2017 C-Peptide Standardization Manufacturer Meeting
Minutes

Wednesday August 2 7:00 AM – 9:00 AM
Marriott Marquis San Diego Marina, San Diego, CA

Participants:

C-peptide Standardization Committee Members
Randie Little—University of Missouri
W. Greg Miller—Virginia Commonweath University

Committee members not present
Judith Fradkin—NIDDK
Carla Greenbaum—Benaroya Research Institute
Gary Myers—AACC
Jerry Palmer—University of Washington
Kenneth Polonsky—Washington University
Lisa Spain—NIDDK
Daniel Stein—Albert Einstein College of Medicine

Guests
Valerie Arends—University of Minnesota
Shawn Connolly—University of Missouri
Daniel Holmes—Univ. of British Columbia
Kuanysh Kabytaev—University of Missouri
Vicky Makky—University of Minnesota
Santica Marcovina—University of Washington
Michael McPhaul—Quest Diagnostics
Curt Rohlfing—University of Missouri
Amy Saenger—University of Minnesota
Michael Steffes—University of Minnesota
Gwen Wark—UKNEQAS/IFCC

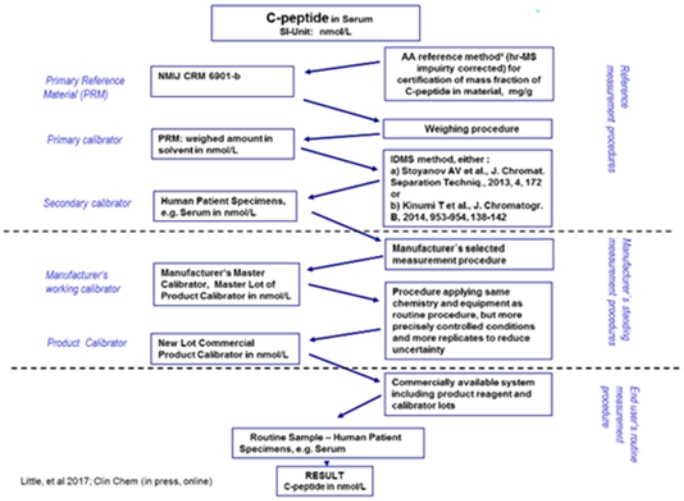
Manufacturer Representatives
Jeanette Axelsson—Mercodia
Bethany Bell—Alpco Diagnostics
Philip Bryan—Ortho Clin Diagnostics
Sean Conley—Alpco Diagnostics
Carole Dauscher—Siemens
Holly Groth—Ortho Clin Diagnostics
Carissa Jones--Mercodia
Iris Kutschera--Diasorin
Lori Lai—Tosoh Bioscience
Stefaan Marivoet—Tosoh Bioscience
Tomomi Murakami—Kyowa Medex
Eri Nibe—Kyowa Medex
Koichi Saga—Tosoh Bioscience
Lata Sundaram—Beckman
Hisao Tsukamoto—Tosoh Bioscience

1) **Welcome and Introduction—Randie Little**
R. Little welcomed those in attendance, the 2016 meeting minutes were approved.

2) **C-peptide Standardization Update—Randie Little**
- In 2002, the NIDDK organized a C-peptide standardization committee and funded an international comparison study of C-peptide assays.
- C-peptide Standardization: Comparison Studies
  - WHO material was ineffective in improving the comparability of C-peptide results among methods/laboratories.
  - Use of pooled serum calibrators greatly reduced variability of results.
  - Showed that pooled serum calibrators with LC-MS assigned values can be used for method re-calibration by the manufacturer.
  - Between-lab/manufacturer CVs were much lower after calibration using pooled serum calibrators.
- C-peptide Reference Method/Laboratory Comparison
  - In order for manufacturers to re-calibrate their C-peptide assays to the reference method we were told that we must have the reference method listed with the JCTLM. This required a comparison between two reference laboratories.
  - The reference method at D. Stein's lab in New York was replicated in our lab at the University of Missouri.
  - We published a comparison between the two laboratories in 2012 that showed good correlation between them (r^2=0.9647).
  - This comparison data was used to submit the method for listing in the JCTLM database; the method is now listed with JCTLM.

- A later 2014 comparison between the two reference laboratories showed a better correlation (r^2=0.9921).

- C-peptide Reference Material: NMIJ CRM (CRM 6901-b)
  - Produced by the National Metrology Institute of Japan
  - A lyophilized synthetic peptide with high purity
  - Concentration determined by two independent amino acid analyses using liquid and gas phase hydrolyses.
  - Is listed in the JCTLM database
  - Evaluation
    1) Serum with zero C-peptide was spiked with native NMIJ reference material and analyzed by LC/MS as a routine sample.
    2) Results closely matched the theoretical values.
- NMIJ also published a reference method in the JCTLM that is different from the D. Stein/DDL method.
  - Comparison between the reference methods showed that results from the NMIJ method were ~25% lower compared to D. Stein/DDL method.
    1) NMIJ used a different sample prep
    2) NMIJ uses a derivatization procedure
    3) NMIJ and DDL use different internal standard (IS)
  - Another set of samples (12 single-donor, 9 pooled) were sent to NMIJ along with the D. Stein IS.
  - The second comparison showed that when both labs used the D. Stein IS, results from serum samples were equivalent between the labs.
  - Concluded that there was an issue with the NMIJ IS.
- We now have a new more sensitive MS at the DDL and have validated that the results are equivalent to those from our previous MS.
- Proposal for Standardization of C-peptide
  - Primary Reference Material: NMIJ CRM 6901-b
  - LC/MS method (Stoyanov, et al, Kinumi, et al)
  - Secondary Reference Material: pooled and single-donor serum.
  - Recently published a paper in Clinical Chemistry (Little et al., DOI: 10.1373/clinchem.2016.269274 Published June 2017) that shows a proposed traceability scheme. G. Miller and G. Myers wrote an accompanying editorial:



- Is there any reason NOT to begin implementing this traceability scheme? Is it time to begin recalibration?

Discussion:

New reference materials, reference methods

A. Saenger and M. McPhaul asked what the differences are between the NJIM and Stein internal standards. D. Holmes asked what the IS used by DDL is, and asked if there is any explanation as to why the results did not match

before but match now. K. Kabytaev said the NMIJ is very different from the Stein/DDL method, they calibrate based on native endogenous C-peptide, use MS/MS instead of MS and utilize a chemical derivatization step. Their explanation for the different results was that there is something in their IS that co-elutes with the labeled C-peptide when it spiked into serum. The DDL IS was synthesized by D. Stein's laboratory. It is N and C labeled multiple times, the NMIJ IS is deuterium labeled and is similar to one produced by Bachem. The DDL has experience with the Bachem standard which is +16, and for example a water adduct is +18; the two can be indistinguishable on MS. R. Little said that Dr. Kinumi's group at NMIJ agrees that the current results are correct. We have a good supply of the Stein IS to maintain ongoing comparisons between the reference labs but will eventually have another IS made to ensure a transition period and continuity.

JCTLM database

A. Saenger noted that there are a number of different reference methods for a lot of different analytes listed in the JCTLM database; are these methods maintained? R. Little said they are not necessarily maintained, reference methods are developed and listed but sometimes the laboratories do not continue to run them depending upon the function of the lab, demand and/or funding. Just because a method is on the list does not mean the method is still being run by the lab, this can be a problem. Reference methods are expensive to develop and maintain.

Issues with C-peptide standardization

R. Little said that the national metrology institutes (NMIs) develop reference methods but unless there is a standardization program in place they don't get translated to the clinical level. For example there was a recent C-peptide survey where pure materials were sent to a number of NMIs to see how well they compared, but this was only among the NMIs. We are trying to bring the different parties together, we have struggled with C-peptide standardization; there were different parties involved that have not always communicated. Sometimes there are new developments that then cause us to have to backtrack and fill in the pieces, all of this is described in the new Clin Chem paper. It describes C-peptide standardization efforts that were going on in various countries with little or no coordination between them. It also discusses the WHO material and shows the original traceability scheme for it. The idea was that manufacturers would use it to calibrate their methods, but the material was not commutable. There is a new WHO C-peptide material made by NIBSC in the UK, but it does not appear to be fully commutable either. This is why we are proposing that manufacturers use commutable serum samples, either pooled or single-donor, with values assigned by a reference method that is traceable back to a primary reference material. G. Miller noted that a problem with WHO materials, which are pure recombinant proteins, is that they are intended to be dissolved in the appropriate matrix. If the matrix is not appropriate they will not be commutable with patient samples and bias will result. People are becoming more aware of this issue, if the pure substance is simply dissolved into a buffer that might be suitable for a MS method but not an immunoassay. What R. Little described represents the appropriate use of the reference material where it is used to calibrate the MS method which in turn assigns values to matrix-appropriate serum specimens. R. Little said the DDL noted a similar issue with the NIST glucose standards. The NIST processed material showed a bias in the routine glucose assay, but when more matrix-appropriate reference materials from Japan were analyzed the results matched closely with the reference values.

International Consortium for the Harmonization of Clinical Laboratory Results

R. Little noted that the editorial written by G. Miller and G. Myers that accompanies the new paper discusses the new ICHCLR which is trying to solve the problems mentioned in the paper. G. Miller said it has not been completed yet but the goal is to have a website listing of all of the harmonization activities going on worldwide with the different analytes. If this had existed R. Little could have gone onto the web site and found out about the different C-peptide standardization efforts going on in China, Japan and elsewhere and there could have been better coordination among them.

Re-calibration of manufacturer methods

R. Little said that the pieces are now in place for manufacturers to begin re-calibration. Some methods already match well with the reference method and those will require little adjustment, others will require more. There are regulatory issues, we were told that in the case of the FDA it is not a long involved process since C-peptide is not a CLIA-regulated analyte. We learned from HbA1c that once the values are re-adjusted we then need to see how well the process is working in clinical laboratories. With HbA1c we are able to look at CAP survey data. There are not a large number of labs running C-peptide right now. The reason NIH became interested is that there are ongoing trials looking at maintaining and possibly increasing insulin secretion in patients with T1 diabetes and C-peptide is the best indicator of beta cell function. Studies in recent years have shown that some T1 diabetes patients actually have

a small amount of C-peptide that increases with exposure to glucose; these levels can be measured with the newer ultrasensitive assays. There has been some progress in this area, so it is important that we standardize C-peptide before there is an increased demand for it once therapies are developed and people are recruited for clinical trials to evaluate them. S. Marcovina asked about laboratories running C-peptide for studies where maintaining longitudinal comparability of results is important, how will they be able to determine how their results will be affected prior to re-calibration by the manufacturer. Can labs obtain value-assigned samples in advance to determine how their results will be affected? R. Little said it should be possible to provide samples to labs that need them, especially labs performing clinical trials. The standardization effort started with comparisons among such labs. The results could be fine within a study where a central lab is used as long as the laboratory uses a good method, good QC protocol, etc. The goal was to be able to compare results across studies; the problem was that the different labs were using different methods and the results were not comparable among them. We then decided to go to manufacturers to get them to standardize so that results match across methods. L. Sundaram asked if there are any total allowable error/precision recommendations for C-peptide. R. Little said that at the beginning blinded replicates were used in the comparisons to look at the precision of different methods, there were differences, there may have been improvement since then. Once we get the methods better aligned we will need to look more closely at the performance of the individual methods including precision, sensitivity, lower limit of detection, etc., and set goals for performance. Regarding sensitivity, we will need to make sure our reference method can measure the low levels. It was noted that in the Faustman et. al paper the levels examined were down to ~1.5 pmol/L. R. Little said we have value-assigned samples to provide to manufacturers and the ADA has officially requested standardization, so can we begin the process? L. Sundaram asked how important urine C-peptide is, R. Little said urine was included in the traceability chain because most assays measure urine as well as serum C-peptide. The standardization should apply to urine as well as C-peptide but right now we are focused on serum.

C-peptide and renal function

D. Holmes noted that they look at C-peptide in islet cell transplant patients and it is very GFR-dependent. It is really only useful in patients with constant renal function, renal failure can muddy the water. R. Little said that right now they are the most interested in looking at patients that have recently developed diabetes who still have some insulin secretion, these patients will not be likely to have renal disease.

3) IFCC Working Group for Standardization of Insulin Assays (SWG-IA) Update — Amy Saenger,

- Goal
  - Achieve calibration traceable to an ID-LC-MS/MS reference measurement procedure for all commercially available insulin assays
  - Manufacturers require a reference system listed by JCTLM to enable recalibration of assays
- IFCC Working Group on Standardization of Insulin Assays (SWG-IA)

Name	Role	Country
A. Saenger	Co-Chair	US
M. Steffes	Co-Chair	US
J. Dekker	Member	NL
D. Holmes	Member	CA
R. Little	Member	US
M. McPhaul	Member	US
G. Miller	Member	US
D. Sacks	Member	US
K. Van Uytfanghe	Member	BE
G. Wark	Member - IFCC	UK
B. Akolkar	Consultant – NIH/NIDDK	US
V. Arends	Coordinator – UMN	US

In Collaboration with: American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), CDC, NIDDK, International Diabetes Federation (IDF)

- IFCC Working Group on Standardization of Insulin Assays (SWG-IA): Corresponding Members

Name	Full and Affiliate Member Societies
Paul Glendenning	Australasian Association of Clinical Biochemists
Syuu Meguro	Japan Society of Clinical Chemistry (JSCC)
Andrejus Coj	Lithuanian Society of Laboratory Medicine
Fayeofori Abbiyesuku	Association of Clinical Chemists Nigeria (ACCN)
Oguzhan Zengi	Turkish Biochemical Society (TBS)
Gary Myers	American Association for Clinical Chemistry (AACC)
Name	**Corporate**
Tanja Dubravcic	Siemens

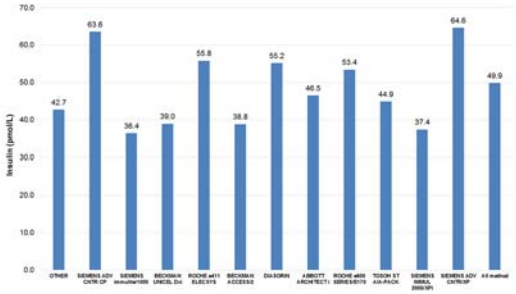
- C-peptide traceability scheme described by R. Little applies to insulin as well.
- Background / Previous Progress

- LC-IDMS RMP developed and published (University of Ghent, K. Van Uyfanghe, L. Thienpont): no longer active
- Commercial methods not standardized despite claimed traceability to WHO 1st IRP 66/304
  1) Use of pure recombinant insulin in immunoassays was not effective to achieve harmonization of results (Marcovina et al, 2007)
  2) Different pure recombinant insulin reference material in immunoassays was not effective to achieve agreement with results with an ID-LC-MS/MS reference method (Miller et al, 2009)
  3) Standardized results achieved by re-calibrating with ID-LC-MS/MS values assigned to individual donor sera and to serum pools
- Harmonization by traceability to IDMS was demonstrated to be achievable using single donor sera
- Harmonization using pooled sera was effective over the concentration interval covered by the pools (>50 pmol/L)

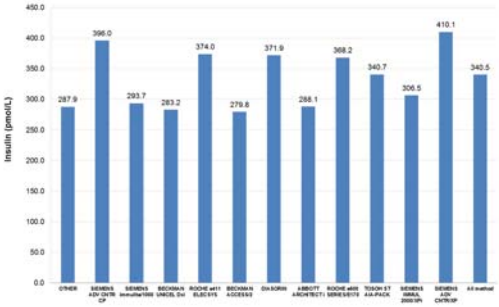
- NIBSC / WHO International Standards
- WHO 1st IRP 66/304
  - Human pancreatic insulin in sucrose and dilute acetic acid (lyophilized)
  - Not suitable for calibration traceability
  - NIBSC/WHO international standard 83/500
  - Development of new international standard needed to move forward
- Insulin Reference Method Procedures: RMP must be established in 2 laboratories, generate documentation for JCTLM submission
  - ID-LC-MS/MS University of Ghent (K. Van Uyfanghe, L. Thienpont) (no longer active)
  - Quest/Nichols: M. McPhaul
  - University of Minnesota (M. Steffes, A. Saenger)
  - Albert Einstein (D. Stein): on hold
- Insulin serum biobank
  - Development of Patient Pools: Specimens collected and processed according to CLSI C37A
  - Patient Pools: Storage of Aliquots
    1) Five levels of reference-method value assigned pools (49.8, 217.3, 236.6, 512.9, 676.1 pmol/L)
    2) Individual donors (45), donor pools (5)
    3) Total aliquots stored at the University of Minnesota: 16,591 aliquots/vials (281 boxes)
- Comparison of results

LC-MS/MS, Thienpont (pmol/L)	Insulin, Intact, LC/MS/MS (pmol/L)	Absolute Diff (RMP-Quest)	% Diff	UMN Insulin, Roche (pmol/L)
49.8	30	19.8	39.8	64.75
217.3	174	43.3	19.9	273.3
236.6	228	8.6	3.6	278.4
512.9	486	26.9	5.2	641.5
676.1	636	40.1	5.9	762.2

- CAP Proficiency Testing / Wild Card Pools
  - Insulin, C-peptide
  - Consent, collection, processing, shipping, storage conducted at the University of Minnesota
  - Donors were fasting; specimens collected when donors were in fasting and non-fasting state (post-glucose load)
  - Results (~700 participating labs)
    1) Insulin Serum Pool (Low)



    2) Insulin Serum Pool (High)



3) Results summary

Method	Survey Specimen Method CV (%)				
	INGW-98 (Low Serum Pool)	INGW-99 (High Serum Pool)	Y-04	Y-05	Y-06
OTHER	55.5	52.8	35.3	25.5	34.4
SIEMENS ADV CNTR CP	0.0	0	3.0	6.2	2.4
SIEMENS Immulite/1000	6.2	5.4	9.9	9.1	9.1
BECKMAN UNICEL Dxi	6.2	5.6	6.4	6.5	6.1
ROCHE e411 ELECSYS	7.1	5.3	8.2	7.7	6.4
BECKMAN ACCESS/2	4.1	4.3	5.7	5.2	4.9
DIASORIN	14.6	11.5	6.0	5.4	5.9
ABBOTT ARCHITECT i	6.0	3.6	4.5	2.9	3.4
ROCHE e600 SERIES/E170	4.6	3.9	4.8	4.9	7.3
TOSOH ST AIA-PACK	4.4	2.5	3.0	1.9	2.9
SIEMENS IMMUL 2000/XPi	9.2	5.5	18.8	25.9	22.4
SIEMENS ADV CNTR/XP	5.7	5.2	7.3	6.6	6.4
All Method %CV	**22.4**	**16.9**	**27.1**	**31.3**	**27.1**

- Insulin Conversion Factor (SI Units)
  1) Conversion factor from mIU/L to pmol/L = 6
  2) Recognized in Diabetes Care, used by the CAP for participants to convert insulin concentrations into SI units if labs report in mIU/L or non-SI units
  3) However, manufacturer package inserts generally provide incorrect or no conversion factors

- Insulin Standardization: Future Initiatives
  - Accuracy based CAP proficiency testing for insulin/c-peptide will be included in accuracy based grading and continuous beginning Q1 2019
  - Continued support from ADA and corporate sponsors
  - Evaluation of NIBSC insulin reference material
- Upcoming Meetings
  - IFCC WorldLab Meeting, Durban
    1) October 22-25, 2017
    2) Half-day meeting
    3) http://www.durban2017.org/
  - Diabetes Biomarker Meeting, Cape Town, ZA: October 26-27th, 2017

Discussion:

New insulin standard commutability study

G. Wark said there were problems with the new NIBSC/WHO insulin standard last year, but there is now agreement among all participants regarding the actual content of insulin in the standard. The next stage is a collaborative study; they were originally focused on immunoassays but are considering inclusion of MS assays as well. We are looking for laboratories to volunteer to participate in the study. Previous NIBSC studies did not evaluate commutability, that will be evaluated in this study, the problem is access to patient samples. I have volunteered to obtain patient material, if anyone wants specific patient groups included let us know and we will try to include them. They have not given me a time frame yet but we want to get it done soon, I am in regular contact with them. R. Little asked if they are looking for laboratories that run different immunoassay methods. G. Wark said yes, they normally like to include as many current methods as possible to get a better idea of how commutable the standard is. R. Little said the DDL can participate using their Tosoh AIA method, G. Wark said they tend to look at labs that participate in UKNEQAS but like to include international labs as well. M. McPhaul asked about inclusion of MS assays, G. Wark said NIBSC is aware that there are now MS insulin assays out there and will probably want to include them. G. Miller asked if the new standard is pure recombinant material, if so it has been shown that these materials are not commutable if dissolved in a buffer. Part of the project should be to figure out, and make recommendations regarding, the best way to prepare a matrix-appropriate calibrator with this material such that it has a chance of being commutable in an immunoassay. G. Wark said she believes that it is a pure recombinant

material and the NIBSC is aware of the matrix issue and is working on it, although she has not seen data yet. R. Little asked if the WHO material was shown to be commutable, how would it fit into the traceability chain? Would manufacturers have the option to use it either way? A. Saenger said they are developing their MS method and would presumably use it to calibrate that method but would then use the reference method to assign the value to serum samples for the manufacturers. Manufacturers would not use the WHO standard to calibrate their assays. G. Miller agreed. R. Little asked if there is currently an insulin reference material listed in the JCTLM database. G. Miller and A. Saenger did not think so. The old WHO insulin standard, which was a pancreatic extract, is no longer available. G. Miller said the new WHO standard should be suitable for calibrating the reference method. Previously the committee looked at insulins supplied by Novo and Eli Lilly, they were assessed in Belgium and were both found to be of high purity and equivalent. The only issue is WHO material is not generally submitted to JCTLM. It stands on its own, but it is generally accepted as a provider of IVD reference materials. R. Little said it is important that the proper use of the WHO standard is made clear.

Patient samples

G. Miller noted that there are already insulin samples that were prepared and assigned values by a reference method that could be value-assigned and used in the project. A. Saenger and M. Steffes said they are currently being stored at their institution. R. Little asked if the stability of these samples, which have been stored at -70 degrees C, is still OK. A. Saenger said they assume so, M. Steffes said they are looking at this, the question is how well they were stored prior to being moved to the Minnesota location. G. Miller said they include older samples that were already value-assigned by the lab in Belgium; those can be used to assess stability. A. Saenger noted that Quest MS results compared to those from Belgium, but we do not know if there is a difference between the methods or it is a specimen stability issue. M. McPhaul noted that since the Quest results were lower, would it would be possible for the lab in Belgium to re-analyze the samples to verify stability of the samples? A. Saenger and M. Steffes said no, the lab is no longer running the method. Quest will run C-peptide on the samples as well, stability is a bigger issue for C-peptide than for insulin. M. Steffes said another issue is that the samples were not adequately cataloged initially. They are now in Minnesota and in our database; we are working with G. Miller to try to resolve which labels correspond with the IDs used in the Belgium analyses but we have not fully resolved this. R. Little said that the DDL ran insulin as well as C-peptide on their routine assay for one set of samples collected early on, and found that if samples have a good range of C-peptide there is also a good range of insulin results. Perhaps in the future the same samples could be used for both? The DDL has been doing collections every few years.

CAP survey

A. Saenger said the serum samples were shipped from Minnesota to a central facility in Texas that distributed them to the labs. There were no international labs included due to shipping constraints. Unfortunately there was some degradation of the C-peptide presumably due to improper handling/storage, we know this because the lab tested them before shipment and then again after they were received as part of the survey. The insulin results were comparable before and after, but the C-peptide results were lower. For the next wild card survey we will try to address the specimen handling/storage issue. R. Little said this is an important piece of the standardization program; we need to be able to evaluate results in the field pre and post-recalibration. It will also be important to eventually assign target values to the specimens in order to have an accuracy-based survey.

Insulin conversion factor

A. Saenger noted that incorrect conversion factors are still common, not only in package inserts but on the web sites of some laboratories. This has been a cause of confusion, and impacts the CAP survey results, we know there have been labs that fail the survey because of the use of incorrect conversion factor. Hopefully in the process of standardization we can address this issue in terms of education. M. Steffes said G. Wark and NIBSC will provide some confirmation of this as they will be providing material for insulin manufacturers and for the insulin reference method with defined units. G. Wark noted that the units other than 6 were used historically and they were not well-established. The correct unit of 6 was established relatively recently; many manufacturers still list the old factors.

Cross-reactivity

L. Sundaram asked about cross-reactivity with proinsulin, it is not an issue for the reference method but can be an issue with immunoassays, what should manufacturers be aware of when developing assays? M. Steffes said the papers published by the Insulin Committee over the years describe this issue. R. Little said early on in the C-peptide standardization process proinsulin was analyzed and examined to see if there was a relationship between PI and C-peptide results. It is very assay-dependent, we could assist manufacturers in looking at this. M. Steffes noted that

one of the split products has quite a bit of cross-reactivity with insulin, the other does not. The one with cross-reactivity exists in low concentrations. It is generally not a problem but manufacturers need to be aware of it. D. Holmes said that many package inserts do not have information on PI cross-reactivity. We should encourage everyone to systematically measure and report it, as PI cross-reactivity could impact standardization. It will be patient-to-patient variable so it would be difficult to build in a "fudge factor". Also, I would expect the insulin to proinsulin ratio to be different in glucose-stimulated versus fasting specimens. R. Little said the Tosoh assay used at DDL was listed in the insert as having some cross-reactivity with PI but we did not see evidence of it, maybe some of the studies need to be redone? We also might want to check this in a future wild card CAP study by including a sample with high PI. There will be some fine-tuning to be done in the future as far as looking at the performance characteristics of assays. Right now we are focused on getting the results to match. C. Jones said there is a risk to manufacturers in terms of trying to address PI cross-reactivity, it might mean having to re-construct entire assays. D. Holmes agreed but noted that it would be helpful for manufacturers to report cross-reactivity so labs can be aware of it. R. Little said that standardization will not help with individual method interferences, but once the process begins we can help in addressing these issues with each method.

Standardization process

R. Little asked manufacturers to begin the process of standardization. We now have a reference method in place that is listed with the JCTLM and have serum samples available with reference values assigned. Manufacturers can request samples any time. C. Jones asked if the data showing that the two reference methods now match has been published. Do we know that the current data are correct? R. Little said it is not in the C-peptide paper that was just published as we did not have the data at the time the paper was submitted. G. Miller suggested publishing the new data as a letter to the editor; R. Little agreed to this. C. Dauscher asked about how the process would be rolled out, once the process begins, do we set a date where the patient results will change over to standardized results? In the meeting with L. Thienpont regarding free T4 and TSH there was much discussion regarding this. R. Little said one option is to inform the labs of the relationship between the old and new values, this is especially important for labs involved in long-term trials. It would be good if this could be provided ahead of time. C. Dauscher said there needs to be physician education as well. R. Little agreed and said labs could hopefully assist in this process. G. Miller said this is an excellent suggestion, a date could be set and also we should work with the clinical organizations. We need to make them aware of when this will happen, what is being done and why, maybe have a session at the ADA. M. McPhaul asked if there are links between this group and other groups such as PATH. They are looking to extend hormone testing standardization efforts out to all of the relevant groups, ADA is a participant. R. Little said ADA would support educational efforts. Everything will not change at exactly the same time but we need to give a time frame. The impact will not be as large as with tests that are used more in clinical settings, but it will impact labs performing research trials. Most of the people involved in these studies are likely aware of what we are doing. Some of the labs were involved in the early studies and people from those labs sometimes attend these meetings, we also send the minutes out to them to keep them informed.

R. Little thanked everyone present for their attendance, the meeting was adjourned at 8:45 AM.

Minutes prepared by Curt Rohlfing 8/11/2017. Modified by Randie Little 8/14/2017.