Internal Quality Control and its place in the Big Picture

Michael Thompson
Birkbeck University of London
m.thompson@bbk.ac.uk

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?

Fitness for purpose
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Expert opinion
Decision theory

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

Preventive action
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


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.

Run-to-run conditions

![Run-to-run conditions diagram](image)
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 $\mu$ and $\sigma$: 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.**

![Graph A](image1)

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

![Graph C](image2)
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 $1.6 \times$ 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

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 $\sigma$, then differences $(x_1 - x_2)$ have zero mean and an SD of $\sigma_{\text{dif}} = \sigma \times \sqrt{2}$.
- But the random order of the duplicates can easily get disturbed.
- This biases and skews the distribution of differences, so that $\sigma_{\text{dif}}$ is inaccurately estimated.
Biased duplicate differences

Median absolute difference (MAD)

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

![Histogram showing frequency and difference distribution](image)
MAD as an estimator of $\sigma$

- $\text{MAD} = 0.675 \times \sigma_d$
  
  $= 0.675 \times \sqrt{2} \times \sigma$

  $= 0.96 \times \sigma$

- Thus MAD is sufficiently close to $\sigma$ for most purposes.
- Complication: $\sigma$ 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).