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Global Biomarkers Standardization Consortium

Reference Materials Teleconference MINUTES

February 24, 2012

ATTENDANCE: Christopher Spedaliere, Irena Baburina, Tobias Bittner, & Jodi Courtney, Paul Contestable, Beth Mcquiston, Bob Dean, Ingo Curdt, Holly Soares, Maria Carrillo, Piotr Lewczuk, David Stuart MSC, Henrik Zetterberg, Pankaj Oberoi, Mary Savage

DOCUMENT AND MEETING MATERIAL LOCATIONS:

Hidden Link: contains all materials and dates for future meetings

http://www.alz.org/research/funding/_global_biomarker_CSF_docs.asp

Public Link: contains general information and dates for future meetings.

http://www.alz.org/research/funding/global_biomarker_CSF_materials.asp

1) Henrik and Piotr on IFCC visit. September Int Fed Clin Chem proposal was submitted for ref method and ref material project. Meeting was held this month and project approved. IFCC is supportive, which means they will provide no money but make a working group and provide suggestions of names for the working group and at this time it is not formed. Will be headed by IFCC.

    a. Also had contact with International Reference Methods and Materials (IRMM) and collaborate with IFCC. IRMM also thought the project was mature enough and ready. Meeting focused on reference materials for calibration and reference method establishment and aware of the methods for Abeta that look promising. It was decided that Piotr, Henrik and Kaj would be working on Abeta first though Tau is important also.

    b. Also discussed Ref Materials for QC. Project Piotr says is focused on calibration material but also want to run parallel project on establishment of ref material as end user QC material. This institute makes public the protocols that people should follow and they certify calibration material. So will compare different matrices such as native CSF and artificial solutions in terms of their compatibility. Could we combine those efforts to establishment of reference method and reference. calibrators. Main focus is on calibrators. But will add QC material establishment for end users. IRMM is located outside Brussels and a unit of 150 people, with great experience of reference materials.

c. Hope to get some information on how the IFCC working group will be formed. But needs to be global working group and Les Shaw was suggested as a US researcher along with Kaj etc. and it is not known if there are requirements about academic vs industry participants. Important that spokesperson for this GBSC be Henrik, Kaj and Les.

d. Most positive outcome would be 2 short term deliverables. FRM based methods to be certified by IFCC used to assign concentrations to reference materials aliquots made and stored by IRMM and used for calibration purposes by kit vendors for Abeta1-42. Major issue might be whether FRM ref method if measures abeta 1-42 and stability of measurements to others might be difficult. Piotr adds that in Germany there is no approval yet for assays but there is a EU project on biomarker standardization and harmonization and with Henrik, Piotr will lead work on this. Biomarker projects sometimes approved by EC don't happen because though approved by EC the money needs to comes from local government . IFCC has approved the project and this will help the project.

e. IFCC says that the GBSC will help disseminate the knowledge of the efforts. IFCC will do nothing until the working group has a proposed reference method and material.

f. Asked IRMM for advice on Tau issues because they have experience with difficult peptides. They stated that one way forward for Tau would be to speak to immunoassays and decide upon one assay giving similar results and label those as the reference method as good as it can get. Then assign the concentrations using standard units etc. So there may be a possible way forward.

g. Holly asked how much money would be involved in this project? There is no clear answer and depends on the project and can get the proper calibrators in first time or repeat experiments are required. IRMM will provide expertise even though they wont provide money. How do other projects get funded? There will be money coming from EU to sponsor some of the efforts. So could be incorporated into this project.

h. Henrik says IRMM is nonprofit paid for by EU countries. IFCC approval they put some resources in the project so no need to pay for material for assay or stability assays. But there will be need for funding from different labs involved. Parts of the EU money can be used that Piotr already mentioned. Bob mentions that this frames the issue but we need to create a work plan. We need the key steps and put them into a work plan. Henrik and Piotr have

a 2 page proposal. IFCC is a slow working organization but is key to getting global approval. Piotr mentioned that he would try to create a work plan and send to IRMM for approval.

i. Ref Method paper draft is almost completed and was presented to IRMM, draft will come to co-authors in a few weeks.

2) Paul Contestable will be presenting, Principal Scientist at Ortho Clinical Dx. Working with BMS and Saladax on development of assay for abeta42. High level presentation will be made on their calibration strategy. Paul described the platform they use, calibration methods and absence of reference method/material and consequence of this. Also discussed calibration options they are proposing to use.

a. In absence of globally agreed upon method, there needs to be a globally established method to standardize the method of the protein being measured.

b. Caliration methodology starts with reference material or method which should be internationally agreed upon and is the standard of truth for the measurement of analyte. Primary calibrator needs to be prepared from reference material based on acceptable scientific rationale and links assay to the "truth". Reference calibrator of selling calibrators needs to be manufacturable for others to use and precise and stable. Selling calibrators then need to be manufactured specifically for every lot, precise, stable and customer friendly.

c. Paul gave a PSA antigen assay example.

d. Calibration options that Paul's group has considered without a reference method. First is a PSA approach, link to an existing assay and they selected en ELISA assay to test a panel of CSF samples covering the assay range with the predictable assay to assign values to reference calibrators. 2nd possibility is LC-MS/MS to analyze a panel of CSF covering the assay range to assign values to ref calibrators. 3rd option is to develop a primary calibrator to assign values to reference calibrators which are value traceable and anchors assay performance but primacy calibrators development is still needed.

e. This 3rd option is what their group has decided to peruse.

f. Primary Calibrator optimization efforts they have looked at for this method involves methods for value assigning, UV method and gross weigh method. This was reviewed by Paul for the method they have selected.

3) Ref material may not be developed too soon, but IRMM method might be developed soon. Primary calibrator is important, would it help if all agreed to use same primary calibrator? If we agree on what peptide to use and net weight based on purity, perhaps there should be some consistency. Vendor might add additional consistency as well. Punkaj joined and has seen within same vendor lot to lot variability, which adds difficulty. Bob mentions that he has also heard variability within vendor. Perhaps manufacturer of kit assays could be approached and attempt to have produced a sufficiently large quantity of material that could be adopted as a consensus starting material. Would that be helpful? Possible? Pankaj also mentions that where vendors are with their assays could be challenging if they are already assigned. Pankaj's organization has some quantity material stored for this but vendors of peptides are of concern, longevity of their compounds etc.

4) Bob mentions that current state of the field is that we are all trying to move forward on sound analytical approaches and consensus material may not be possible. Pankaj mentions a possible round robin with different kits from different vendors. Other issue is having each vendor reveal their method to manufacture material and whether that is possible for sharing. Pankaj thinks it is possible to a certain extent. Paul mentioned that he thinks logistically may be difficult but intermediate reference preparation is where this would lead not a gold standard.

5) So Maria will follow up with Holly and Bob to see which vendors would be invited to talk separately about this round robin possibility. Question would be to see if they would be willing to engage in an effort to pool material and conduct a round robin.

6) Mary Savage asked about the peptide source. Have we heard about this issue and does it make sense to have only one vendor source for a peptide? We were going to put together a list of vendors and their materials as we have heard from MSD and PPD. Holly will work with Maria to get that list together and talk to vendors about this as well.

ACTION ITEMS TO TRACK:

I. Maria will follow up with Holly and Bob to see which vendors would be invited to talk separately about this round robin possibility. Question would be to see if they would be willing to engage in an effort to pool material and conduct a round robin.

II. We were going to put together a list of vendors and their materials as we have heard from MSD and PPD. Holly will work with Maria to get that list together and talk to vendors about this as well.

III. Maria will work with Kaj and Henrik to bring a special overview of the QC program. We will attempt to include a discussion of a possible IRMM work plan and cost. THIS HAS BEEN SCHEDULED MARCH 5th.

Upcoming TC Dates/Times:

Monday, March 5, 2012 – 7:30 am PST / 9:30 am CST / 10:30 am EST / 4:30 pm Sweden: AA QC Program Overview CALL

Wednesday, March 14, 2012 – 7:30 am PST / 9:30 am CST / 10:30 am EST / 4:30 pm Sweden

Thursday, April 5, 2012 – 7:30 am PST / 9:30 am CST / 10:30 am EST / 4:30 pm Sweden

Thursday, April 19, 2012 – 8:30 am PST / 10:30 am CST / 11:30 am EST / 5:30 pm Sweden

Wednesday, May 2, 2012 – 7:30 am PST / 9:30 am CST / 10:30 am EST / 4:30 pm Sweden

Wednesday, May 16, 2012 – 7:30 am PST / 9:30 am CST / 10:30 am EST / 4:30 pm Sweden

Tuesday, May 29, 2012 – 7:30 am PST / 9:30 am CST / 10:30 am EST / 4:30 pm Sweden