Meeting of the NGSP Steering Committee
Minutes
Monday July 28, 2025 2:00 PM – 3:30 PM
Fairmont Chicago Millenium Park, Chicago, IL

Participants:

*David Sacks —NIH, Chair, NGSP Steering Committee
*Carla Siebelder—IFCC HbA1c Network Coordinator, ERL, NGSP
*Kuanysh Kabytaev—Univ. of MO
*Erna Lenters—ERL, IFCC, NGSP
*Julie Myers—Bio-Rad Laboratories
*Elizabeth Selvin—Johns Hopkins University
*Hubert Vesper—CDC
*Mathew Wagner—Sebia
Shawn Connolly—Univ. of MO, NGSP
Emma English—Chair, IFCC C-EUBD
Curt Rohlfing—Univ. of MO, NGSP Network Coordinator
Salvatore Secchi—NIDDK/NIH

Virtual:
Beena Alkolkar—NIDDK/NIH

Steering Committee members not present:
*Robert Cohen—Univ. of Cincinnati
*David Nathan—Massachusetts General Hospital
*John Higgins--Massachusetts General Hospital
*Michael Steffes—Univ. of Minnesota

***Member of the NGSP Steering Committee**

1) **Welcome and Introduction—David Sacks, Chair, NGSP Steering Committee**
D. Sacks welcomed those in attendance, thanked outgoing manufacturer representative Monica Swenson for her contributions to the committee and welcomed new manufacturer representative Julie Myers. Those present introduced themselves and the 2024 minutes were approved. D. Sacks and others present noted that longtime NGSP Coordinator Randie Little retired July 1 and acknowledged her immense contributions to HbA1c standardization and the success of the NGSP.

2) **NGSP Progress Report—Curt Rohlfing, NGSP Network Coordinator**
- NGSP Network Monitoring
  - The PRLs and SRLs continue to demonstrate excellent comparability (May 2025 between-lab CVs were 1.13% and 0.77% for the PRLs and SRLs, respectively).
  - Monthly between-lab CVs for the NGSP network were all <1.5% over the past year.
  - The SRLs are also monitored against each other using an acceptance ellipse, which is based on the slope and intercept of the differences between the individual SRLs results and the medians of all SRLs.
- Long Term Quality Controls (LTQC)
  - Provides another estimate of long-term consistency of NGSP results
  - Three levels of frozen whole blood aliquots
  - Analyzed monthly by the Missouri SRLs and quarterly by all SRLs
  - The original LTQC samples were analyzed from 2010 to 2019
  - New LTQC samples were prepared and have been analyzed from 2018 to the present
  - In all cases the mean CVs for the LTQC samples were all ≤1.5%
- NGSP Certification
  - The number of certified methods continues to increase, while the number of laboratories has leveled off.
  - There are ~400 methods and ~150 laboratories currently certified.
  - Most certified labs are Level I and are outside of the U.S.
- Variability of Level 1 Labs May 2024
  - Level 1 labs are monitored quarterly
  - In May, the between-lab CV for the L1 labs was 1.67% (n=24)
- Status of HbA1c Measurement (CAP data)
  - Current CAP limits (2013-2024): Each result must be within ±6% of NGSP assigned target value (mean of 8 SRLs, multiple results from each).

- There has been much improvement in within and between-lab variability since 1993 as the CAP and NGSP certification criteria have been tightened over the years.
- Variability among methods improved dramatically from 1993 to 2014 but the improvement has been more subtle in recent years.
- CAP 2025A survey
  - Pass Rates (±6% CAP Accreditation Limit)

Specimen	NGSP Target (% HbA1c)	Acceptable Range (±6%)	Pass rate % (Low/High)	Cumulative Pass Rate % (±6%)
GH-01	9.84	9.2 - 10.5	88.5/100	96.8
GH-02	5.60	5.2 - 6.0	94.5/100	98.8
GH-03	7.97	7.4 - 8.5	92.2/100	98.4
GH-04	8.45	7.9 - 9.0	93.2/100	98.2
GH-05	6.00	5.6 - 6.4	92.3/100	98.1

  - Cumulative pass rates were all >96%.
  - For individual methods, pass rates ranged from 88.5% to 100%.
  - All-method CVs have dropped over time since 2000.
  - All-method CVs for the 2025A survey were all <3%.
  - CAP data Summary (2025A)
    1) Method-specific, between-laboratory CVs ranged from 0.4% to 4.0%.
    2) Overall, only 60% of laboratories are using methods with CVs ≤2.5% at all five HbA1c levels.
    3) All-method CVs for the most recent survey ranged from 2.5-2.8%.
    4) Overall Pass rates are between 96.9 and 98.8% for the current 6% accreditation limits

- Conclusions
  - The NGSP network is still doing well with very low CVs.
  - CAP survey results show that the all method CVs (including all laboratory & methods' results) have been ≤3% since the 2020C survey. We would like to see this get to ≤2.5% as recommended in the ADA/ADLM guidelines (Sack et.al. Diabetes Care 2023;46(10):e151–e199. https://doi.org/10.2337/dci23-0036)
  - Measurement of HbA1c continues to improve but there are still a few methods with between lab CVs >3%.

Discussion:

D. Sacks asked about the possibility of getting another PRL in the network, C. Rohlfing said he would look into it. D. Sacks and E. English noted that there was recent issue with the Premier method in the UK, the method developed a positive bias which resulted in overdiagnosis of diabetes and expensive corrective actions. D. Sacks mentioned that the 2 of 24 LI labs that had high biases for 3 of 10 monitoring samples in May only showed these biases on the high end of the range (≥9% HbA1c). C. Rohlfing said that whenever there are bias issues with manufacturers or labs it is almost always in the upper HbA1c range. D. Sacks noted that the between-laboratory CVs have leveled off in recent years after dropping significantly before that, it is possible that between-lab imprecision cannot be further improved. H. Vesper asked if removing point-of-care methods in the CAP survey data would significantly change the overall data. C. Rohlfing responded that it would not change the numbers much, the number of labs using POC methods on the survey is relatively low, although one POC method on the survey has had issues recently and is showing higher between-lab CVs in the last several surveys. E. Lenters and E. English said the variable performance and limited regulation of POC methods continues to be problematic.

3) CAP Proficiency Testing Update—David Sacks

- Proficiency Testing (PT)
  - In US all labs that measure patient samples are required by law to perform PT
  - Regulated by CMS (Centers for Medicare & Medicaid Services) through CLIA
  - CAP (College of American Pathologists) is largest provider of PT material in the world

- CAP Grading
  - Initially, CAP used peer group grading for PT for HbA1c
  - Subsequently, introduced whole blood PT, but maintained peer group grading
  - In 2007 changed to accuracy-based grading
  - Target values assigned by NGSP network
  - ±15% acceptable
  - 99% of laboratories passed
- PT Criteria Tightened
  - In 2008 acceptability reduced to 12%
  - 2009 - 10%
  - 2010 - 8%
  - 2011 - 7%
  - 2014 - 6%
- Proposed CAP PT Criterion 2020: ±5%
- Pass Rates for CAP 2020 GH5-C: ±6% vs. ±5%

Sample ID	Target (%)	±6%	±5%
GH-11	5.5	97.9	**95.2**
GH-12	8.3	97.7	**95.4**
GH-13	5.1	97.6	**97.6**
GH-14	10.1	96.9	**95.1**
GH-15	6.0	97.6	**96.6**

- CLIA Proposed PT Rule 2019 (CLIA 88 update)
  - Hemoglobin HbA1c would become a regulated analyte
  - Criterion for acceptable performance: Target ±10%
- Implications of New CLIA Proposal
  - HbA1c would become, for the first time, a regulated analyte
  - CAP is not permitted to fail a lab if it meets CLIA criteria
  - If CLIA accepts ±10%, CAP will have to loosen acceptability from ±6% to ±10%
- Response to CMS 2019 Proposal
  - Multiple organizations (clinical and lab) and individuals sent comments to CMS
  - Almost all the 107 comments received by CMS protested loosening HbA1c criteria
  - Delegation from ADA went to speak to CMS
  - An editorial was published in 2019 in a clinical diabetes journal criticizing the proposal (Klonoff et. al, J Diabetes Sci Technol 2019 May;13(3):424-427).
- CMS Response
  - Not persuaded by comments
  - Acknowledge improvement in accuracy
  - Concerned that "…tighter criteria will limit access to testing…"
- Final CLIA Rule
  - Acceptance limits for HbA1c are 8%
  - Effective January 1, 2025
- CAP Conundrum
  - CAP has 2 separate programs
    - PT
    - Accreditation
  - Grading of regulated analytes by **PT providers** must follow rules in Federal Register
  - **Accrediting agency** can require better accuracy for lab to remain accredited, but **PT provider** must grade HbA1c at 8%

- Formal grading had to change to 8%
- CAP PT 2025: CAP has three HbA1c PT surveys
  - Accuracy-based GH5 survey: Main survey, >2,500 labs
  - Waived accuracy-based GH2 survey: Waived assays, ~400 labs
  - International GH5I survey: Not accuracy-based, >425 labs
- CAP Solution: Have 2 sets of criteria (dual grading)
  - Labs not using accuracy-based PT OR not accredited by CAP have to be graded by +/- 8%
  - Labs using accuracy-based PT and accredited by CAP graded by +/- 6%
  - Evaluation reports sent to the participating labs show if lab passed at both 6% and 8%
- GH5-A 2025 Overall Pass Rate

Specimen	NGSP Target (% HbA1c)	Acceptable Range (+/- 8%)	Cumulative Pass Rate % for 8%	Acceptable Range (+/- 6%)	Cumulative Pass Rate % for 6%
GH-01	9.84	9.0 - 10.7	98.8	9.2 - 10.5	96.8
GH-02	5.60	5.1 - 6.1	99.4	5.2 - 6.0	98.8
GH-03	7.97	7.3 - 8.7	99.2	7.4 - 8.5	98.4
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- Summary
  - Acceptable performance for HbA1c PT changed to 8%
  - Effective January 1st, 2025
  - Labs accredited by CAP that use accuracy-based PT will have to meet 6% criterion

Discussion:

D. Sacks noted that the GH2 waived accuracy-based whole blood survey is new for 2025, many labs running POC methods have moved to this survey. He clarified that GH2 is 3 samples rather than 5, so one factor is probably that it is less expensive to participate, and the GH5I survey is for international labs that cannot participate in the whole blood survey due to shipping logistics. C. Rohlfing added that the GH2 survey doesn't meet CLIA requirements, but since it is only waived POC methods it does not need to. E. Lenters acknowledged that shipping samples internationally presents logistical issues and shipments can get delayed, and asked why the GH5I survey is not accuracy-based. D. Sacks said since it utilizes lyophilized materials there could be matrix effects. E. Lenters and C. Siebelder suggested that nonetheless it would be worthwhile to examine the data against an accuracy base, E. English agreed noting that the survey could be done both ways (peer group and accuracy-based). D. Sacks agreed and said CAP might try doing this. M. Wagner asked if there are any plans to tighten the CAP accreditation criteria to 5% now that the CLIA issue has been settled, D. Sacks said there are currently no plans to do so but he may bring this up with CAP at a later date. D. Sacks also noted that CAP received no calls from laboratories regarding the change in grading, which he found very surprising. S. Secchi asked how CAP obtains the survey samples, and how hemoglobin variants are addressed. D. Sacks responded that CAP works with a company that finds donors and makes pools with the HbA1c levels specified by CAP, and variants are excluded. In the past CAP has included a variant sample in the survey on a few occasions, but these samples cannot be used for grading since methods with variant interference would fail. It is a major undertaking, the company has to find donors with variants and they have said they cannot find enough donors for variants other than HbS trait. Additionally the law now required 5 graded samples in each survey, so CAP would have to include a 6th sample which would be expensive for CAP. It might be possible for CAP to include a variant sample for a subset of methods. H. Vesper asked if variant samples are ever incorporated into NGSP certifications, C. Rohlfing said they are deliberately excluded.

4) 2025 Clinical Advisory Committee Meeting Update—David Sacks

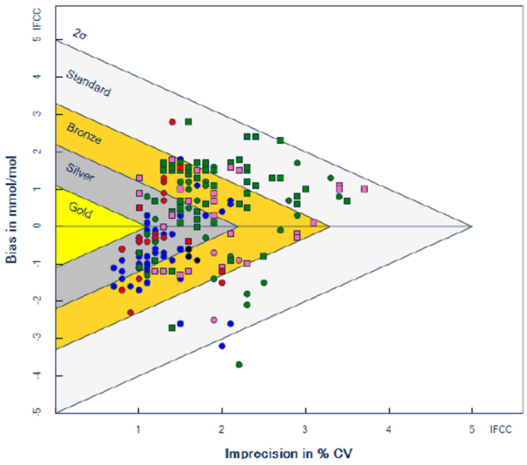
- The 2025 CAC meeting took place at the ADA annual meeting in Chicago in June.
- CAC: To facilitate communication between the NGSP and the clinical community
- The meeting is normally chaired by Dr. Christopher Holiday, Director of Diabetes Translation at the CDC, but he was unable to attend so K. Kabytaev chaired the meeting in his place.

- Summary
  - C. Rohlfing presented a NGSP/CAP update
  - Robert Cohen presented data regarding estimated HbA1c by CGM vs. actual measured HbA1c
    - Many CGM proponents claim that HbA1c estimated from CGM measurements is more accurate than measured HbA1c in cases where there is a discrepancy between them.
    - R. Cohen did a large study that examined the effect of red-cell lifespan on measured HbA1c
      1) Healthy volunteers
      2) Gave them N15 labeled glycine and measured red-cell lifespan
      3) Found reduction in the difference between estimated and measured HbA1c when the latter is corrected for red-cell lifespan
  - E. Selvin and D. Nathan had a debate on the topic of considering race-based HbA1c targets
  - Irl Hirsch presented an update on diabetes and kidney disease along with related data.

5) Update IFCC Network—Carla Siebelder

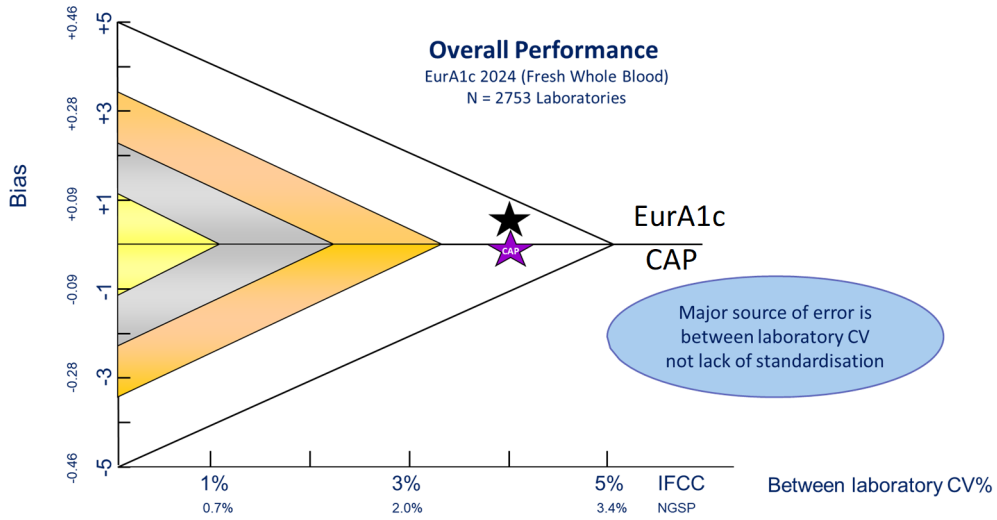
- There are currently 15 approved laboratories and 1 candidate laboratory in the IFCC laboratory network. The laboratories are spread around the globe and include labs in the U.S., Europe, South America and Asia. (www.ifcchba1c.org)
- The IFCC/NGSP master equation is still being monitored via sample comparisons between the two networks performed twice a year. The equation remains very stable, after over 20 years.
- Performance Manufacturers 2024 (total 243)
  - Gold 0: 0%
  - Silver 100: 41%
  - Bronze 90: 40%
  - Standard 43: 18%
  - IFCC criteria not met 2: 1%

	Lab Instr %	POCT %
Ion-exchange HPLC	28	0
Immuno Assay	13	31
Affinity	1	14
Cap Electroph	1	<1
Enzymatic	9	2



- IFCC Model Quality Targets
  - Bias has a more significant impact (on the risk of misinterpretation) than imprecision when using HbA1c for diagnosis of diabetes. (Weykamp et. al, Clin Chim Acta 548 (2023) 117495).
  - Criteria are being reconsidered by the IFCC C-EUBD
- Monitoring Quality: EurA1c 2024
  - A project of the IFCC C-EUBD and EQA/PT organisers
  - Once a year EQA Organisers use the same 2 samples

- 2024: 23 countries - 27 EQA - 4284 laboratories
- Ultimate check performance in the field



Discussion:

D. Sacks noted that it is good to see that the overall performance seen with the EurA1c data matches that of CAP. S. Connolly said that the IFCC reference method has become easier for him to run due to more experience with the method and this is probably the case for the other network labs. That may be part of why the ME is more stable now, also maybe some of the labs that have since dropped out were not performing well. C. Siebelder said she has noticed that the overall performance of the network labs has shown some improvement.

D. Sacks noted that the Manufacturer Forum would take place after this meeting in the same room, and thanked everyone for their attendance. The meeting was adjourned at 3:25 PM.

Minutes prepared by C. Rohlfing 9/19/2025. Modified by D. Sacks 9/30/2025 and C. Siebelder 10/01/2025.