Meeting of the NGSP Steering Committee
Minutes
Sunday July 24, 2022 2:00 PM – 4:30 PM
Marriott Marquis, Chicago, IL

Participants:

*David Sacks —NIH, Chair, NGSP Steering Committee
*Randie Little—Univ. of MO, NGSP Network Coordinator
*Elisa Noll—Roche Diagnostics
*Carla Siebelder—Queen Beatrix Hospital (NL), IFCC Network Coordinator
*Michael Steffes—University of Minnesota
*Monica Swenson—Abbott Diagnostics
*Hubert Vesper—CDC

Via Zoom:

*John Higgins—Massachusetts Gen. Hosp.
*Garry John—Chair, IFCC C-EUBD
*David Nathan—Massachusetts General Hospital
Erna Lenters—ERL, IFCC, NGSP
Kuanysh Kabytaev—Univ. of MO
Curt Rohlfing—Univ. of MO, NGSP

Steering Committee members not present:

Robert Cohen—University of Cincinnati
Philippe Gillery—University Hospital of Reims (FR), IFCC Scientific Division
Elizabeth Selvin—Johns Hopkins University

***Member of the NGSP Steering Committee**

1) **Welcome and Introduction—David Sacks, Chair, NGSP Steering Committee**
D. Sacks welcomed those in attendance and those present introduced themselves. D. Sacks thanked J. Felberg for her service to the NGSP and welcomed new manufacturer representative Monica Swenson to the Committee. The 2021 minutes were approved.

2) **NGSP Progress Report—Randie Little , NGSP Network Coordinator**
- NGSP Network Monitoring
  - The PRLs (3) and SRLs (11) continue to demonstrate excellent comparability (May between-lab CVs were 1.29% and 0.95% for the PRLs and SRLs, respectively).
  - There are currently two PRLs, the CPRL and EPRL, APRL dropped out and is currently not active.
  - ASRL#2 in China switched from the Variant II Turbo 2.0 method to the D-100 (ASRL#3).
  - We continue to experience shipping issues with ASRL#3, and are generally getting their monitoring data late because of this.
  - 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.
  - Monthly between-lab CVs for the NGSP network were all <1.2% over the past year.
- Long Term Quality Controls (LTQC)
  - Provides another estimate of long-term consistency of NGSP results
  - Three levels of frozen whole blood (5.1%, 7.9% and 11.2% HbA1c) were analyzed from 2010 to 2019.
  - The original LTQC samples were replaced by new LTQC samples analyzed from 2018 to the present (5.0%, 7.5% and 10.0%).
  - Analyzed monthly by Missouri SRLs and quarterly by all SRLs.
  - Results show consistency in SRL results over time since 2010.
- NGSP Certification
  - The number of certified methods continues to increase, while the number of laboratories has leveled off.
  - There are 300 methods and ~130 laboratories currently certified.
  - Most certified labs are Level I and are outside of the U.S.
- Status of HbA1c Measurement (CAP data)
  - Current CAP limits (2013-2021): Each result must be within ±6% of NGSP assigned target value (mean of 8 SRLs, multiple results from each).

- 2019 proposed CLIA amendment: A Roadblock to Further Improvement in HbA1c
  - CMS and CDC proposed a rule change to update proficiency testing regulations under CLIA 88
  - They proposed making HbA1c a "regulated analyte" with an acceptance limit of ±10%.
  - The proposed loosening of acceptance limits (from ±6% to 10%) would reduce the effectiveness of HbA1c assays and compromise the safety of patients.
- 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.
- CAP 2022A survey
  - Five fresh whole blood samples
  - 2022A CAP Pass Rates (±6%)

Specimen	NGSP Target (% HbA1c)	Acceptable Range (±6%)	Pass rate % (Low/High)	Cumulative Pass Rate % ±6%
GH-01	8.42	7.9-9.0	87.0/100.0	97.5
GH-02	6.31	5.9-6.7	92.4/100.0	98.3
GH-03	9.05	8.5-9.6	90.7/100.0	96.9
GH-04	5.18	4.8-5.5	92.9/100.0	98.5
GH-05	6.72	6.3-7.2	92.3/100.0	98.6

  - Cumulative pass rates were all >96%.
  - For individual methods, pass rates ranged from 87% to 100%.
  - All-method CVs have dropped over time since 2000.
  - All-method CVs for the 2022A survey were all <3%.
  - Between-lab CVs by method type show that there are samples of all method types that perform well, and only one method showed a CV>3%. The three POC methods that appeared in the survey performed well.
  - Biases by method type showed that the degrees and directions of bias were not specific to particular method types.
  - CAP data Summary (2022A)
    1) Method-specific, between-laboratory CV's ranged from 1.0% to 3.5%.
    2) Overall, 83% of laboratories are using methods with CVs < 3% at all five HbA1c levels.
    3) All-method CVs for the most recent survey ranged from 2.2-2.7%.
    4) Overall Pass rates are between 96.9 and 98.6% for the current 6% limits
- Hb variant interference publication: Rohlfing, et al. Evaluation of interference from hemoglobin C,D,E and S traits on measurements of hemoglobin A1c by fifteen methods. Clinica Chimica Acta 2021:522;31-35
  - One ion-exchange HPLC method and two POC immunoassay methods showed clinically significant interference from one or more of the four common variants (AS, AC, AE, AD).
  - E. Lenters has since evaluated interference for two of these methods and did not find clinically significant interferences.

- Conclusions
  - The NGSP network is still doing well with very low CVs.
  - CAP survey results show that the all-method CVs (including all laboratory results) have been <3% for the last 4 surveys. We hope to see this continue.
  - Measurement of HbA1c continues to improve but there are still a few methods with Hb variant interference..
- Raw data from Manufacturers
  - After last year's Steering Committee meeting, we began requesting raw data from manufacturers submitting certification data for POC methods.
  - Between April and July 2022, data from 12 manufacturers for 38 methods were requested; all complied.
  - All raw data matched data sent for certification.
  - There were 2 manufacturers (11 methods) that failed certification.

Discussion:

APRL and ASRL#3

D. Sacks asked if we know why APRL has not been active and if their absence presents a problem. R. Little replied that we do not really know, they had some issues with their instrument and her impression is that it will eventually come back online. The CPRL is still functioning and the EPRL is still active as a backup, so it does not present a problem at this time. D. Sacks asked if the issues with shipping to the SRL in China are due to Covid. R. Little replied that shipping to China has always been difficult, but since Covid problems with shipping to China, and for that matter many other countries, have been worse.

Variant Interference

D. Sacks asked about the discrepancies between the findings from the 2021 paper and the recent study by E. Lenters, why were the results different for two of the methods? R. Little said it could be differences in reagent lots or software versions. C. Rohlfing added that with ion-exchange methods such changes can cause differences in how peaks are separated resulting in changes in interference. R. Little noted that for the DCA Vantage the difference with AS was seen previously when CAP included a AS sample in the survey. She did not know why we are seeing this, they did not see it when the method was evaluated previously a number of years ago. E. Lenters said she looked at the interferences using both her and the Rohlfing et. al criteria and both showed no clinically significant interference in her data. However, the interferences in both studies were in the same direction and were "borderline". One good thing is that Tosoh is now checking their ion-exchange methods for interferences from common variants each time reagent lots or software is changed. E. Lenters and C. Rohlfing said that the distribution of values for the variant samples were not ideal, there were very few high HbA1c values for some, it is difficult to obtain these samples. R. Little noted that the results were actually similar between the two studies, it is just that in one the differences reached clinical significance and in the other they did not. E. Lenters noted that both groups have seen interference from AE with the b101 method, and asked E. Noll if the company was previously aware of this. This represents a significant concern when this POC device is used in Asian countries where AE is very prevalent. R. Little agreed, noting that even if the interference is listed in the package insert, users may not be aware that the patient has HbE trait. D. Sacks added that users do not always pay attention to package inserts. E. Noll said that she does not know what the current situation is with the b101 method at Roche as she is not in the POC division, but said she would address this with POC R&D. D. Sacks asked about clinical significance when looking at interferences, how do you determine what constitutes clinical relevance? What does the ±6% actually mean? R. Little noted that in the paper there is a table showing the actual biases at 6 and 9% as well as whether the differences were statistically or clinically significant. C. Rohlfing and E. Lenters noted that defining clinically relevant differences is difficult, when clinicians are asked what they consider relevant they give many different answers, E. Lenters has done surveys that demonstrate this. They found some nurses consider differences as small as 0.2 or even 0.1% NGSP to be significant. Physicians seem to understand a little more but still some make changes in therapy based on very small differences. When subsequently asked if they felt they needed help in interpreting results most said no. These studies were done in the Netherlands, R. Little and E. Lenters agreed that it would be good to do these kinds of surveys in other countries including the U.S. E. Lenters said that students actually developed an app to assist primary care nurses with interpretation of the results but they do not use it. R. Little said the lack of understanding of variability is a problem for other analytes as well, not just HbA1c. G. John said that in terms of clinical relevance we are talking about analytical effects, there is also the issue of whether variants are having biological effects. D. Sacks said from a practical clinical standpoint there is the issue of diagnosis in addition to management. If an instrument has a positive bias and the results are being used to screen for or diagnose diabetes, you will over-diagnose people, and vice-versa. In terms of management, he has asked clinical experts on the NGSP Clinical Advisory Committee what should be considered a clinically relevant change in HbA1c, the general answer is 0.5%. The FDA actually uses 0.5% as their criterion for new diabetes therapeutics. However, what is used in everyday patient care may be completely different. E. Lenters said for variants she looks at whether the distribution of the variant sample differences are within the dispersion of the differences for non-variant samples. Is looking at the variant vs. non-variant samples at fixed cutoffs, i.e. 6 and 9% HbA1c, necessarily appropriate given the limited distributions of the HbA1c results for the variant samples? R. Little said even though the variant studies may not be perfect but they can give a good idea of whether interference is present. M. Steffes noted that many papers have been published over the years based on data from the DCCT/EDIC study looking at diabetes complications over time. Embedded in this is the idea that the HbA1c results have remained constant over

decades. There is a very high level of trust in the laboratory processes that maintain these results. R. Little said that the EDIC patients get results from other labs with the central lab only analyzing one result per year, and asked M. Steffes if they ever hear about discrepancies. M. Steffes said there were times where a GRADE study patient's HbA1c result would be within the study criteria locally, but the result from a sample sent to their laboratory would be out, although the actual differences between the results were small. The result from their laboratory is trusted, which is a statement about how the University of Missouri laboratory, which their lab has been anchored to over the years, has been able to maintain consistency over time. In terms of variants, their laboratory gets push back from physicians, they report that a variant was detected but the physicians want to know why they do not identify which variant it is. What about reporting of elevated HbF? C. Rohlfing said that in the case of elevated HbF the lab does not provide a comment, unless the elevated HbF is above the level at which non-interference is documented. M. Steffes said that on HPLC elevated HbF can affect HbA1c measurements, R. Little said that is only true for some methods. D. Sacks noted that CAP sometimes includes AS in their survey and they see that there are methods where there is AS interference but a result is still reported. They would like to periodically include other variants but the blood supplier says they are not able to collect enough blood to send to all of the participating labs.

Raw Data from Manufacturers

E. Lenters asked if the raw data received from the manufacturers showed the date and time stamp in addition to the result, R. Little said yes. D. Sacks asked what will be done if data are requested from a manufacturer and they do not send it. R. Little said the data analyses will not be performed, so far this has not happened. D. Sacks asked if the number of methods that failed is consistent with what has been seen in the past, R. Little said it is hard to say since they were new methods. E. Lenters suggested requesting the raw data for all of the methods, D. Sacks agreed that this was a good idea. R. Little said this can be done and agreed to do so. There may be cases where the raw data cannot be printed out, but in that case they could provide pictures. M. Swenson asked what kind of raw data format is acceptable, R. Little responded that any format is acceptable as long as it includes the date, time and result. Printouts from most lab instruments and even many POC devices contain this information, if not they have to provide pictures.

3) Clinical Advisory Committee Meeting Update—David Sacks

- The CAC met at the 2022 American Diabetes Association annual meeting in New Orleans.
- The purpose of the CAC is to facilitate two-way communication between the NGSP and the clinical community.
- The CAC is composed of representatives from major global clinical diabetes organizations.
- Summary
  - R. Little presented an update on NGSP progress.
  - There were two main topics of discussion, both related to continuous glucose monitoring systems (CGMS).
    - Sue Kirkman presented an update on the current status of CGMS
      1) Much has changed with CGMS over the last decade.
      2) The use of CGMS among T1 diabetes patients has gone up dramatically.
      3) There are financial costs associated with increasing use of CGMS.
    - Guido Freckmann, chair of the IFCC working group on CGM, gave a presentation on efforts to standardize CGMS.
      1) Goal of the WG is to define the standard procedures used to assess the analytical performance of CGMS.
      2) He presented data from a recent study where a group of patients were put on two different CGM systems.
         - The results from the two systems were not the same.
         - 11% of the results would have led to different treatments.

Discussion:

CGMS

D. Sacks asked D. Nathan if he knew the percentage of pediatric T1 diabetes patients in the U.S. that are currently using CGM. D. Nathan replied that he did not have the latest numbers from the registry, but he estimated that about half of these patients are on CGM and the numbers are rising. The use of hybrid systems

that include insulin pumps is also rising, the accuracy of CGMS is central to these developments. D. Sacks noted that there is some talk of using CGMS more often in patients with T2 diabetes. D. Nathan said that much of this talk is being promoted by the CGMS manufacturers and those with ties to those companies. The actual evidence supporting the efficacy of CGMS use is much less clear than is the case for T1. D. Sacks said there was a recent article which even discussed the use of CGMS in people without diabetes, for example athletes. Regarding standardization of CGMS, it is a difficult problem. When different systems produce different results it is not easy to determine which one is right, you cannot simply measure blood glucose because it is not the same thing as interstitial fluid glucose measured by CGM. At the same time it is really important because CGM is now so widely used, and in particular some of the newer systems interface with an insulin pump. If the patient is injecting their insulin they are supposed to utilize a meter, but with these newer hybrid systems the CGMS determines when and how much insulin is injected. D. Nathan said the measurement that is used to assess CGMS and compare the results to lab measurements is the MARD (mean absolute relative difference). Current CGM monitors are moving toward <10%, where they used to be 12-15%. The fact that they measure glucose about every 5 minutes helps overcome some of the inaccuracies, because even if a single result is off there are many measurements contributing to the average. There will always be a systematic difference between CGM and blood glucose, because the CGMS measure glucose in interstitial fluid and there is a lag time between the two. Even so there are now several hybrid systems on the market and overall they seem to perform well in patients with T1 diabetes. J. Higgins said that a bias in the individual sensor will make the long-term measurements inaccurate. G. Freckmann actually put out a recent paper where they used 4 different sensors in ~25 subjects. The average bias for the Dexcom G5 was about 3%. This means that because of the low CVs for HbA1c, HbA1c is actually going to give a more precise measurement of mean glucose even if the patient wears the CGMS for 120 days. D. Nathan said there has been the suggestion from the CGMS manufacturers that CGM can replace HbA1c. However, that is not possible for patients who are not on CGM, which is currently the vast majority of people with diabetes. Also, the two measurements do not provide the same information, and the relationship between HbA1c and risks for complications have been established by results of long-term trials. This has not been, and likely never will be, done for CGM. He did not think CGM will ever replace HbA1c in terms of its clinical utility. Getting the HbA1c measurement is easier, it is more precise, and it is much less expensive. G. John agreed, and noted that there is much work to be done in terms of standardizing CGM. It does need to be done given that more and more T1 patients are using CGM. R. Little said there are clinicians that are using the GMI (Glycemic Management Indicator) estimates from CGM and trusting them more than HbA1c. D. Sacks said that people need to be made aware of the issues with CGM, as there are people pushing for CGM to replace HbA1c including in symposia at national meetings.

4) CMS Guideline Update—David Sacks

- Proficiency Testing (PT)
  - Evaluation of lab performance against pre-established criteria by interlaboratory comparisons
  - Also termed EQA (external quality assessment)
  - 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 is largest provider of PT material
- 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%
- CAP 2010, 2012 & 2013 GH2A Pass Rates at ±6% HbA1c Cutoff

	2010	2012	2013
Low (5.1/5.6%/6.07)	91.0	95.8	93.4
Medium (6.0/7.2%/7.1)	91.6	92.9	95.3
High (8.4/9.4%/9.3)	88.6	92.5	94.3

- As the CAP criteria were tightened, the comparability of HbA1c results improved dramatically.
- Proposed CAP PT Criterion 2020: ±5%
- CLIA Proposed PT Rule 2019 (CLIA 88 update)
  - Hemoglobin HbA1c would become a regulated analyte
  - Criterion for acceptable performance: Target ±10%
- Effect of Change in PT
  - True HbA1c is 6.5%
  - If criterion is ±5%, acceptable value is 6.2% - 6.8%
  - If criterion is ±10%, acceptable value is 5.8% - 7.2%
- 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%
  - CAP elected NOT to reduce criteria from ±6% to ±5% in 2020
- Potential Outcome of CLIA Proposal
  - Accuracy of HbA1c assays likely to deteriorate
  - Patient care likely to suffer.
- Response to CMS 2019 Proposal
  - Presented at CAC meeting at ADA in June 2019
  - 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).
- CAP 2010, 2012, 2013 & 2022 GH2A Pass Rates at ±6% HbA1c Cutoff

	2010	2012	2013	2022
Low (5.1/5.6%/6.07)	91.0	95.8	93.4	98.5
Medium (6.0/7.2%/7.1)	91.6	92.9	95.3	98.3, 98.6
High (8.4/9.4%/9.3)	88.6	92.5	94.3	97.5, 96.9

- 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

- What Did CMS Do? Final rule published July 11, 2022

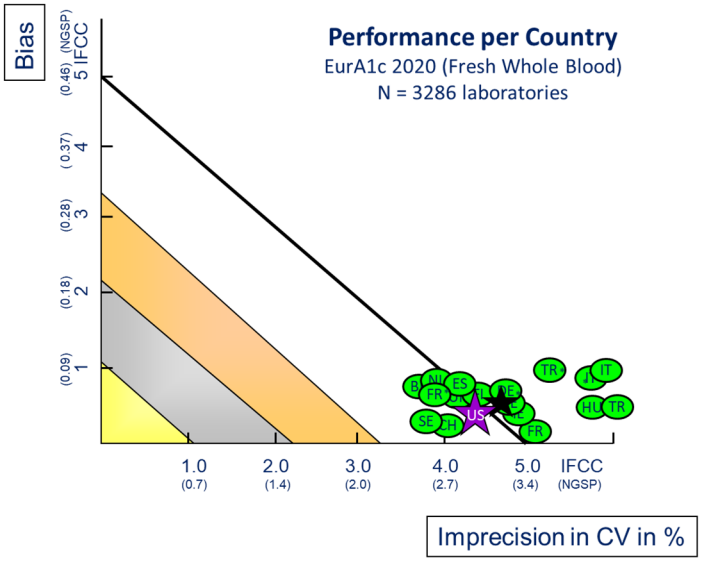
- CMS Response
  - Not persuaded by comments
  - Acknowledge improvement in accuracy
  - Concerned that tighter criteria will limit access to testing
  - Laboratories that use non-commutable PT will be punished
  - Looser CLIA acceptance limits will not cause manufacturers to allow accuracy to deteriorate
- Final CLIA Rule
  - Acceptance limits for HbA1c are 8%
  - Effective July 11, 2024
- Implications of New CLIA Regulation
  - CMS indicated accreditation organizations can require labs to meet more stringent criteria
  - Option of using 8% and adding more stringent limit "…for educational purposes"
  - CAP will consider options
  - Plan to engage clinical community

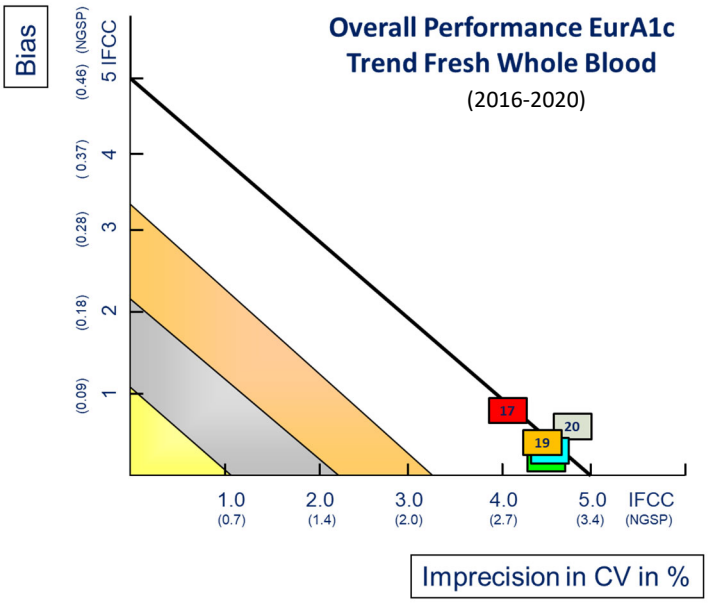
Discussion

CLIA Final Rule
R. Little noted that in the CMS response they stated that PT providers have the flexibility to require labs to pass criteria that are more stringent than CLIA. D. Sacks said that is what they stated, but based upon the wording of the CLIA law CAP believes that they will not be able to actually fail labs as long as they meet the CLIA criterion. D. Nathan said this is egregious on the part of CMS, it is harmful for patients. He did not think established manufacturers would have any reason to lower quality, although there could be newer vendors that bring in assays of lesser quality. HbA1c has been an important part of improving the quality of patient care over the recent decades. He suggested that clinical organizations go to the press, as this could adversely impact patient care and it represents an unnecessary step backwards. D. Sacks agreed and noted that this requires pushback from the clinical community. D. Nathan felt that this issue would resonate with the ADA leadership. R. Little said that if CAP finds out that they cannot fail labs as long as they fall within the CLIA limits it will be a bigger problem, but if it turns out they can, then we need to encourage them to move forward. D. Sacks agreed but said that CAP does not know at this point. There has been strong reaction at CAP regarding this, CAP has seen HbA1c as a "poster child" for improving test quality. D. Nathan asked D. Sacks to circulate the original CMS final rule document to the meeting participants, D. Sacks said he would do this. Regarding CMS concerns about limiting the availability of HbA1c tests, what is the evidence to support this. HbA1c is currently widely available even under the current CAP criteria. D. Sacks thought it might have to do with PT surveys other than CAP that are used by a much smaller number of labs. Since these surveys do not use commutable materials they would likely fail a larger number of labs under more stringent criteria. E. Lenters asked how many laboratories participate in surveys other than CAP, D. Sacks said he did not know, he has not been able to obtain that information. However, we do know it is much smaller number of labs than those that participate in CAP. R. Little said the other surveys use lyophilized materials because they are much more stable, and those surveys are less expensive than CAP. R. Little noted that manufacturers would still have to pass the NGSP criteria in order to be certified, and that will not change. E. Lenters said that in Germany there is the opposite problem. E. Noll said Germany is tightening their criterion to 3% for internal controls (mmol/mol). This is very challenging for manufacturers. R. Little asked how they assess the internal controls and who looks at the data and decides if the lab passes or fails. E. Noll said it is part of the inspection and accreditation process, if the lab falls outside of the limits they cannot run the test. E. Lenters said 3% is not realistic, it leaves little room for variability, especially in the low end of the range. Clinicians came up with the 3% criterion, they do not understand that there is uncertainty around the measurements. Manufacturers have performed their own tests and even the best available methods cannot consistently meet this criterion. D. Sacks said it is likely that this law will have to be changed since no method can meet this requirement, otherwise the test will become unavailable. D. Sacks asked the manufacturer representatives what they thought about the new CLIA rule, will this cause lower test quality? M. Swenson said no, the products have already been developed to meet current standards and there is no reason to change them. E. Noll added that their product standards have to apply globally. D. Sacks asked if manufacturers might lower test quality to save money, E. Noll, M. Swenson and E. Lenters said no. E. Lenters noted that they still have to pass IFCC and NGSP criteria. D. Sacks and R. Little acknowledged this but said the CAP criteria are still important.

5) Update IFCC Network—Carla Siebelder

- After working with Cas Weykamp for 30 years, I replaced him as the Network Coordinator after his retirement in 2020.
- C. Weykamp was recently presented with a Dutch royal award, Knight in the Order of the Dutch Lion, for exceptional achievements in clinical chemistry and the worldwide standardisation of blood tests for diabetes in particular
- Since early 2020 Covid-19 has posed challenges for our studies in terms of planning, personnel and logistics.
- There are currently 19 approved laboratories and 2 candidate laboratories in the IFCC laboratory network. They are spread around the globe and include labs in the U.S., Europe, South America and Asia.
- The IFCC/NGSP master equation is still being monitored via sample comparisons performed twice a year. The equation remains very stable.
- EurA1c: A Project of the IFCC C-EUBD & EQA/PT organisers
  - Once a year EQA Organisers use the same 2 samples
  - 2020: 22 countries - 27 EQA - 5120 laboratories
  - Criteria were developed by the IFCC Task Force and a based on TAE of 5 mmol/mol
  - Results (will be published in September):





Discussion:

EurA1c
C. Siebelder said the results show that all of the participating countries are well standardized, but imprecision still varies among them. The main focus at this point should be reducing imprecision. Also, the 2020 study was impacted by the pandemic, they were unable to draw blood from diabetic subjects so they were only able to use two samples from non-diabetic subjects. It is interesting that the overall mean performance in the 2020 EurA1c study was very close to that obtained from the U.S. based on the CAP survey. M. Steffes asked where the EurA1c results are published, C. Siebelder replied that they are available on the IFCC HbA1c standardization web site (ifcchba1c.org). R. Little asked if the results of the earlier studies have been published in a journal, C. Siebelder said only the first (2016) study. There are plans to publish another paper. H. Vesper asked about the differences among countries, how do you explain this? C. Siebelder said it could be that some countries focus more on quality than others, or there could be differences in education. E. Lenters said it also depends upon what assay methods the different countries are using, and technician training also varies.

Master Equation
It was noted that the ME has remained very stable, especially over the last several years.

D. Sacks thanked everyone for their attendance, the meeting was adjourned at 4:20 PM.
Minutes prepared by C. Rohlfing 8/24/2022.