Educational Discussion: Newly Graded Analytes

2022-A Accuracy-Based Testosterone, Estradiol (ABS)

In the CAP Accuracy-Based Testosterone, Estradiol Program, participating laboratories test 3 specimens twice per year. Specimens used in accuracy-based program are produced from pooled, off-the-clot, freshly frozen serum samples using procedures that minimize matrix effects. Off-the-clot serum forms after donor whole blood clots in the absence of anti-coagulant, resulting in material highly representative of patient specimens. Such *commutable* specimens enable a more accurate comparison of results within and across laboratory peer groups and methods.

Peer group evaluation to assess method precision was performed for all analytes (except for PSA) and reported to accreditation programs. PSA is a new addition to this program; therefore, it was evaluated for educational purposes and not graded at this time. A second evaluation using an "accuracy-based target" compared testosterone and estradiol results to a reference value established by mass spectrometry performed at the CDC Clinical Chemistry Branch (Atlanta, Georgia). Accuracy-based results are NOT reported to accreditation agencies and are provided to participating laboratories for informational purposes only; comparisons to reference targets may be used to guide assay improvement and inform harmonization of results across methods and laboratories. Each laboratory must assess the accuracy and precision of its instrument, and if necessary, initiate appropriate actions.

Only mass spectrometry met the minimum of 10 participating laboratories for peer group evaluation and demonstrated 84.6-92.3% acceptability for estradiol and 92.0-100.0% acceptability for testosterone. In contrast, use of accuracy-based target values showed lower pass rates for estradiol methods (Table 1). ABS-01 and ABS-03 were evaluated by absolute difference in pg/mL (Figure 1) and ABS-02 was evaluated by % mean bias (Figure 2) to account for maximum flexibility of acceptance criteria.

The lower overall accuracy-based pass rate for estradiol may be due to inconsistent assay calibration and/or sample specific effects. As may be expected due to known sensitivity issues in estradiol methods, the best performance (88.1% overall pass rate) was observed in the sample with the highest concentration (ABS-02, target 45.9 pg/mL). Accuracy-based evaluation for estradiol demonstrates an overall positive bias in samples with low estradiol concentrations (ABS-01, target 14.0 pg/mL and ABS-03, target 2.1 pg/mL). Interpretation of these results is complicated by the lower limits of quantitation for many assays exceeding the sample concentrations (Figure 1). Accurate determination of low estradiol concentrations is essential in certain clinical situations, therefore the need to improve sensitivity of estradiol assays remains. Bias was not a significant concern for testosterone (Table 2).

The results summarized here highlight the critical need for accuracy-based programs. While peer comparisons provide insight into routine performance among clinical laboratories, they do not

provide an assessment of accuracy. Although true comparisons could only be made using the mass spectrometry method, the difference between peer group and accuracy-based pass rates for estradiol methods highlights the utility and overall need for improved assay harmonization to support patient care.

Table 1. Accuracy-based evaluation of estradiol

Specimen	Target pg/mL	Acceptable Range ± 30% or 9 pg/mL	Overall Pass Rate %	Mass Spectrometry Agreement %
ABS-01	14.0	5-23	72.2	92.3
ABS-02	45.9	32-60	88.1	92.3
ABS-03	2.1	0-12	68.8	88.9

Figure 1. Accuracy-based estradiol method performance for ABS-01 and ABS-03. Dotted lines indicate acceptability ±9 pg/mL.

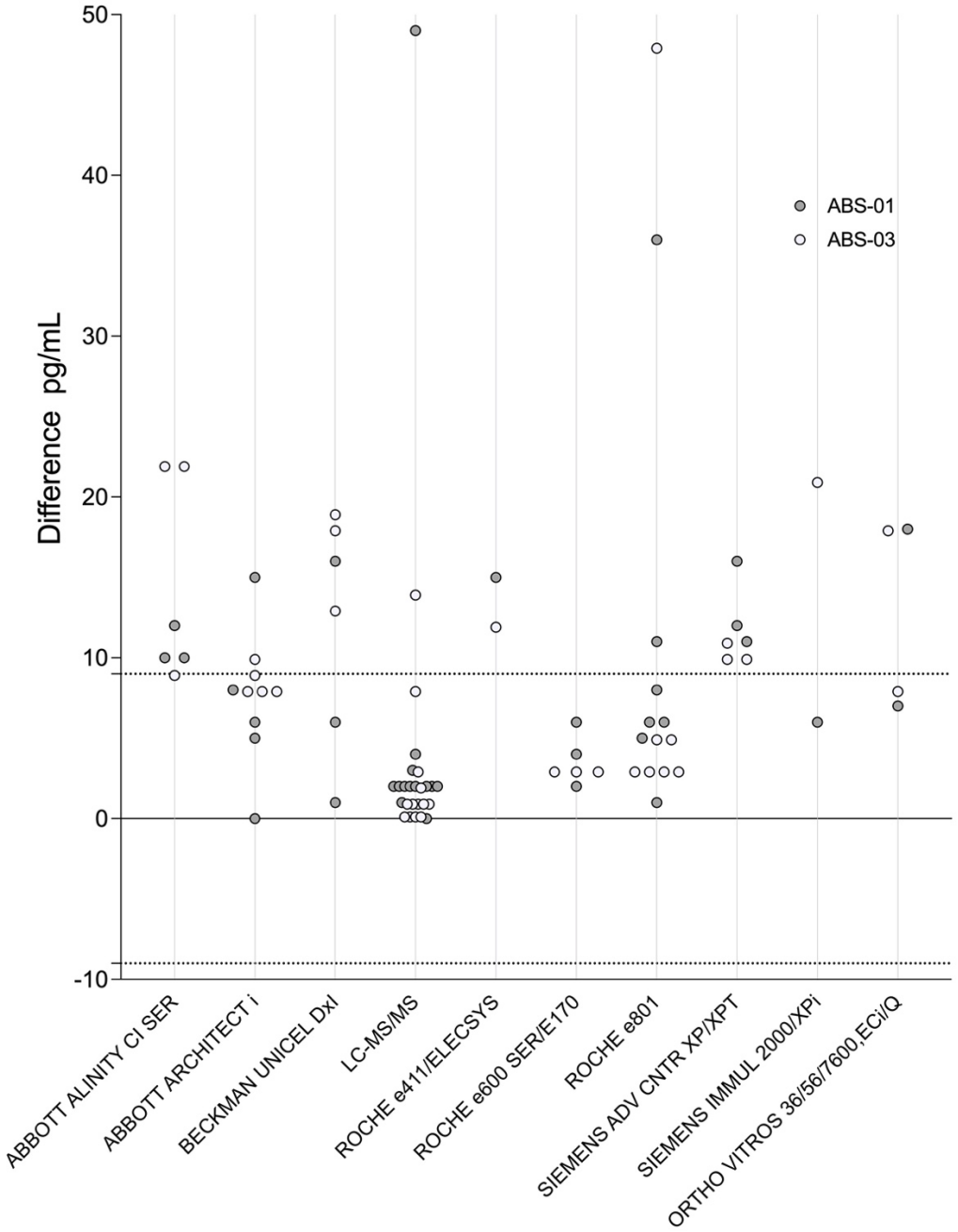

Figure 2. Accuracy-based estradiol method performance for ABS-02. Dotted lines indicate acceptability ±30%.

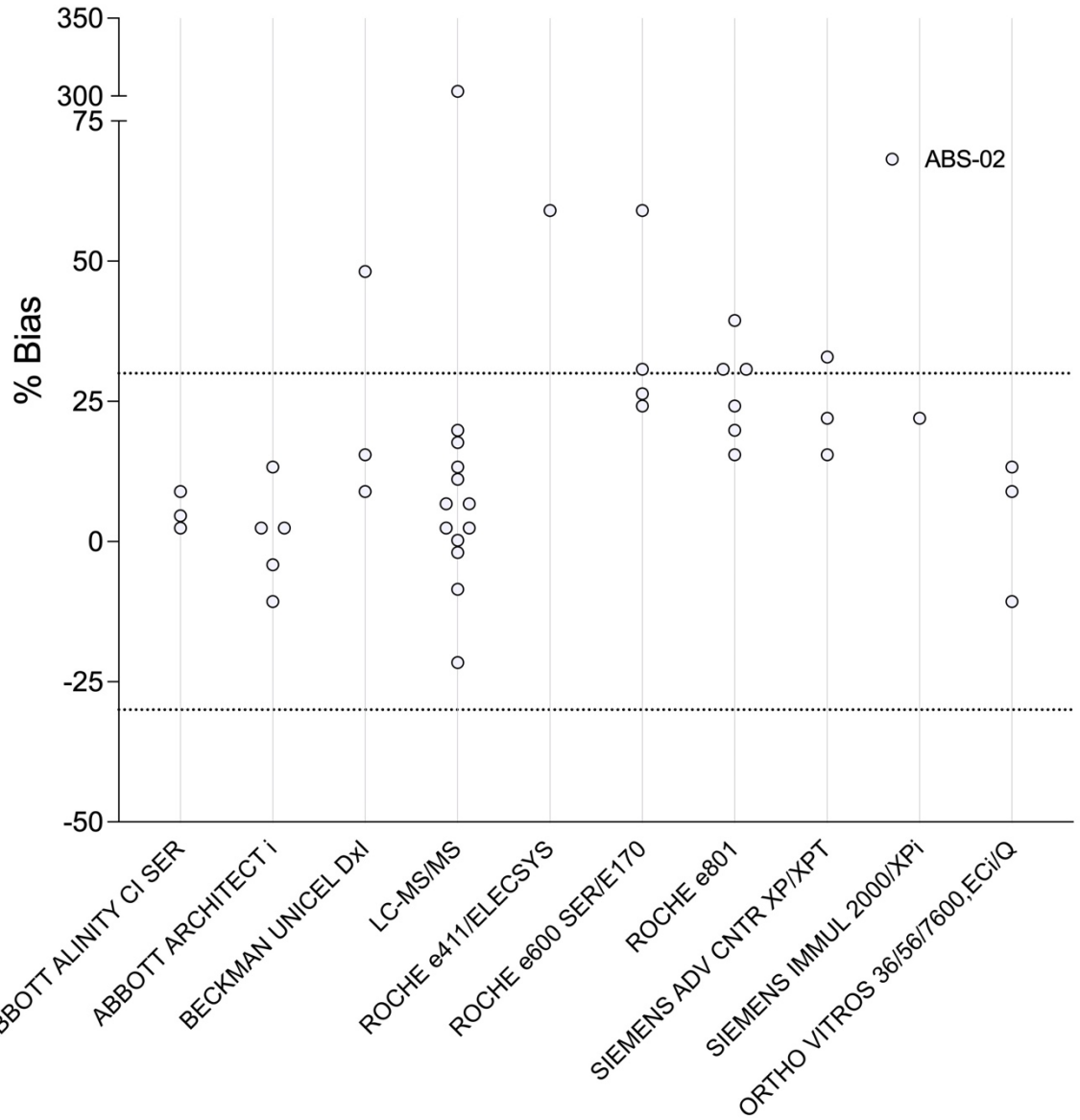

Table 2. Accuracy-based evaluation of testosterone

Specimen	Target ng/dL	Acceptable Range ± 20% or 20 ng/dL	Overall Pass Rate %	Mass Spectrometry Agreement %
ABS-01	432.0	345-519	91.0	92.0
ABS-02	30.1	10-51	100.0	100.0
ABS-03	11.2	0-32	98.0	100.0

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