

ISO 17025, Section 5.9

Or... How I Learned To Stop Worrying And Love The Bomb

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Florida Pesticide Residue Workshop
19 July 2010
St Pete Beach, Florida

Our experiences

- Challenges
- Approaches
- Failures
- Successes

ISO 17025, Section 5.9

Assuring the Quality of Test and Calibration Results

It is very brief...less than half a page.
It has two subsections, 5.9.1 and 5.9.2

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ISO 17025, Section 5.9.1

- The laboratory shall have quality control procedures for monitoring the validity of tests and calibrations undertaken. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to the reviewing of the results. This monitoring shall be planned and reviewed and may include, but not be limited to, the following:
 - a) use of CRMs and/or RMs;
 - b) proficiency-testing;
 - c) replicate tests;
 - d) retesting;
 - e) correlation of results for different characteristics.

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ISO 17025, Section 5.9.2

- Quality control data shall be analyzed and, where they are found to be outside pre-defined criteria, planned action shall be taken to correct the problem and to prevent incorrect results from being reported.

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Our starting point: USDA PDP recovery criteria

- Absolute Range
 - Within 50 – 150 %
- Statistically Calculated Range
 - Within control chart UCL / LCL (i.e. +/- 3 sd)
- NOTE: PDP applies this requirement to “marker” pesticides, not to ALL pesticides.

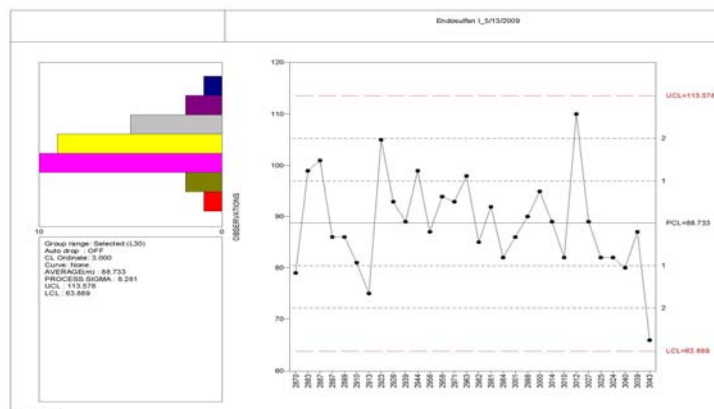
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Non-conformance against 5.9.1

- Initial A2LA assessment, Dec 2006...
- “Quality control data have not been trended for LCMS analyses in the Chemical Residue Laboratory.”

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SPC-PC IV, from Quality America, Inc



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[Endosulfan I in PDP Oranges; QuEChERS]

Challenge: Workflow logistics

- QC data is not entered into lab database by the chemists, but later...by clerical staff.
- So bench chemists were not able to use control charts while processing a batch.

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Challenge: WHAT do we trend?

- Over 150 individual recoveries per batch
- Yielding over 22,000 recovery data points per year

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GCMS Mix: 68 compounds

d-Allethrin, Amitraz Metabolite, Atrazine, Azinphos-methyl, Bifenthrin, Carfentozone-ethyl, Chlordane-Cis, Chlordane-Trans, Chlorfenapyr, Chlorothalonil, Chlorpropham, Chlorpyrifos, Chlorpyrifos-Methyl, Clomazone, Coumaphos, Cyfluthrin, Cyhalothrin, Total, Cypermethrin-Cis, Cypermethrin-Trans, Cyprodinil, DCPA, Deltamethrin, Dichlobenil, Dicloran, Diphenamid, Diphenylamine, Endosulfan I, Endosulfan II, Endosulfan Sulfate, Fenarimol, Fenpropathrin, Fenvalerate, Fluvalinate, Heptachlor, Hexachlorobenzene, Metalaxyl, Methoxychlor, Metolachlor, Mevinphos, MPCPS, Myclobutanil, Oxyfluorfen, Parathion-Ethyl, Parathion-Methyl, PCNB, Pebulate, Pendimethalin, Pentachloroaniline, Pentachlorobenzene, Permethrin-cis, Permethrin-Trans, Phenothrin, Phosalone, Phosmet, Piperonyl Butoxide, Pirimiphos Methyl, Pronamide, Propargite, Pyridaben, Pyriproxyfen, Resmethrin, Tebuconazole, Tefluthrin, Tetramethrin, Triadimefon, Triadimenol, Triallate, Trifluralin

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LCMS Mix: 110 compounds

3-OH Carbofuran, Acephate, Acetamiprid, Aldicarb, Aldicarb sulfone, Aldicarb sulfoxide, Ametryn, Azoxystrobin, Bendiocarb, Bitertanol, Boscalid, Buprofezin, Carbaryl, Carbendazim, Carbofuran, Chlorantraniliprole, Clothianidin, Diazinon, Diazinon Oxy Analog, Dichlorvos, Difenoconazole, Dimethoate, Dimethomorph, Dinotefuran, Diphenylamine, Disulfotone, Disulfotone Sulfone, Ethiofencarb, Ethion, Ethoprop, Etoxazole, Fenamidone, Fenamiphos, Fenamiphos Sulfone, Fenamiphos Sulfoxide, Fenbuconazole, Fenhexamid, Fenpropimorph, Fenpyroximate, Fenthion, Flonicamid, Fluazifop-Butyl, Fludioxonil, Fluoxastrobin, Fluridone, Fonofos, Forchlorfenuron, Furathiocarb, Halosulfuron-Methyl, Hexaconazole, Hexythiazox, Imazalil, Imidacloprid, Imiprothrin, Indoxacarb, Malathion, Malathion Oxon, Mandipropamid, Metaldehyde, Methamidaphos, Methidathion, Methiocarb, Methomyl, Methoxyfenozide, Monocrotophos, Napropamide, Norflurazon, Norflurazon Desmethyl, Novaluron, Omethoate, Oryzalin, Oxadixyl, Oxamyl, Oxamyl Oxime, Oxydemeton Methyl, Oxydemeton Methyl Sulfone, Phorate, Phorate Sulfone, Phorate Sulfoxide, Phosphamidone, Pirimicarb, Prallethrin, Profenofos, Propamocarb HCL, Propetamphos, Propiconazole, Propoxur, Propoxur D3 (For IS), Pymetrozine, Pyraclostrobin, Pyrimethanil, Quinoxifen, Saflufenacil, Saflufenacil I, Saflufenacil II, Spinosad A, Spinosad D, Spirodiclofen, Spiromesifen, Tebufenozide, Terbufos, Tetramethrin, Thiabendazole, Thiacloprid, Thiamethoxam, TPP (For IS), Trifloxystrobin, Triflumizole, Triticonazole, Vernolate

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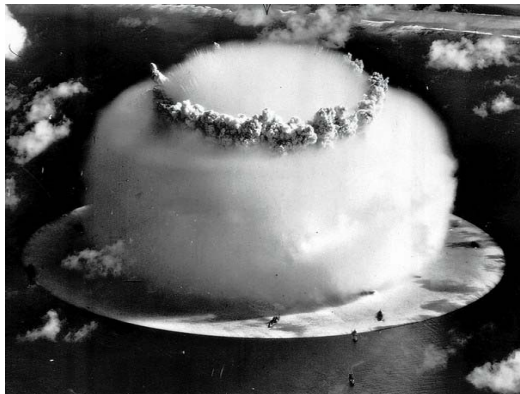
Challenge: AOAC (2006) 5.9

- Statistical process control charts **SHALL** be prepared for the QCS sample analyses...
- Corrective action **SHALL** be taken for all control samples that are outside of the acceptance criteria of the control chart.

Note: our lab has no argument w/ this for single parameter methods

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But we will have a corrective action triggered in EVERY batch!



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[Gail's opinion: That's about as smart as starting a nuclear war.]

Lots of Corrective Actions? Too Bad!!!



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The assessment was over... Our fix...

- Acceptance Criteria for **ALL** Spike Recoveries:
 - 50-150% = acceptable
 - Within +/- 3 sd = acceptableCorrective Action required if any compound exceeds both criteria.
- Trend analysis performed on analytes for which there are findings in that batch.
Corrective Action required if run tests are triggered.

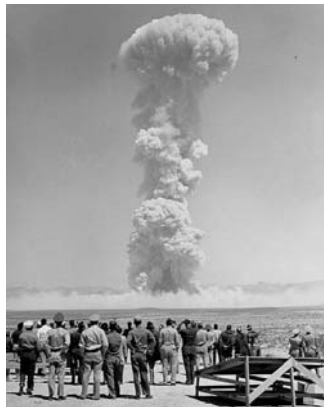
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We did have a corrective action triggered in almost EVERY batch!



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Having many CAs was no surprise...



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...but it was very sad nonetheless.

NELAC Quality Systems (2003) Appendix D.1.1.2.1.e

- MARGINAL EXCEEDANCE
- Recovery outside ± 3 SD, but inside ± 4 SD

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NELAC 2003, Appendix D.1.1.2.1.e

Analytes in LCS	Analytes allowed in ME
> 90	5
71-90	4
51-70	3
31-50	2
11-30	1
< 11	none

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Our fix evolves...

Acceptance Criteria for Spike Recoveries:

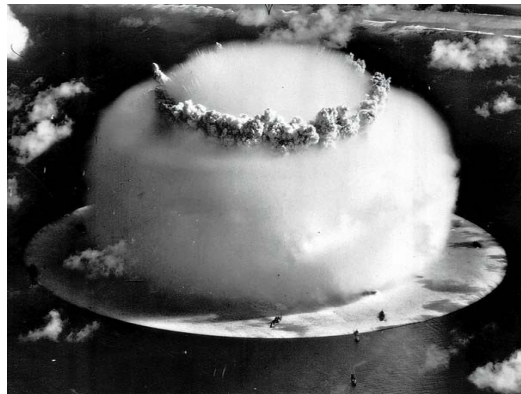
- 50-150% = acceptable
- Within +/- 3 sd = acceptable
- Within +/- 4 sd = acceptable provided no more than 10% fall in this ME range

Corrective Action is required if:

- More than 10% fall into 3rd category above
- ANY exceed +/- 4 sd

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We still had corrective actions triggered in many, many batches!



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Many discussions and meetings...



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...and much angst...

**"Gentleman, you can't fight here!
This is the war room!"**



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...as well as conflict.

Our fix continued to evolve...

- Acceptance Criteria for Spike Recoveries:
 - 50-150% = acceptable
 - Within +/- 3 sd = acceptable
- Corrective Action is required if more than 30% of analytes are unacceptable

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How did we pick 30% and why?

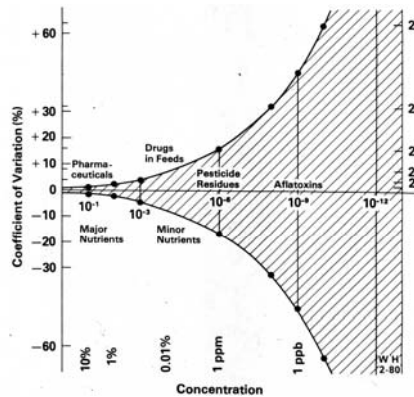
Goal for corrective action triggers:

- Maximize ability to see non-random events
 - Assignable root causes
- Minimize corrective actions triggered by random variation
 - Unknowable root causes

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Much variation in residue analysis...

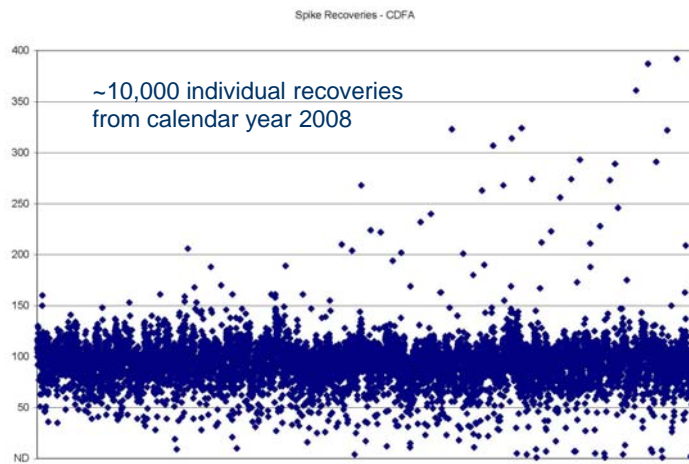
Horwitz Curve, or "Trumpet"



27

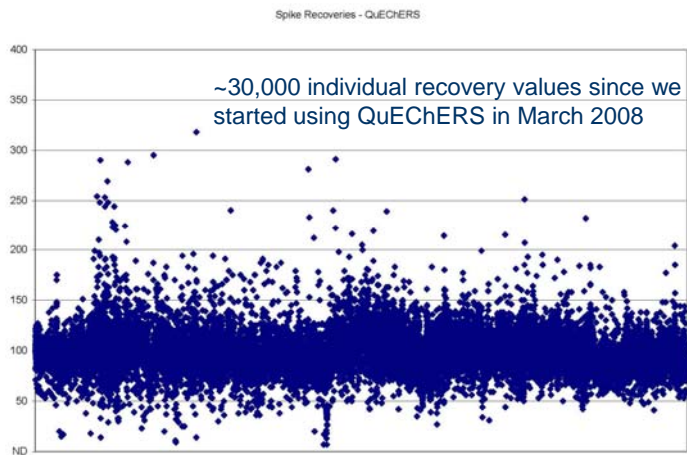
Horwitz, et al, JAOAC, Vol 63, No 6, 1980, pp 1344-1354

Recoveries using CDFA extraction



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Recoveries using QuEChERS extraction

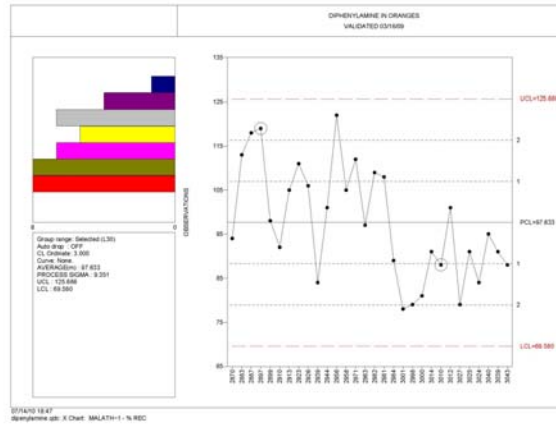


How to “manage” variation...

- Institute “aggregate” recoveries, for trending.
- Aggregate = the average recovery of all quantifiable analytes in a given spike mix, analyzed on a given instrument.
- Aggregates smooth the data.

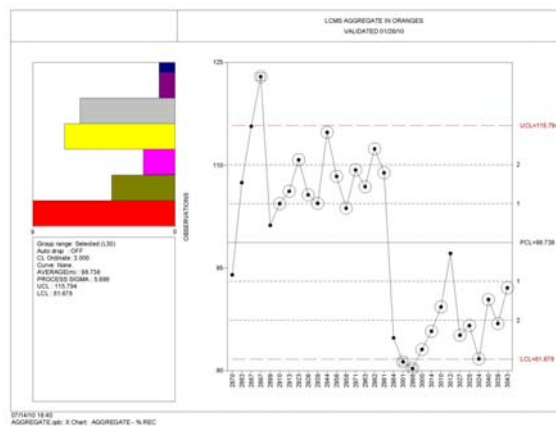
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Individual analyte behavior - Diphenylamine in PDP Oranges; LCMSMS



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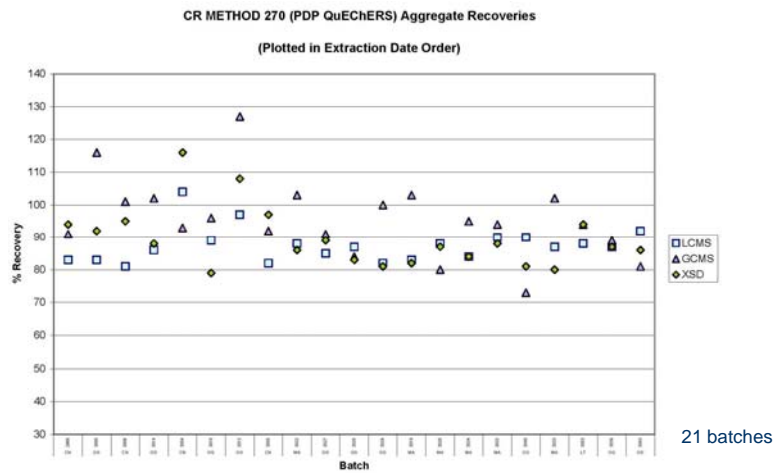
Aggregate behavior - LCMSMS aggregate in PDP Oranges



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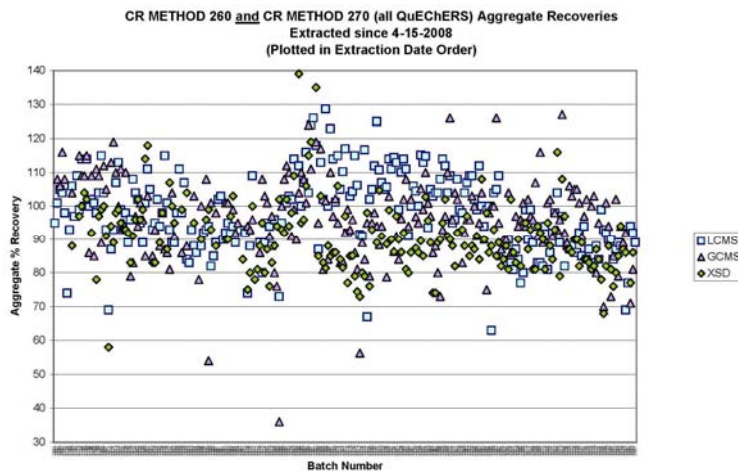
Comparison of Aggregates within a batch

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Are there patterns in this data?

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Pesticide residue proficiency test (PT) samples since January 2000

Provider	PTs
SSCS	13
AOAC	18
FAPAS	12
PDP (n = 1 or 2)	8
EU	1
Total	52

35

(as of June 2010)

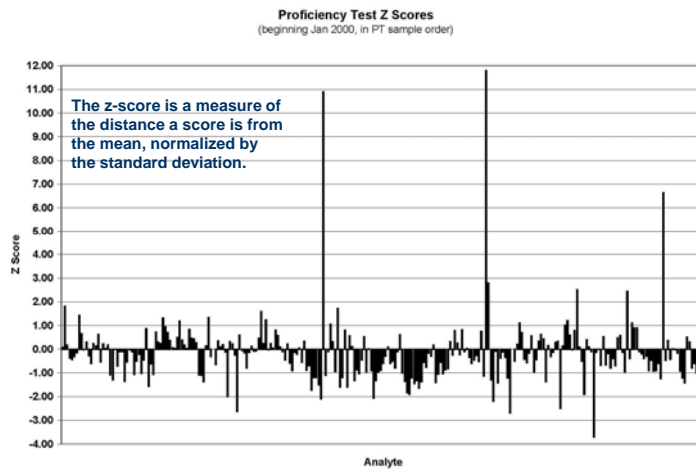
402 Results Reported to PT Providers

# of Results	Type of Score
265	Z-score
101	% recovery
36	no score

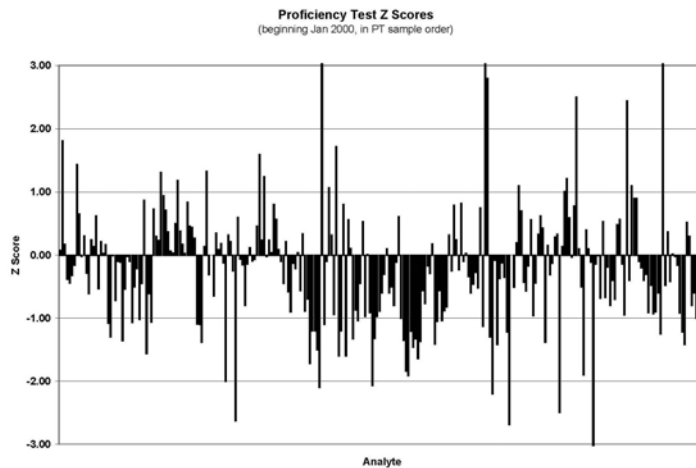
36

(as of June 2010)

265 Z-scores; all but four within +/- 3

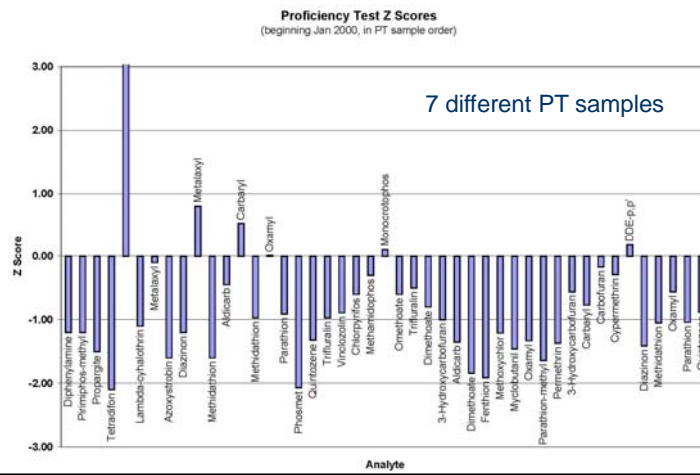


Expanded y axis...



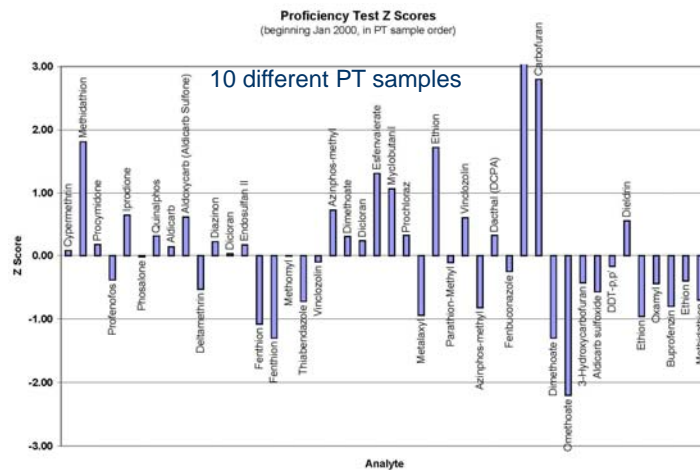
Filter: "CR 250" extraction

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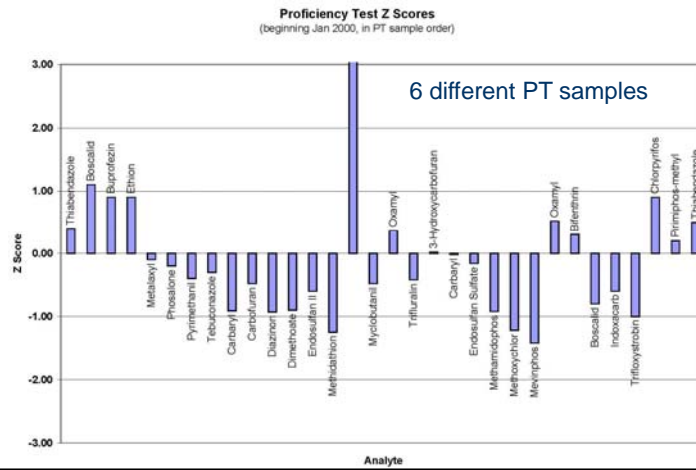
Filter: CDFA extraction method

40



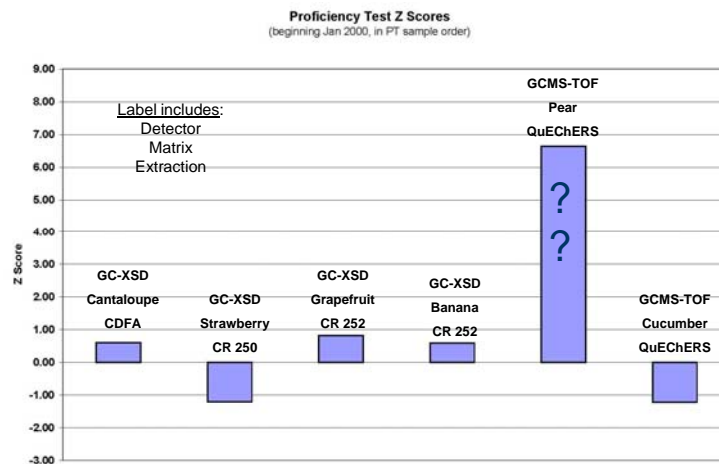
Filter: QuEChERS extraction

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Filter: Methoxychlor

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What's ahead?

- More change

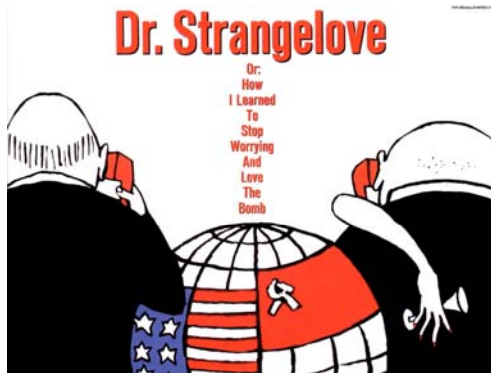
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December 2006, 3½ years ago

- Quality Control SOP
 - Rev 3 (at time of assessment)
 - Rev 9 now in draft
- Corrective Action SOP
 - Rev 1 (at time of assessment)
 - Rev 6 now in draft

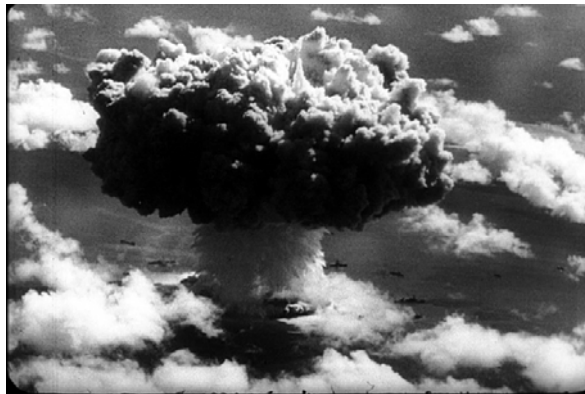
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Thank you Stanley Kubrick



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Any Questions?



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Please note...

- The Bureau of Chemical Residue Laboratories maintains A2LA accreditation to ISO/IEC 17025 for the specific tests listed in A2LA Certificate 2534.03.