



Meeting of the NGSP Steering Committee Minutes

Sunday July 26, 2015 3:00 PM – 5:30 PM
Hyatt Regency, Atlanta, GA

Participants:

*David Sacks—NIH, Chair, NGSP Steering Committee
*Randie Little—Univ. of MO, NGSP Network Coordinator
*Philippe Gillery—University Hospital of Reims (FR), IFCC Scientific Division
*Garry John—Norfolk and Norwich University Hospital (UK), Chair, IFCC Task Force on HbA1c Std.
*W. Greg Miller—Virginia Commonwealth Univ.
*Ross Molinaro—Siemens Diagnostics
*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

Susanne Adams—Roche Diagnostics
Shawn Connolly—Univ. Of MO, NGSP
Christine Flandre—Sebia
Kuanys Kabytaev—Univ. of MO
Curt Rohlfing—Univ. of MO, NGSP
Mark Schmid—Roche Diagnostics
Carla Siebelder—Queen Beatrix Hospital (NL)
Alexander Stoyanov—Univ. of MO
Masao Umemoto—Ref. Material Inst for Clin Chem Standards

Steering Committee members not present:

Robert Cohen—University of Cincinnati
David Nathan—Massachusetts General Hospital

1) Welcome and Introduction—Randie Little, NGSP Network Coordinator

R. Little welcomed those in attendance (D. Sacks was delayed), those present introduced themselves.

2) The 2014 Steering Committee minutes were approved by the members present.

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

- NGSP Network Monitoring
 - PRL1 has been down for a few months and not sending data. We hope they will be back up and running soon.
 - We have a new PRL in Japan (ReCCS) as of April 2015.
 - The PRLs and SRLs continue to demonstrate excellent comparability.
 - Monthly between-lab CVs for the NGSP network were all <2% over the past year.
- Certification
 - The number of certified methods and laboratories had recently leveled off but increased again over the past year.
 - There are ~150 methods and ~170 laboratories currently certified.
 - Most certified labs are Level I and are outside of the U.S.
 - There are clusters of certified labs in South Africa, Columbia and various locations in Asia.
- Current criteria
 - Current Manufacturer Certification Criteria: 37/40 individual results must be within $\pm 6\%$ of the SRL (one SRL) mean.
 - Current CAP limits (2013-2014) :Each result must be within $\pm 6\%$ of NGSP assigned target value (mean of 7 SRLs, multiple results from each).
- CAP Data
 - There has been much improvement in within and between-lab variability since 1993.
 - There has been more subtle improvement over the last several years (2010-2015).
 - 2015A survey
 - This year there were 5 samples, 2 were duplicates.

- Method-specific, between-laboratory CV's ranged from 1.3% to 8.4%, the method with the highest CV is being phased out.
 - Over 76% of laboratories are using methods with CVs <3.5% at all five HbA1c levels.
 - The all-method CVs were 3.4-3.6%, we are getting close to the goal of consistently achieving $\leq 3.5\%$.
 - Overall pass rates were ~93-96%, a few individual methods had much lower pass rates while others had 100%.
 - The mean absolute differences between the duplicate samples for individual methods were all <0.2% HbA1c
- Issues for discussion
 - Manufacturer certification failures and process to re-certify; how many chances should they get?
 - A manufacturer failed certification with only 25/40 results within $\pm 6\%$
 - Their explanation was as follows:
 - 1) “the calibrator value assignments were improperly performed; it is believe the IFCC material utilized had been opened and refrozen...”
 - 2) “A new tech that performed the certification work did not properly thaw and mix the samples prior to analysis...”
 - 3) “After the submission of data, the xx System was found to have random performance issues and preventative maintenance was required (replacement of lamp).”
 - The method failed again with 29/40 results within $\pm 6\%$
 - How many opportunities should a manufacturer get to re-certify after failure?
 - 1) For POC
 - 2) For lab methods
 - Rare variant data on web site
 - The NGSP web site currently lists information regarding interference from common hemoglobin variants (HbS, HbC, HbE, HbD, elevated HbF).
 - Recently we published a paper on interference of 49 rare variants using eight methods
 - Would it be useful to add this information to the NGSP website along with results from other published data?
 - NGSP Clinical Advisory Committee says “Yes”, it may be useful.
 - Rare Variant Interference: JDST 2015
 - 1) 49 rare Hb variants
 - 2) Trinity ultra2 boronate affinity HPLC and Roche Tinaquant immunoassay were primary and secondary comparative methods
 - 3) Methods evaluated were G7, G8, D-10, VII Turbo 2.0, enzymatic, and Capillarys 2.
 - 4) Results acceptable if within the 99% prediction interval of the regression line for non-variant samples.
 - 5) Following manufacturer instructions, would an inaccurate result be reported?
 - 6) Results:
 - For the ion-exchange and CE methods most, but not all, interfering variants were visible on the chromatograms/electropherograms such that the affected HbA1c result would not be reported if manufacturer guidelines were followed.
 - For some methods/variants inaccurate results would have been reported for some, but not all, samples of a particular variant
 - The way in which this information is presented on the website has not yet been decided
 - Other published data would be included; there are several papers including small numbers of variants/methods
 - Interest: Labs using ion-exchange HPLC or CE are noticing more and more variant peaks on their chromatograms/scans and may be interested in this information
 - Other Issues that will need to be explained:
 - 1) Few samples for most rare variants (some only n=1)
 - 2) Results are not always clear-cut; In some cases a wrong result would have been reported for some, but not all, samples with a given method.
 - 3) Study focused on analytical interference
 - Hb Raleigh is known to have a lower glycation rate compared to HbA

- Other rare variants may result in altered glycation or shortened red cell lifespan that has not been well studied
- Would this information about rare variants be useful for laboratories?
- Could presenting this information cause confusion?

Discussion:

Manufacturer re-certification attempts after failure

R. Little noted even if a method fails re-certification and is therefore no longer on the list of certified methods it will still be in use in the field. Sometimes the failure is due to calibration while other times it may be due to variability. D. Sacks asked about the time interval between certification attempts, is there a minimum time? R. Little said there is no minimum but it usually takes several months for the manufacturer to investigate, that was the case for this manufacturer. We currently require them to provide an explanation for the failure and explain corrective actions taken, and also how any changes will be communicated to end-users. D. Sacks asked if there is a requirement for a manufacturer to notify the FDA in the event their method is no longer certified, R. Little did not think so. G. John asked if there is notification on the NGSP web site when a method fails, R. Little said no, the method just comes off of the list. There could be other reasons why a method is no longer certified besides a failure, for example the manufacturer may have decided to stop promoting it. The problem is some users may not be aware that the method is no longer certified. D. Sacks asked how often a method loses its certification status in a year, R. Little did not know exactly but said maybe five per year. C. Weykamp suggested imposing a minimum of three months between certification attempts rather than limiting the number of attempts. R. Little noted that this had been discussed before, it is a possibility. M. Steffes asked if the manufacturer is charged for each attempt, R. Little said yes. C. Flandre said that if the investigation involves checking the calibration and system maintenance it takes a short period of time, but if there is a substantial defect in the system that requires going back to R&D it could take months. T. Prestigiaco said new methods submitted to FDA have to show traceability to the NGSP and this is listed in their package inserts. If they fail NGSP certification the use of that method by a customer is considered off-claim, they need to escalate their troubleshooting and work with the NGSP to solve the problem. They may need to recall the particular lot and/or perform a re-calibration, or make other adjustments. R. Little said it is not as big of an issue if the method is not yet on the market, we have a box on their submission form that asks for this information. T. Prestigiaco agreed and added that NGSP certification should just be the “final check”, for a new method the manufacturer should have already performed checks against the NGSP via sample exchanges to establish their in-house calibration. G. Miller said that for methods already on the market it would seem reasonable to have a table on the web site showing methods that have been de-certified in the previous 12 months, they could be moved back onto the certified list if they subsequently pass. R. Little agreed. D. Sacks said the concern is that a lab using a certified method that fails would not know that the method is no longer certified. R. Molinaro said that if a method that has gone thru the FDA process fails certification the manufacturer would be compelled by their internal QA processes to inform their customers, R. Little and G. John said this might not happen with some manufacturers. M. Schmid said their customers routinely ask for up-to-date proof of NGSP certification. Countries often require that this information be made available to customers. T. Prestigiaco asked if a method that is no longer certified would be indicated on the CAP survey, R. Little said many methods do not appear on the survey. Also, because of the way methods are grouped on the survey it might not always be clear, that is why we no longer put a star next to methods that are certified on our CAP summary, it could be misleading. Even if we were able to put this information on the web site it is unclear if customers would look at it. H. Vesper asked about the timeframe in which manufacturers are required to notify FDA of a certification failure. T. Prestigiaco said the general requirement is that an assessment which includes impact on patient care and a corrective action plan need to be submitted within two weeks. The corrective actions taken depend upon how bad the problem is based on risk assessment. If there is significant risk to patients a recall of the lot may result. R. Molinaro said each manufacturer has their own quality and risk management systems, if there is a systematic bias that could put patients at risk it would spark discussions with the FDA and a major investigation into the problem. D. Sacks suggested asking the FDA if they want the NGSP to notify them of failures, R. Little agreed. T. Prestigiaco said their company performs annual re-certification using a lot that is not yet in the hands of end-users, that way if there is a problem it is not sent out and there is no risk to patients. R. Little questioned whether all manufacturers do this, some may just pick a lot off the shelf or choose a lot they know is good. H. Vesper said the timeframe between certification attempts should not be too long, we need to help manufacturers get back on track in a timely manner. M. Schmid agreed and said we should not have a time limit, we want manufacturers to be certified, however they do need to explain and document corrective actions. G. John suggested placing a time limit on the manufacturer’s response to the NGSP after a failure. T. Prestigiaco

noted that this may be a bigger problem for small manufacturers, larger companies get notified by customers if their calibration is off because they fail surveys. R. Little noted that many methods that are NGSP-certified are not available in the US and are therefore not FDA approved. D. Sacks asked if POC devices should be held to the same standard, it was agreed that they should.

Rare variants on web site

D. Sacks asked how many residues on the beta chain terminus are recognized by the Roche antibody, M. Schmid said four. C. Weykamp asked how the rare variants were identified, R. Little responded that they were sequenced. R. Little noted that for the G8 method in particular there were variants that were either not visible on the chromatogram or looked like a different variant where the result is considered reportable. C. Weykamp asked if we know the prevalence of some of these variants, some may exist only in a few individuals in the world. R. Little said we really do not know, D. Sacks said the prevalence may vary by region. R. Little said that there is increased interest in variants. We could even have links to variant chromatograms. G. John said with ion-exchange a variant may be visible in a fresh sample but not one that has been stored. M. Schmid said it is good to have the information but clinicians will want to know if it is relevant to them, how prevalent are these variants? R. Little said clinicians will likely not be the ones looking at this information, mainly it will be labs. C. Flandre said that if this information is provided for labs it is important for them to know the prevalence of these variants, especially in their populations. R. Little said she did not know how to obtain this information, there are no studies. This information might help to make labs more aware that if they come across something that looks different from normal, it could be one of these variants and they may not want to report a HbA1c result. M. Steffes said it is really up to the clinician, sometimes we see variants on the G8, we tell the physician that if this is a concern for them they need to proceed with a hemoglobin identification. C. Flandre said that is fine as long as you can see the variant, some methods do not indicate that a variant is present. P. Gillery said the information could be useful in terms of making people aware that a rare variant may be present if a strange peak is seen or there is a discrepancy between the HbA1c result and other parameters, but we need to decide the best way to present this information. G. John agreed and noted that in his institution they discovered that a patient had J Baltimore because of a discrepancy between the HbA1c result and clinical impression. R. Little said one of the variants in the study looked like HbD on the G8, results are considered reportable in the presence of HbD but the result for this variant was inaccurate. M. Schmid asked if this means that each time there is evidence of an unusual variant it would then need to be sequenced, this could be costly. R. Little said not necessarily, it is more about increasing awareness, if a lab sees an unusual peak they would know it may indicate an uncommon variant and the HbA1c result might be affected. They could also compare their chromatogram to chromatograms of confirmed variants run by the same method to get an idea of what the variant might be. M. Schmid asked if the CE and ion-exchange methods can identify unusual variants based on elution times, C. Flandre said the Sebia methods have defined windows that can help distinguish the possible variants. T. Prestigiacomo said Bio-Rad has a library of variants showing what the chromatograms look like on their instruments. R. Little asked if the NGSP web site could have a link to this information, T. Prestigiacomo said yes. However, immunoassays are different, they are not affected by most variants but you cannot tell if a variant is present. R. Molinaro expressed mixed feelings about presenting this information: while it could be useful we may get very relevant questions for which we have no answers. R. Little suggested that we could come up with a list of anticipated questions and discuss how to respond, also we could have disclaimers relating to questions that we cannot answer regarding prevalence, etc. C. Flandre said that 1500-2000 variants have so far been identified and there are likely more that have not yet been identified, we cannot possibly get data on all of them. R. Molinaro agreed and asked what kind of precedent this would set in terms of new variants. R. Little said we would just have to say in general that labs need to be aware of a possible interference from a rare variant if they see something strange or the HbA1c result doesn't match clinical impression. D. Sacks asked if clinicians would look at this information if it were posted on the web site, R. Little did not think so unless they had a problem patient where they see a discrepancy and the lab is not helping them. D. Sacks noted that NIDDK is enthusiastic about presenting this information, R. Little said we will come up with a draft and send it to the Steering and Clinical Advisory Committees for review. C. Weykamp said it would be important to scientifically distinguish these variants from the four major ones, we need to make it clear that these are much less common and therefore have limited impact on daily clinical practice. C. Flandre said most clinicians have little understanding of these variants, they trust the lab to give them correct numbers. D. Sacks agreed and said they generally just want to know if the result is correct or not. C. Flandre said prevalence is important, the information could confuse labs with limited understanding of variants. They could be presented as two tiers, some rare variants are more uncommon than others. D. Sacks said there would have to be a caveat such as a paragraph explaining that these variants are very rare. G. John noted that there may be a variant present that you cannot see, it ultimately comes back to questioning a result that does not

match clinical impression. D. Sacks asked how ARUP identified the variants in the study, if they did electrophoresis and saw nothing did they then do sequencing? R. Little said if they detected the presence of a variant on the Variant II beta thal method then they performed sequencing.

4) 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 2015.
 - R. Little presented an update on NGSP progress and discussed rare variants.
 - I gave an update on CAP Proficiency Testing
 - In USA labs that perform patient testing are required by law to participate in PT
 - Historically, CAP sent out 2 PT surveys annually for HbA1c
 - Each survey contains 3 samples
 - Originally artificial, now whole blood
 - Participation in the survey increased from ~2500 labs in 1998 to ~3500 today
 - Regulated analytes
 - 1) CLIA mandated 86 analytes (“regulated”) that require PT
 - 2) Mainly diagnostic tests regularly performed whose results are “important to health care treatment decisions”
 - 3) HbA1c is not included i.e., not a “regulated analyte”
 - Regulated Analytes – Future
 - 1) CMS (Centers for Medicare and Medicaid Services) and CDC are examining a list of non-regulated analytes
 - 2) Plan to add more to mandated list requiring PT – when?
 - 3) Commission on Laboratory Accreditation (LAP) suggested increased frequency of monitoring
 - 4) Selected tests “critical to patient safety”
 - 5) Analytes: BNP/NT-proBNP, Troponin, HbA1c
 - 6) Increased frequency of PT to 3 mailings per year, with 5 samples in each shipment
 - 7) Require 4/5 correct (ie, +/- 6%) to pass
 - 8) Optional - labs can choose whether to participate in the new 5 sample GH5 survey or the 3 sample GH2 survey (for now)
 - PT Failure
 - 1) In past, CAP worked with labs that failed PT
 - 2) CMS recently reminded CAP to adhere to CLIA mandate
 - 3) If lab has repeat unsuccessful performance in PT for a regulated analyte, it is required to cease testing for 6 months (fail either 3 consecutive or 3 of 4 surveys)
 - FDA approval of methods (high variability, interferences)
 - There is a POC immunoassay method that has been approved by the FDA for monitoring despite the fact that the package insert notes interference from HbS, HbC, HbE, HbD and elevated HbF.
 - With this type of method there would be no way of knowing that a variant is present.
 - We asked the FDA if it is possible to prevent a method with these interferences from being approved, the answer is no.
 - “Substantial equivalence”—If manufacturer can show that their method is equivalent to one that has already been approved, even if that method is old, the FDA has to approve it due to how the law is written.
 - NGSP web site
 - Leonard Pogach at the Veteran’s Administration believes that HbA1c should be reported as a range reflecting the analytical variability of the test.
 - He wanted changes to the clinical use page on the NGSP web site, feeling that it was biased toward the ADA recommendations which the VA and CMS do not agree with, especially use of POC methods and the general guideline of <7% HbA1c for patients with diabetes.

Discussion:

CAP Survey

D. Sacks says there currently is no timetable for when HbA1c will become a regulated analyte. R. Little asked if CMS sets the criteria for passing the survey, D. Sacks said no, CAP sets the criteria. H. Vesper said CMS publishes their own criteria for regulated analytes. R. Little then asked what happens if CMS decides to publish criteria that are less strict than CAP, e.g. $\pm 12\%$. Would labs then just switch to a different PT survey in order to have a better chance to pass? Conversely, if CMS specifies $\pm 6\%$ this may be too tight for surveys other than CAP that use processed specimens. Also these surveys likely would not have assigned target values so would this be based on the peer group? H. Vesper said that CDC normally get input from CAP and other PT providers when they put together recommendations for CMS. D. Sacks said that CAP is by far the largest PT provider in the U.S. C. Weykamp asked how many labs chose to participate in GH5, D. Sacks said roughly 2500. H. Vesper asked if the GH2 survey will disappear if HbA1c becomes a regulated analyte, D. Sacks said yes, at least in the U.S. (15% of participants are outside the U.S.). T. Prestigiacomo asked how the increased number of samples for GH5 will affect required performance specifications as calculated by C. Parvin, would the CAP requirements be tighter than NGSP. D. Sacks said this is a good point, C. Parvin may need to look at this again.

FDA Approval of Methods

M. Schmid asked if a method with interference(s) gets approved regardless of the FDA criteria for variant interference. D. Sacks and R. Little said that the criteria regarding variant interference only applies to a diagnostic claim, the method being discussed would not be approved for this. If there is an interference the manufacturer is required to put a "black box" warning in the package insert. R. Little said the FDA has not approved a method for diagnosis that has an interference where the interference cannot be seen and therefore a result would be reported. M. Schmid acknowledged this but said nonetheless the FDA set a requirement but is allowing a disclaimer. T. Prestigiacomo asked if the NGSP could make variant interference part of the certification requirement, that way the method would not be able to claim traceability to NGSP. R. Little said this would probably not affect FDA approval due to the law regarding substantial equivalence, they would still have to approve a method with interferences. T. Prestigiacomo and M. Schmid noted that the method would not be NGSP certified which is part of the FDA requirements, the question is whether this would override substantial equivalence. R. Little said it would be difficult for the NGSP to do this, T. Prestigiacomo acknowledged this adding that it would be difficult to develop specific criteria, e.g. would interference from one common variant be acceptable but not 2, or 3? This has likely been an issue for the FDA as well. R. Little said the important thing is that if there is an interference, it can be seen so that an inaccurate result is not reported. D. Sacks said POC is a whole different issue, they methods are generally not used by sophisticated labs. C. Weykamp asked what the definition of POC is, there will likely be hybrid methods on the market soon. R. Little and D. Sacks said the important thing in the U.S. is whether the method is CLIA-waived, POC methods want this designation so that they can be used in physician offices, etc. D. Sacks said almost all POC devices are CLIA-waived. H. Vesper asked if there should be different requirement for POC since they are used in different settings, maybe require multiple lots of reagents to be tested since there are typically multiple lots in use in the field. R. Little said we already have the requirement that if a POC method fails certification they need to re-submit with three different lots. It is hard to know how many lots are in use in the field, it is likely different for different methods, there is also the question of what constitutes a lot (reagents, calibrators, etc.). POC manufacturers have suggested in the past that they need to make HbA1c more widely available and should not have to meet requirements that are as stringent as those applied to lab methods, but we feel that since the test is being more-or-less used for the same purposes in patient care they should meet the same requirements.

NGSP web site

R. Little said that based on discussions with L. Pogach we have already made some revisions to the clinical use page on the web site. He is very concerned about the goal of $<7\%$ HbA1c, that this is not appropriate for many patients, especially those that are elderly and/or have co-morbid conditions. This has resulted in overtreatment with negative consequences. We still include the summary of the ADA recommendations but expanded this section based on the more recent ADA guidelines that include more discussion of individualizing HbA1c treatment goals. We have added links to other guidelines and added a disclaimer that the NGSP does not endorse any particular guidelines. We propose further revisions including removing the statement regarding use of POC methods and adding the NDEP guiding principles (GP) which elaborate on the concept of individualizing treatment goals (although the VA and CMS have not signed off on the NDEP GP). We also propose adding a summary of the National Diabetes Information Clearinghouse guidelines for interpreting

HbA1c results. E. Selvin said she agreed with the revisions with the exception of the first bullet under the NDIC guidelines (“consider that all laboratory test results represent a range, rather than an exact number”). The number is the best estimate of the true value, we know that there is inherent variability. The statement is not really accurate, there is variability in test results but they do not really “represent a range”; moreover the statement has nothing specifically to do with HbA1c. D. Sacks agreed and said we do not have to quote everything from each guideline on the web site. R. Little said it would be difficult for labs to report results as a range; most labs do not really know how to determine their “range” for reporting results and it would vary from method to method and lab to lab. H. Vesper added that reporting as a range would mean you could not have single decision cutpoints. C. Weykamp said we are talking about uncertainty of test results, this is an issue in Europe, the new accreditation guidelines state that each laboratory should know the uncertainty of each of their assays. Laboratories are unhappy about this and clinicians are not asking for it to be implemented. G. John and C. Weykamp said there has been discussion of reporting results as a range but clinicians do not want this and they do nothing with the additional information. E. Selvin said the number represents a best estimate, and clinicians look at the results along with other test results when looking at the clinical picture. H. Vesper suggested not using “Taken From” when referencing the source for the guidelines, it implies that those quoted are considered the most important, perhaps just say “From”. R. Little and D. Sacks noted that the ADA POC statement is controversial, some studies do not show that POC significantly improves patient care. The committee agreed to H. Vesper’s suggestion and the other proposed revisions, additionally the bullets regarding POC and “results represent a range” should be removed.

5) IFCC Task Force on HbA1c Standardization—Garry John

- Successes
 - Several Publications including:
 - JAMA
 - Clinical Chemistry
 - Clinical Chemistry and Laboratory Medicine
 - Collaborations:
 - International Diabetes Federation
 - World Health Organisation
 - Ongoing projects:
 - IFCC/IDF/WHO International questionnaire on diabetes clinical practices (AACC & ADA no response)
 - WHO Handbook on Laboratory aspects of Diabetes Monitoring and Diagnosis.
- The Next Stage
 - To maintain and further develop the network of reference laboratories for the measurement of HbA1c (through collaboration with C-TLM)
 - To work in partnership with WHO and IDF to continue to promote the reporting of HbA1c in line with the consensus statement
 - To work in partnership with WHO and IDF to facilitate the development and implementation of international guidelines for the use of HbA1c in the diagnosis of diabetes
 - To work with IFCC Corporate Members to develop a consensus position on the information to be included in the Instructions for Use (IFU) as it relates to the clinical use and interpretation of HbA1c methods
 - Develop quality targets for the measurement of HbA1c and other biomarkers, and on the basis of these targets, and in conjunction with professional bodies, advise on the use of biomarkers for monitoring, diagnosis and screening of diabetes and glucose intolerance.
 - To work with WHO and TF-POCT to recommend best practice in the use of POCT methods for the measurement of HbA1c
 - To evaluate the clinical value of emerging biomarkers (e.g. glycated albumin) for the management of patients with diabetes and to establish whether there is a case for method harmonisation of effective new biomarkers
 - To evaluate the emerging importance of post translational modification derived products (PTMDPs), and especially Advanced Glycation End-Products (AGEs), and work with Professional bodies on the best way of developing these for use in diabetes.
 - To monitor the literature and advise on best practice in relation to laboratory aspects of diabetes.

Discussion:

IFCC Task Force on HbA1c Standardisation

G. John noted that the U.S. is the only major country which has not responded to the survey. The Task Force has a new committee and is moving away from focusing just on standardization and more toward more education efforts, especially in developing countries that are not experienced with HbA1c. H. Vesper asked if WHO has a laboratory that is working with the TF, G. John said no, WHO has a specific department that will be looking more closely at diabetes. One area will be POC testing in developing countries.

Addition of another SRL

R. Little said that a Level 1 laboratory in Japan wants to join the NGSP network as a SRL. The laboratory has performed well, the question is do we need/want another SRL in Japan? It is additional work for us to prepare additional samples and ship them to an additional SRL and we would have to do another network certification involving a 100 sample comparison. Would it be of benefit in terms of being able to certify additional manufacturers/laboratories? We currently have 8 SRLs, 3 in the U.S., 4 in the Netherlands and one in Japan. D. Sacks asked what method the requesting lab uses, R. Little said the G8 which is already the method used in two SRLs. There are also other ion-exchange methods used by several SRLs. I am not sure if there is a reason to have another SRL in Japan. Would it be of benefit in terms of being able to certify additional manufacturers/laboratories? G. John asked what the criteria are for selecting a new SRL. R. Little replied that we have not added any SRLs in a while, do we want to have a large network like the IFCC? Having a larger network makes it more difficult to make sure all of the labs stay on track and also makes it more expensive to ship monitoring samples. ASRL#1 actually pays for the monitoring shipments to their laboratory, I am not sure the lab in Japan that wants to join the network can do so. G. John noted that if there are no set criteria a lab can ask why they cannot join the network. R. Little said the reasoning up until now is whether it would benefit the NGSP to add the SRL in terms of reaching more manufacturers/labs. H. Vesper noted that in the CRMLN they normally ask for an endorsement from an appropriate national body, perhaps we should ask for this. In this case there is already a network laboratory in the same country. R. Little said we did not ask for this with the other SRLs but we may be able to in the future. D. Sacks asked what the cost is per shipment to send the samples to Japan, M. Umemoto said ~\$1000.00. G. John suggested that the added SRL could be required to cover shipping costs to their lab as well. C. Weykamp asked if it is necessary to perform the monitoring every month given the stability of the network. R. Little said we do the monitoring monthly because the SRLs certify manufacturers/labs on an ongoing basis, if they fail in a given month we need to question all certifications performed over that time period. C. Siebelder noted that the last NGSP monitoring shipment contained enough monitoring sets for the next three months. R. Little said we were able to do this the last time around and may be able to in the future to save on costs. If we could do this, costs might not be as big of an issue, especially if the SRL is able to cover at least some of the cost. M. Umemoto said their SRL (ASRL#1) can certify any additional Japanese manufacturers. D. Sacks asked what the negatives of adding another SRL would be besides cost. Is getting sufficient quantities of samples an issue? R. Little said we are pushing the limit on sample volumes now but adding one more SRL is probably feasible if there is a need. D. Sacks said it is difficult to define a need, R. Little said it's mainly a matter of whether this will mean certifying more methods/labs. M. Steffes said adding one more SRL would not appreciably improve the quality of the estimates (means of SRLs) for these samples. C. Weykamp and G. John suggested that the NGSP should adopt a policy that defines the number of laboratories that will be allowed to be in the network. R. Little asked if there would be an exception if a lab wanted to become a SRL in an area of the world where we do not currently have one. E. Selvin said this is why adopting general criteria would be helpful. The committee agreed. C. Weykamp said the IFCC network is encountering the same issue. The international aspect is very important to the IFCC, we look at a candidate laboratory's background and role in a given country. Up until now we have been able to accept more laboratories but the number of network labs will eventually become an issue. R. Little said we will develop criteria, G. John suggested part of it could be regional in terms of defining where there already are SRLs vs. areas where there aren't. R. Little said yes but for example we already have 4 SRLs in the Netherlands and we are able to ship samples to other parts of the world, where the SRLs are located may not be that important. G. John suggested that the number of NGSP SRLs could be limited to 8, if one drops out the laboratory that is wanting to join the network could then be added. C. Weykamp said variation in methodology could also be an argument. R. Little noted that another issue is we currently may not have the samples to do the 100-sample SRL certification. Preparing new sets is time-consuming and labor intensive, perhaps we could consider another way to perform network certification? Maybe compare the results to the

means of all of the SRLs rather than the CPRL? C. Weykamp and D. Sacks said that we should take some time to consider such major changes. R. Little agreed but said we could consider this for the future, maybe prepare the next set of 100 samples with this change in mind, we will need to perform more SRL certifications in the future in any case since the SRLs periodically upgrade to newer and better methods. C. Weykamp suggested that rather than using a separate set of 100 samples, the candidate SRL could analyze the monitoring samples each month in parallel with the network labs and if they pass a given number of months they would be accepted.

D. Sacks thanked everyone for their attendance, thanked outgoing manufacturer representative C. Flandre for her service to the NGSP and welcomed new manufacturer representative R. Molinaro. The meeting was adjourned at 5:30PM.

Minutes prepared by C. Rohlfing 8/12/15, modified by R. Little 8/12//15, revised by C. Rohlfing 9/17/15.