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Global Consortium for the Standardization of Biomarkers

Reference Materials Teleconference MINUTES

December 12, 2011

Attendance: Irena Baburina Saladax Biomed, Chris Spedaliere, Gary Feiss, George Bashir Ortho Clinical Diagnostics, Mary Savage, Bob Dean, Les Shaw, Beth Mcquiscon, Lisa DiMagno OCD, Tad Fox OCD, Stefan Jaeger Roche, Punkaj Oberoi, Tobias Vitner Roche, Adam Simon, Henrik Zetterberg & Holly Soares

I. Introduction of Co-Chairs and Membership – Maria Carrillo

   a. Henrik, Holly and Piotr will be co-chairs for this group.

II. Review of key issues for Reference Materials Objectives:

   a. We have invited Roche, Abbot, OCD to this meeting to make sure that what we do doesn't happen in without others knowing what we are trying to accomplish. We have action items from the Holly started with action items, contact Roche, OCD and GE. Slide 2 does outline what we are trying to accomplish. We are trying to create a methods and a reference calibrator that is a gold standard. George Green is going to join us hopefully and can give us an overview on his efforts.

   b. Generating a cert ref material discussion, settled on using native human CSF and Henrik and kaj are driving this to get a CRF approved through the IFCC which will meet Dec 16th to coordinate this next step.

   c. Action items, H and K were going to give us an update from IFCC which will require a reference method and hopefully on the next call we will be hearing more about this. Next also we were going to ask companies to share information with us on their validation efforts. MDS, Abbot, Roche, OCD have joined now and hopefully will be able to share what they have.

   d. Punkaj mentions that the amount of CSF to sustain these products long term, need liters/10s of liters to sustain controls. Mid January we can do a more formal update. Bob mentions that ref material will be a native material collection and storing etc is a challenge and needs to have longitudinal stability, this would give us the needed assurance that this is a stable material and have a value assigned. The other issue is a reference standard

which one could use to build calibrators and one of the questions discussed as a group, that when this group selected a reference material ab or tau substance that we would use to start to prepare reference standards we would pool manufacturers to make sure that companies thought this was sufficiently good material to be used at a corporate level. Punkaj says this is in line with their thoughts. Punkaj mentions they have challenges with the aggregation with AB42 and handling is very critical and the sample handling between the diff labs, there are up to 2 fold diff in quantification so this is a big challenge between sites with reference materials. More so with CSF and less so in calibrator. Ref materials group challenge is that when you go out of native CSF, the calibrators will alter the material. Bob mentions that MDS is many steps down from issues we are needing to contend with. Issue is what commercial source of ref material are companies using to prepare the calibrator. So rather than having this consensus group select one of those, what are manuf using commonly because we can then use that for a common calibration and that this group can use that material so that we do not choose something so different from what manuf use.

e. Punkaj said there were huge variations in values of CSF. So if this group could collect high quality CSF this would be better state than many of the vendors that they get their materials from. Getting the right pre analytical collections is a challenge. 5-10 liters of reference material needs to be consistent. So having a good clinical site to collect this as a WHO Standard Ref Material would be an advantage.

f. George from OCD says having a large pool of CSF is ideal but how will that value be assigned in the first place? Holly mentions that the Ref Method group will be establishing this, they are trying to come up with a gold standard method group, AB independent method and mass spect base method currently the goal. Would this method be years away? Should not take many years, but the main issue would be defining some of the fractions.

g. George mentions that starting with an artificial matrix would be less challenging to make sure you are measuring the right species and has stability. Collecting native CSF is a long term goal in his estimation. So perhaps short term use artificial and long term use native. Short term would be easier to measure and establish. Value signing CSF is a formidable task and agreeing a source of high pure relevant abeta and tau and deciding how to handle it, would be a starting point to move closer to the standard, would not be solution but will help in the interim. Bob Dean says that we are all in agreement with the concept that these two tasks may prove difficult. But

there is an effort to try and identify native human CSF in quantities large enough to use for value assignment and this is very challenging and may take loner. The 2nd is to try to identify a pure ref material that could be used to spike a proper solution in an artificial material to use this as a calibration solution. These 2 pieces would move us forward. We would have to identify a purified source for the ab42 and handling of material to make sure it didn't aggregate to make it available. Each who have attempted to build a commercial assay have grappled with this issue and we would benefit from learning how you individually did this to help us with our plans.

h. Pujkaj says that in January he should have approvals to share this with us, but was the only company that was able to speak to this possibility. Provisions for providing standards in their kits are frozen to a certain concentration because of challenge of going from stock to a frozen working stock is very reproducible. Bob Umek has shared that when they look at inter vial reproducibility they are very stable at that frozen stock level. This is less so for Tau but AB42 requires this because of aggregation and changing the concentration. This will be the challenge for an artificial material.

i. Bob mentions that this group will be making some decisions that may be contrary to what has been done with the commercial side. And so we don't want to cause issues with what has been used to date. We would like the companies to advise us. George cannot agree to share OCD but they will be willing to share what they learned and make suggestions and collectively make decisions, agree together on supplier and purity and diluents and how to handle it, that will go a long way in the spirit of standardization. George says they may be able to provide basic information on this approach.

j. Beth from Abbott will need to go back to check for permission and perhaps be able to come back. ACTION ITEM, various companies will go back to ask for the ability to share information. What information? Source of the AB42 and Tau, how pure it is? Etc. Specific questions would be helpful for George and perhaps others.

    i. Source of Ab42, Tau and commercial source of chem. entity starting material?

    ii. Some of companies have in public domain this information? Can they share also?

k. Manu from Innx, Innx got a green light from company to share with the group the basic principles of standard materials in assay. There wasn't time to

prepare an overview. But for the next call would like to do this. ACTION ITEM: INNX presentation. INNX source materials externally and steps standardized by fractional testing and weighting it on the assay as was designed.

l. For the next call, we will go through all manufacturers to see what they will be able to share.

III. Reference Calibrator,: proposal on the table to get a 3rd party in to get ref calibrators and not languish in precompetitive space so we will wait a bit more to see what standard practice is and see what the QC program.

IV. Maria will work with Kaj and Henrik to bring a special overview of the QC program in January.

V. Henrik will also be able to tell us about the IFCC and the meeting on the 16th of December. Henrik reports that there is no letter yet that was an approval. Things are a bit slow with IFCC, but others that have been involved with other standardizations move slowly, so there hasn't even a formal letter that the project has been approved by IFCC, only oral approval.

VI. EU initiative, standardization initiative application and looks like project will be funded but is a complicated process because individual companies will state their budgets so there is no direct knowledge about this. So can report outcome of this effort for this context on the next call.

VII. Debate, large pool of QC material for the group to use, this might be beyond the scope of this group. Henrik mentions that Piotr was a proponent of this, but perhaps we should start with this other direction described here. Henrik and Piotr will continue to work towards this separately but if we focus on CRF for purposes described by IRMM and IFCC and have a s a goal to deliver a material with calibrator and assigned value will be the idea;

VIII. Fox from OCD perspective, will draft answers to questions and they will have to go through a review as if they were going to be a public disclosure. This will take about 3 weeks. Abbott shuts down last 2 weeks of December.

IX. Maria will schedule call in 3rd week of January, and QC overview call early part of January for all interested to attend.

X. NEXT CALL DEC 19th IS CANCELLED due to the holiday.

Next calls: TO BE SCHEDULED