Quality assurance challenge 11

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We would like to invite you to participate in the Analytical Challenge, a series of puzzles to entertain and challenge our readers. This special feature of “Analytical and Bioanalytical Chemistry” (ABC) has established itself as a truly unique quiz series, with a new scientific puzzle published every other month. Readers can access the complete collection of published problems with their solutions on the ABC homepage at <http://www.springer.com/abc>. Test your knowledge and tease your wits in diverse areas of analytical and bioanalytical chemistry by viewing this collection.

In the present challenge, quality assurance is the topic. And please note that there is a prize to be won (a Springer book of your choice up to a value of €75). Please read on...

Meet quality assurance challenge 11

Earlier challenges focussed on method development and the steps for the validation of an analytical method. We have learnt that in principle validated analytical methods are suitable for routine analysis. But the question is whether the data produced by a certain method are still *fit for purpose each time*. This is realized by methods of *internal quality control* (QC), which is the subject of this challenge. Monitoring analytical performance on an ongoing basis is an important question in quality management in the laboratory.

Whereas *quality assurance* involves the overall measurements taken by the laboratory to regulate quality, QC relates to the individual measurements of samples. QC can be realized by analysis of QC materials under the same conditions. If there are no significant differences according to tests of trueness and precision, the analytical method is still under statistical control. The QC material required is a

material of known composition which is similar to the test materials in terms of the matrix and the analytical concentration. It may be, for example, a certificated reference material or an in-house reference material.

Internal QC is preferably verified by *control charts*. There are a number of different types of control charts, but the Shewhart chart is mainly used. The general pattern of a Shewhart chart at the start of routine analysis is shown in Fig. 1. The central line of the control chart is a mean value $\bar{x}$, which is the “true value”, and s is the standard deviation obtained by measurements of a QC material in the pre-period.

The upper and lower action limit lines UAL and LAL, respectively, and the upper and lower warning limit lines UWL and LWL, respectively, are obtained by the following expressions:

For the warning limit lines,

$$\bar{x} \pm 2s \quad (1)$$

and for the action limit lines,

$$\bar{x} \pm 3s. \quad (2)$$

On the assumption that the measured values are normally distributed, the three-sigma limits include 99.7% of the area under a curve of the normal distribution and the two-sigma lines include 95.5% of the values. When the QC results are averaged by replicates per run, the standard deviation s must be calculated from separate estimation of within-run and between-run variances calculated by

$$s = \sqrt{s_{\text{bw}}^2 + \frac{s_{\text{in}}^2}{n_j}}, \quad (3)$$

where n_j is the number of replicates per run.

Note that outliers must be rejected for the construction of the control chart.

Data obtained in the routine analysis are plotted in chronological order and they are inspected to see whether the process is in control or whether an out-of-control situation can be

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Fig. 1 The general pattern of a Shewhart chart at the start of the routine analysis and the curve of the normal distribution of the analytical results obtained in the pre-period with the “true” value $\bar{x}$ and the limits at significance levels $P=95\%$ and $P=99\%$. *LAL* lower action limit, *LCL* lower control limit, *UAL* upper action limit, *UCL* upper control limit

detected. In the latter case, the process should be stopped, and the causes of this variation must be sought and eliminated.

ISO 8258 [1] gives rules for the recognition of an out-of-control situation:

1. One measured point lies outside the upper or the lower action line.
2. Nine consecutive measured points lie on one side of the central line.
3. Two consecutive measured points lie outside the warning line.
4. Nine consecutive measured points show an upward trend.
5. Nine consecutive measured points show a downward trend.

A Shewhart chart constructed according to Fig. 1 can be applied as a mean control chart, primarily used for detecting *bias* in an analytical system.

The *range chart* is applied for monitoring the analytical *precision*. The range R_i , i.e. the difference between the largest and smallest values obtained by repeated measurements within each analytical run, is given by

$$R_i = x_{i,\max} - x_{i,\min}. \quad (4)$$

The average range $\bar{R}$ is calculated by

$$\bar{R} = \frac{\sum R_i}{n}.$$

Fig. 2 Format of a range chart. *UWL* upper warning limit

Table 1 Analytical results for the determination nitrite nitrogen by ion chromatography for ten sets of three replicates obtained from a control solution

Observation no.	c_i (mg L ⁻¹ N)	Observation no.	c_i (mg L ⁻¹ N)
1	0.152	6	0.152
	0.153		0.155
	0.153		0.154
2	0.156	7	0.158
	0.154		0.156
	0.155		0.158
3	0.151	8	0.153
	0.156		0.154
	0.155		0.152
4	0.161	9	0.156
	0.156		0.158
	0.156		0.155
5	0.154	10	0.153
	0.153		0.155
	0.154		0.154

The format of a range chart is shown in Fig. 2. The upper action limit line *UAL* or upper warning limit line *UWL* is obtained by multiplying the average range $\bar{R}$ by tabulated multipliers D_{WL} and D_{AL} , which, for example, are given in [2].

The warning limit line is given by

$$WL = \bar{R}D_{WL} \quad (5)$$

and the action limit line is calculated by

$$AL = \bar{R}D_{AL}. \quad (6)$$

Table 2 The first eight analytical results obtained by a in-house reference material for the determination nitrite nitrogen by ion chromatography obtained by the quality control in routine analysis

Observation no.	c_i (mg L ⁻¹ N)	Observation no.	c_i (mg L ⁻¹ N)
1	0.154	5	0.158
	0.152		0.155
	0.155		0.157
2	0.152	6	0.151
	0.154		0.158
	0.155		0.152
3	0.164	7	0.151
	0.168		0.153
	0.166		0.152
4	0.150	8	0.154
	0.152		0.155
	0.154		0.156

An out-of-control situation can be detected by the rules given above.

The challenge

The challenge concerns the determination of nitrite nitrogen in surface water by ion chromatography according to the EU norm given in [3]. Table 1 presents the analytical results obtained in the pre-period from each of three replicates using an in-house control solution, and the first eight results in the routine analysis are summarized in Table 2.

- (a) Check the mean values $\bar{x}_j$ of the i observations of the measured values in the pre-period for a normal distribution and outliers at the significance level $P=95\%$.
- (b) Construct the corresponding chart for controlling the mean values and determine whether the analytical system is under control.
- (c) Construct the corresponding chart for controlling the precision and determine whether the homogeneity of variances is given. Note that the D factors for $n_j=3$ are $D_{WL}=2.176$ and $D_{AL}=2.575$ [2].

References

1. ISO 8258 (1991) Shewhart control charts. International Organization for Standardization, Geneva
2. Reichenbacher M, Einax JW (2011) Challenges in analytical quality assurance. Springer, Heidelberg
3. DIN EN ISO 10304-1 (2009) Water quality-determination of dissolved anions by liquid chromatography of ions-part 1: determination of bromide, chloride, fluoride, nitrate, nitrite, phosphate and sulfate (ISO 10304-1:2007)

We invite our readers to participate in the Analytical Challenge by solving the puzzle above. Please send the correct solution to abc-challenge@springer.com by April 1, 2013. Make sure you enter "Quality assurance challenge 11" in the subject line of your e-mail. The winner will be notified by e-mail and his/her name will be published on the ABC homepage at <http://www.springer.com/abc> and in the journal (volume 405, issue 17), where readers will find the solution and a short explanation.

The next Analytical Challenge will be published in 405/12 (May 2013). If you have enjoyed solving this Analytical Challenge, you are invited to try the previous puzzles on the ABC homepage.