

# 2011 C-Peptide Standardization Manufacturer Meeting

## Minutes

Wednesday July 27 8:00 AM – 10:00 AM  
Marriott Marquis, Atlanta, GA

### Participants:

#### C-peptide Standardization Committee Members

Randie Little—University of Missouri  
Daniel Stein—Albert Einstein College of Medicine

#### Committee members not present

Judith Fradkin—NIDDK  
Carla Greenbaum—Benaroya Research Institute  
W. Greg Miller—Virginia Commonwealth University  
Gary Myers—AACC  
Jerry Palmer—University of Washington  
Kenneth Polonsky—Washington University  
Lisa Spain—NIDDK

#### Guests

Kelly Chun—Esoterix  
Curt Rohlfing—University of Missouri  
Michael Steffes—University of Minnesota  
Alexander Stoyanov—University of Missouri  
Linda Thienpont—Ghent University, Belgium

#### Manufacturer Representatives

Margherita Banci—IDS Ltd  
Gabriella Bobba—Diasorin  
Thomas Ciesiolka—Roche Diagnostics  
Sean Conley—Alpco Diagnostics  
Masuo Inoue—Tosoh Bioscience  
Shuichi Horikawa—Fujirebio  
Susan Kolarik—Tosoh Bioscience  
Patrick Lindstedt—Mercodia  
Yu Nashida—Tosoh Bioscience  
Tadashi Ninomiya—Fujirebio  
Judy Ogden—Tosoh Bioscience  
Heather Pham—IDS Ltd  
Susan Retka—Beckman Coulter  
Kouichi Saga—Tosoh Bioscience  
Hisao Tsukamoto—Tosoh Bioscience

#### 1) **Welcome and Introduction—Randie Little**

R. Little welcomed those in attendance, those present introduced themselves. The minutes of the 2010 meeting were approved.

#### 2) **Update on Clinical Trials for Diabetes Prevention—Daniel Stein**

- Main points
  - > 1.4 million in the US; incidence rates rising
  - Type 1 diabetes is (usually) an autoimmune disease.
  - Adolescent (obese) Type 2 Diabetes rapidly increasing.
  - It is a predictable disease with different phases.
  - Preventing future, maintaining and/or restoring beta cell function is the goal.
  - C-peptide is the most accurate biomarker of beta cell area and function in beta cell depleted diabetes.
- Goal is to identify those at risk for beta cell destruction and take steps to preserve beta cell function.
- Why preserve beta cell function?
  - Prevent short-term complications (hypoglycemia)
  - Prevent long term complications (retinopathy, nephropathy, neuropathy, etc.)
- Insulin secretion in-vivo
  - Pro-insulin is cleaved to insulin and C-peptide.
  - Insulin (but not C-peptide) is cleared by the liver.
  - Insulin is not the best marker for insulin secretion because of its rapid clearance; the liver quickly removes 50-80% of the insulin secreted.
  - Circulating C-peptide (but not insulin) accurately reflects what is secreted by the pancreatic beta cells.
- Which tests to measure beta cell function in clinical trials?
  - Glucagon Stimulation Test (GST) or Mixed-meal Tolerance Test (MMTT): MMTT is more physiological and better stimulates C-peptide (Greenbaum et. al 2008)

- Urinary C-peptide/Creatinine Ratio
  - 1) Single-sample UCPCR is stable and reasonably reproducible, and is proportional to 24 hour UCPCR ( $R^2 = 0.64$ ) (Hattersley et. al, Clin Chem 2009;55, 2035-39).
  - 2) 2 hour UCPCR is highly correlated with 90 minute MMTT C-peptide overall ( $r=0.87$ ) and in detecting stimulated C-peptide  $<0.2\text{nM}$  (95% sensitivity, 100% specificity), and correlates highly with home post-prandial 120 minute UCPCR( $r=0.8$ ) (Hattersley and colleagues, ADA 2010 Orlando)
  - 3) UCPCR represents an excellent tool for distinguishing HNF 1- $\alpha$ /HNFactor 4- $\alpha$  maturity-onset diabetes of the young (MODY) from long-duration Type 1 Diabetes (ROC curve ~99%) (Hattersley and colleagues, Diabetes Care February 2011 34:286-291).
  - 4) Fasting urine C-peptide are much lower in lean (~4 ng/ml) as opposed to obese (~30 ng/ml) subjects, subjects with T2 diabetes had levels of ~12 ng/ml (Stein et. al)
- Immunobiology of T1 diabetes
  - Activated T-cells cause stimulation of immune cells.
  - Release peptides that are recognized by T-cell receptor.
  - Secretion of cytokines and growth factors.
  - Proliferation of T-cells that are cytotoxic and kill beta cells
- Treatment Approaches for Type 1 Diabetes
  - Intensive Insulin Therapy
  - Antigen specific interventions
  - Non-antigen-specific interventions (anti-CD3 monoclonal antibodies)
  - Regenerative Therapies
- Studies
  - Results from the Trialnet glutamic acid decarboxylase (GAD) autoantibody vaccine trial have not shown it to be effective in preserving beta cell function in patients with recent-onset Type 1 diabetes (Lancet 2011;378:319-27).
  - Anti-CD3 Trials
    - 1) Mechanism of Action: Anti-CD3
      - Blocks co-stimulation between dendritic and T cells
      - Prevents augmentation of the response in terms of proliferation of toxic cytokines and attack of the T3 cells on the beta cells.
    - 2) Abatacept immunoglobulin trial results show a trend toward beta cell preservation that was not significant; it appeared to slow but not stop beta cell loss (Lancet online June 28, 2011)
    - 3) Protégé trial (Teplizumab) one year results showed no difference in primary outcomes between treatment and control groups. However, several subgroups (8-11 years of age, USA only, patients initially treated early) did show improvement in C-peptide preservation (Lancet online June 28, 2011).
    - 4) DiaPep 277
      - 24 amino acid synthetic peptide derived from HSP60
      - Induces anti-inflammatory T-cells (Th2, Treg)
      - Bloc Phase I, II studies are now complete, results show an excellent safety profile and a trend toward efficacy in newly diagnosed patients.
      - Phase III studies are now underway.
- The Dream of Beta-cell Regeneration
  - 1) In type 1 and type 2 diabetes there is apoptosis or programmed death of beta cells due to cytokines and toxic intermediates.
  - 2) Ideally would like to stop the immune attack on beta cells to preserve them and also grow new cells
  - 3) There is evidence that growth of new beta cells is possible and does occur (for example in bariatric surgery).
  - 4) GLP-1
    - Evidence in animal models that it can grow new beta cells and help prevent apoptosis.
    - Increases insulin synthesis and secretion of insulin

- Our studies indicate that GLP-1 is highly effective in stimulating insulin biosynthesis in vivo under hyperglycemic conditions in normoglycose tolerant and Type 2 diabetic subjects.
- Types of Beta Cell Intervention Trials
  - Immunosuppression
  - Beta Cell Rest
  - Immunostimulation
  - Immunomodulation
  - Miscellaneous
  - Regenerative (proposed)
  - Transdifferentiation
- Summary
  - Antigen specific therapy trials in new onset subjects are being undertaken.
  - Immunomodulatory trials with anti-CD3 are encouraging.
  - Prevention of Beta cell apoptosis; stim regeneration/neogenesis attractive
  - Level of C-peptide may be an important indicator of potential response.
  - Multicenter trials and networks will help us find effective therapies during the next decade.
  - Combination therapy targeting multiple pathways may hold the greatest hope for prevention and cure.

**Discussion:**

RL asked if DS feels that C-peptide will be used in T2 patients when they are on insulin. DS said yes, we must bear in mind that in T2 diabetes half of the problem is insulin resistance, not just beta cell loss. The correct way to evaluate beta cell function in this case is beta cell function normalized to the degree of insulin resistance. People have attempted to do this by doing OGTTs and measuring insulin, this to me is a bad thing to do. Insulin clearance by the liver can vary from 50 to 80%. The most appropriate biomarker for beta cell function is C-peptide, but then you need an appropriate indicator of insulin sensitivity. Currently the gold standard is the hyperinsulinemic euglycemic clamp, this is very involved. IVTT can be used but is not as good. Epidemiologically insulin measurement is often used, but there are two caveats. Liver clearance may vary, the other issue is the glucose level; higher glucose levels will result in higher beta cell activity and vice-versa. So, the role for insulin as a marker of insulin sensitivity is mainly in large epidemiological trials, it may also be useful for clinical screening but there are caveats.

**3) Update on C-peptide Standardization Studies—Randie Little**

- In 2002, the NIDDK organized a C-peptide standardization committee and funded an international comparison study of C-peptide assays.
- Phase I Study
  - WHO normalization was ineffective in reducing the variability of C-peptide results within and among lab/methods.
  - Normalization with sample calibrators was effective in reducing variability of C-peptide results.
- Phase II Study: Normalization of C-peptide results using patient samples that have been assigned values by a reference method greatly reduces the variability among methods and laboratories.
- Phase III Study
  - Standardization of C-peptide results to a Mass Spectrometry Reference Method significantly reduces between-lab variability
  - Calibrators can be prepared from either single donors or samples pooled from more than one donor
  - Serum is acceptable for the Reference Method and can be used for calibrators
  - Some methods still have relatively high CVs in some labs
- Phase IV Study: Pilot Re-calibration Study: To evaluate the use of pooled serum calibrators with LC-MS assigned values for method re-calibration by the manufacturer.

- Manufacturer calibration of methods using reference value-assigned pooled serum substantially improved the comparability of C-peptide results.
- The fasting and 2-hour specimens from one subject showed much greater variability among the methods than the other samples with both the manufacturers' usual and pooled serum calibrations. We subsequently discovered that the person was taking Accutane at the time, we do not know if this was the cause.
- Comparison of C-peptide Results from two Reference Laboratories
  - In order for manufacturers to re-calibrate their C-peptide assays to the reference method we must have it listed with JCTLM which requires a comparison between two reference laboratories.
  - We have been setting up a second C-peptide reference assay at the University of Missouri.
  - Initial comparison data between the two laboratories shows good correlation between them with both pooled and individual donor sera ( $r^2=0.97$  and  $0.93$ , respectively).
  - We will continue to work on developing the second reference lab/method.
- Next steps
  - Complete method setup in second reference laboratory (MO)
  - Publish comparison
  - Submit Reference method to JCTLM
  - Prepare another set of pooled sera for calibrators (#, levels?)
  - Collect another set of individual test sera
  - Ship to manufacturers for assay re-calibration

#### **Discussion:**

##### ***Sample Type***

MS asked DS about the use of EDTA vs. serum for C-peptide. DS said that EDTA alone actually accelerates C-peptide degradation, serum is reasonably stable, EDTA plasma with aprotinin and DPP4 inhibitor is the best. MS said rapid processing is also important, DS agreed saying that this may not always be done properly in clinic settings where samples for large trials are typically processed. MS said they are using the TrialNet protocol in a study with EDIC seeing if subjects have remaining beta cell function, he does not know if aprotinin is specified in the protocol. DS said that his laboratory has received a large cohort of specimens from TrialNet for cross-referencing against the immunoassay method, he is also not sure if they used aprotinin or DPP4. In some situations it may not be practical to use aprotinin plus DPP4 but it is best if feasible. MS said that Hattersley and colleagues showed that freeze/thaws are fine for urine C-peptide. DS said that for serum, C-peptide is reasonably stable for one rapid freeze/thaw but not multiple freeze/thaws. MS asked if EDTA plasma specimens with aprotinin that were drawn in the DCCT and have been frozen for 30 years would still be suitable for C-peptide analysis. DS said they probably should be OK as long as they have been kept frozen and not subjected to freeze/thaws. RL asked if they were ever stored at -20, MS said they have been at -70. They also obtained urines for measurement of creatinine clearance, those might be better. DS said urine samples should be pretty stable. RL asked if we should be thinking about urine C-peptide measurement. DS said he does not know the specifics as far as which assays are validated for measuring C-peptide in urine, some researchers have been measuring it. Hattersley et al. used the Roche assay, and we can measure it by IDMS, we may need to consider this.

##### ***Discrepant specimens from Phase IV***

DS said that Accutane can cause hypertriglyceridemia, could this be the cause of the discrepancies. RL said this would probably have caused noticeable lipemia. DS said that the medication is no longer commonly prescribed due to issues with liver toxicity. PL thought that the issue might be interference from a heterophilic antibody such as a mouse antibody. This type of interference is generally dependent upon the assay, reagents, conditions, etc. It was noted that the samples could be tested for this type of interference and if it is present a blocking agent can be added to the specimens. RL asked if specimens to be used to make calibrators could easily be screened for this interference. PL said that it is more complex than this, it may not be possible to use a single blocking agent with all assays. CR and RL noted that the subject was drawn again after going off of the medication. The new specimens

were analyzed by several of the methods that showed the most discrepancy in the study and the initial large differences were no longer evident. RL noted that all of the samples were assayed for proinsulin and there was nothing unusual with results for these specimens.

#### ***Number of samples and levels needed***

RL asked the manufacturers if the range of calibrators used in the last study is appropriate. DS said that the high end is relevant, with insulin resistance we have seen levels around 7nmol/L under stimulation but this is very unusual. The highest level of calibrator used in this last study was ~9nmol/L which is pretty high. MS said the range is appropriate, at least from a T1 point of view. RL said an advantage of making pooled calibrators is we can pool samples at the lower end of the range with near-zero C-peptide samples from long-term T1 subjects and thereby cover the very low range. DS said that for the intervention trials levels between 0 and 1 nmol/L are the most important, anything more is mainly relevant for T2 diabetes. RL said the low ones are the most difficult to get, DS said T1s will be low or pharmacological intervention could be used. RL asked about required specimen volumes. Would manufacturers need much larger sample volumes if manufacturers were actually doing recalibration “for real”? PL said that at his company they would need 200-500uL, RL said that is very doable. It was noted that different assay methods will require different volumes. TC said that 2ml would be sufficient for re-calibration of their methods, single donor samples would be preferred and additives should not be used. From a convenience and practical point-of-view pools may need to be used, but the data showing that use of pools vs. single samples will achieve equivalent harmonization is limited. Also, you can learn more useful information with single samples, for example the case of the individual with unusual results in the current study. There is also the risk of getting an unusual sample included in the pool. MI agreed that this is a concern, it is best to use single donor calibrators. RL suggested there might need to be a “pre-test” of the samples prior to pooling. TC asked how this would be done, RL and DS said it may be possible to analyze the samples on a limited number of methods. TC said that there is also the issue of the traceability chain. If native samples are analyzed by the reference method and manufacturer’s can use them as working calibrators this makes a shorter traceability chain with less uncertainty. DS asked PL if he could make their reference material available for the reference method, they have compared against the WHO standard but it would be good to compare against another good standard. PL said they could do this.

#### ***Stability of samples***

PL said sample integrity is an issue. RL noted that this is why DDL performs the sample drawing and handling at their site. PL said aprotinin and DPP4 should be used in the serum calibrator samples, there may be issues with degradation so why not include them? DS said that with serum the clotting cascade is activated, he is not sure that serum with aprotinin and DPP4 is stable, is there data? PL said they have some data, there are individual differences between samples, we should just take out any variables we can. They have also tried freeze-drying, it does not work, there is degradation even after freeze-drying. RL said we do not intend to freeze-dry the samples, but if freeze-drying doesn’t work what do manufacturers/labs do about controls? DS said their control is liquid-based and frozen at -70 in a albumin/creosol buffer, this seems to be stable. PL said they sell freeze-dried controls for their diabetes assay panels (insulin, pro-insulin, C-peptide) and have been doing so for many years. Roughly one of 15 batches showed instability for one of the levels. They investigated and there actually was C-peptide degradation. This was pooled serum that was freeze-dried and stored at 4 degrees C. Stability studies were performed at high temperature, long-term, etc. over 36 months; in terms of stability it all came down to which individual sera were pulled. DS said that in his experience they do occasionally see a rather large amount of C-peptide degradation in individual samples. PL said they do not know exactly why this occurs, C-peptide has a pentapeptide structure at one of the ends, which is biologically active. They believe this is connected to its stability in serum but do not know how. RL asked about short-term stability of lyophilized materials, PL said it is excellent. RL said that for the CAP survey, which uses lyophilized samples, data for the different methods looked similar to what we observed with the different methods in our study. This would seem to suggest that freeze-dried materials may be sufficient for CAP surveys. DS asked whether the freeze-dried samples in the stability studies were serum or EDTA with additives, PL responded that they were serum-based. DS said it would be interesting to see if there was any difference in stability for freeze-dried EDTA with additives vs. serum, at least for the problem samples. PL said they compared them and did not see a

difference in the short-term. RL asked what the time interval is for short vs. long-term stability, and when did you start to see degradation? PL replied 6 months for short-term, three years for long-term, they observed degradation at two years (4 degrees C). They did not previously have any data on stability of freeze-dried controls, they had already prepared 30-40 batches. KC noted that in their reference laboratory they make their own QC by pooling human EDTA plasma and making small single-use aliquots that are kept frozen. They are not lyophilized and seem to be very stable for at least 2-3 years. PL said that was their experience as well, after this finding they did a larger study with different types of samples. This showed individual differences between samples, some are very stable while some degrade. It is therefore understandable that if a number of individuals are pooled you might not see this effect as it would be diluted out. RL asked what the frequency is of this happening, PL did not know but it does exist, it may be caused by an enzyme. DS agreed, noting the C-peptide has a di-peptide at the end which is a substrate for DPP4 so addition of this might solve this problem although they have not investigated this. PL said that they have been looking at this.

#### 4) Insulin Standardization Update—Michael Steffes

- Background
  - Initial work done by an ADA, NIDDK, CDC work group (2002)
  - Marcovina et al, Standardization of Insulin Immunoassays: Report of the American Diabetes Association Workgroup. Clin Chem 2007;53:711-716.
    - 1) Results for 10 immunoassays were not standardized despite claimed traceability to WHO 1st IRP 66/304
    - 2) Use of a pure recombinant insulin reference material in immunoassays was not uniformly effective to achieve harmonization of results. Some manufacturers could utilize the pure reference material. Some could not.
    - 3) Cross reactivity with proinsulin and split-products was minimal for most, but not all, assays
  - Joint Working Group formed with IFCC
    - 1) Toward standardization of insulin immunoassays. Miller et al, Clin Chem 2009;1011-1018, 2009.
      - Results for 10 immunoassays were not standardized despite claimed traceability to WHO 1st IRP 66/304
      - Use of a different pure recombinant insulin reference material in immunoassays was not effective to achieve agreement of results with an ID-LC-MS/MS for many assays. Satisfactory for some.
      - Standardized results could be achieved by recalibrating with ID-LC-MS/MS values assigned to individual donor sera or to serum pools over a limited concentration interval
      - Unresolved if single donors are required or if serum pools can be used as secondary reference materials
      - Unresolved if pure recombinant insulin preparation can be used to calibrate immunoassays
- Next Steps
  - WHO project to replace 1st IRP 66/304, insulin for immunoassays, with a recombinant preparation in conjunction with replacement of WHO 83/500, IS for human insulin, used to assay pharmaceutical preparations (Chris Burns, NIBSC, UK)
    - 1) Insulin WG continues to provide input on the laboratory requirements for the new WHO insulin international standard
    - 2) Benefit from efforts of the insulin manufacturers
  - Project plan outline for 5-10 years currently pursued by the WG. We have the following goals:
    - 1) Commercial methods have calibration traceable to IDMS RMPs
    - 2) Sustain resources for calibration traceability; e.g. RMP labs and primary RMs
    - 3) Sustain resources for surveillance of traceability, e.g. EQAS, certification process

- 4) Manufacturers require a reference system listed by JCTLM to enable recalibration
  - Primary reference material from WHO
  - cRMP LC-ID-MS/MS (Daniel Stein, Albert Einstein, NY, USA)
- 5) Provide a panel of single donor sera with IDMS values to assist manufacturers with internal method improvement and procedures for calibration traceability
  - NIDDK/CDC has funded preparation and preliminary value assignment of serum samples and pools
- 6) Continue to explore collaboration with the NIDDK work group for c-peptide standardization (Randie Little, chair)
- 7) Letters to manufacturers
- o Outcomes
  - 1) Manufacturers have the option of working with the new WHO insulin preparation
    - Basically upgrading the current status for many
  - 2) Serve as a model for other standardization schemes
    - Laboratory to complete the IDMS measurements
    - Extend beyond the research area to the whole of clinical medicine
  - 3) Weigh the investments in the current and planned efforts
    - ADA and NIH have provided nearly all the currently available resources
    - Resources from the diagnostic community

**Discussion:**

MS said that insulin standardization needs financial support from manufacturers, and noted that insulin and C-peptide standardization efforts are similar.

***Calibrators and Samples***

RL asked if the calibrators just collected are single donor or pooled, MS responded that some are pooled and some are single donor. RL asked how many sets there are, MS said there are 40. Manufacturers can use either single or pooled. PL said the number of samples is the most important, a panel of 20-40 samples for recalibration. If there is one unusual sample it is not as important if there are more samples. RL said that for C-peptide we have both pooled calibrators and also individual samples used to test the calibration. MS said that for insulin standardization we are asking manufacturers to calibrate with the new WHO reference materials, we will provide samples to test how good the calibration is. LT said that for recalibration manufacturers need a place to start, with insulin they can start with the new WHO standard and if this does not enable them to achieve the needed accuracy single-donor samples can be used to readjust the calibration. RL noted that this approach is different than for C-peptide where we do not have a WHO material but we have pooled sera to use as calibrators and single-donor samples to verify the calibration. PL said that from the manufacturers' point of view a reference material is not needed, they need reference-assigned samples to set their calibration, they can use these in-house to set their calibration. He does not believe in standardization first, the first and second tiers are harmonization. Standardization comes later and is probably not achievable for all biomarkers. The goal is to achieve agreement, of course there are other factors that need to be considered including imprecision and interferences. TC agreed and added that variation between lots of materials, whether it be native pools or some other material, is also a consideration. If you have a large number of native sera this helps sustain the harmonization over time. LT said that a reference material is needed to calibrate the reference method procedure. RL said that for C-peptide we do not have a WHO reference material that is of sufficient quality to do this and it may be some time, perhaps years, before we do. DS suggested that C-peptide manufactured by the pharmaceutical industry may be suitable for this purpose even though it is not WHO material. LT agreed but said it should be accepted as the primary calibrator of the reference system. The WHO insulin material may end up being from a pharmaceutical manufacturer, if it is accepted by the BIPM and NMIs after additional testing then it can be used as a primary calibrator. RL asked if we wait for this. LT said if there is no primary material for this purpose you cannot wait, you can only ask NIBSC to develop a new C-peptide standard you can use. DS asked if Mercodia can share their reference material, PL said

this is not a problem but it is formulated specifically for their assay. There was general agreement that harmonization efforts need to proceed even without a suitable WHO standard.

**5) Insulin and C-peptide IDA LC/MS assay Progress Report—Daniel Stein**

- Ultrahigh sensitivity IDA LC/MS candidate reference method for C-peptide established (Rogatsky et al 2006)
- Harmonization of well validated C-peptide immunoassays successfully completed based upon single and pooled donor specimens
- Second site for IDA LC/MS C-peptide in progress (Missouri)
- Initial IDA LC/MS insulin assay method reported (Rodriguez-Cabaleiro Clin Chem 53:1462-69).
  - Limit of Quantitation 12 pmol/L (72 ng/L)
  - CV 3.2-6.3% intra-assay, 3.8-10.3% interassay
  - Achieved goal <32% error as per ADA guidelines
- Our laboratory has been successful in procuring funds for development of a high-throughput analytical biomarker laboratory based around automated robotic specimen handling
- We have acquired an additional mass spec and have made progress in setting up the laboratory.
- Progress in insulin method development
  - We have obtained synthesized U-<sup>13</sup>C h-insulin (mw 6064)
  - Initial step will be affinity purification
  - Microheterogeneity
    - 1) **Problem:** Insulin is susceptible to protein microheterogeneity due to deamidation
    - 2) **Solution:** Generate stable tryptic peptide (GFFYTPK) after HPLC purification
  - Still have some work to do with method optimization, LT has offered to help us with this
  - We hope to be able to compare with results from the LT laboratory
  - The Missouri lab may eventually set up an insulin method as well.
  - Future goals
    - 1) Purification and quantification of U-<sup>13</sup>C h insulin IDA standard, but need reference unlabeled insulin std for comparison!
    - 2) Design and optimization of IDA isotope std and plasma reformatting on automated liquid handler system
    - 3) Optimization of online affinity capture and trypsinization
    - 4) Optimization of ultrahigh sensitivity 2D RP/RP LC/MS detection. Fasting insulin 3-20 μU/ml
      - Goal LOQ < 2μU/ml = 12pmol/L = 72pg/ml
      - Total max CV 3% (7% at LOQ), bias limit 5%
    - 5) Cross validation vs Thienpont LC/MS method and ? Other immunoassays w/ single, donor pools 10-1000pM

**Discussion:**

DS said that funding support is needed, they have obtained the needed equipment but there is not money for the needed staffing. There has been good progress in establishing comparability between the NY and Missouri C-peptide reference laboratories, the goal is to achieve agreement within +/-5%.

*RL thanked everyone for their attendance, the meeting was adjourned at 10:00 AM  
Minutes prepared by Curt Rohlfig, 9/2/11. Modified by Randie Little 9/9/11.*