



Introduction

Within the CPA UK Ltd Standards for the Medical Laboratory v2 2008, two new terminologies have been introduced that refer to traceability and uncertainty of result. The purpose of this paper is to provide assessors with information on how these terms should be interpreted during the assessment process.

Traceability

Traceability is defined as the property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties.

There are seven SI (Le System International d'Unites) base units of measurement (see table 1). These are all well defined and have international standards.

Table 1. The seven base units

| Measurement | Unit | Sign |
|---------------------|---------|------|
| length | metre | m |
| mass | gram | g |
| time | second | s |
| electric current | ampere | A |
| temperature | kelvin | K |
| amount of substance | mole | mol |
| luminous intensity | candela | Cd |

From these base standards it is possible to derive other standards that may be used for standardisation or other physical, chemical and biological systems. Primary reference standards are generally held at national level by organisations such as the National Physical Laboratory (NPL) or the National Institute for Biological Standards and Controls (NIBSC). For most applications it is not practical or cost effective to use primary standards for calibration and so a hierarchy of calibration materials has been developed that may be traced back to reference material. Laboratories should ensure that there is an unbroken chain back to a national or international standard for any calibration systems used. This will involve the laboratory performing a risk assessment of the importance of accuracy of a measuring system and how to obtain appropriate calibration materials to ensure that any measurements are accurate (see table 2 for examples). Where a CE marked manufacturer's kit is used the manufacturer should provide this information within the kit information sheet. Where laboratories produce their own "in house" measuring systems any apparatus and reagents used to produce calibrators should be of appropriate quality.

Table 2. Examples of calibrated materials

| Measurement | Material |
|------------------|------------------------|
| temperature | calibrated thermometer |
| mass | calibrated weights |
| volume | grade A pipette |
| centrifuges | calibrated stroboscope |
| assay calibrator | CE marked kit |

It is important to note that many analytical systems use relative measurements to a standard curve. Under these circumstances it is not necessary to achieve absolute accuracy of the measuring system as any errors will be corrected automatically (e.g.

optical systems to measure the intensity of a colour produced by a biochemical reaction).

Within the non-numeric disciplines of medical laboratories is often not possible to use reference material or standards. Under these circumstances other mechanisms such as second opinion or published descriptions of pathology may be considered useful reference material.

Measurement Uncertainty

Measurement Uncertainty (MU) is defined as a parameter, associated with the result of measurement that characterises the dispersion of the values that could reasonably be attributed to the measurand [1]. By quantifying the possible spread of measurements an estimate of confidence in the result may be obtained. In any assay system there may be bias due to systematic effects leading to inaccuracy. Measurement uncertainty stems from imprecision as a result of random effects on the assay system (see figure 1).

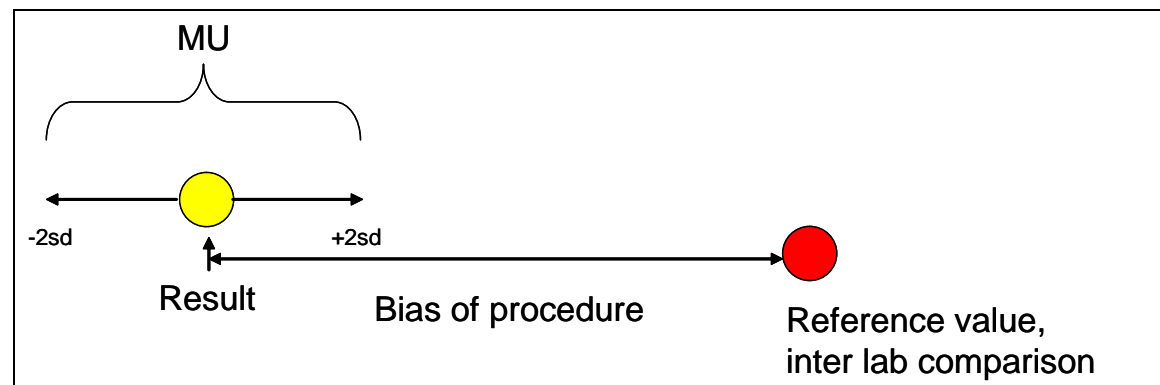


Figure 1. Measurement uncertainty v Bias

In 1995 the International Organization for Standardization produced a guide to the expression of uncertainty in measurement (GUM) [2]. This provides a model for expressing uncertainty in measurement and allows a “bottom up” approach where individual uncertainties are quantified and summed to provide an overall uncertainty. Whilst this approach may be easily applied to electrical and optical laboratories it is not so straightforward in medical laboratories where there are numerous other potential factors that may contribute to overall uncertainty of result.

GUM describes two types of uncertainty:

Type A

That may be derived from repeated measurements and statistical analysis. Within medical laboratories that produce numeric results it is relatively easy to quantify. Sources of such data may range from imprecision studies carried out at the time of assay verification to real time observation of results from internal quality control material.

Type B

That may be derived from other non-statistical means. Examples may include manufacturer’s assay validation data, intra individual biological variation or professional opinion.



Within a medical laboratory, Type B errors may be categorised into three areas:

- 1 Pre-examination.
Within the pre examination phase many results will be subject to variability due to how the specimen is collected or stored. This could be the patient's state (e.g. fasting), the site from which the sample is collected or other parameter such as time of sampling. For each procedure any factors that could lead to significant variability of results should be identified and steps taken to reduce potential errors as much as possible.
- 2 Examination
Within any examination procedure there are numerous factors that may introduce variability. In any analytical system there may be variability of calibrators, volumes of sample and reagents, technical performance of equipment. These tend to produce a Gaussian distribution so results that may be used define the imprecision of an analytical system. This would generally be expressed as standard deviation or percentage coefficient of variation. There may also be substances present (e.g. bilirubin or drugs) that interfere with examination processes.
- 3 Post-examination
Many examinations produce raw numerical data that is then manipulated to produce a final result. It is possible for calculations to introduce errors (e.g. rounding numbers) and lead to variability of results. Interpretation of any result is also subject to variability. There may be biological differences between individuals that lead to difficulties in interpreting results. Where an examination is used for confirming the presence or absence of a disease the sensitivity and specificity of an examination process must be well understood. Many examination processes produce results that are equivocal or on the borders of abnormality.

Whilst it may not be entirely possible to quantify uncertainty relating to these areas, it should be possible for CPA assessors, through the assessment process to obtain confirmation that a laboratory is accounting for them (see table 3).

Table 3. Examples of uncertainty

| Pre examination | Applicable CPA standard |
|--------------------------------|---|
| Patient state | E 1 Information for users |
| Patient preparation | |
| Time of sample collection | |
| Site of collection | E 3 Specimen collection |
| Collection method | |
| Sample transport | E 4 Sample transport |
| Third parties | E 6 Referral to other laboratories |
| Sample storage | C 4.2 Storage facilities |
| Examination | |
| Calibration | F2 Examination procedures |
| Cross reactions | |
| Combination with other results | |
| Calculations | |
| Internal Quality Control | F3 Assuring the quality of examinations |
| Post examination | |
| Report | G 2 The report |
| Reference ranges | |
| Interpretation | G 5 Clinical advice and interpretation |



Conclusions

Where possible examinations should be referenced to a known reference material or accepted standard. In non-numeric disciplines this standard may be a normal sample, a known pathology or reference documentation.

There should be evidence that actions are taken to eliminate, reduce to a minimum or take into account any uncertainty of measurement when interpreting results.

CPA assessors should be able to satisfy themselves that those providing diagnostic and monitoring services have a good knowledge of factors that may introduce variability within any part of the examination process. Much of this evidence may not be explicit and will become apparent when confirming compliance with other CPA standards.

References

- 1 National Pathology Accreditation Advisory Council (NPAAC). *Requirements for the estimation of measurement uncertainty*. Canberra: Commonwealth of Australia, Australian Government Department of Health & Ageing; 2007. ISBN 1-74186-164-0.
- 2 International Organization for Standardization. Guide to the expression of uncertainty in measurement 1995:101 ISO Geneva.

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October 2008