



FOR PEPTIDE HORMONES AND RELATED SUBSTANCES

SCHEME HANDBOOK

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ILLUSTRATIVE EXAMPLES OF THE INTERPRETATION OF CUMULATIVE PERFORMANCE DATA

Calculation of BIAS and VAR by combining results from different pools at different concentrations over 6 months is designed to make maximum use of the data, but introduces certain constraints in the interpretation of these performance statistics. These are illustrated in the examples below. Interpretation of BIAS and VAR is always assisted by examining the table showing your performance by pool and distribution (Appendix 2, page 17)

Low BIAS, low VAR

Your assay is precise and giving results close to the target value in the concentration range assessed. The desirable place to be, assuming accuracy of the target value.

Low BIAS, high VAR

There is wide scatter of your bias on individual specimens, although the mean ratio to the target value is near unity. There are several sources of high variability, eg:

- a. Between- and within-assay imprecision
- b. Dose-related differences in bias
- c. Pool-related differences in bias

The table of performance by pool and distribution will help identify which, if any, of these sources is most important.

As the VAR is essentially the confidence with which the mean BIAS can be estimated, it would be wrong under these circumstances to feel too complacent about your low BIAS!

High BIAS, low VAR

Your assay is clearly biased relative to the target value, the ratio of your result to the ALTM (or GLTM) being relatively constant over the concentration range assessed. Common causes of this are errors in standardisation (wrongly prepared, or degraded standards), errors in conversion of results to the units used by EQAS (wrong factor, or wrong mathematics!) and differences in assay specificity.

High BIAS, high VAR

There is a wide scatter of deviation from target on individual specimens, superimposed on a shift from unity in your mean ratio to the ALTM (or GLTM). The above comments on high VAR apply. The BIAS cannot be reliably estimated while the VAR remains high, and elimination of the sources of variability should be a first priority.

Note that if your assay is biased and you take steps to correct this, you will temporarily have a high VAR while the changing BIAS passes through the 6 month window.

NOTE BIAS and VAR describe important aspects of performance but you should also examine your performance on special specimens, eg recovery and baseline security.

APPENDIX 1

PERFORMANCE CRITERIA (1997)

The following limits of acceptable performance in respect of BIAS and VAR have been set by the National Quality Assurance Advisory Panel for Chemical Pathology.

	BIAS	VAR
PEPTIDE I		
FSH	±20%	+15%
LH	±20%	+15%
Prolactin	±20%	+15%
Growth Hormone	±20%	+20%
PEPTIDE II		
PTH	±25%	+25%

Performance criteria have not been set for ACTH and calcitonin.

AFP, CEA and hCG		
AFP	±15%	+15%
CEA	±20%	+20%
hCG	±20%	+20%

MATERNAL SERUM SCREENING		
NTD AFP	±10%	+15%
Down's AFP	±10%	+15%
Total/Intact hCG	±15%	+15%
Free β -hCG	±10%	+10%
Unconjugated Oestriol	±20%	+15%

The performance criteria for the Maternal Serum Screening scheme refer to results in concentration units. Performance limits of 20% are under examination for BIAS and VAR of all results in MoMs, but these limits have not been approved by the Panel.

APPENDIX 3

STATISTICAL CALCULATIONS

Specimen and laboratory performance statistics are calculated after logarithmic transformation of results, using the trimming method of Healy MJR (Clin Chem; 25:675-677, 1979). Logarithmic transformation allows for skewness in the data and appropriate computation of errors while trimming improves the reliability of the mean and measure of scatter.

SPECIMEN STATISTICS

1. All laboratory trimmed mean (ALTM) and its geometric coefficient of variation (GCV)

For each specimen non-numeric results, including those reported as "less than" or "greater than" are discarded. All remaining individual results are ranked and transformed into their natural logarithms. The lowest and highest 5% of results (rounded up to the nearest whole number) are trimmed (Healy, 1979). The excluded results play no part in the calculation of the estimate of the mean of the results (ALTM) or the scatter of values (GCV), but **are not necessarily outliers** and are therefore retrieved for the later identification of between-laboratory, within-specimen outliers and calculations of individual laboratory BIAS and its variability (see below).

2. Grouped laboratory trimmed mean (GLTM) and its GCV

Calculations exactly analogous to those described above can be performed on results from groups of similar methods, such as those immunometric assays of hCG employing only monoclonal antibodies, or on results from individual methods. The estimate of the mean is referred to as the GLTM, and its associated estimate of scatter is the GCV.

LABORATORY PERFORMANCE STATISTICS

3. Cumulative bias and its variability

Cumulative bias (BIAS) and the variability of the bias (VAR) are calculated for each laboratory from all results returned by that laboratory on all usable specimens during the most recent six months to date (12 months for Peptide II).

Non-numeric results are discarded, as above, and the remaining results are transformed by taking natural logarithms. Deviations are calculated by subtracting the natural logarithm of the chosen target for the analyte in question (ALTM or GLTM) from these logarithmic values. (This is equivalent to division of untransformed values). The values are ranked and trimmed as above. The mean and LSD are calculated and within-laboratory, between-specimen outliers identified. The BIAS is then the antilog of this mean expressed as a percentage difference from 100 and the VAR is the GCV of the deviations.