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Assessing the Performance of Point-of-Care Hemoglobin A1c Systems

To the Editor:

Lenters-Westra and Slingerland (1) recently reported results of a comparative performance study of several point-of-care (POC)1 tests for hemoglobin A1c (Hb A1c), and we commend them for providing useful new information on instrument performance. We also believe that the results should be interpreted strictly in terms of the facts, including consideration of discrepancies between the study design and the instructions provided by the manufacturers.

Bayer’s A1CNow+-® Multi-Test A1C System was included in the initial phase of this study, but testing was not continued for the main phase of the study after the local distributor of that product concluded that the preliminary CLSI EP-10 results did not warrant further testing. The authors reported that these results were probably due to EDTA interference. As a POC test, the A1CNow+ test is primarily intended for capillary blood samples, and the instructions for use specify use of heparin-containing collection tubes when using venous blood.

The authors’ title, “Six of Eight Hemoglobin A1c Point-of-Care Instruments Do Not Meet the General Accepted Analytical Performance Criteria,” and its conclusion are misleading when 7 instruments at most were used according to the manufacturers’ operating instructions; thus, performance conclusions are warranted only for these 7 instruments. No conclusion should be drawn regarding the performance of the A1CNow+® test because it was not used according to manufacturer’s labeling in the preliminary stage and thus was not included in the final study. In the Results section of the Abstract, the authors state that 2 of 8 manufacturers decided not to continue the study because of the disappointing EP-10 results, a simplification that omits the relevant fact that inappropriately obtained blood samples were used for the A1CNow+® test.

In the same issue of this journal, Bruns and Boyd (2) contributed an editorial offering further interpretation and an opinion of the Lenters-Westra and Slingerland report. They paraphrase the same misinterpretation by stating, “Two of the 8 manufacturers withdrew from the study after initial unpromising results with their POC methods.” This statement again misrepresents the reason for the withdrawal in the case of the A1CNow+® test and further supports our belief that there will be misunderstandings because of the conclusions and overall impression provided by the report.

Furthermore, the Results section and the Acknowledgments at the end of the Lenters-Westra and Slingerland report indicate that the study authors communicated directly with a local unaffiliated distributor for the Bayer A1CNow+® device in lieu of direct communication with the manufacturer (Bayer). We point out that Bayer was not asked to comment on the study protocol before its execution and thus did not have the opportunity to comment on the resulting negative bias when the test was used with EDTA-containing blood.

A challenge to future researchers (and their reviewers) examining the performance of POC Hb A1c devices would be to include an analysis of all the relevant information to provide a broader context for interpretation. In Lenters-Westra and Slingerland’s report, it is apparent that there was variation among the laboratory reference methods, although they were all controlled and calibrated in the authors’ laboratory. Reference 17 in their report is cited as a source of concern regarding the accuracy of

1 Nonstandard abbreviations: POC, point-of-care; Hb A1c, hemoglobin A1c.
POC instruments, yet this reference describes an accuracy drift over time that was as large in the central laboratory instrument as it was in the POC device (3). Survey results from the College of American Pathologists (4) indicate that in the field, variation within and between laboratory-based methods can be comparable to or greater than some of the POC results reported by Lenters-Westra and Slingerland, and an analysis of these trends was given in the report by Holmes et al. cited by these authors. Including such considerations would shed light on realistic performance expectations with the current state of laboratory methods for Hb A1c. Although performance should be of primary concern, additional clinical considerations, such as patient access, cost, portability, convenience, and the impact of immediately available Hb A1c results, would also bring added value to the context of this discussion.

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References

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In Reply

We thank Drs. Irvin, Knaebel, and Simmons for their questions, and appreciate the opportunity to reply.

The evaluation protocol was designed by the authors and sent for comment either to the manufacturers, or to their local distributors. We expected local distributors to communicate with their manufacturer regarding the protocol. We reject the notion that we approached an unaffiliated distributor, because the distributor we contacted is registered on the Bayer HealthCare website (1). This local distributor had no comments on the study proposal. Moreover, the local distributor gave us the results of 9 A1CNow® InView™ field evaluation studies, all of which used whole-blood samples anticoagulated with EDTA. Although the professional-use product insert (2) states that heparin tubes are preferred for venous blood collection, it does not give specific warnings regarding the disadvantages of EDTA blood. If these disadvantages are important, their omission in the Warnings and Precautions section is a major oversight, because EDTA tubes are commonly used for the determination of hemoglobin A1c in the clinical laboratory. Such information should have been provided to the local distributors and further detailed in the product insert.

The EP-10 results were sent to the local distributor and discussed in person. The possible effect of EDTA was discussed and we offered the option of repeating the study with capillary blood at the diabetes care center, but the local distributor was not interested.

After publication of our article (3) we offered the manufacturer an option of repeating the study with heparin blood and sent them a draft proposal. Our only requirement was that regardless of outcome, the study results could be published. The manufacturer declined our initial offer, but suggested that we apply for a Bayer Diabetes Care Independent Research Grant. We understand that the manufacturer has very specific regulatory and compliance measures to meet to satisfy legal requirements, but in this case we felt their response was somewhat overcautious. In addition, to maintain our investigative independence, up to that point we had accepted only reagents from the various manufacturers, and no other support or grants from involved industries. Therefore, we respectfully declined the invitation to apply for further research grants. However, in our opinion, the manufacturer, by declining our offer to repeat the study with heparin blood, missed an opportunity to further extend the knowledge regarding the analytical performance of the A1CNow+ Multi-Test A1C System.