BIOLOGICAL VARIATION AND ANALYTICAL QUALITY SPECIFICATIONS

Callum G Fraser
Scottish Bowel Screening Centre, Kings Cross, Dundee DD3 8EA, Scotland

Many quantities vary over the span of life due to natural biological factors involved in ageing: these variations often occur rapidly at critical points in the life cycle and age stratified reference values may be needed. Other quantities have predictable biological rhythms that may be daily, monthly or seasonal: this has implications for sample collection, reference values and clinical utility. However, most quantities have variation that can be modelled as random fluctuation around a homeostatic setting point: this is termed within-subject biological variation. Moreover, the homeostatic setting points of individuals usually differ, which is termed between-subject biological variation.

It is relatively easy to determine the magnitude of within-subject [CV_I] and between-subject [CV_G] components of biological variation in numerical terms, through replicate analysis of series of samples collected from each of a cohort of individuals, followed by exclusion of outliers and nested analysis of variance [ANOVA]**.** Much work continues in this area and more data continue to appear with time.

The literature and the intranet contain large databases on the components of biological variation in both the healthy and in groups with specific diseases. These are easy to access. It is generally appropriate to use these data in everyday practice. Numerical data on the components of biological variation in the healthy can be applied in:

- determining the change that must occur in an individual's serial results before the change is significant [the reference change value] and using these "reference change values" in auto-verification and delta-checking,
- deciding the utility of traditional population-based reference values,
- a plethora of other uses in laboratory quality management including assessment of professional guidelines and recommendations, and
- setting quality specifications for imprecision, bias, total error, and other reliability analytical performance characteristics,

With regard to the setting of quality specifications, the general formulae are that:

- imprecision: $CV_A < 0.5\ CV_I$
- bias: $B_A < 0.25\ [CV_I^{\ 2} + CV_G^{\ 2}]^{1/2}$
- total analytical error: $TE_a < 1.65 \times 0.5\ CV_I + 0.25\ [CV_I^{\ 2} + CV_G^{\ 2}]^{1/2}$

However, biological variation-based quality specifications may not be able to be met with current technology or may be easily surpassed. In such cases, different multipliers [0.75 and 0.375: 0.25 and 0.125] may be applied for imprecision and bias to give minimum and optimum quality specifications for imprecision and bias respectively. In external quality assessment and proficiency testing, it has been recommended that quality specifications for total allowable error be applied.