Internal Quality Control and its place in the Big Picture

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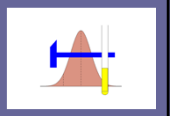
The Three Pillars of Quality

The Big Picture—how it all fits together



Fitness for purpose
What accuracy best suits end-user needs?

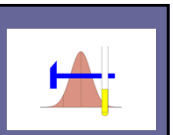
→

Method validation
What accuracy can my method supply?
Is it fit for purpose?

→

Quality control
Does my method consistently stay fit for purpose?

The Big Picture—how it all fits together



Fitness for purpose
What accuracy best suits end-user needs?

Expert opinion

Decision theory

→

Method validation
What accuracy can my method supply?
Is it fit for purpose?

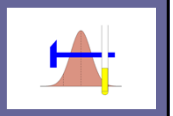
Collaborative trials
Precision studies
Reference materials
Calibration studies
Ruggedness tests
Etc. Etc.

→

Quality control
Does my method consistently stay fit for purpose?

Preventive action
Control materials
Control charts
Duplication
Proficiency tests

IQC

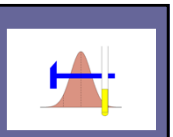


Preventive action

IQC
- Control materials
- Control charts
- Duplication

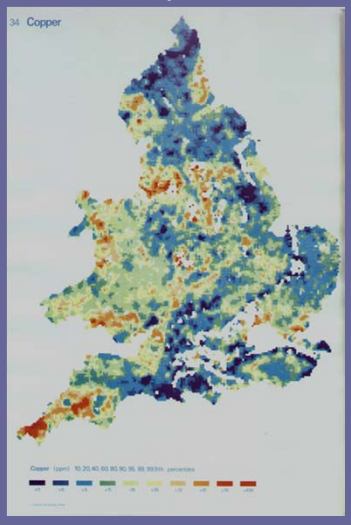
Proficiency tests

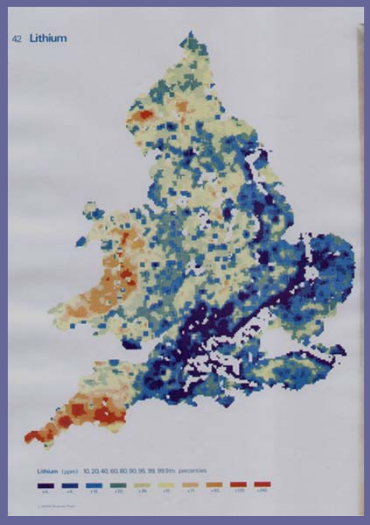
Why do IQC?



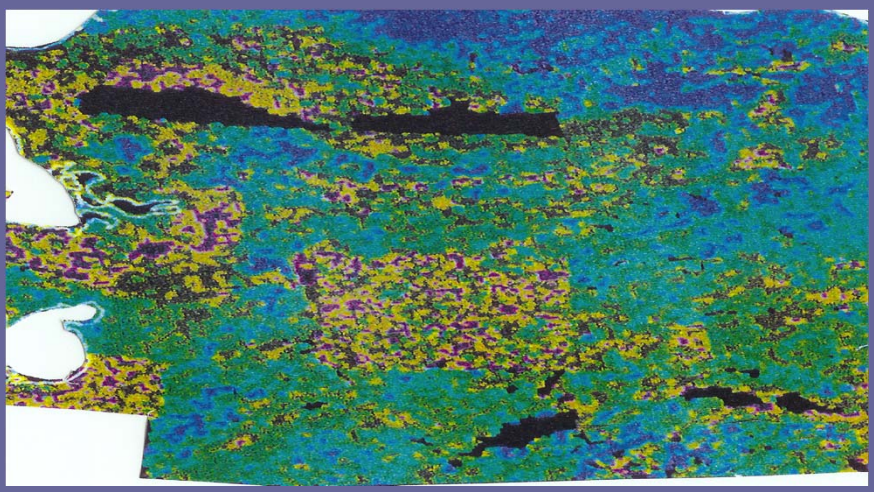
- To ensure that the uncertainty found during validation remains true for successive runs of the measurement.
- To ensure that the factors determining the magnitude of uncertainty have remained constant. (Same thing) **But**…
- You can't estimate uncertainty within a routine run.

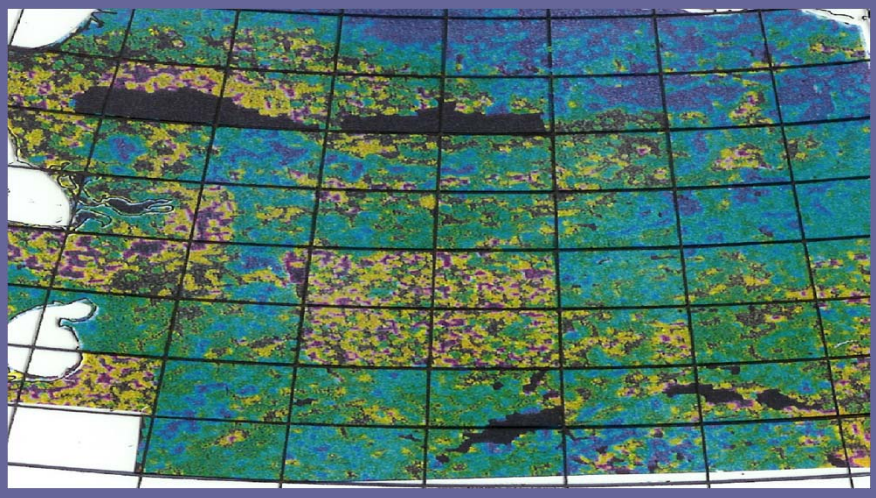
The Wolfson Geochemical Atlas of England and Wales
(Clarendon Press 1978)
50,000 samples; 25 elements





But elsewhere…

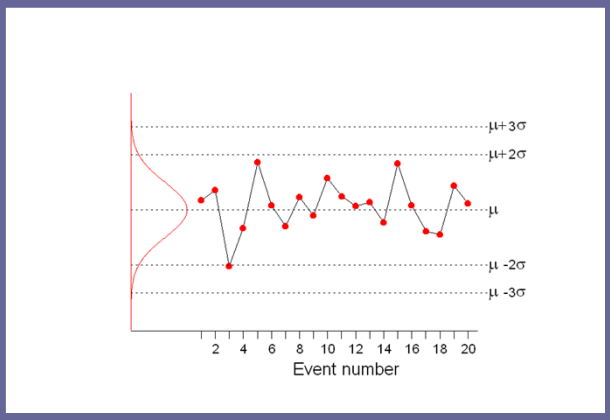




The meaning of statistical control

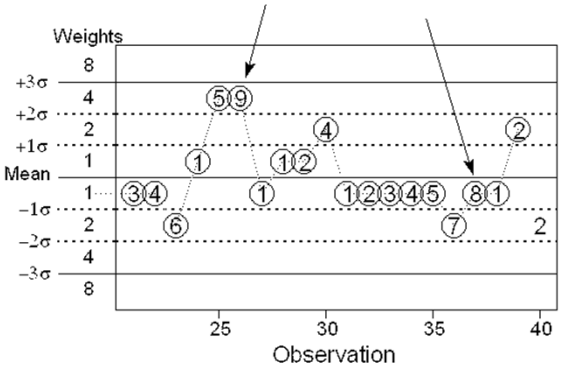
- A *representative* aspect of the process behaves like an independent random variable from a normal distribution.
- The parameters of the distribution (mean and standard deviation) have to be estimated by observing the process itself.
- Results are plotted on a control chart.

Shewhart chart



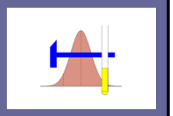
- See the ISO/IUPAC Harmonised Guidelines for Internal Quality Control for details. (*Pure Appl Chem*, 1995, **67**, 649-666. Free download from www.iupac.org)

Range chart (or 'J-chart')



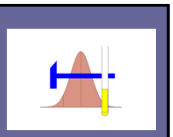
See *AMC Technical Briefs* No 12.
Free download from www.rsc.org/amc

Deviation from statistical control



- If the surrogate variable deviates from the normal, we assume that the system is out of control, that is, the factors that control the size of uncertainty have changed.
- The analytical results for the run are not reliable and must be considered for rejection.
- If the cause of the problem can be identified, it must be remedied before continuation of the analytical process.

What do we measure?

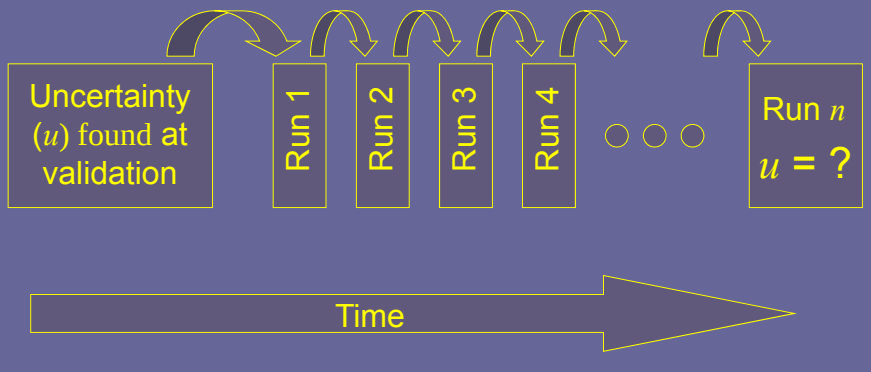


- One or more surrogate reference materials (control materials) inserted into the sequence of test materials that make up the run.
- The surrogate results are plotted on a control chart.
- The control materials must be typical of the type of material being analysed, and contain the analyte at a typical (or critical) concentration. **But…**
- The materials are never quite typical because they are homogenised and often stabilised.

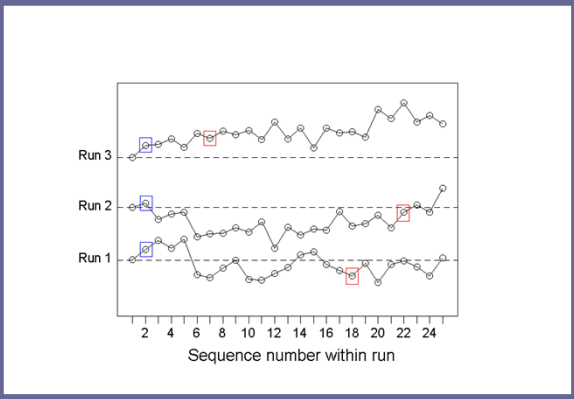
What do the surrogate results portray?

- The dispersion measured is not standard uncertainty but run-to-run precision, a subset of VIM3 intermediate precision.
- Run-to-run SD is usually smaller than standard uncertainty by a factor of 0.5.
- *Inference*—you cannot validly use standard uncertainty, or repeatability SD, or fitness-for-purpose criteria or reference levels for setting up control charts.
- See *Precision in chemical analysis: a critical survey of uses and abuses*. *Analytical Methods* (2012) DOI 10.1039/c2ay25083g.

Run-to-run conditions



Replication within-run

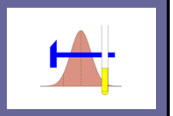


- *Inference*—the control material needs to be in a random position within each run of real analysis to be representative.

More complications

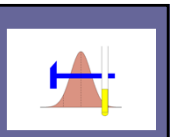
- Real runs of analysis are not replications of the same material.
- All of the materials are different and there may be blanks and other check materials.
- This gives rise to extra uncertainty, e.g., from memory effects.
- *Inference*—you can estimate the parameters for the control chart accurately only when the process is in routine operation, i.e., not during an initial one-off validation.

Even more complications: setting the control limits



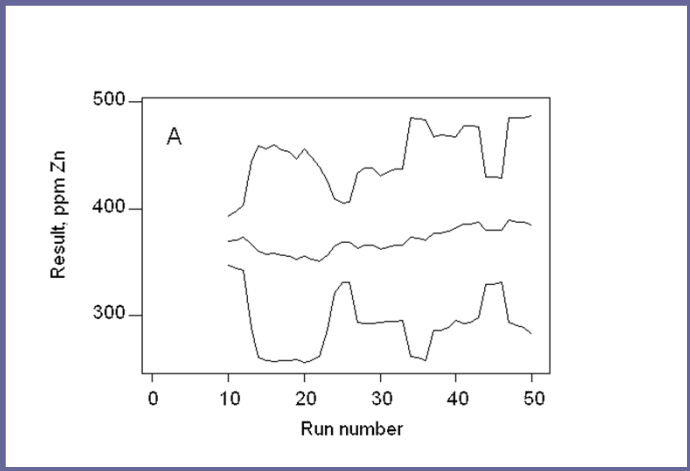
- We don't know μ and σ: they have to estimated from run-to-run replicated results, not within-run results.
- At first the estimates will be based on only a small number of observations (say 10) and hence very variable.
- For a new process, the analysts will be inexperienced and the results less precise and may contain outliers.
- After some experience with the system, the estimates should be reviewed.

Example

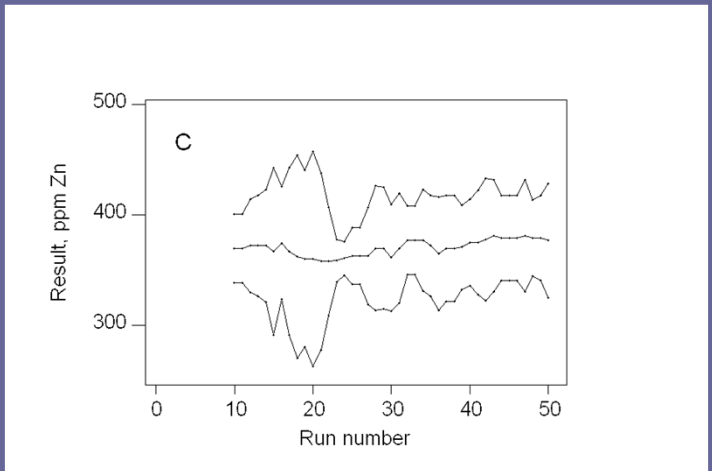


- Zinc in samples of soil by acid extraction and ICPAES.
- About 100 samples per run.

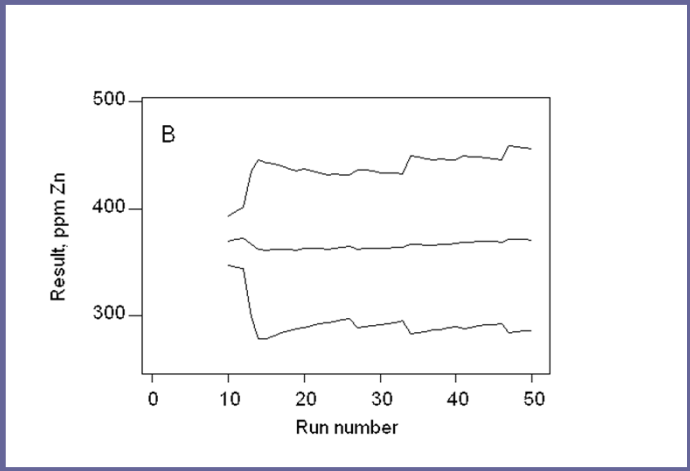
Control lines based on mean and SD estimated from rolling groups of 10 results. Classical statistics.



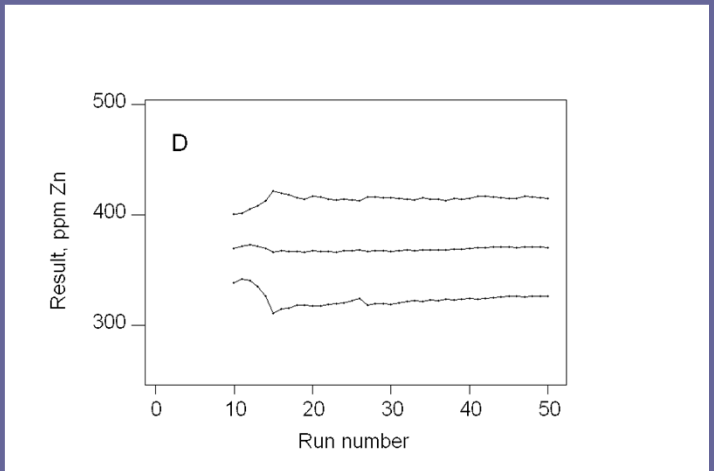
Control lines based on mean and SD estimated from rolling groups of 10 results. Robust statistics.



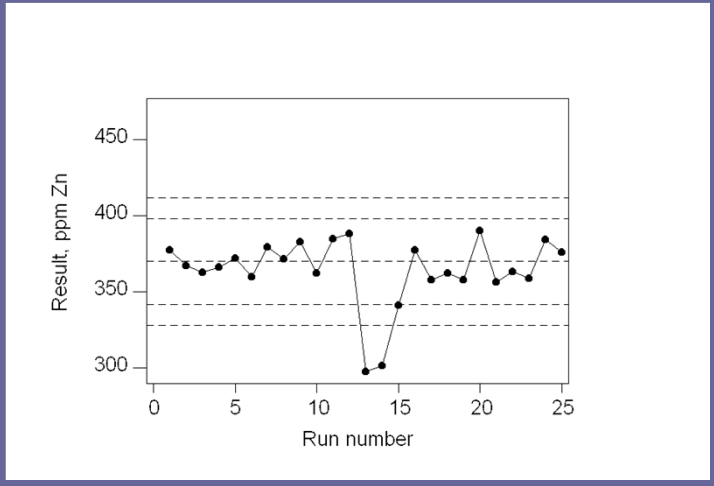
Control lines based on mean and SD estimated from all results up to *n*-th run. Classical statistics.



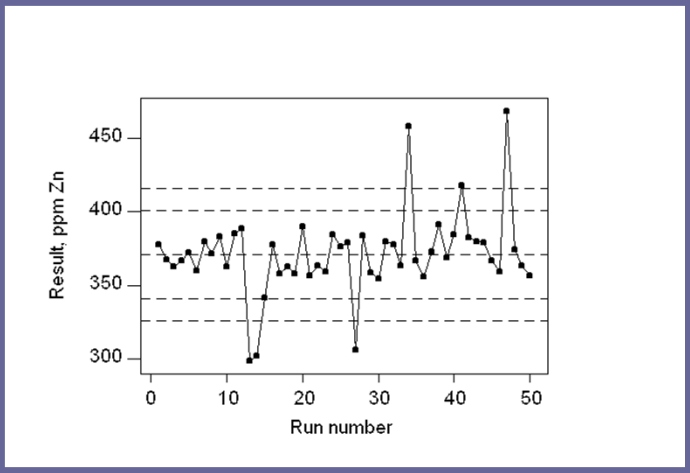
Control lines based on mean and SD estimated from all results up to *n*-th run. Robust statistics.



Interim control chart based on validation results: repeatability mean and 1.6 × repeatability SD



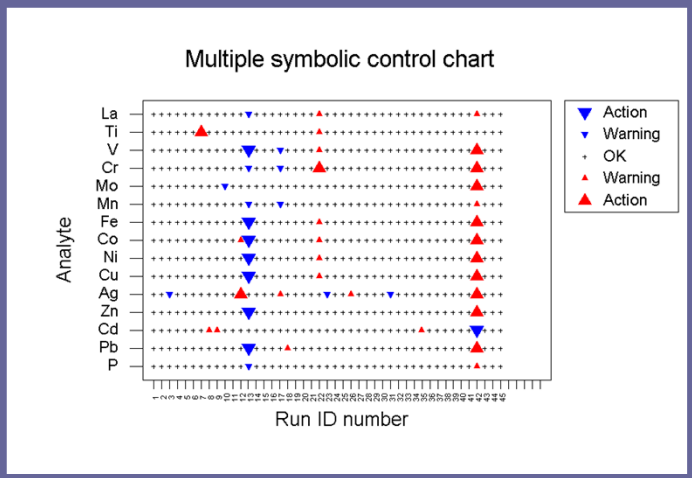
Updated control chart based on robust statistics from the first 50 runs.



Limitations of IQC

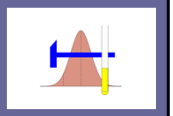
- IQC is retrospective.
- IQC does not protect against sporadic blunders (gross errors).
  See *AMC Technical Briefs* No 49, March 2011.

IQC in simultaneous multianalyte analysis



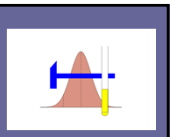
See: Multiple univariate symbolic control chart for internal quality control of analytical data. *Anal. Comm.* **35**; 205-208.

One-off analysis



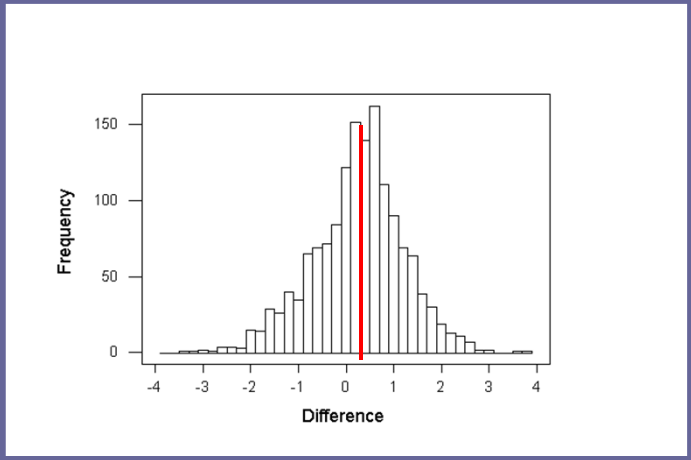
- The concept of statistical control is not applicable.
- Base accuracy criteria on fitness for purpose considerations.
- If a CRM is available, analyse that alongside the test materials.
- Analyse the test material(s) in duplicate.
- Plot the absolute differences against the means.

Duplicate results



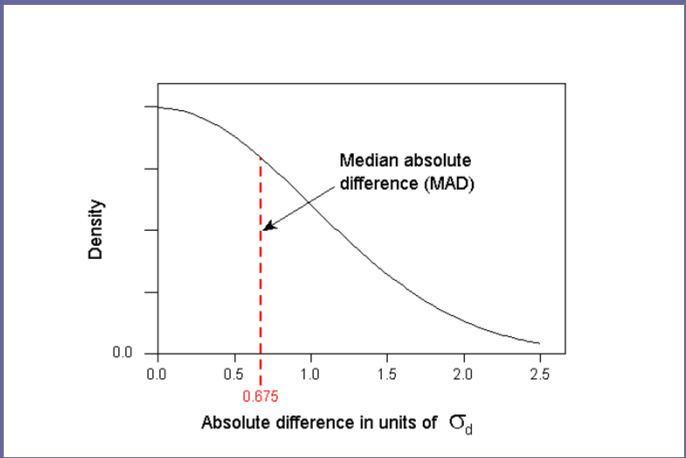
- If x_1, x_2 are independent random normal duplicates from a population SD of σ, then differences (x_1-x_2) have zero mean and an SD of $\sigma_{dif} = \sigma \times \sqrt{2}$.
- But the random order of the duplicates can easily get disturbed.
- This biases and skews the distribution of differences, so that σ_{dif} is inaccurately estimated.

Biased duplicate differences



Median absolute difference (MAD)

- Resolve the issue by using absolute differences $|x_1-x_2|$.

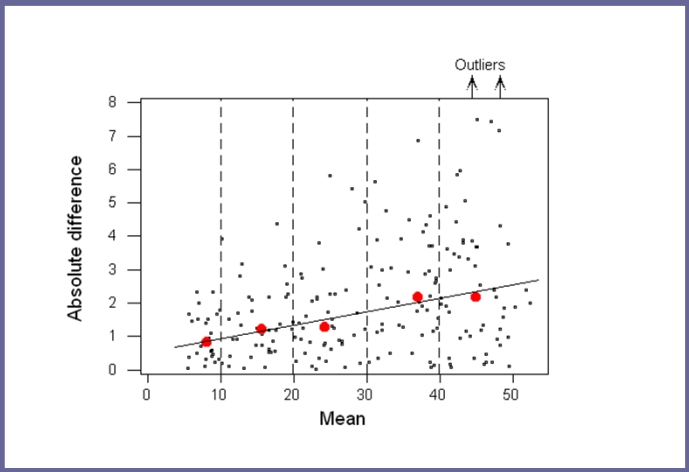


MAD as an estimator of σ

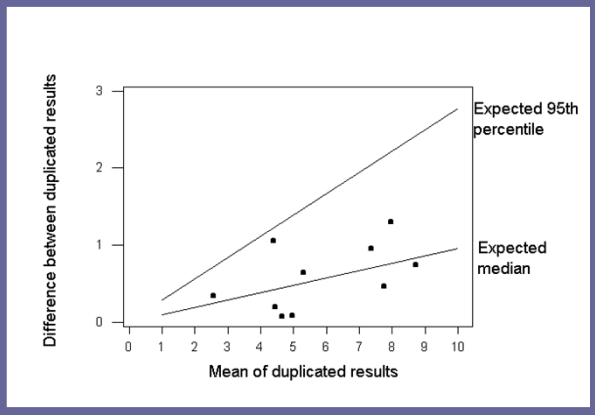
- MAD = 0.675 × σ_d
  = 0.675 ×√2 × σ
  = 0.96 × σ

- Thus MAD is sufficiently close to σ for most purposes.
- Complication: σ varies with concentration.

With a large dataset



With a small dataset



- The plot shows the data points and the expected percentiles for an RSD of 10%.
- More details of duplicate plots from *AMC Technical Brief* No 9 (free download from www.rsc.org/amc).