UK NEQAS for General Haematology

Uncertainty of Measurement in the Laboratory and UK NEQAS (H)

Paul McTaggart[1], Ciaran Mooney[2], Barbara De la Salle[1] and Keith Hyde[1]

[1]UK NEQAS (H), PO Box 14, Watford WD18 0FJ, UK
[2]Department of Haematology, Rotunda Hospital, Dublin, Ireland

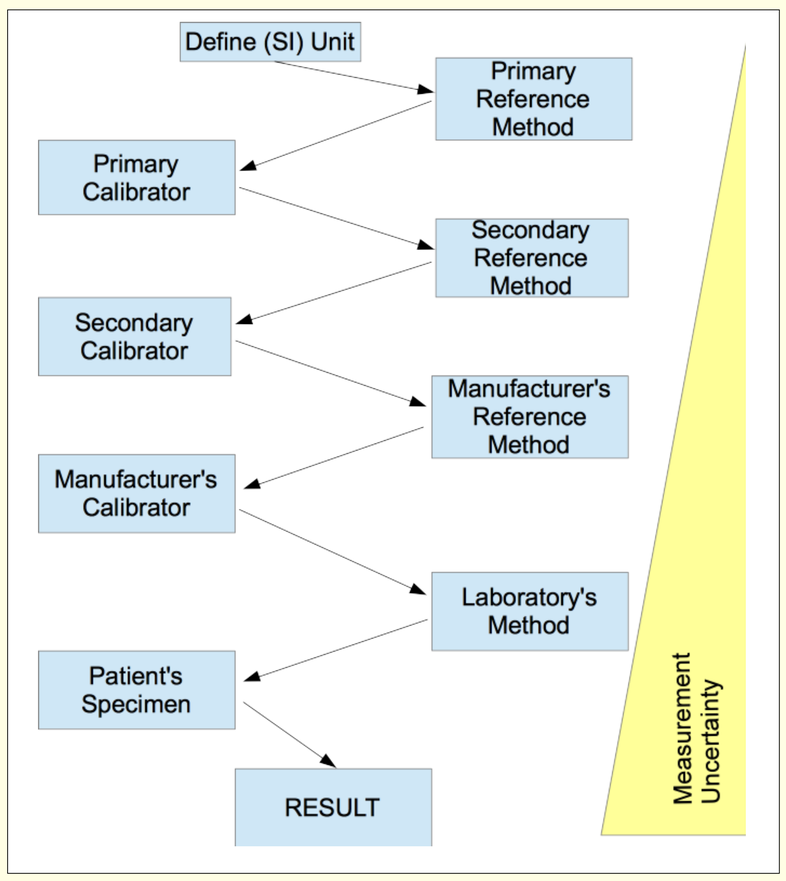
Introduction

Uncertainty of Measurement provides a quantitative estimate of the quality of a test result, and therefore is a core element of a quality system for laboratories[1]. The same principle applies to External Quality Assessment (EQA) because the uncertainty of the assigned value is a measure of the quality of the EQA material.

ISO 15189, 5.6.2 requires that "*The laboratory shall determine the uncertainty of results where relevant and possible.*"

Uncertainty of measurement is one of two inter-dependent metrological concepts, the other being traceability.

Healthcare scientists have for many years sought to achieve traceability by reference to primary standards which have international recognition, and to determine uncertainty of measurement by determining the various components of total analytical error.



The relationship between traceability of measurement and uncertainty of measurement.

Uncertainty of measurement increases as one moves down the traceability pathway from the definition of the SI unit to the result.

"A measurement result is complete only when accompanied by a quantitative statement of its uncertainty. The uncertainty is required in order to decide if the result is adequate for its intended purpose and to ascertain if it is consistent with other similar results"
National Institute of Standards and Technology, Background to Uncertainty of Measurement; www.physics.nist.gov

The challenges

ISO 15189, 5.6.2 states that "*Sources that contribute to uncertainty may include sampling, sample preparation, sample portion selection, calibrators, reference materials, input quantities, equipment used, environmental conditions, condition of the sample and changes of operator.*"

Automated instruments are highly complex and to dissect out the individual contribution to total uncertainty of measurement by each variable would not be feasible in a routine medical laboratory. In addition, most of the automated instruments are closed systems in terms of reagents, calibrators and controls. Manufacturers seldom supply full information regarding traceability and uncertainty of measurement.

Therefore, the only uncertainty we can determine is the reproducibility of the final result produced by the instrument which is dependent on a combination of all of the above factors.

Uncertainty may be calculated using Internal QC data or by using commercial controls. For the accuracy component; the QC material chosen for reproducibility studies must be within the tolerance limits dictated by manufacturer and may not show any evidence of bias, proportional or systematic.

The within run uncertainty is calculated from the mean and standard deviation (SD) of repeated estimations (minimum 20) from a single sample in a single run.

The between run uncertainty is calculated from the mean and SD of the results from the daily IQC runs over a period of working days to obtain a minimum of 20 results

ISO 13528 9.2.1 states "*If the standard uncertainty of the assigned value is large in comparison with the performance evaluation criterion, then there is a risk that some participants will receive action and warning signals because of inaccuracy in the determination of the assigned value, not because of any cause of the participant.*"

The standard uncertainty of the assigned value in EQA depends upon the method used to derive it, the number of laboratories (consensus values) and other factors including homogeneity and stability.

Worked examples

Estimation of Haemoglobin in the laboratory.

Haemoglobin was estimated 30 times, the mean was 135.6 g/L with an SD of 0.76 g/L.

The within run uncertainty (U_a) is calculated using the formula;

$$U_a = SD/\sqrt{n} = 0.76/\sqrt{30} = 0.14 \text{ g/L}$$

From the QC files over last 20 working days, the mean was 135.7 g/L with an SD of 0.86 g/L

The between run uncertainty (U_b) is 0.19 g/L.

These uncertainties are combined to give the Combined Uncertainty (U_c) using the formula;

$$U_c = \sqrt{(U_a^2 + U_b^2)}$$
$$U_c = \sqrt{((0.14)^2 + (0.19)^2)} = 0.24 \text{ g/L}$$

To calculate the 95% confidence interval, this combined uncertainty must be multiplied by a "coverage factor" of 2. The result is known as the "expanded uncertainty".

Thus, the 95% confidence interval for Haemoglobin at a level of x g/L is x +/- 0.48 g/L.

Estimation of Haemoglobin in UK NEQAS (H)

In a recent Full Blood Count Survey, 529 participants returned data for Haemoglobin, the concensus mean value was 181.33 g/L with an SD of 1.013 g/L. The SD used to calculate the Deviation Index (DI) (SD_{pt}) was 1.012 g/L.
The standard uncertainty of the consensus mean ($u(x_{pt})$) is calculated using the formula;

$$u(x_{pt}) = 1.25 \times SD/\sqrt{n} = 1.25 \times 1.013/\sqrt{529}$$
$$u(x_{pt}) = 0.066 \text{ g/L}$$

How do we know if this uncertainty would have an effect on performance assessment? ISO 13528 9.2.1 requires that the standard uncertainty of the consensus mean be less than 0.3 times the SD_{pt}. In this case, $0.3 \times SD_{pt}$ was 0.304 which is greater than the uncertainty of the concensus mean ($u(x_{pt})$) of 0.066.
At this level the uncertainty of the consensus mean has negligible effect on the DI.

UK NEQAS (H) has been assessing uncertainty for FBC parameters and will be including the uncertainty value on reports in the near future.

Acknowledgements

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References

1 White G H, Farrance I Uncertainty of Measurement in Quantitative Medical Testing – A Laboratory Implementation Guide. Clin Biochem Rev Vol 25 Suppl (ii) November 2004 S1-24