Internal Quality Control Survey – Results and Recommendations

Background /introduction

The Joint Working Group on Irish Laboratory Accreditation (JWG ILA) have been aware of anecdotal reports of a lack of uniformity among Irish laboratories in the application and use of internal quality control procedures.

It was therefore agreed by the JWG ILA to explore developing a consensus on Internal Quality Control procedures which could form the basis of a draft policy on IQC. As a first step, it was decided to issue an IQC questionnaire, which would provide useful information about current practice in Irish Laboratories. The questionnaire was issued to Quality Managers (approx. 40) who were asked to arrange for completion of one questionnaire for each major section of the Blood Sciences Laboratories and to state the laboratory or section. There were 28 responses from Clinical Biochemistry Laboratories, 26 from Haematology / Coagulation Laboratories and 6 from a variety of specialised laboratories. This represents a return rate of approx. 65 – 70% for Haematology / Coagulation and Clinical Biochemistry Laboratories. The majority of the 26 responses from Haematology / Coagulation Labs included both Haematology and Coagulation, but 7 responses were from Coagulation Labs separately.

Subsequently a Sub-group on IQC Procedures was set up by the JWG ILA with representatives from the three professional bodies to consider results of the survey and make comments and recommendations on the areas addressed in the questionnaire. These recommendations apply to Biochemistry, Haematology and Coagulation Laboratories except where specific recommendations are listed separately for these disciplines. The scope of these recommendations includes biochemistry, immunoassay, cell counting and routine coagulation tests. The recommendations do not cover flow cytometry, protein electrophoresis, molecular diagnostic tests, qualitative tests and point-of-care tests.

Questionnaire, Results, Comments and Recommendations:

1. *Do you routinely use the analyser Supplier's own controls - only?* ☐
   or independent controls only? ☐ *or both?* ☐

   Results: In Biochemistry (Clinical Chemistry) just 3 labs use analyser supplier's controls only. About half of the remainder use independent controls only and half use both.
   In contrast, in Haematology (Haematology / Coagulation) 16 of 26 labs use supplier's controls only, one uses independent controls only and 9 use both supplier's and independent controls.

   Comments: The Committee appreciates that some of the differences between Biochemistry and Haematology are due to difficulties with suitable IQC material in Haematology,

particularly for cell counting, as whole blood is not stable and synthetic cell matrices may give different results on different analysers. In regard to FBCs, laboratories may often be obliged to use Supplier's own controls as there may be blood cell parameters specific to that Supplier's analyser. The use of independent controls should be considered as per ISO 15189:2012, which states in paragraph 5.6.2.2 Note 2 "Use of independent third party control materials should be considered, either instead of, or in addition, to any control materials supplied by the reagent or instrument manufacturer".

Recommendation:

Clinical Biochemistry: The use of independent controls is recommended, where possible. Haematology / Coagulation: Use of independent third party controls should be considered, either instead of, or in addition to supplier's own control, where possible. In cell counting, laboratories may be obliged to use Supplier's own controls. In these circumstances, or where the use of independent controls is not feasible, the use of additional forms of QC should be considered, eg patient means (Bull BS et al Am J Clin Pathol 1974, 61: 473-481; Levy WC et al Am J Clin Pathol 1986, 86: 193-9).

2. *What are the selection criteria for the QC material?*

a) *Assayed* ☐ *or unassayed?* ☐

Results: In Biochemistry, 18 labs use assayed controls and 14 use unassayed controls (some use both). In Haematology, all 26 labs use assayed controls: 3 labs use both.

Recommendation:

Assayed controls should be used where possible, either instead of, or in addition to, unassayed controls. This is particularly important when a method is being established in the lab.

b) *Liquid, frozen?* ☐ *or lyophilised?* ☐

Results: In Biochemistry, almost all labs use liquid frozen controls, 12 also use lyophilised controls. In Haematology, 14 labs use liquid controls and 16 use lyophilised controls. In general, liquid QC is used for FBCs, lyophilised controls are used for coagulation tests and liquid frozen QC are used for haematinics.

Comment: The Committee makes no recommendation on the choice of liquid, liquid frozen or lyophilised QC material, which will depend on factors such as stability, ease of use etc.

Type of matrix?.....

c) *Other criteria (please specify)?*.....

Results: Biochemistry Labs specified criteria for QC material such as human, serum / plasma /protein based, stability, analyte levels covering testing range and medical decision points, cost and not requiring reconstitution. Haematology Labs specified criteria such as whole blood (FBC), human blood cells / cell matrix, plasma (Coag.), long shelf life and infrequent lot number changes.

Comment: The above comments are in line with ISO 15189 5.6.2.2 which states "The laboratory shall use QC materials that react to the examining system in a manner as close as possible to patient samples".
In addition, the Committee consider that good stability of QC material in use is also very important.

d) *If lyophilised QC are used, are these reconstituted with bulb pipettes* ☐ *or automatic pipettes?* ☐

Results: Bulb pipettes were used for reconstitution of controls by almost half of the Biochemistry respondents and by only one of the Haematology respondents.

Comment: While bulb pipettes are considered more accurate than automatic pipettes, the Committee considered that well maintained and calibrated automatic pipettes are sufficiently accurate for this purpose. It is important to have certified calibration checks at intervals.

3. a) *How many levels of QC are used for common analytes?.....*
b) *Do you choose QC material that covers low,* ☐ *medium* ☐ *and high* ☐ *analyte concentrations?*

Results: a) The large majority of labs use 3 levels; four Biochemistry and 7 Haematology labs use less than three. b) Labs using 3 controls use low, medium and high.

c) *Do you choose QC material that covers the medical decision cut point for analytes?*
Yes ☐ No ☐

Results: c) 22 of 26 Biochemistry labs and 19 of 25 Haematology labs do choose QC material that covers the clinical decision cut point for analytes.

Comments: ISO 15189:2012 states in 5.6.2.2 Note 1:
"The laboratory should choose concentrations of control materials, whenever possible, especially at or near clinical decision values".

Recommendation:

The use of 3 levels of control is preferable; however, use of 2 levels is acceptable. We recommend choosing control material with analyte levels which are close to the clinical decision threshold(s), where possible.

4. *Do you run all levels each time?* ☐ *or fewer?* ☐ *or sequentially?* ☐

Results: 15 of 27 Biochemistry labs and 20 of 26 Haematology labs run all levels of QC each time. The remainder run fewer controls or run them sequentially.

Comment: The Committee made no recommendation on this issue.

5. *On the main analyser(s), what is the frequency of running controls?*
For urea and electrolytes:……
For thyroid function tests:……
For full blood count:……..
For D-dimers:……..'
For more specialised tests:……
Results: The frequency of running controls for routine tests (eg U/Es) in Biochemistry varies a lot, from once daily to once hourly. The median response was 3-4 times per day. The most common frequency of running controls for thyroid function tests was once or twice a day. The frequency of running controls in Haematology labs (FBC) varied almost as much as in Biochemistry, from once per day to eight times per day (median was 3 times per day). D-Dimers generally had QC run once or twice a day.

Comment: See below in Q7

6. *How did you decide on QC frequency?*.....

Results: A variety of responses were given. The responses given were as follows (frequency of response in brackets): Analyser performance / analyser stability (10), historical or previous experience (11), workload (8), manufacturer's recommendation (8), published guidelines / best practice (7), INAB Assessor advice (4), Sigma metric (1).

Comment: See below in Q7

7. *Is QC run: After (daily) maintenance?* ☐ *After any calibration?* ☐ *Out of hours?* ☐

Results: All labs run QC after daily maintenance and after any calibration. Almost all labs run QC during on call periods, but two Biochemistry labs stated that they do not. Four labs responded N/A and it is assumed they do not provide an on call service.

Comment: ISO 15189:2012 states in 5.6.2.2
"QC materials shall be periodically examined with a frequency that is based on the stability of the procedure and the risk of harm to patients from an erroneous result."

Recommendations:

It is recommended to run QC before analysis begins and following daily maintenance, calibration and any troubleshooting procedures. For continuous workflow, QC should be run at a minimum of 3 times in each 24 hour period. In Coagulation, certain assays may have been demonstrated to be very stable eg D-Dimers and may only require QC once per 24

hours. In Haematology cell counting it is recommended to use the X bar mean as a running control which produces mean values for key red cell indices after every 20 patient samples (Bull BS et al Am J Clin Pathol 1974, 61: 473-481; Levy WC et al Am J Clin Pathol 1986, 86: 193-9). Where tests are performed in a discrete batch , QC should be placed at the beginning and end of each batch. However the frequency of running QC should be based on the stability of the analyser / method / reagents, the workload and frequency of the assay and the risk of harm to patients from an erroneous result.

8. *How does your lab determine the acceptable range of values for QC?*

a) *accept suppliers range for the QC*? ☐

b) *establish own range from mean and CV of replicates?* ☐ *If so, how many replicates?.....*

Are replicates within assay? ☐ *Between assay?* ☐ *Both?* ☐

Are outliers excluded first? *Yes* ☐ *No* ☐

Results: Almost all Biochemistry labs establish their own QC ranges and only three use Supplier's range. In Haematology, 18 of 26 labs establish their own ranges, while 16 labs accept the Supplier's range. All labs who responded use either between assay replicates or a combination of within and between assay replicates. The majority of labs exclude outliers before calculating QC ranges. The number of replicates used to establish own range from mean and SDs varied from as little as 5 to over 40.

c) *Is your acceptable range for QC:*

Mean ± 1SD? ☐ *Mean ± 2SDs?* ☐ *Mean ± 3SDs* ☐

Results: 20 Biochemistry and 20 Haematology labs use mean ± 2SDs. Five Biochemistry and five Haematology labs use mean ± 3SDs.

d) *When QC mean and range is established, is this adjusted later and if so after what period of time?.....*

Results: Almost all labs do adjust the QC mean and range after it is established; one Biochemistry lab and three Haematology labs say they do not adjust. The criteria used for adjustment and the period before review and adjustment varies considerably.

Recommendations:

In Clinical Biochemistry, the Committee recommend that users should establish the QC means and ranges in their own labs. In establishing or verifying the QC range, a combination of between and within assay replicates eg 5 x 5 (ACB website) or 20 x 2 (CLSI) should be used. Outliers should be excluded before calculating mean and SDs (but only if the root cause of the outlier is known. An appropriate statistical tool should be used). The use of QC ranges of mean ± 2 SDs is considered standard practice. Review the QC target range after one month or when sufficient data (60 – 100 values for routine tests) have been accumulated

and adjust, if necessary. Review the QC data at intervals and investigate the cause of any shifts in mean or SDs. Further adjustment of QC means and SDs is not a surrogate for trouble-shooting problems.

In Haematology laboratories, we recommend verifying the Manufacturer's QC target ranges. Repeat analysis of new lots of QC should be carried out to verify lot to lot stability (for each analyser).
In Coagulation, we recommend verifying the Manufacturer's QC target ranges.

9. *Does your lab use the same QC target and ranges for the same test on multiple analysers?*
Yes ☐ *No* ☐

Results: In Biochemistry, 12 labs do, 7 labs do not and 8 labs stated N/A (presumably do not have multiple analysers). In Haematology, 16 labs do, 4 do not and 6 stated N/A.

Comments: To use the same QC target and ranges for the same test on multiple analysers is more pragmatic but the use of different targets and ranges may be more correct from a purist point of view. The Committee does not make a recommendation in this regard. Laboratories should evaluate the comparability of results from multiple analysers at intervals; if significant differences are found, it is important to identify and eliminate the cause.

10. *Which IQC error detection rules do you use?*

Does your laboratory -

a) *reject results if a single QC is 2SDs out once?* *Yes* ☐ *No* ☐

Results: In Biochemistry only 3 labs reject results if a single QC is 2SDs out once and 22 labs do not reject. In Haematology 12 labs reject results and 11 labs do not.

b) *reject results if a single QC is 3SDs out once?* *Yes* ☐ *No* ☐

Results: 26 of 28 Biochemistry labs and 22 of 24 Haematology labs reject results if a single QC is 3 SDs out once. Two Biochemistry and two Haematology labs do not reject results in this circumstance.

c) *reject results if the same QC level is 2SDs out twice consecutively?* *Yes* ☐ *No* ☐

Results: Most laboratories reject results if the same QC level is 2 SDs out twice consecutively. Four Biochemistry and one Haematology labs do not reject results in this circumstance.

d) *reject results if 2 levels of QC are 2SDs out in a single run or consecutively?*
Yes ☐ No ☐

Results: The majority of labs reject results if 2 levels of QC are 2 SDs out in a single run or consecutively. Eight Biochemistry labs and 3 Haematology labs do not reject results in this event.

Comment: Question d) is really two questions. One refers to a 2-2S rule within-run and the other to a 2-2S rule across-run. This may have caused some confusion.

e) *Do you use criteria for warning (in addition to rejection criteria)?* *Yes* ☐ *No* ☐

Results: 16 Biochemistry labs state that they do use criteria for warning (in addition to rejection criteria) and 11 do not. 11 Haematology labs do use additional criteria for warning, while 14 do not.

f) *Do you use other rules for rejection or warning?* *Yes* ☐ *No* ☐
If yes, please specify:……..

Results: Four of 26 Biochemistry labs and 7 of 25 Haematology labs stated that they use other rules for rejection or warning. The additional rules used included R 4S rule, 10-1S rule, "mx bars, X on rc indices, electronic values on wbc, moving average programs.

Recommendation:

It is recommended that Laboratories establish a policy for QC failure criteria, which should be based on an accepted statistical approach, as part of a total quality control program.
In Clinical Biochemistry, the Westgard Rules approach is commonly used. The one 2S rule should be regarded as a warning. If results are rejected on the basis of the one 2s rule, it is estimated that many runs will be falsely rejected. Results should be rejected on the basis of the one 3S rule, otherwise poor quality results may be released. Results should also be rejected if the same QC level is 2SDs out twice consecutively or if two levels of QC are 2SDs out in a single run or consecutively. The 10 X rule, if used, should be regarded as a warning that the process needs investigation.
In Haematology, a combination of rules including mean ± 2 SDs, the X bar mean using patient red cell indices (Bull's Algorithm, see references above) and delta checks are commonly employed

11. *Does your lab use automatic blocking of patient result reporting based on QC rejection criteria?* *Yes* ☐ *No* ☐

Results: Less than half of the respondents (11of 27 Biochemistry and 9 of 26 Haematology /Coagulation labs) stated that they do use automatic blocking of patient result reporting based on QC rejection criteria.

Comment: Automatic blocking of result reporting based on QC failures is desirable but this functionality may not be available on some analysers / middleware / LIS systems.

12. *Does your laboratory use auto-verification of results to fully authorised status if QC is acceptable -*
    for some results? ☐ *for all results?* ☐ *not at all?* ☐

    Results: A number of labs (10 of 27 Biochemistry and 8 of 25 Haematology) use auto-verification of results to fully authorised status if QC is acceptable for some results, but the majority of labs do not.

    Comment: Where this autoverification is used for some results, it is usually for results in a narrow (eg normal) range for which delta checks have passed. Any such rules should be checked at intervals to ensure that they are working as intended. It is worth noting that on occasion, analytical problems may be identified during analytical / postanalytical non-automated authorisation even when QC checks are passed.

13. *Does your laboratory audit and review IQC failure data?* *Yes* ☐ *No* ☐
    If so, do you use this data to influence frequency of IQC used?.....
    How else do you use this data?.....

    Results: Most labs (23 of 27 Biochemistry and 25 of 26 Haematology labs) state that they do audit and review QC failure data and approximately half of labs use this data to influence frequency of IQC used. A wide variety of responses were given to the question "how else do you use this data", but most related to assessing method performance or trouble shooting.

    Recommendation: It is recommended that QC failure data is audited and reviewed at intervals and that the information gained is discussed at staff meetings.

14. *Does your lab use methods other than IQC material to assess analytical performance?*
    eg Patient means? ☐ *Delta checks?* ☐ *Other?* ☐

    Results: Patient means were used by 12 Haematology labs but just two Biochemistry labs. Delta checks were used by 15 Biochemistry and 14 Haematology labs. Other methods were used by 9 Biochemistry labs and 11 Haematology labs; the responses given included EQA, verification material, moving average program, inter-lab comparison and MCHC / CHCM correlation errors.

    Comments: Although both IQC and EQA are essential components of an overall quality policy, is important to distinguish between them. IQC is used in the decision to accept or reject results on patients' samples and enables the laboratory to describe and monitor the quality of its work; EQA is retrospective and does not give information about today's results.

EQA permits a comparison of quality between laboratories and also methods and may be used in troubleshooting assay / analyser problems.

Recommendation: The use of patient means and similar measures are very valuable tools and should be used where analysers / software have this capability; the laboratory should use every such means at its disposal, particularly since there are no consumables costs involved.

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