Meeting of the NGSP Steering Committee
Minutes
Sunday July 27, 2014 3:00 PM – 5:30 PM
Fairmont Chicago, Chicago, IL

Participants:

*David Sacks —NIH, Chair, NGSP Steering Committee
*Randie Little—Univ. of MO, NGSP Network Coordinator
*Christine Flandre—Sebia
*Phillip Gillery—American Memorial Hospital (FR), IFCC Scientific Division
*W. Greg Miller—Virginia Commonwealth Univ.
*Curtis Parvin—Bio Rad Laboratories
*Tony Prestigiacomo—Bio-Rad Laboratories
*Elizabeth Selvin—Johns Hopkins University
*Michael Steffes—University of Minnesota
*Hubert Vesper—CDC
*Cas Weykamp—Queen Beatrix Hospital (NL), IFCC Network Coordinator
***Member of the NGSP Steering Committee**

David Armbruster—Abbott Diagnostics
Shawn Connolly—Univ. Of MO, NGSP
Anita Durairaj— Univ. Of MO
Emma English—IFCC Task Force on HbA1c Std.
Dennis Mertens—Roche Diagnostics
Violeta Raneva—ReCCS Japan
Scott Reutten—Abbott Diagnostics
Curt Rohlfing—Univ. of MO, NGSP
Alexander Stoyanov—Univ. of MO

Steering Committee members not present:

Robert Cohen—University of Cincinnati
Garry John—Norfolk and Norwich University Hospital (UK), Chair, IFCC Integrated Project on HbA1c
David Nathan—Massachusetts General Hospital

1) Welcome and Introduction—David Sacks, Chair, NGSP Steering Committee

D. Sacks welcomed those in attendance including incoming manufacturer representative Tony Prestigiacomo and thanked outgoing manufacturer representative Scott Reutten. Those present introduced themselves.

2) The 2013 Steering Committee minutes were approved by the members present.

3) NGSP Progress Report—Randie Little , NGSP Network Coordinator

- NGSP Network Monitoring
  - The PRLs and SRLs continue to demonstrate excellent comparability.
  - Monthly between-lab CVs for the NGSP network were <2% over the past year.
- Certification
  - There are ~130 methods and ~130 laboratories currently certified.
  - The number of certified methods and laboratories has recently leveled off, this may be due to more labs/methods failing because of the tightening of the criteria in September 2012.
  - The criteria were tightened again this year which might result in fewer certified labs/methods.
  - Most certified labs are Level I and are outside of the U.S.
  - There are a few clusters of Level II labs, most notably in Colombia.
- Current criteria
  - Current Manufacturer Certification Criteria: 37/40 individual results must be within ±6% of the SRL (one SRL) mean.
  - Current CAP limits (2013-2014) :Each result must be within ±6% of NGSP assigned target value (mean of 7 SRLs, multiple results from each).
- Changes in Certification Failure Rates: First 6 months 2013 (±7%) vs 2014 (±6%)

	2014	2013
Manufacturer	15.5%	7.9%
Level I Lab	18.6%	5.1%
Level II Lab	16.0%	6.3%

- CAP Data
  - There has been much improvement in within and between-lab variability since 1993
  - There has been little improvement over the last several years (2010-2014).
  - 2014A survey
    - There are two groups of methods that clearly showed high bias which may explain the decreased overall pass rates compared to the previous survey.
    - The method-specific bias was over 0.30% HbA1c for 7 methods for at least one level.
    - Method-specific, between-laboratory CV's ranged from 0.5% to 5.6%. CVs were <5% at all levels for all but one method.
    - Overall pass rates were 88.8 to 94.2% which is lower than the rates for the previous survey.
    - The all-method CVs are still not consistently ≤3.5%.
    - There is still room for improvement!
    - Pass Rates

      1) 2014A

Specimen	NGSP Target (% HbA1c)	Acceptable Range **(±6%)**	Pass Rate % (Low/High)	Cumulative Pass Rate %
GH2-01	6.49	6.1-6.9	57.0/100	88.5
GH2-02	6.97	6.5-7.4	60.7/100	89.1
GH2-03	9.65	9.0-10.3	74.5/100	94.2

      2) 2013A

Specimen	NGSP Target (% HbA1c)	Acceptable Range **(±6%)**	Pass Rate % (Low/High)	Cumulative Pass Rate %
GH2-01	7.11	6.6-7.6	77.5/100	95.3
GH2-02	9.32	8.7-9.9	80.0/100	94.3
GH2-03	6.07	5.7-6.5	63.6/100	93.4

    - All-method CVs
      1) All-method CVs are still consistently ≤3.5% which is the goal
      2) The CVs for the low, middle and high levels in the 2014A survey were 3.8%, 3.8% and 3.4% respectively.
- Issues for discussion
  - Change the total imprecision requirement limit for SRL certification (CV currently must not be statistically significantly >3%) to 2% (this was agreed to by the committee)
  - Manufacturer certifications failures/possible misuse of certification
    - Currently if a method fails the manufacturer must determine the cause of the problem, then document the changes made and how this will affect customers prior to re-attempting certification. For POC methods they are also required to submit data from 3 different lots.
    - In this case a manufacturer submitted certification data from 6 lots
      1) Three lots passed, the other three failed.
      2) Although the lots used for certification are included on the list of certified methods, putting the method on the list implies that the method meets the certification criteria even though in this case half of the lots failed.
      3) The manufacturer says that the lots that passed are a different type than those that failed (type B vs. C) and the ones that failed are not on the market.
    - Another manufacturer stated that they do not fill reagent packs until they receive notice of certification.
    - According to the NGSP protocol methods must be operated in the same manner as a customer
    - Questions:
      1) Should manufacturer certification be used to certify reagents prior to being placed on the market?
      2) Can we (should we) control the way the certification is used?
      3) Should the manufacturer indicate up front whether the reagents are currently on the market?
  - Acceptable limits for variant interference (Compared to boronate affinity SRL3 and after calibration adjustment)
    - 2000-2010 (6 papers): S, C, D & E, acceptance limits for clinical significance were within ±10% at 6 % 9% HbA1c (based on regression vs. AA samples)
    - 2012 (1 paper): S, C, D & E, acceptance limits for clinical significance tightened to ±7%

- 2014 abstract: rare variants, acceptance limit was defined by 99% prediction interval of the regression line for AA results (poster in handout)
- Questions
  1) Should we tighten the clinical significance limit to 6%?
  2) Should we use some other calculation?

Discussion:

Increase in percentage of methods/labs failing

P. Gillery asked about the absolute numbers of labs, R. Little said there were ~130 each of certified methods and laboratories for the whole year so roughly half of those numbers for the first two quarters. D. Sacks asked if the methods and labs that failed were generally marginal with the earlier criteria, R. Little said she did not look at that specifically. In general that is the case with methods but with labs they can sometimes be using a good method but there may be a shift in calibration resulting in failure due to bias. C. Weykamp asked what happens if the 2014 criteria are applied to the 2013 data, are the number of failures then similar for 2014 vs. 2013? The increase in failures is substantial. R. Little said she has not looked at this, D. Sacks noted that she had looked at this last year with the 2013 data when the committee was considering tightening the criteria.

Change in imprecision limit for SRLs

M. Steffes asked if within-lab SRL imprecision is routinely monitored, R. Little responded that it is only assessed when a new SRL is certified but the SRLs are monitored monthly against each other as well as the CPRL. S. Ruetten asked if there would be any impact as a result of this change, R. Little said no, the current SRLs meet the 2% criterion anyway. D. Sacks asked if we need to notify the SRLs of this change and when it would be made effective. R. Little said that we could notify the SRLs, it will become effective immediately but will only apply when new SRLs are certified which is infrequent.

Manufacturer certification failures/potential misuse of certification

D. Armbruster noted that the NGSP does not certify every lot, only the method, so it is sort of "luck of the draw". R. Little said that manufacturers usually submit data for only one lot. S. Reutten said that it is not the responsibility of the NGSP to serve as quality control for manufacturers, they should design methods where all lots will pass then use a representative lot to certify the method. R. Little noted that a manufacturer could submit data from multiple lots hoping that at least one will pass, S. Reutten agreed that this is an abuse of the certification process. R. Little said that in this case it appears that the process of using the instrument is different between the two types even though it is the same instrument. D. Armbruster added that at a minimum the manufacturer should have been more transparent regarding which lots are the ones are on the market vs. not. S. Reutten said this process should be sorted out prior to the instrument entering the market. The NGSP and IFCC both offer the opportunity for assistance when manufacturers design a product prior to market entry. During this design phase the best process needs to be determined; then, when the method is ready it could be certified prior to market entry. T. Prestigiacomo agreed, noting that the NGSP provides value-assigned samples that manufacturers can use in method development. The NGSP cannot police every lot. D. Mertens asked if lot-to-lot variations are mainly observed with POC methods. R. Little said that it is confusing with POC because there are often many lots available. C. Flandre said that when POC works like larger assays where large amounts of reagents are manufactured at one time, they can be normalized and thoroughly tested such that you have a better chance of obtaining consistency over thousands of tests performed by end-users. When it comes to testing of individual units as is the case with many POC methods, the best you can do is a random sampling. Even if doing the best job possible, there is no guarantee that the remaining units on the shelf will perform in the same way. This is why all POC methods should not be placed in the same basket. R. Little noted that the manufacturer in question may have simply been testing the newer method type, but this was not made clear when the data were submitted for certification. Should we specify that manufacturers need to indicate at the time data are submitted for certification whether the method is currently on the market? Now that we know that the 3 lots in question are not on the market, should we go ahead and certify the method? The problem is that if we fail the method, they have to then submit data from 3 different lots if they try again but they have already submitted 3 lots that passed. M. Steffes said he does not understand why there are so many lots, typically in laboratory assays we use lots that may be good for a year or more, why should POC be different? C. Flandre said stability may be an issue for some methods, C. Weykamp added that some POC methods have shown rapid deterioration of the cassettes/reagents used. Maybe the expiration date and lot numbers should be stated on the certificate. R. Little noted that the lot numbers are listed on the certificate and certified methods list, D. Sacks said the problem is that no one looks at them and the certification is good for one year. R. Little said if the lot numbers that failed were on the

market we would definitely have to fail the method but they are not. D. Sacks noted that the difference between the three lots that passed vs. the three that failed are dramatic, how come the manufacturer did not see this? C. Flandre added that they should have noticed this in their testing, unless there was a problem that happened after testing such as a stability issue. Sometimes with a new product there can be an issue with shelf life. D. Mertens said it may be an issue with their quality control processes, in the end you want to have a method that will continue to be traceable to the NGSP after it is on the market. S. Reutten said that if all six lots were subjected to the same internal quality control processes and calibrated using the same IFCC calibration materials, and all six lots were deemed acceptable, then all six lots are suspect. R. Little said she does not know what calibrators they used or what their internal QC processes are. D. Sacks asked how many lots are normally submitted, R. Little said usually one lot. D. Sacks said if we certify type B there is nothing to prevent them from releasing type C. R. Little asked if we could certify B and specify this on the list and certificate. D. Sacks asked what the criteria are for saying that one method is different from another method, should these be considered to be two different methods. S. Reutten said they should have two different registration IDs if they are separate products, R. Little asked if this is true in every country, S. Reutten said yes. Unless they have two separate product IDs they should be considered the same product. R. Little said the manufacturer said the latest type is a different test kit package with a different procedure. D. Sacks said the question is: are they different methods? If so pass the one that passed and fail the one that failed. D. Sacks asked how we could find out if they have two different product IDs. S. Reutten said the manufacturer could provide this information. R. Little asked if we should go ahead and certify the first type if it has a different product ID from the second, the committee approved. WG. Miller said there is a danger here, the manufacturer failed to indicate that these were two different methods. The lots were submitted as if they were all from the same method, we are not sure at this point that they are different, it is possible that a manufacturer could submit a whole series of lots in the hope that one of them passes and the method gets certified. We need clarification on how these are promoted and sold in the marketplace, if they are promoted and sold as basically the same thing they should be failed; if they are promoted and sold as two different methods the method that passed could be certified. S. Reutten asked if they indicated that the newer method type was indeed a new method, R. Little said that after she questioned them they submitted a description of the two different procedures. They use the same instrument but the procedures for getting the sample into the product are different. C. Flandre noted that this sounds like two different products, but sometimes there are reasons not to claim the two are different. D. Sacks said this information was not submitted up front, WG. Miller reiterated that there is the risk that the manufacturer is using a manipulative process to obtain certification. S. Reutten said that another possibility is that there is a lack of predictability in the performance of their product which would make their QC and calibration processes suspect. R. Little asked if she should find out if the two types have two different product IDs then inform the committee in order to make a decision. This was agreed. C. Flandre said we need to discourage companies from doing this in the future. R. Little said there are a few examples where companies have different products under different names from the same company, one may be cheaper but not as good, the sampling procedure may be different, they may be sold in different markets, etc. D. Sacks asked if we should require the product ID to be submitted along with the certification. Do the product IDs stay the same over time or can they change? D. Mertens said it can be different in Europe vs. the U.S. for the same product, the base number is identical but the last 3 digits may be different, a different method will have a completely different number. S. Reutten said the product IDs stay the same over time. The issue here is that manufacturers need a predictable process in obtaining the raw materials for their products such that if they produce multiple lots over the course of a year they should have predictable performance, any lot should be able to pass certification. S. Reutten said you can ask for the unique product ID. C. Weykamp and C. Flandre reiterated that the manufacturer should have noticed these differences between lots in development prior to attempting certification. R. Little said she can make sure that manufacturers only submit one lot in the future, and if a manufacturer still submits more than one lot for the same method she will tell them that if any lot fails the method fails. WG. Miller suggested randomly picking one of the lots. R. Little asked if we should ask manufacturers to specify whether the product is currently on the market. T. Prestigiacomo noted that manufacturers sometimes want NGSP certification in order to file with FDA and/or launch their product prior to it being on the market. R. Little said that if a product that is not on the market fails certification we do not need to be concerned about how changes made prior to another certification attempt will affect end users, this is a concern for methods that are already on the market. S. Reutten and T. Prestigiacomo noted that the FDA requires methods to be NGSP certified. D. Sacks asked: if a product is NGSP certified then gets FDA approval and goes on the market, then two years later it fails certification, then fails a second attempt after trying to fix the problem, who is responsible for notifying FDA? The manufacturer representative present responded that the manufacturer is legally obligated to notify the FDA. D. Mertens added that there are also customers that request a copy of the certificate as well as market pressure.

Acceptable limits for variant interference

R. Little said that when evaluating methods for variant interference we have to test for clinical significance because with methods that show tight correlations to the reference there can be statistically significant differences that are not necessarily clinically relevant. The original limits (based on the difference between the regression lines for the variant vs. AA samples) were ±10% relative at levels of 6 and 9% HbA1c, these were tightened to ±7% for the 2012 paper, do we need to tighten them again to ±6%? For our latest study of rare variants we could not use this scheme since we only had one or a few samples of each variant so we used the 99% prediction interval of the AA regression line as the acceptable limits. This was not originally a NGSP issue but it has become one due to the heightened interest in potential variant interference with HbA1c results, we post information on variant interference on the NGSP web site. D. Sacks said the NIDDK, which funds the NGSP, is very concerned about this issue. It is important to come up with criteria for stating whether there is interference that is clinically relevant. R. Little said that the original ±10% criteria seemed reasonable at the time, it was tightened to ±7% when CAP and NGSP tightened their acceptable limits to ±7%. T. Prestigiacomo said manufacturers have claims in their inserts based on FDA requirements, the concern is that there might be inconsistencies between these claims and what is listed on the NGSP website due to the use of different cutoffs. FDA looks at each individual variant sample being within the limits, not the regression line. R. Little noted that on the NGSP website we show methods that showed no significant interference at ±10% but also highlight the methods that passed ±7% in the most recent study. D. Mertens said that for the diagnosis claim approval from FDA the limits of ±7% were used, it is unclear what effect tightening the limits to ±6% would have. T. Prestigiacomo added that the study designs are different, S. Reutten said that the FDA is using ±7% as their limits now. D. Mertens asked what the argument is that ±6% is better than ±7% at the medical decision point. R. Little said that determining the performance required at medical decision points has always been a problem, about the only thing that has been stated is the significance of a change of ±0.5% HbA1c, that is more or less where the ±7% limits came from. C. Weykamp asked if anyone is checking to see if the criteria are met as they are changed. R. Little said the FDA will not change their criteria, while the NGSP and CAP have tightened their criteria over time. D. Sacks asked what the basis was for the FDA ±7%, the response is that it was based on NGSP. S. Reutten said it was derived at least somewhat from ±0.5% at the medical decision point, there was discussion of the clinical requirements at the meeting in Washington DC. R. Little said it sounds like the FDA criteria are effectively tighter if they require every point to be within the limits. S. Reutten responded that they evaluate bias based on regression going thru and including the medical decision point, also seeing if there is any significant slope indicating a change in the effect with HbA1c concentration. D. Mertens said he has not seen any recent scientific papers on the topic of potential medical effects of hemoglobin variants, for example there are claims that some methods have no interference from HbAE but no one really knows if red cell lifespan is affected and if so to what degree. Given the medical picture as a whole is there justification for ±6% vs. ±7%? D. Sacks asked if there are any methods that passed for a given variant at ±7% but would fail ±6%, R. Little said she has not looked at this specifically but it is likely that there would be a few instances. When the limits were tightened from ±10% to ±7% there was at least one method for which a variant passed the former but failed the latter. C. Weykamp noted that NGSP is based on 40 samples where the variant studies may use fewer samples which might justify wider limits. R. Little added that we cannot control the levels of HbA1c with the variant samples like we do for NGSP certification so the range may not be evenly divided across the range of HbA1c values. D. Sacks said that the CAP survey would be another way to test for variant interference but it is difficult to obtain enough blood, C. Weykamp noted the uncertainty of the NGSP value assignments for variant samples would be larger since fewer SRLs would be used. S. Reutten asked if the NGSP goal is to certify methods that are to be used for diagnosis as well as monitoring, if so the manufacturer could submit data to NGSP showing that their method is not impacted by variants. Manufacturers already have to do these analyses anyway, they could send the results to NGSP, the actual testing could be done by a independent laboratory rather than the manufacturer. R. Little said this is a FDA issue; the NGSP would be judging the manufacturer's data. T. Prestigiacomo suggested that the NGSP is already doing so to some extent by posting the variant information that is based on studies in the literature. D. Mertens said with public literature you can never be sure of the results, it depends upon the evaluation criteria used, whereas the FDA now uses 7%, this is true for monitoring and risk identification as well as diagnosis. D. Sacks noted that methods previously approved for monitoring would not have to be evaluated based on the FDA 7% unless the manufacturer decides to seek a diagnosis claim. S. Reutten suggested that the NGSP could have manufacturers submit the data to them regardless of whether the manufacturer is seeking a diagnosis claim. C. Weykamp suggested that all of the manufacturers may seek diagnosis claims for their methods. D. Sacks said we do not know if that is the case because the clinicians are using it for diagnosis regardless of if it is specified for that use. Also what if the method is sold outside the U.S.? D. Mertens responded that Asia is heavily affected by the FDA requirements; manufacturers are getting requests from Asia for methods to have the diagnosis claim, customers want this. R. Little asked what

kind of data manufacturers are required to submit to the FDA in terms of interference from common variants. S. Ruetten said 15-20 of each variant across the range of values and across the range of concentration of the variant, T. Prestigiacomo added that they concentrate on 6.5 and 8% HbA1c. The samples are value-assigned by boronate affinity (NGSP SRL). E. English suggested looking at data from previous studies of variant interference to see how methods would look if more stringent criteria were applied. D. Sacks asked if the consensus it to stay with ±7% for now, the committee agreed to this. S. Reutten asked if this would be applied to all of the samples and how frequent will the variant evaluations be? R. Little said we look at the difference in the regression lines (AA vs. variant) and will continue to do so. As far as the variant studies are concerned we try to do them periodically whenever there are a significant number of new methods coming out, one limitation is the ability to get variant samples, especially D and E. D. Sacks suggested getting samples from Thailand, R. Little said the shipping is difficult. C. Weykamp asked if frozen samples can be used or if fresh is needed, R. Little said aliquots of fresh samples are needed prior to freezing in order to be able to analyze the samples on multiple methods. C. Weykamp said that their laboratory gets a significant number of D and E samples, we can discuss this at a later time. Shipping as fresh whole blood would be expensive due to the number of shipments that would be required.

4) Rationale for Changes in NGSP Certification Criteria?—Curt Parvin

- Paper recently published in Clin Chim Acta (433 (2014): 259-263)
- Goal: Develop NGSP certification criteria that are comparable to CAP's criteria.
- CAP criteria:
  - 2011-2012 criterion
    - 3 samples are tested by the lab.
    - The assigned values are obtained from 7 SRLs testing each sample on 2 days in triplicate.
    - If 2 or 3 of the lab's results are within 7% of the assigned values the lab passes, otherwise the lab fails.
  - 2013 criterion
    - If 2 or 3 of the lab's results are within 6% of the assigned values the lab passes, otherwise the lab fails.
- New NGSP Criteria
  - 40 samples are tested once by the lab and in duplicate by a reference lab.
  - The lab's 40 sample results are compared to the reference lab's average values.
    - The allowable difference between a lab's result and the reference lab's average value is set to match the CAP requirement.
    - If N or more of the lab's 40 results are within allowable limits then the lab passes, otherwise the lab fails.
  - N is determined so the chance of a lab passing the NGSP criterion is approximately the same as passing the CAP criterion.
- Evaluating and Comparing NGSP Criteria
  - Consider a range of possible bias and imprecision combinations for a laboratory
  - For each bias and imprecision combination;
    - Compute the probability of passing the CAP criterion
    - Compute the probability of passing the new NGSP criterion for different values of N
  - Determine lab bias and CV combinations with the same probability of failing a criterion (contours)
    - Contours for failure rates of 0.1%, 1%, and 5%
  - Overlay contours to compare criteria
- Results: NGSP Criterion to Match 2011-2012 CAP
  - For an NGSP criterion requiring ≥ 37 out of 40 results to be within ±7%
    - If laboratory bias is < 3%
      1) The NGSP criterion is comparable to the CAP criterion at a 95% chance of passing
      2) At higher probabilities of passing the CAP criterion is more stringent
    - If laboratory bias is > 3%
      1) The NGSP criterion is more stringent than the CAP criterion
- Results: NGSP Criterion to Match 2013 CAP
  - The comparability of an NGSP 37/40 within 6% criterion to the 2013 CAP criterion is similar to the comparability of an NGSP 37/40 within 7% criterion to the 2011-2012 CAP criterion.
- Conclusion

- Based on these results the NGSP Steering Committee recommended that 37 of 40 results need to be within ± 6% of the NGSP for method certification beginning in January 2014.

Discussion

Change in Certification Criteria

C. Weykamp noted that when the CAP criteria and NGSP criteria were tightened in similar ways there were corresponding decreases in pass rates as would be expected; were these similar in proportion? C. Parvin said these calculations were based on modeling in which assumptions were made, it is important to look at the resulting data. D. Sacks noted that for CAP the 6% is rounded to favor the participant, so sometimes 6% and 7% may be the same. Another issue with the most recent CAP survey is some methods showed larger biases than usual vs. the NGSP targets which increased the failure rates for those methods. R. Little added that both the most recent and previous CAP surveys used the ±6% limits but the pass rates were clearly lower in the most recent one. C. Weykamp said it would be good to be able to test the theoretical model with actual data. S. Reutten asked how much data would be required in order to do this, how do we assess whether tightening the criteria is the correct thing to do? C. Parvin said that it is difficult to test for statistical differences when looking at relatively small differences in proportions, especially with limited sample sizes. R. Little said the goal is to achieve all-method CVs under 3.5% on the CAP surveys. C. Weykamp asked whether there is any action, formal or informal, on the part of CAP or NGSP whenever you see a consistent bias from survey to survey with a given method. R. Little said we have no way to do this other than to show everyone that this is happening in the summary reports on the NGSP web site. Sometimes we see it in the certification but sometimes there is a disconnect between performance on certification vs. on the CAP survey. D. Sacks said that if there is a large bias on the CAP survey labs fail, if this happens these labs have to document corrective action, they generally contact the manufacturers and demand corrective action. C. Weykamp noted in Denmark, the EQA organizer was not satisfied with the performance of one manufacturer, they sent a report to all of the countries of the EU and it became a big issue. We subsequently saw improved performance of the method in our EQA program. T. Prestigiacomo noted that the calculations assumed 3 of 3 samples passing on the CAP survey, does CAP now require this or is it still 2/3? D. Sacks it is still 2/3 for participants in the CAP survey. R. Little asked if there is a possibility of HbA1c becoming a CLIA regulated analyte, and would this be a good thing? D. Sacks said it is being considered; this would be good for patients as the penalties for failing a CAP survey are stricter. C. Weykamp said in Germany the penalties for failure are very strict but because of this the EQA criteria are very wide, the acceptable limit for HbA1c is ±18%. R. Little asked if CMS has the power to decide what the criteria are; D. Sacks said no. H. Vesper noted that the testing frequency would increase to three times/year. His understanding is that CMS has contacted PT providers to get input on which analytes are high priority and what criteria should be used.

5) Clinical Advisory Committee Meeting Update—David Sacks

- The CAC is composed of representatives from major clinical diabetes organizations. The purpose is to facilitate interchange between these organizations and the NGSP.
- The CAC met at the ADA in June 2014.
  - R. Little presented an update on NGSP progress.
  - There was a lot of discussion of hemoglobin variants.
  - There was a lot of discussion about ethnic differences in HbA1c
    - Elizabeth Selvin of Johns Hopkins University presented findings from a recent study that concluded there are no significant differences in HbA1c between ethnic groups independent of glycemia and HbA1c is a better risk predictor than glucose in these groups.
    - Bruce Wolfenbuttel of the Univ of Groningen presented data from a recent study that concluded that there are differences in HbA1c among ethnic groups that necessitate different thresholds and treatment goals.
- Issue of clinical recommendations listed on the NGSP web site
  - Representatives from the VA and CMS were concerned about the ADA clinical recommendations posted on the NGSP web site. They felt that this made it appear that the NGSP was endorsing the ADA guidelines but not all clinical organizations subscribe to these guidelines.
  - There was much discussion and disagreement regarding whether the NGSP should list any clinical guidelines on the web site.
  - In response to the CAC meeting we have since changed the web site listing
    - ADA recommendations have been updated to reflect the current guidelines

- Now provide links to other clinical guidelines
- Added a disclaimer saying the NGSP does not endorse specific clinical guidelines.

- Should we continue to list this on the web site?

Discussion:

E. Selvin noted that there is not disagreement about whether there are differences in HbA1c among ethnic groups. The issue is whether these differences are due to differences in glycemia or other factors.

Clinical recommendations on the NGSP web site

D. Mertens said that many healthcare organizations follow the ADA recommendations so it would seem to make sense to have them posted, since there are links to other guidelines as well it seems fine. E. Selvin noted that ADA guidelines are informed by a international panel of experts. E. English said perhaps the heading could be changed to "Clinical Recommendations" rather than "ADA Recommendations". D. Sacks noted that we need to check the guidelines every year for revisions, for example new pediatric targets just came out. E. Selvin suggested the heading could be "Clinical Use" rather than "Clinical Recommendations". D. Armbruster noted that based on the CAC minutes the majority of clinical organizations seemed to support having clinical recommendations on the web site. E. Selvin said that is it important for the NGSP to connect to clinical translation. R. Little and D. Sacks agreed saying we are trying to educate the laboratory side, not many clinical chemists go to the ADA web site. The committee agreed that the information should remain on the web site after making the aforementioned revisions.

Manufacturer Forum

C. Flandre and S. Reutten said that the issue of multiple lots submitted by the manufacturer discussed earlier should be presented at the forum. D. Sacks agreed, it was not listed under its own heading on the forum agenda but it would be brought up.

D. Sacks thanked everyone for their attendance, the meeting was adjourned at 5:05PM.

Minutes prepared by C. Rohlfing 8/12/14. Modified by R. Little 8/19/14.