Accuracy and precision of methods for measurement of paracetamol in serum

Matthew Gist[1], Kathleen Barnett[1] & John F. Wilson[2]
[1]Cardiff Bioanalytical Services Ltd, 16 Mount Stuart Square, CARDIFF CF10 5DP
[2]Dept. of Pharmacology, Therapeutics & Toxicology, Wales College of Medicine, Cardiff University CF14 4XN.

Introduction

A bimodal peak has been a feature of participant paracetamol results reported to the Heathcontrol EQA Scheme for Toxicology since at least August 2004 (Figure 1). The scheme has investigated the source of this divergence by sub-analysis of results for different analytical techniques.

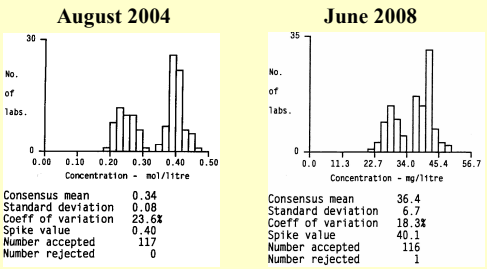

Figure 1

Material and Methods

Three liquid samples of human serum containing weighed-in concentrations of paracetamol, salicylate and a volume of ethanol plus bronidox preservative were circulated to members of the Heathcontrol scheme for analysis monthly. Concentrations of paracetamol ranged from zero to 500 mg/L. Data of fifteen samples from May 2008 to October 2008 were analysed (3 zero spike samples were excluded).

Results

Thirteen methods were used to report paracetamol measurements to the Heathcontrol EQA Scheme. The number reporting by each method are shown below (figure 2).

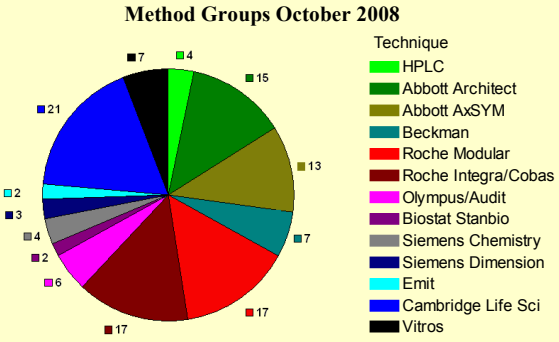

Figure 2

Precision

The Olympus/Audit Kits, Biostat Stanbio Kits and both Siemens methods (the Dimension and the Chemistry analyser) were significantly less precise than some of the least variable techniques (Figure 3).

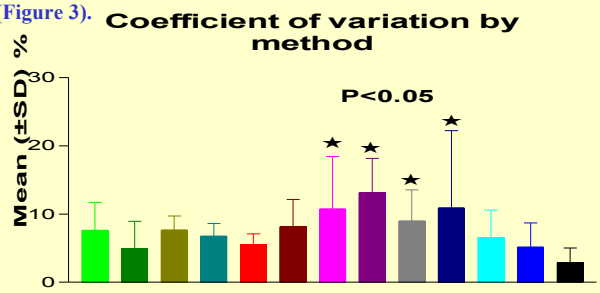

Figure 3

Accuracy

Figure 4 is a plot of the mean average deviation from the spike value expressed as a percentage. The error bars represent one standard deviation. Four techniques stand out as having negative bias that were statistically different form zero ($P < 0.001$); the Roche Modular, Roche Integra/COBAS C, Olympus/Audit Kits and the Biostat Stanbio Kits.

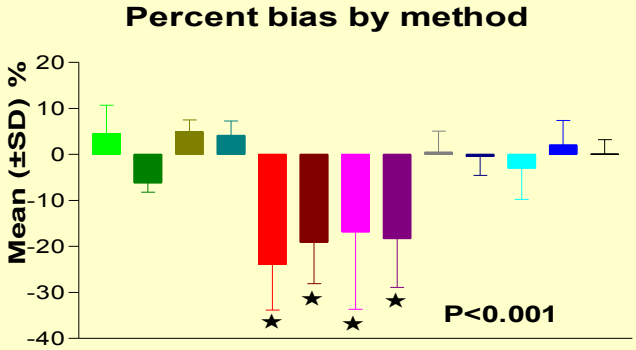

Figure 4

The mean bias value hides interesting variation with drug concentration. The Roche Modular, Roche Integra and Olympus/Biostat kits all have negative biases which increase as the concentration of paracetamol decreases (Figure 5). The Olympus method presents an interesting case as there was an apparent change in the data that occurs in August 2008. There was a marked improvement in the method which coincided with a change in the product number of reagent used in the assay.

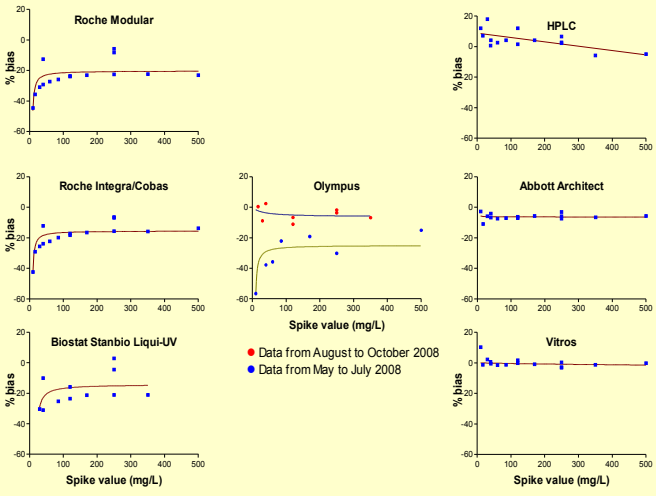

Figure 5

Summary

A bimodal peak evident in serum paracetamol results submitted to the Heathcontrol scheme is caused by four separate methods. the Roche Modular; Roche Integra/COBAS C; Olympus/Audit Kits and the Biostat Stanbio Kits which produce results in EQA samples with significant negative bias. In August 2008, Olympus 'fixed' their assay by issuing new reagent.

[Queries to heathcontrol@btinternet.com]