COLLEGE of AMERICAN PATHOLOGISTS

2018-A Hemoglobin A_{1c} Survey Discussion

The GH5/GH2 Survey samples were prepared from pooled whole blood obtained from healthy or diabetic individuals. The target values were determined from the means of all results from seven National Glycohemoglobin Standardization Program (NGSP) Secondary Reference Laboratories (SRLs). Each laboratory analyzed each sample in triplicate on two separate days. These NGSP Network Laboratories use methods that are calibrated and traceable to the method used in the Diabetes Control and Complications Trial (DCCT). Comparison to the NGSP Network allows both manufacturers and clinical laboratories to trace their glycated hemoglobin results to the DCCT. The target HbA_{1c} values for the Survey are as follows: GH-01, 7.15%; GH-02, 5.19%; GH-03, 8.42%; GH-04, 9.79% and GH-05, 6.12%.

The Survey uses an accuracy-based evaluation against the NGSP reference method targets with an acceptable limit equal to ± 6% of the target value. Because the PT samples are prepared from human whole blood, the bias observed for the PT samples is expected to reliably reflect the bias that exists for patient samples analyzed with the same method.[1] The percentage is a mathematical fraction, not the HbA_{1c} reporting unit. For example, the acceptable range for GH-01, which has an HbA_{1c} value of 7.15%, would be HbA_{1c} values between 6.7 and 7.6%.

In addition to the 6% grading criterion used by the CAP for HbA_{1c}, a second "dual grade" with an acceptable limit equal to ± 5% of the target value is shown on your laboratory evaluation. This second "dual grade" is provided for **educational purposes only** and is not reported to CMS, nor will it be used by any accreditation program. Each laboratory must assess the accuracy and precision of its instrument, and if necessary initiate appropriate actions. **Note that the acceptable limit for grading will be reduced to ± 5% of the target value in 2020.**

[1]EDTA in the PT sample has been shown by the manufacturer of Bayer A1cNOW+ to cause artificially low results by this method. Routine patient samples for this method are from fingerstick and do not include EDTA. The manufacturer recommends the use of heparin anticoagulant instead of EDTA when testing venous samples. Peer group grading was employed for Bayer A1cNOW+ users.

For the five specimens, the pass rates vary considerably depending on the HbA_{1c} method (data for all methods $n \geq 10$ are summarized in Table 1.) While the overall pass rate ranged from 95.6% to 97.3%, depending on the target value, the lowest pass rate was 72.7%. Nevertheless, some methods were able to achieve 100% (or close to 100%) pass rates for all five samples.

Table 1. Pass Rates for Peer Groups ≥ 10 Participants

Specimen	NGSP Target % HbA_{1c}	Acceptable Range ± 6%	Pass rate % Low/High	Cumulative Pass Rate %
GH-01	7.15	6.7-7.6	81.8/ 100.0	95.9
GH-02	5.19	4.8-5.6	72.7/ 100.0	97.3
GH-03	8.42	7.9-9.0	79.1/ 100.0	96.8
GH-04	9.79	9.2-10.4	81.8/ 100.0	95.6
GH-05	6.12	5.7-6.5	84.6/ 100.0	97.1

Examination of the HbA_{1c} results obtained by participants in the Survey reveals that in general the mean values measured by the participants did not differ markedly from the values determined by the NGSP Secondary Reference Laboratories. The method-specific HbA_{1c} means for GH-03 (target value 8.42%) exhibited the least variation, ranging from 8.16% to 8.60% HbA_{1c} (these are differences of -3.1 and +2.1%, respectively, from the target value). The method-specific means for GH-01 (target value 7.15%) ranged from 6.93% to 7.42% HbA_{1c} (differences of -3.1 and +3.8%, respectively, from the target value). GH-02 (target value 5.19%) had method-specific means ranging from 4.89% to 5.41% HbA_{1c} (differences of -5.8 and +4.2%, respectively, from the target value). GH-04 (target value 9.79%) had method-specific means ranging from 9.39% to 10.03% HbA_{1c} (differences of -4.1 and +2.5%, respectively, from the target value). GH-05 (target value 6.12%) had method-specific means ranging from 5.88% to 6.33% HbA_{1c} (differences of -3.9 and +3.4%, respectively, from the target value). Abbott Architect c System and Tosoh G8 Automated HPLC had CVs ≤1.5% for all five samples. ARKRAY Adams HA-8180 series, Bio-Rad

D-100, Sebia Capillarys 2 Flex Piercing and Trinity Biotech Premier Hb9210 HPLC had CVs ≤2.0% for all five samples. Guidelines from The National Academy of Clinical Biochemistry and the American Diabetes Association recommend an inter-laboratory CV <3.5% ([Sacks DB, et al. *Clin Chem*. 2011;57:e1-e47] and [Sacks DB, et al. *Diabetes Care*. 2011;34:e61-99].) Most methods were able to achieve this criterion. However, Beckman AU Systems - Beckman reagent had CVs >3.5% for four samples and Siemens Dimension Xpand had CVs ≥3.5% for three samples. Roche cobas c311 had the lowest mean value for three samples.

In addition to the tables, the data obtained for each method (with a peer group $n \geq 10$) are also presented in the style of box-and-whisker plots (Fig. 1). Each method is listed individually, with the number of participants using that method in parentheses after the name of the method. The individual lines extend from the minimum to maximum difference, expressed as a percentage from the target value (the percentage is a mathematical fraction). The thicker line indicates the distribution of the middle 90% of values. The grey shaded area represents the evaluation limit, ie, ± 6% from the target. The diamond is the median for the particular method. Outliers were excluded. The presentation allows rapid visualization of bias [how far the diamond (median) is from zero], imprecision (length of the line) and the number of laboratories that failed (those that lie outside the shaded area) for each method. This feature provides additional detailed information that should be useful to individual laboratories to assess their method and compare it to both their peers and to other methods.

Manufacturers of methods that have the means furthest from the reference value and those with the largest imprecision are encouraged to improve their performance, especially those methods that consistently exhibit large bias and/or large CVs. This is particularly important in the clinically relevant HbA_{1c} ranges (~5.5% to 8%).

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Chemistry Resource Committee