To the Editor:

We read with great interest the report of Stepmann et al. (1) identifying analytical errors in commercial analytical systems by using an external quality assessment (EQA) scheme with single-donor specimens. The use of such materials provides an assessment of method accuracy that is generally regarded as the gold standard in such comparisons (2). Unfortunately, only a limited number of laboratories can typically participate in such assessments without resorting to pooled or processed proficiency materials. Analytical ranges are also usually limited using single-donor specimens unless these materials are supplemented with additions that potentially obviate the benefits of using such specimens.

Although intermethod bias cannot be definitively assessed with materials that have not been shown to be commutable for the examined analytes and analytical techniques, it is incorrect to assume a priori that pooled or spiked specimens, by their nature, are noncommutable and that method biases seen with such specimens are largely due to matrix effects. The data provided by Stepmann et al. (1) allow for comparison of bias estimated with more commonly used materials in proficiency testing, and we undertook a review of bias estimated by traditional proficiency testing in light of the data reported in that paper.

Through the New York State Laboratory Reference System Proficiency Testing Program, we used pooled human serum, derived from plasma (Bioresource Technology), with analytes added as necessary to prepare specimens with clinically relevant concentrations for each test event. Specimens were sterile-filtered (0.22-μm pore size), aliquoted, and stored frozen at ≤−80 °C until they were shipped in the frozen state to 427 laboratories for analysis. Results for the analytes and instrumentation from participants matching the Stepmann et al. study (1) are shown in Table 1. To approximate the analysis done in the original study (1), we stratified the data into low-, middle-, and high-concentration ranges for each analyte. Target values for each specimen and analyte were established with a robust statistical technique using all the participant data (3), and we calculated, for each assay system, the median bias from those target values within each category.

Comparison of the bias assessed by the 2 EQA schemes shows that processed proficiency fluids largely provide similar estimates of bias for 6 of the 8 analytes examined (Table 1). Excluding LDL and HDL cholesterol, 74 of 90 estimates of bias (82%) differed by less than the threshold criteria proposed by Stepmann et al. (1): ≤4.5% for glucose, phosphate, and triglycerides; ≤4.0% for cholesterol, creatinine, and urate. Using a much stricter criterion of differences of ≤2% (likely within the measurement uncertainty of either study), we found concordance for 63% of the comparisons. Estimates of bias for LDL and HDL cholesterol in our study were substantially greater than those obtained with neat human serum. The lack of commutability of processed materials for lipoproteins and lipid measurements has been demonstrated previously (4), and this was not an unexpected finding. Nonetheless, results for cholesterol and triglycerides were largely within bias thresholds even though processed human serum has been previously shown to be noncommutable for these lipid analytes (4). The notable bias found in the Ortho procedure for phosphate (approximately 6%–15%) was nearly identical in both studies and followed the same degree of dependence on phosphate concentration (Table 1).

In addition to the type of specimens used in the 2 studies, there are other differences in design including the concentration range of analytes, number of participant laboratories, number of specimens distributed, and method for calculating bias that make the similarity in bias estimates all the more remarkable.

Although the comparison we performed here cannot substitute for a full commutability study, it provides insight into the utility of pooled and spiked materials in PT. Whereas there were instances in which the bias of the processed materials differed from those of the patient samples, the more common observation was agreement between the 2 EQA schemes for estimating intermethod bias for 6 analytes. These data suggest that accuracy-based PT with pooled and/or spiked specimens is achievable for at least
Table 1  Comparison of bias estimates (at low, medium, and high concentrations) for 8 analytes and 5 analytical systems.\textsuperscript{a}

<table>
<thead>
<tr>
<th></th>
<th>Cholesterol</th>
<th>Creatinine</th>
<th>Glucose</th>
<th>HDL cholesterol</th>
<th>LDL cholesterol</th>
<th>Phosphate</th>
<th>Triglycerides</th>
<th>Urate</th>
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<tbody>
<tr>
<td>Abbott</td>
<td>3.0</td>
<td>3.4</td>
<td>5.1</td>
<td>5.9</td>
<td>-0.4</td>
<td>-1.8</td>
<td>5.5</td>
<td>14.5</td>
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<td>3.8</td>
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<td>4.2</td>
<td>0.2</td>
<td>0.4</td>
<td>-5.4</td>
<td>5.0</td>
</tr>
<tr>
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<td>-1.8</td>
<td>-0.6</td>
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<td>2.1</td>
<td>-0.5</td>
<td>0.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Roche</td>
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<td>1.0</td>
<td>0.5</td>
<td>-1.1</td>
<td>1.9</td>
<td>-0.3</td>
<td>-3.2</td>
<td>14.6</td>
</tr>
<tr>
<td>Ortho</td>
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<td>-1.0</td>
<td>1.1</td>
<td>-1.3</td>
<td>1.6</td>
<td>0.2</td>
<td>-5.6</td>
<td>7.1</td>
</tr>
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<td>1.2</td>
<td>0.3</td>
<td>3.5</td>
<td>2.8</td>
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<tr>
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<td>1.0</td>
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<tr>
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<td>2.7</td>
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<td>0.6</td>
<td>0.0</td>
<td>1.6</td>
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<tr>
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<td>-3.4</td>
<td>-2.8</td>
<td>0.5</td>
<td>-1.0</td>
<td>1.7</td>
<td>-10.6</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Bias indicates median difference (\%) between results from the specified analytical system and the target value: for Ghent data, target values were determined as specified by Stepman et al. (1); for New York State Laboratory Reference System Proficiency Testing Program (NYSPT) data, target values were calculated by a robust statistical technique using data from all participants (2); NYSPT data are results from 3 proficiency events (15 specimens) from October 2013 to May 2014. Analyte concentration ranges (lowest to highest) were total cholesterol [111–266 mg/dL (2.9–6.9 mmol/L)]; glucose [39–281 mg/dL (2.2–15.6 mmol/L)]; phosphate [2.3–5.5 mg/dL (0.7–1.8 mmol/L)]; urate [2.7–11.4 mg/dL (161–678 μmol/L)].

some measurands, without the need to resort to use of so-called peer grading, which has the effect of perpetuating the sort of analytical bias identified by Stepman et al. (1) and will not result in improvement of trueness (3). Both organizers and participants of EQA schemes benefit from studies such as Stepman et al., where bias observed with single-donor samples can be used as a benchmark.

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