

## Marking scheme for question:

### Question

Define the terms **imprecision**, and **bias (or inaccuracy)**. How can these be assessed when initiating an assay and how can they be monitored long term?

(My suggested changes to question in red)

### Definitions (25%)

**Imprecision:** *'Imprecision is a measure of the closeness of a series of measurements of the same material'*

**Bias (or inaccuracy) definition;** *'Bias (or inaccuracy) is the difference between the mean of a series of measurements of the same material and the true value.'*

A useful diagram demonstrating these definitions (which saves time for the candidate and the examiner) is a circled target with:

- Holes scattered all over the target: high imprecision unable to determine bias/accuracy
- Holes all together but well below the 'bulls eye' demonstrating low imprecision but negative bias
- Holes all together but well above the 'bulls eye' demonstrating low imprecision but positive bias
- Holes all together on the 'bulls eye' demonstrating low imprecision and zero bias good accuracy

### Assessment when initiating a new assay (50%)

#### Imprecision

Estimation of within and between batch imprecision at 2 to 3 different levels of the analyte. Requires multiple measurements within a batch and >10 (if possible) between batch estimates. The answer should include definitions of standard deviation and coefficient of variation

$$\sigma = \sqrt{\frac{\sum (x - \bar{x})^2}{n - 1}}$$

$\sigma$  = lower case sigma

$\sum$  = capital sigma

$\bar{x}$  = x bar

Coefficient of Variation = [SD/mean] x 100

An example of a precision profile should earn marks, showing the typical pattern of greater imprecision at low concentrations and lower imprecision at high concentrations (usually, but other examples acceptable with explanations e.g. imprecision due to dilution of samples with high results)

Although not asked specifically in the question, candidates may mention the impact of imprecision on the assay detection limit and also on critical difference assessment. Formally the standard deviation (SD) of an assay is calculated from both the analytical ( $SD_A$ ) and biological ( $SD_B$ ) variations;

SD= square root of [ $SD_A^2 + SD_B^2$ ]

#### Bias (Inaccuracy)

For a new assay there are a number of alternatives to ensure results are accurate:

- Comparison with independent reference materials (e.g. NISBC)
- Recovery experiments from in human specimens
- Analysis of EQA specimens for which there are method related mean values available
- Sample exchange with other users using the same method or a different method and comparison of results

#### **Long term assessment of Imprecision and Bias (accuracy) (25%)**

##### Imprecision

For established assays this requires regular IQC review of coefficient of variation at each level. Westgard limits deserve a mention here. Evaluation imprecision on EQA schemes (e.g. where repeat circulations are made of the same EQA material)

Bias (Inaccuracy)

Review of EQA performance against ALTM and method mean.

Candidates might discuss the shortcomings of EQA schemes where the majority of participants use the same commercial method which has a strong influence on the 'target' value which in fact may be inaccurate.

Although less popular now, where the number of specimens are analysed ( $> 100$  as a guess) is large then review of the truncated daily mean is a sensitive method of detecting changes in bias/accuracy.

PG 01.06.10