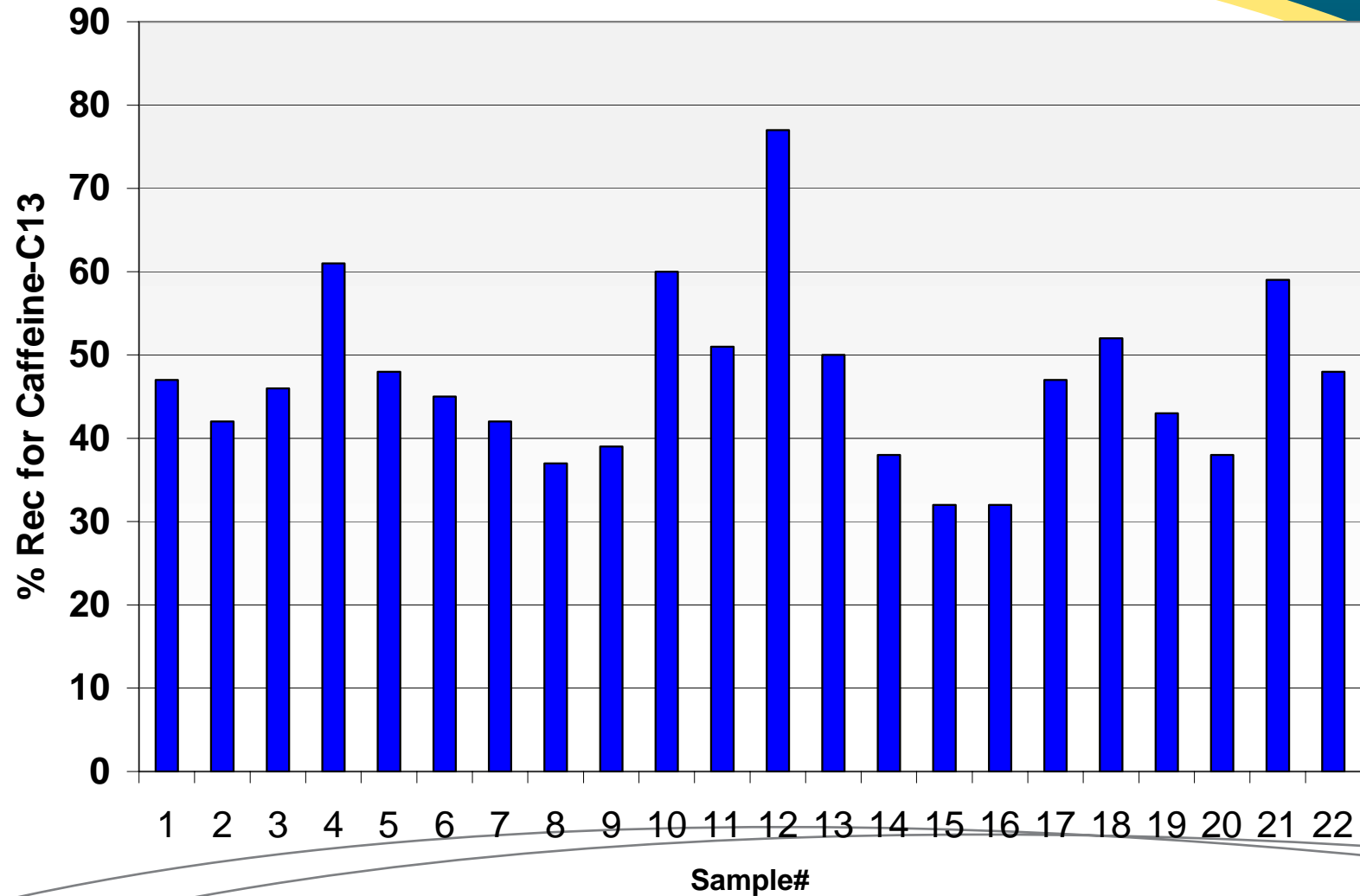
The Impact of Technique and Experience on Triclosan Recoveries is Apparent



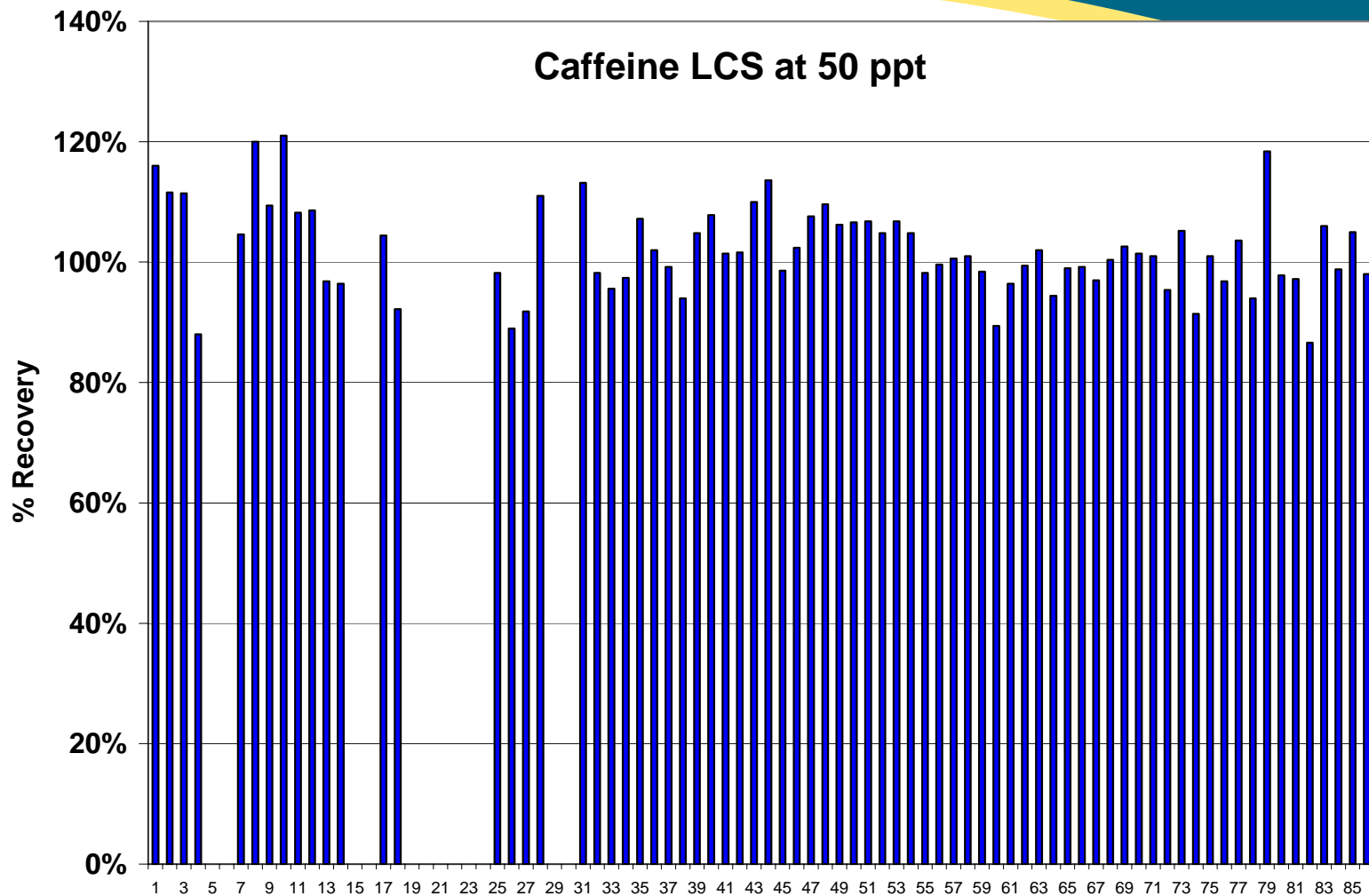
The Same Pattern Holds for Matrix Spikes



Caffeine Surrogate Recovery using SPE-LC-MS-MS is Usually Less Than 50% for Real Samples

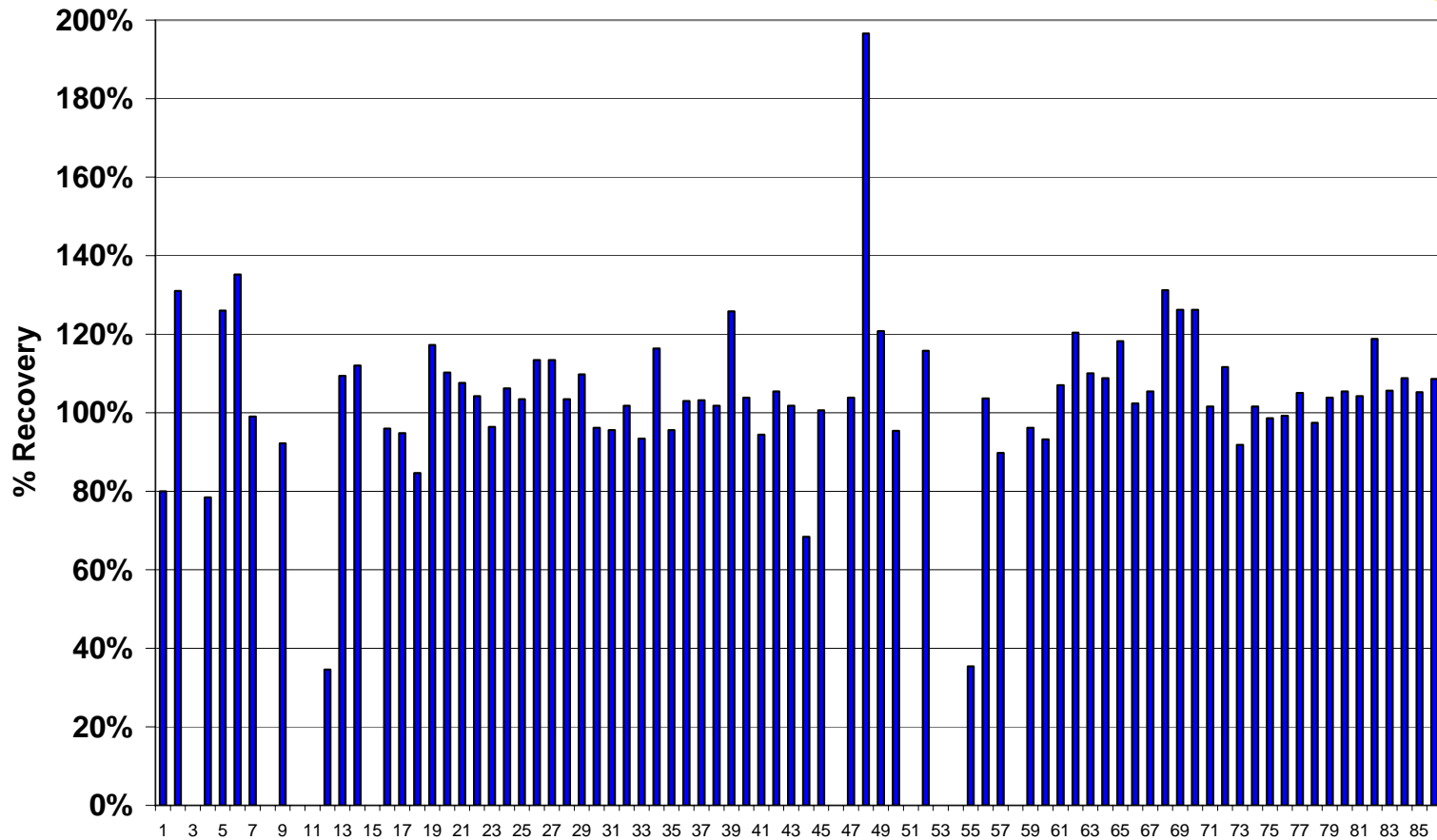


However QC Recoveries for Caffeine by Isotope Dilution LC-MS-MS are Very Tight

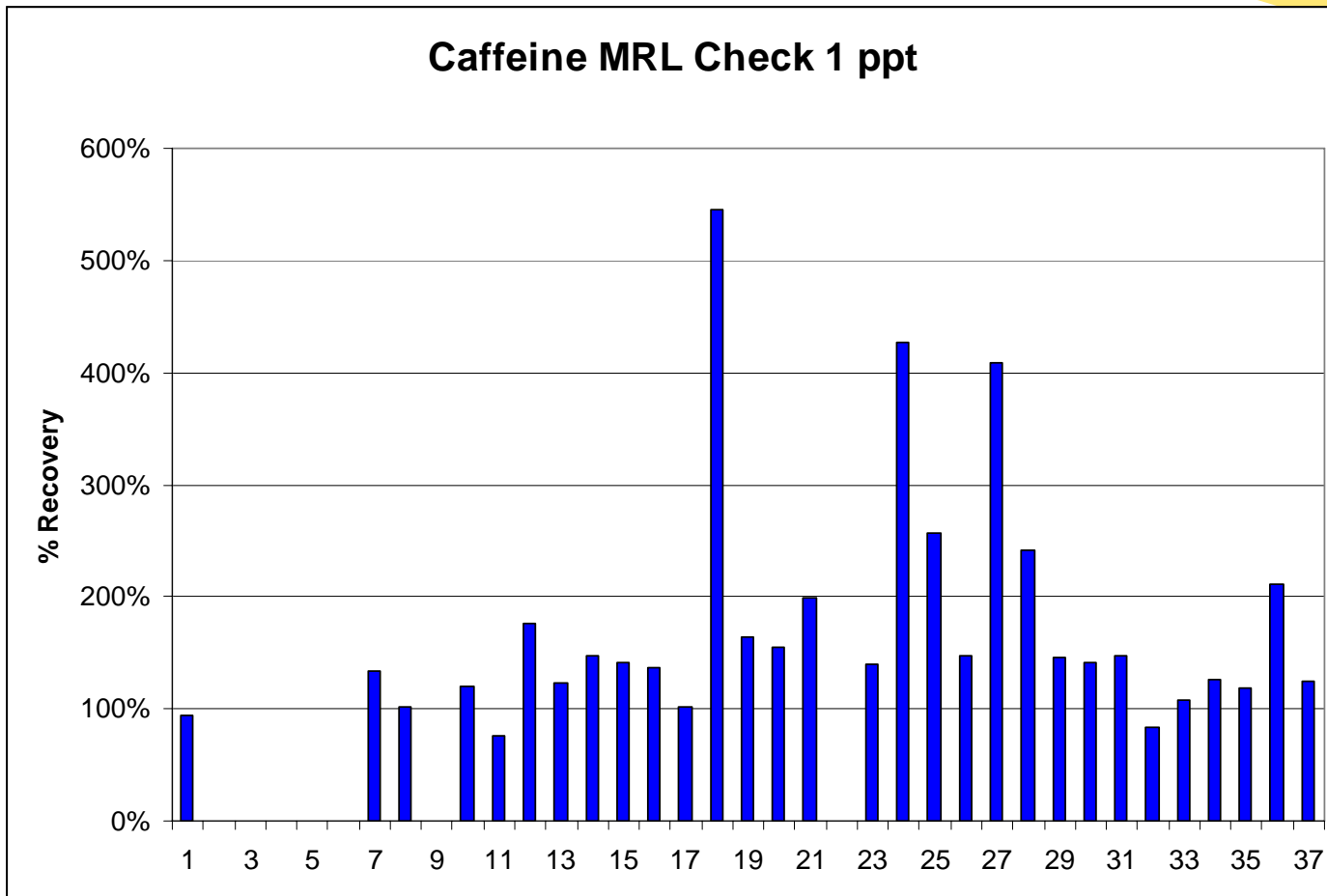


Caffeine Matrix Spike Recoveries are Generally as Precise as LCS with Isotope Dilution

Caffeine Matrix Spike Recoveries at 50 ppt

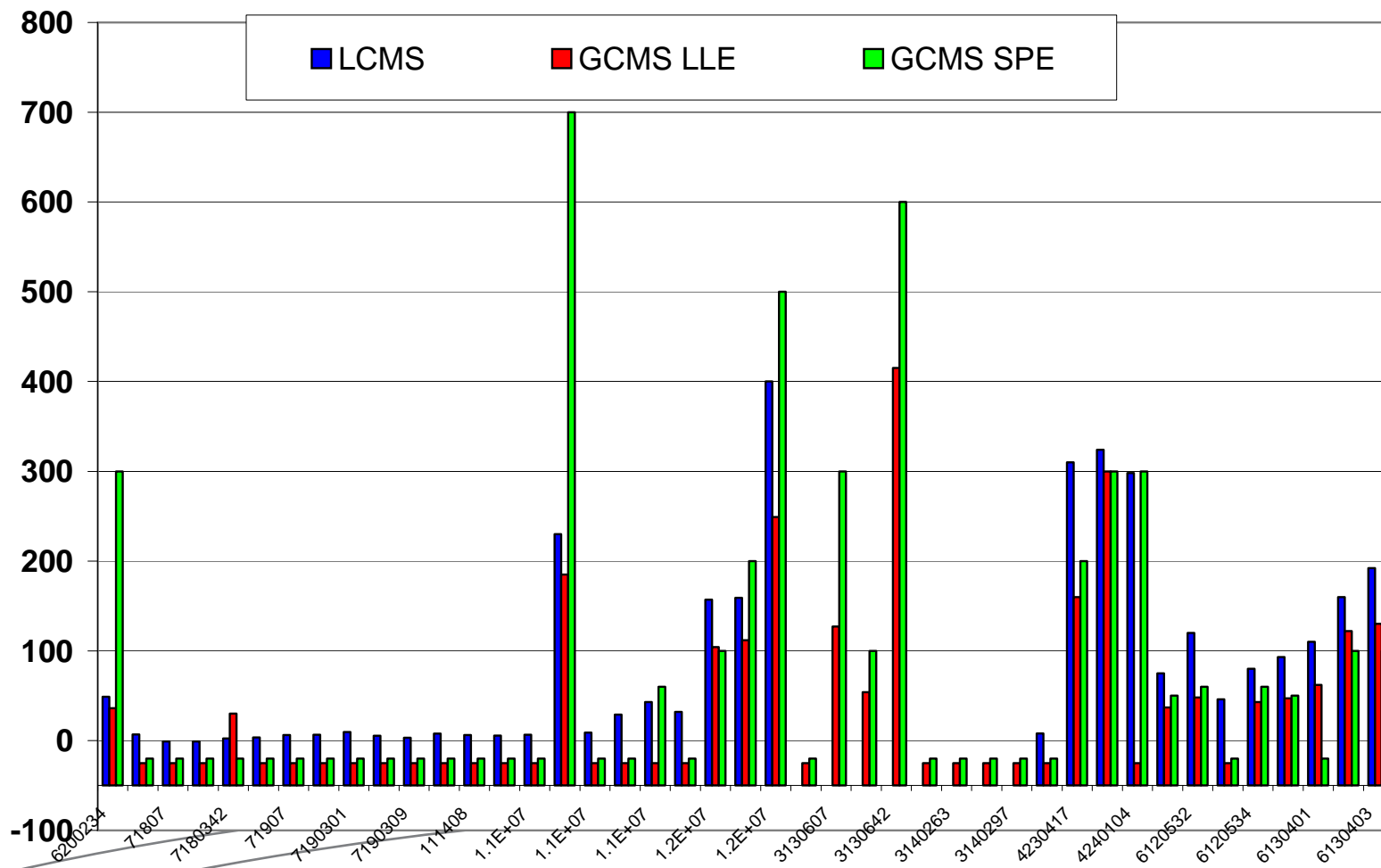


At Trace Levels, False Positives for Caffeine are Common

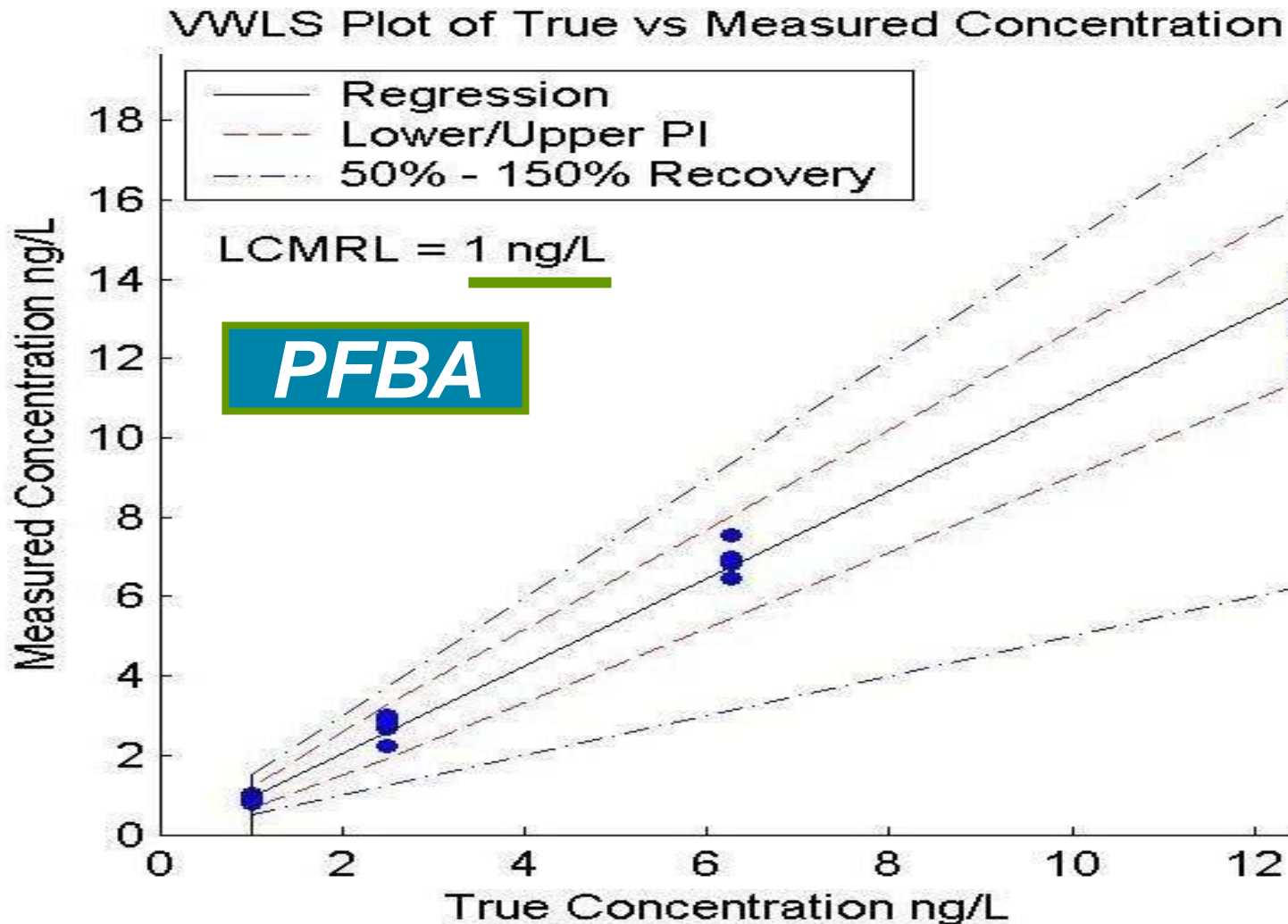


Agreement Among Methods on the Same Sample is Not Always Good

Caffeine (ng/L) by 3 Different Methods on Multiple Samples



To Really Get A Feel for the ML for Emerging Contaminants You May Need to Use Sophisticated Algorithms such as LCMRL



3a. What are the requirements for method approval under 40CFR136?

- There must be permit requirements on the contaminants to actually ‘approve’ a method for compliance monitoring.
- EPA OW uses contractors to prepare methods now (e.g. 1694 prepared by Axyss Analytical out of Canada)
- Methods approved by consensus bodies (e.g. Std Methods, ASTM) may also be approved, but same requirement holds

3b. What about CDPH method development and approval and EPA/CDPH “Certification” Issues?

- CDPH can do whatever they want in terms of approval (e.g. original nitrosamine method came out of CDPH), but in general they are not doing much methods development
- EPA developed 1694 in response to an Agency promise to Congress, but that doesn't mean it's certified (or reliable)
- CDPH won't “certify” a method unless there is a regulatory requirement to monitor.

4. Which chemicals are the best markers?

- There is a lot of literature in this area. (e.g. Oppenheimer et al, 2008, Snyder et al, 2008).

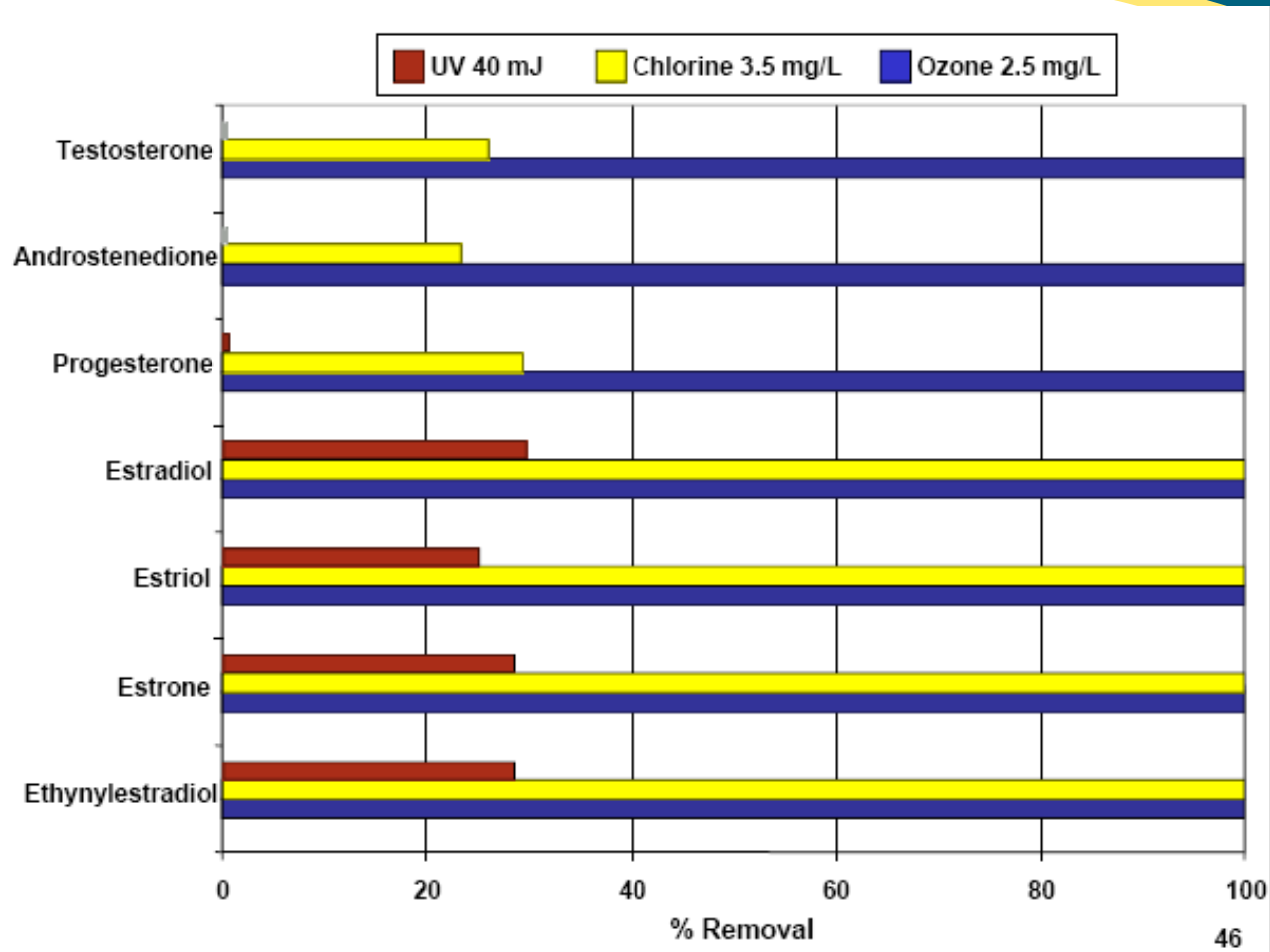
Table 1. SRT Required to Achieve Target Compound Removal of 80 Percent

SRT values of 5–15 days are required to remove several compounds.

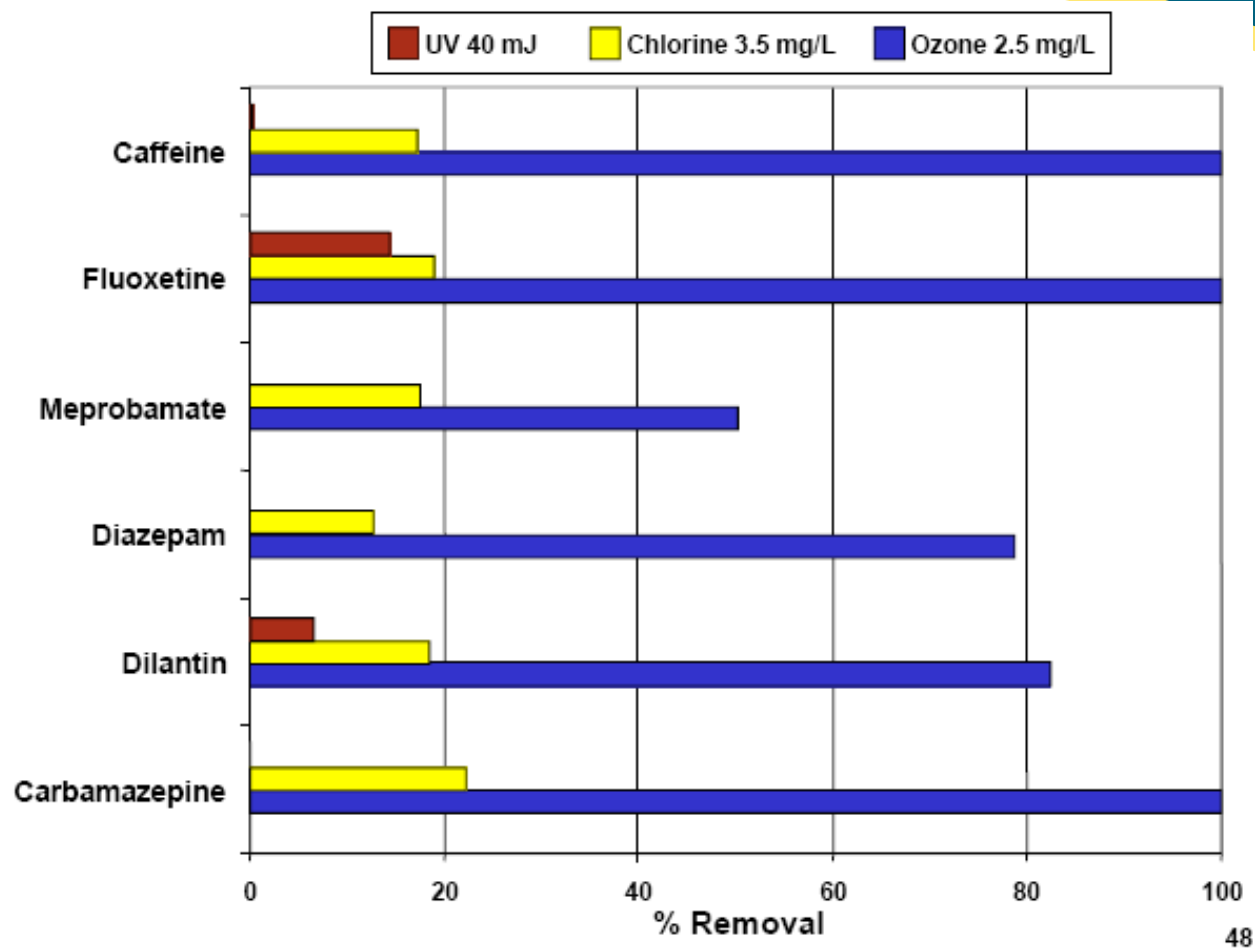
Bins	Compounds	SRT₈₀/days
Excellent Removal	Chloroxylenol	5
	Butylbenzyl phthalate	5
	Oxybenzone	5
	Octylmethoxycinnamate	5
	Benzyl salicylate	5
	Caffeine	5
	Ibuprofen	5
	3-Phenylproprionate	<5
	Methylparaben	<5
	Methyl-3-phenylproprionate	<5
Moderate Removal	Benzophenone	13
	Triclosan	10
	Ethyl-3-phenylproprionate	>5
	Octylphenol	5~28 ¹
Poor Removal	Musk ketone	>15 ¹
	Galaxolide	>15 ¹
	TCEP	>30 ¹
	DEET	>6
	BHA	>5 ¹
	Triphenylphosphate	>5 ¹

¹Although the SRT₈₀ value is indeterminate, consistently good removal wasn't observed even in the plant with SRT as high as 30 days.

Removal of Steroids in Water Treatment (from Snyder et al, 2008)



Removal of Pharmaceuticals with different treatment options (Snyder et al, 2008)



Compounds with Lower Removal Efficiency from Conventional Water Treatment Processes (Snyder et al, 2008)

Ozone 2.5 mg/L

<30% Removal	30-70% Removal
Musk Ketone	Meprobamate
TCEP	Atrazine
	Iopromide

UV 40mJ/cm²

<30% Removal
Testosterone
Progesterone
Androstenedione
Estriol
Ethinylestradiol
Estrone
Estradiol
Erythromycin
Trimethoprim
Naproxen
Hydrocodone
Ibuprofen
Caffeine
Fluoxetine
Meprobamate
Diazepam
Dilantin
Carbamazepine
DEET
Atrazine
Galaxolide
TCEP
Iopromide
Pentoxifylline
Metolachlor
Gemfibrozil
Musk Ketone

Chlorine 3.5 mg/L

<30% Removal	30-70% Removal
Testosterone	Ibuprofen
Progesterone	Metolachlor
Androstenedione	Gemfibrozil
Caffeine	
Fluoxetine	
Meprobamate	
Diazepam	
Dilantin	
Carbamazepine	
DEET	
Atrazine	
Galaxolide	
TCEP	
Iopromide	
Pentoxifylline	

So What Should One Monitor For?

- The ideal indicator compounds are resistant to treatment
- The ideal indicator compounds occur frequently and at relatively high levels
- Ideally one would like to be able to just use 1 method to pick up multiple indicator compounds
- Possible options
 - Caffeine (one of the most common occurring)
 - Carbamazepine
 - Gemfibrozil
 - TCEP and other phosphate based flame retardants

5. Can one Find Reliable Labs? And What Does It Cost?

- There are at present less than a dozen labs nationwide doing pharmaceutical analysis commercially.
 - All have seen a huge increase in workload since 3/08
 - However workload does not necessarily ensure quality
- Several water utilities are collecting data analyzed by multiple labs to look at variability
- AWWARF is sponsoring an inter-lab study (to be awarded later this year)
- Per sample costs vary from ~\$500 to \$2,000

For PPCPs, Few Labs Use the Same Target List or the Same RL

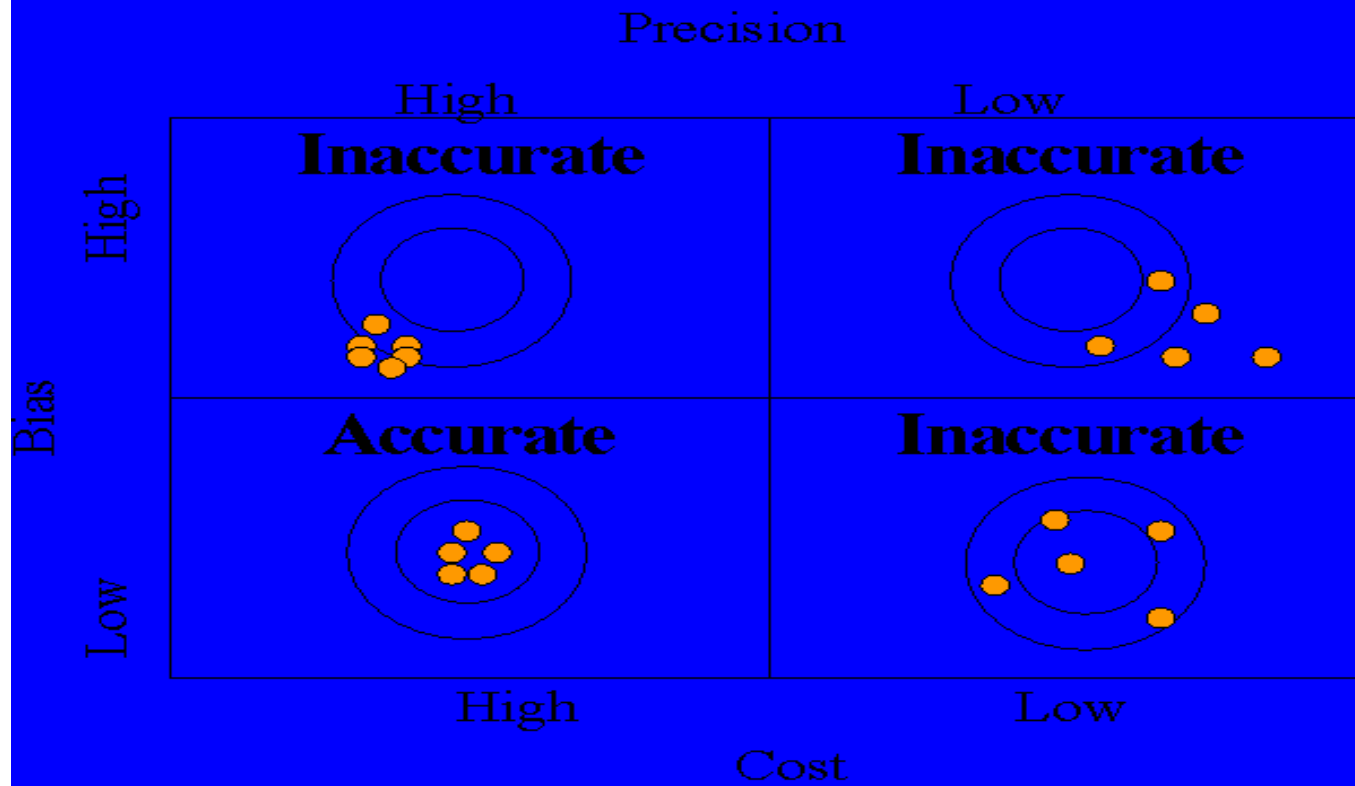
compound	Lab1	Lab2	Lab3	Lab 4 Method 1	Lab 4 Method 2	# of methods listing Compound
# of compounds in lab list	73	32	15	36	53	
Trimethoprim	1	1	1	1	10	5
Triclosan	5	10	2	5	10	5
Sulfamethoxazole	2	1	1	1	10	5
Ibuprofen	50	10	2	1	10	5
Carbamazepine	1	1	1	5	10	5
Caffeine	500	5	1	3	10	5
Acetaminophen	5	10	2	1	10	5
Progesterone	0.1	10		1	10	4
Gemfibrozil	0.5	1		1	10	4
Fluoxetine	1	1		1	10	4
DEET	5	5		25	10	4
Cotinine	1		1	1	10	4
Testosterone		10		1	10	3
Sulfathiazole	5		1		10	3
Sulfamethazine	1		1		10	3
Sulfadimethoxine	0.1		1		10	3
Naproxen	2	1			10	3
Lincomycin	0.1		1		10	3
Iopromide		1		5	10	3
Estrone	0.5	1		1		3
Diclofenac	5	2			10	3
Diazepam		1		1	10	3
Bis Phenol A (BPA)	100	10		10		3

6. What is the impact of matrix on precision and accuracy?

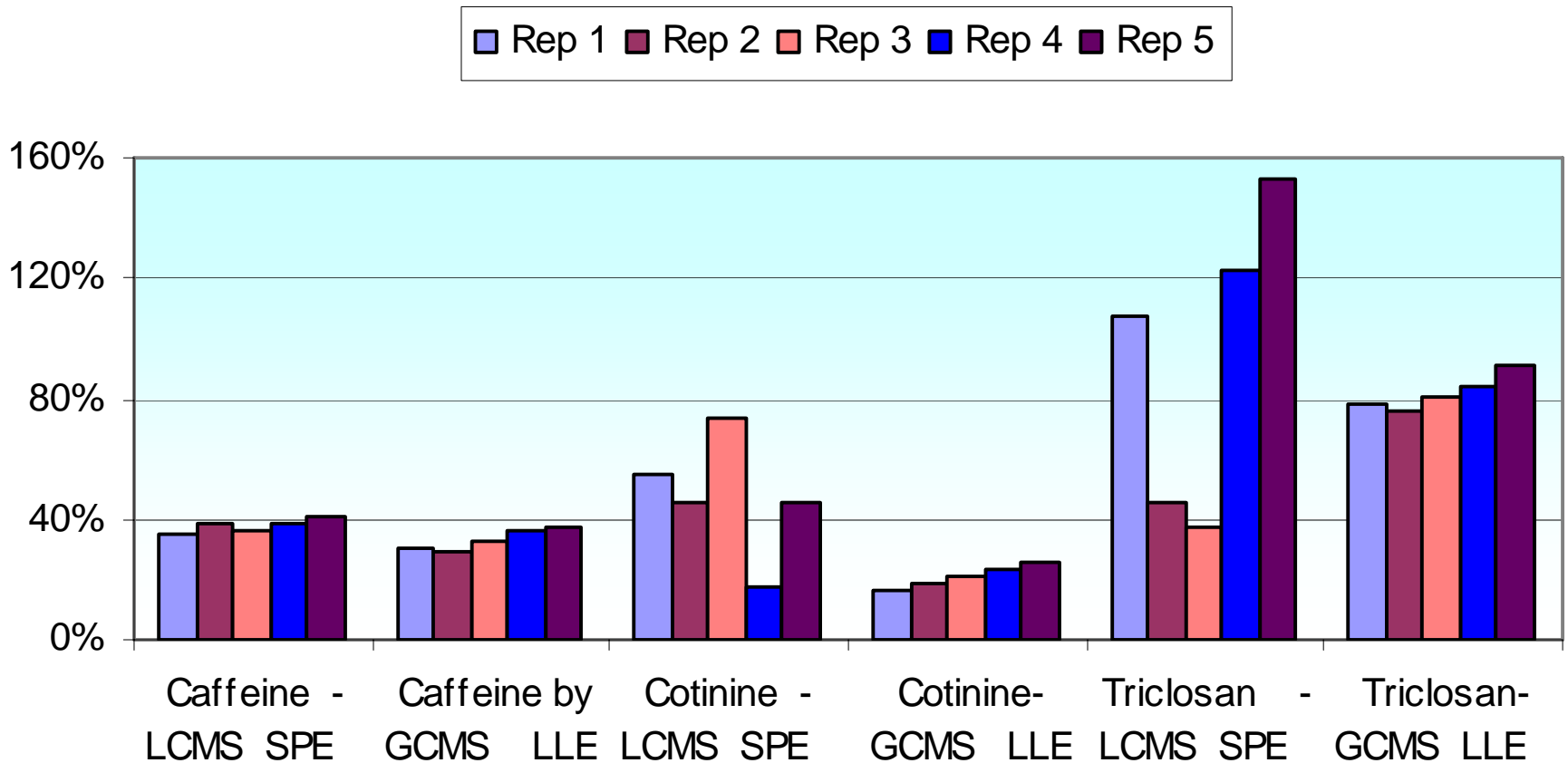
- Compared to all the other uncertainties in this analysis at trace level, wastewater matrices just increase the variability.
 - See 2005 interlab study
 - Accuracy can be improved substantially by using isotope dilution, but a) there aren't isotopes for everything and b) it gets very expensive very quickly
- “I don't care how precise you are, you're off by three orders of magnitude.”
 - Professor Clair Patterson, Caltech ca1970

What is Most Important? Accuracy or Precision?

Precision, Bias, and Accuracy (adapted from EPA 1996)

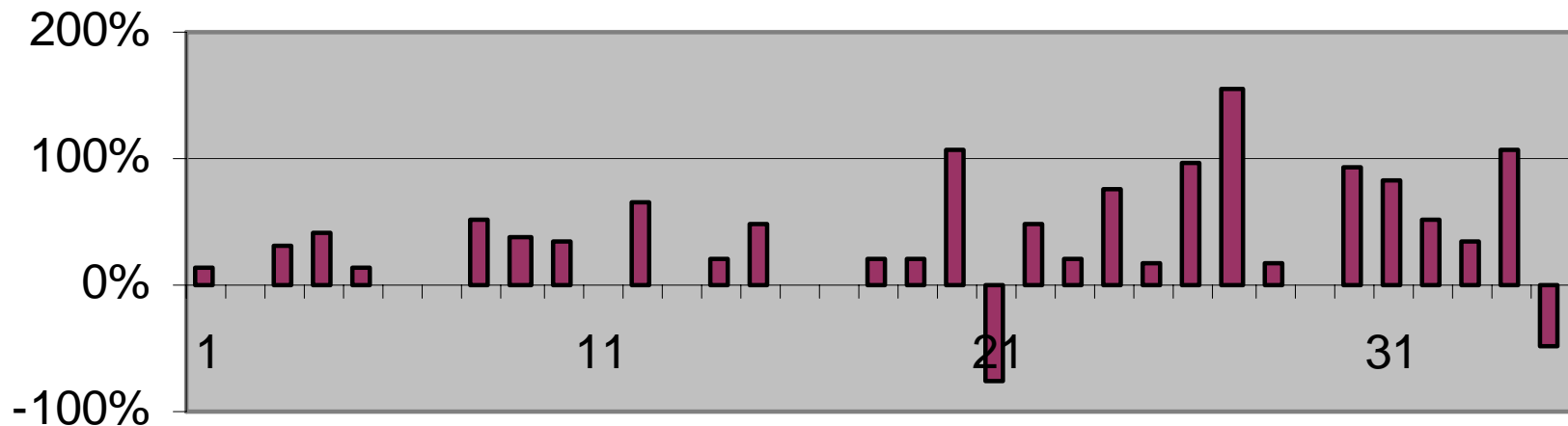


PPCP Intralab variability circa 2005 - % Recovery for Real World Spiked WW Samples (no IDMS)

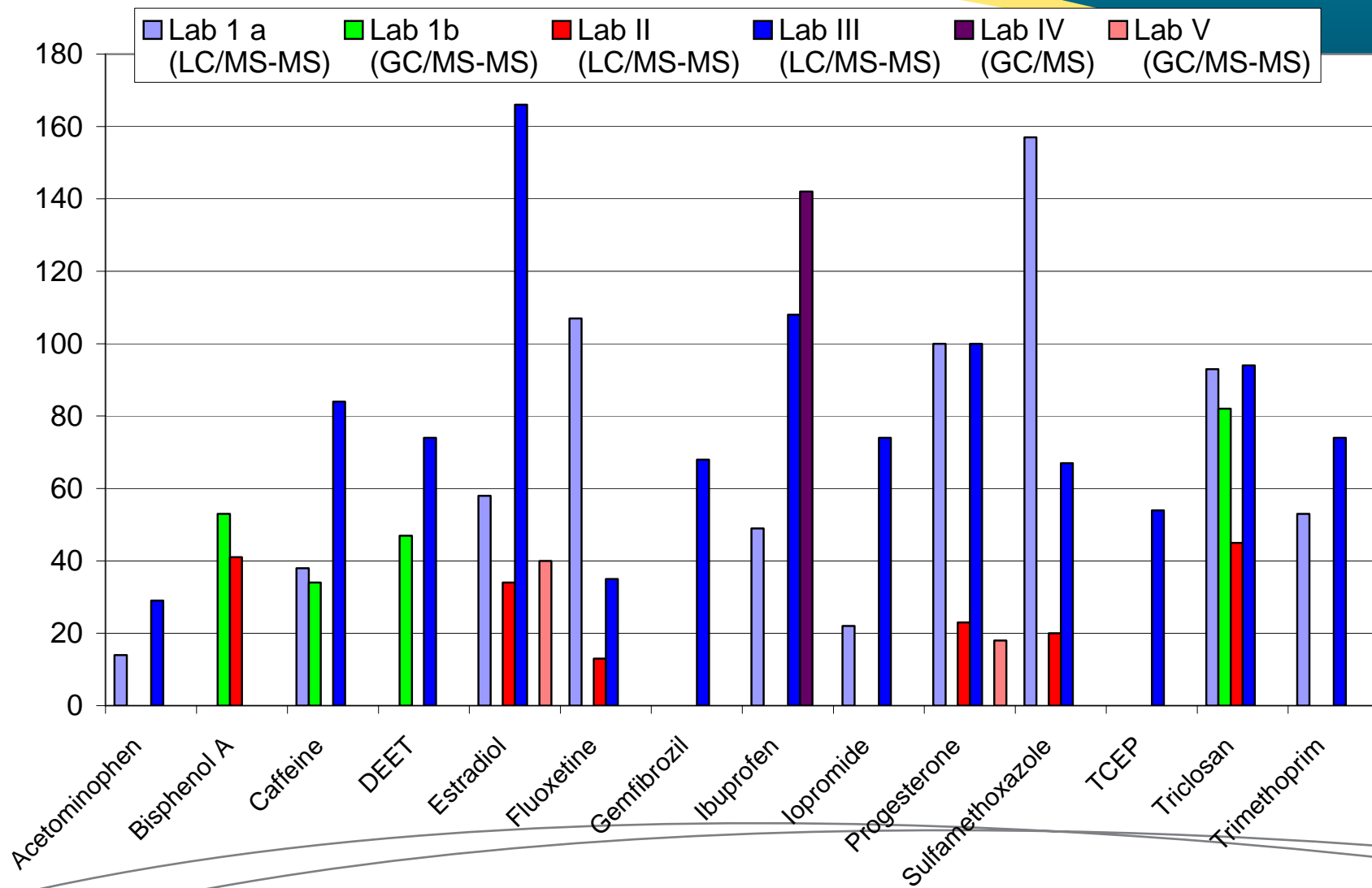


Without IDMS, Even a Little Matrix Can Create Broad Recovery Issues

Recoveries of various PPCPs in secondary effluent when spiked at 50-500 ng/L levels



State of Art in 2005 – Interlab Study for Various PPCPs in Secondary Effluent – None of the Labs Used IDMS.



Words of Wisdom for Emerging Contaminant Analysis

- EC analysis is complex. Isotope Dilution can correct for a lot of “sins”, particularly on ECs.
- Paying attention to quality systems helps ensure better data.
- When you measure at low levels you need to do your QC at low levels.
- Methods get better when they become more standardized.
- We need to beware of the I.I. – the innocently incompetent...

The More QC You Build In the Higher You Are on the Ladder of Quality

Low level MS/MSD



Low level LCS/LCSD

LCS/LCSD &/or MS/MSD

Field and Method Blanks



Preservation?

Just a Few Things to Chew On



Any Questions?

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