

GUIDANCE ON THE INTERPRETATION OF ASPECTS OF ANALYTICAL QUALITY CONTROL (AQC)

1 Introduction and general guidance

- 1.1 The purpose of this document is to provide guidance to Inspectors to aid their assessment of the appropriateness of a laboratory's implementation of AQC in chemistry laboratories. It should be used in conjunction with the reference documents listed in DWI Information Letter (IL) 3/99 and the Technical Auditors' AQC Manual. The guidance should also be of use to water companies and the laboratories they use for compliance analysis, and has therefore been issued under cover of IL 18/99.
- 1.2 The guidance on internal analytical quality control given in IL 8/93 remains valid. However, a number of authoritative documents have subsequently been issued, which have been adopted by the Inspectorate as supplementary reference documents. These have been detailed in IL 3/99. These authoritative documents are entirely consistent with the guidance given in IL 8/93 and would have been referenced if they had been available. The Harmonised Guidelines on Internal Quality Control are particularly welcome because they give clear and unequivocal guidance on what constitutes an out of control condition, and the actions to be taken whenever an out of control condition exists. However, the adoption of these Harmonised Guidelines has brought into sharper focus a number of issues relating to AQC, particularly those relating to out of control conditions.
- 1.3 The definition of an out of control condition as nine successive plotting values falling on the same side of the mean line is not new and is entirely consistent with paragraph 41 of IL 8/93 which states "The (internal AQC) procedures should also include regular and frequent examination and review of all charts and include guidance for checking and investigating significant trends or changes in either random or systematic error...", and with a tighter but similar supplementary decision rule is given in NS 30. The guidance given in IL 8/93 in respect of out of control conditions is that the definition should be consistent with the guidance given in section 5.3.2 of NS 30. The Harmonised Guidelines definition is entirely consistent with NS 30 in respect of single charts/records, but NS 30 does not consider the conjunctive use of two charts and is less authoritative in tone.
- 1.4 As with all out of control conditions, the occurrence of nine plotting values falling on the same side of the mean line is an indication that the data produced by the system are of unknown accuracy and hence they cannot be relied upon, or in the case of compliance analysis do not comply with the requirements of regulation 21(2)(d)(iii). This situation remains until such time as the cause of the out of control condition has been investigated and any necessary remedial action taken. However, it may sometimes be possible to demonstrate that results associated with certain out of control conditions are fit for purpose.
- 1.5 The Harmonised Guidelines do go significantly further than either NS 30 or IL 8/93 in the statement of action to be taken whenever an out of control condition occurs, but do not give any guidance on what action should be taken. NS 30 is somewhat unhelpful in this regard, merely recommending that unspecified action be taken. IL 8/93 is more specific in requiring the laboratory to have properly documented procedures for routine AQC that stipulate what action or

actions should be followed when an out of control condition is shown to exist, including a definition of an out of control condition and detail of the records to be made when such a condition exists. The results of analyses obtained using a method that is not in statistical control should not be released except in exceptional circumstances, when each result so released should carry an appropriate commentary in all records and reports. The circumstances in which such results can be released for compliance purposes should be fully documented and state that the cause of the out of control condition should first be identified and shown not to affect the results of analysis of samples intended for release. This remains the Inspectorate's position.

- 1.6 However, experience has shown that some laboratories have difficulty with determining what is required by this guidance. The following supplementary guidance is therefore intended as a benchmark against which a laboratory's procedures and practice in respect of identifying and acting upon an out of control condition can be assessed by Inspectors. This guidance may be given to laboratories and other interested parties by Inspectors as an aid to the formulation of appropriate laboratory procedures and records provided it is made clear that they are only criteria or benchmarks for assessment and not a detailed list of the procedures, records and actions we expect to see. Alternative but no less effective approaches are to be encouraged, and any recommendations for improvements referencing this supplementary guidance should use terms like "consistent with" or "such as" and not be prescriptive.
- 1.7 It should be remembered that the primary purpose of AQC is to identify changes in the performance of the analytical system. It is not intended to assign either cause or magnitude to that change. However, it can in some circumstances provide some pointers to the types of problem to focus on in any investigation, or an indication of the likely significance and timing of the change. Examples are:
- (a) successive breaches of the same warning limit may be due to changes in either systematic or random error, but successive breaches of the warning limits on opposite sides of the mean are almost certainly due to changes in random error. Scrutiny of the chart may give an indication of when the problem was first observed, but it cannot be assumed that the onset coincided with either a change on the chart or the first out of control condition;
 - (b) breaches of warning and action limits provide no information about the magnitude of the change in performance, but when a change in systematic error, or bias, occurs which is not associated with limit breaches the control chart can give an indication of the magnitude of the change and when the change occurred.
- 1.8 One other aspect of the Harmonised Guidelines that has engendered comment is the recommendation to analyse in duplicate a relatively large number of samples. This recommendation is made because of the problems of sample homogeneity that exist for many sample matrices. This is not generally a problem for drinking water and laboratories are not expected to implement it except in the case of *ad hoc* analyses. The guidance given in paragraphs 27.b. and 33 to 36 of IL 8/93 remains appropriate.

2 Definition of an out of control condition

2.1 The following rules (2.2 and 2.3) should be used as a benchmark for deciding whether a laboratory's definition of an out of control condition is satisfactory. They are expressed in terms of Shewhart charts, but the underlying principle of establishing a reasonably high probability of detecting a significant change in performance in respect of within-batch and between-batch random errors (either separately or combined) and systematic errors (bias) with an acceptably low probability of false alarms is applicable to all chemical and physical determinations. One such system, also applicable to Shewhart charts, is the Westgard Rules. When applied in full this system gives a similar degree of control to the system described below, with the same caveats on bias checks for multiple control determinations in the same analytical run (see 2.5 below). The Westgard Rules are given in figure 2 of the Harmonised Guidelines.

2.2 Single control chart

- (i) The current plotting value falls outside the action limits; or
- (ii) The current plotting value and the previous plotting value fall outside the warning limits but within the action limits; or
- (iii) Nine successive plotting values fall on the same side of the mean line.

2.3 Two control charts

- (i) At least one of the plotting values on either chart falls outside the action limits; or
- (ii) Plotting values for both charts are simultaneously outside the warning limits; or
- (iii) The current plotting value and the previous plotting value on the same control chart both fall outside the warning limits; or
- (iv) Both control charts simultaneously show that four successive plotting values fall on the same side of the mean line; or
- (v) One of the charts shows nine successive plotting values falling on the same side of the mean line.

2.4 For the purpose of implementing these rules the term "two charts" means two charts of the same type for different control solutions, and not two different charts constructed from the same data (ie not mean and range charts for the same solution). The rules for bias checking do not apply to range charts.

2.5 The rules with respect to warning and action limit breaches are generally applicable for all charts. However, the rules with respect to successive values falling on the same side of the mean line assume that for batches of more than 20 samples the mean of a fixed number of control determinations is plotted rather than the individual results. If more than one control determination is carried out for batches of less than 20 samples, the same assumption applies. When adopting the alternative recording strategy of plotting all individual AQC results for long analytical runs an unacceptably high rate of false alarms can occur in certain circumstances. This problem can be overcome either by adopting the use of mean and range charts as recommended in the Harmonised Guidelines or by using two charts, one of individual values for the warning and action limit checks only and one of analytical run means for detecting changes in systematic error only. The more rigorous approach of using mean and range charts as described in the Harmonised Guidelines is to be encouraged by the Inspectorate but not insisted upon, especially as it is not always a practical option either because of extreme variations in the number of samples analysed in one batch or the analytical run consists of a number of small batches. For the purposes of this paragraph 'batch' has the meaning given to 'batch of analyses' in paragraph 34a of DWI Information Letter 8/93 and 'analytical run' means the analysis of one or more batches sequentially using the same equipment and calibration standards, without any break in the analysis and without shutting down or reoptimising the settings of any instrument between batches.

3 Actions to be taken when an out of control condition exists

3.1 The Harmonised Guidelines recommend that the analyst should respond to an out of control condition by:

- (i) cessation of analysis pending diagnostic tests and remedial action; and
- (ii) rejection of the run of results and re-analysis of the test materials.

3.2 This is fine in theory, but any rigorous attempt to implement it in practice runs the risk of preventing the laboratory from functioning correctly. While these recommendations are fine as a starting point for developing a working policy, they must in practice be tempered by common sense. Any policy would be expected to contain the elements given in paragraphs 3.3. and 3.4 below (or satisfactory equivalents).

3.3 In respect of recommendation 3.1(i) the essential elements of a satisfactory policy are:

A For out of control conditions associated with action limit and/or warning limit breaches:

- (a) cessation of analysis pending diagnostic tests and effective remedial action whenever there is evidence of a continuing problem (eg continued warning limit breaches); and, irrespective of whether analysis has ceased;
- (b) a full investigation of the cause of the problem;

- (c) immediate corrective action whenever the cause of the problem is identified, followed by demonstration of the effectiveness of the action before analysis is resumed;
- (d) a review of the fitness for purpose of results obtained before and, if appropriate, during the investigation period and the rejection and re-analysis or resampling of all unfit results; and
- (e) the maintenance of full records of all investigations carried out, details of the outcome of those investigations sufficient to fully support any assignment of cause, the corrective action taken and any decision taken in respect of results of analysis (see paragraph 4.3 below).

B For out of control conditions associated with a change in systematic error, but not associated with action limit or warning limit breaches:

- (a) an assessment of the effect of the change in systematic error on the fitness for purpose of the associated results and the cessation of analysis pending diagnostic checks and effective remedial action whenever there is evidence that results are not fit for purpose; and, irrespective of whether analysis has ceased:
- (b) a full investigation of the cause of the problem;
- (c) immediate corrective action whenever the cause of the problem is identified, followed by demonstration of the effectiveness of the action, if appropriate before analysis is resumed; and
- (d) the maintenance of full records of all investigations carried out, details of the outcome of those investigations sufficient to fully support any assignment of cause, the corrective action taken and any decision taken in respect of results of analysis (see paragraph 4.3 below).

3.4 In respect of recommendation 3.1(ii) the essential elements of a satisfactory policy are:

C For out of control conditions associated with action limit and/or warning limit breaches:

- (a) where there is evidence of a continuing problem throughout the whole analytical run, rejection of all results for the whole run; and

- (b) either:
- (1) where there is evidence that the problem was of short duration, rejection of all data not bracketed by valid AQC results; or
 - (2) rejection of the whole analytical run: this action is always required when mean and range charts are used.

Results of analysis associated with an out of control condition may subsequently be accepted provided the cause of the out of control condition has been established and can be shown not to affect the fitness for purpose of any released results. All released results associated with an out of control condition must carry an appropriate commentary in all records and reports.

D For out of control conditions associated with a change in systematic error, but not associated with action limit or warning limit breaches:

- (a) an assessment of the effect of the change in systematic error on the fitness for purpose of the associated results and the rejection of all results whenever there is evidence that those results are not fit for purpose.

Results of analysis associated with such an out of control condition may be accepted if it can be shown that the magnitude of the change in systematic error does not affect the fitness for purpose of the results. Results initially rejected may subsequently be accepted provided the cause of the out of control condition has been established, and can be shown not to affect the fitness for purpose of any released results. All released results associated with an out of control condition must carry an appropriate commentary in all records and reports.

4 Investigation of out of control conditions

- 4.1 This guidance is relevant to the investigation of all out of control conditions identified by internal AQC and “flagged” external AQC (or proficiency testing) results. Both conditions are referred to as “failures” in the remainder of this section. However, the investigation of external AQC “failures” is more difficult because of the delay between analysis and the reporting of the “failure”. It should be remembered that it is possible for a thorough investigation to reveal no obvious cause for an isolated “failure”, but such an outcome where there are multiple “failures” should result in an even more thorough investigation. A major part of any investigation will be a review of routine system suitability checks which should be carried out as a matter of good practice. These investigations will normally include all of the following items that are relevant to the analytical system being investigated, and should therefore all feature in the standard investigation protocol. Omissions in specific investigations should be justified:

- (a) checking of all freshly prepared standards (stock, intermediate and working) against the “old” standard before using it. This practice is generally not possible for standards which are made up frequently, eg daily, because of deterioration;
 - (b) recording of dates and details of preparation and commencement of use of all new calibration standards, AQC solutions, reagents etc including stocks and intermediate stocks and bought-in solutions. This is not always necessary for items that are prepared fresh daily;
 - (c) calibration and operating records for balances, ovens, incubators etc;
 - (d) system suitability checks eg system response to a known standard, temperature records, indicators of condition of chromatography columns (retention time, retention time drift, peak width, peak skew, peak separation, number of theoretical plates etc), mass calibration and tuning of mass spectrometers;
 - (e) relevant environmental conditions; and
 - (f) a record, log or diary maintained by the analyst of any unusual or abnormal occurrences including any deviations from the documented procedure however trivial.
- 4.2 Once a potential cause of the “failure” has been identified, it should whenever possible be demonstrated whether it is the cause, and the efficacy of any corrective action demonstrated.
- 4.3 A full record should be retained of the investigation, its outcome, and any corrective action and its efficacy, which is cross referenced to the associated “failure(s)”.
- 4.4 If the initial investigation fails to identify the cause of a real problem, further steps which can be taken are given in the BSi Draft for Development “Water Quality – Guide to analytical quality control for water analysis”. The requirement to investigate further in these circumstances should be documented and suitable guidance either given or referenced.

APPENDIX – SUMMARY OF BENCHMARK POINTS

A laboratory's procedures, practice and records relating to internal AQC should, in addition to complying with IL 8/93 paragraphs 33 to 41, have the following features (or equivalent):

- A clear definition of an out of control condition to include

- For a single chart
 - any point outside the action limits; and
 - any two consecutive points outside the warning limits; and
 - either
 - nine successive points on the same side of the mean; or
 - similar rule(s) for quickly identifying changes in bias.

- For two charts
 - any point outside the action limits; and
 - the corresponding single points on both charts outside the warning limits; and
 - any two consecutive points on one chart outside the warning limits; and
 - either
 - four successive corresponding points on both charts on same side of mean, or nine successive points on one chart on the same side of the mean; or
 - similar rule(s) for quickly identifying changes in bias.

- A clear statement of the actions to be taken in response to all out of control conditions

- In response to action or warning limit breaches:
 - stop analysis, carry out diagnostic tests and remedy problem before resuming analysis for a continuing problem; and in all cases, whether or not a continuing problem exists
 - a full investigation followed by appropriate corrective action (with demonstration of effectiveness of corrective action before normal operation is resumed); and
 - rejection of all affected data not known to be fit for purpose; and
 - a full record of all actions to be kept.

- In response to a change in bias not associated with action or warning limit breaches:
 - an immediate assessment of the effect of the change on the fitness for purpose of data, and stop analysis, carry out diagnostic tests and remedy problem if data is not fit for purpose; and
 - rejection of all affected data not known to be fit for purpose; and whether or not data remains fit for purpose
 - a full investigation followed by corrective action (with demonstration of effectiveness of corrective action before normal operation is resumed if results were not fit for purpose); and
 - a full record of all actions to be kept.

- A clear statement of the type of investigation to be undertaken in response to all out of control conditions

- Initial investigation to include checks on records relating to:
 - standards (old vs new) and their preparation, date of first use, age, storage etc;
 - reagents and their preparation, date of first use, age, storage etc;
 - instrument calibration and operation records (including ancillary equipment such as balances);
 - system suitability checks;
 - relevant environmental conditions;
 - analyst's log; and
 - a full record of the details of the investigation, its outcome and any resultant action.

- If further investigation is required (ie no cause has been identified for a continuing problem affecting the fitness for purpose of data):
 - a clear statement of a logical process of further investigations to be undertaken.