

IMCLGS Meeting Summary

18 April 2006

Review manuscript outline and form working groups.

Working Title: Recommendations for the characterization and qualification of analytical performance controls for DNA based genetic tests.

Scope of document discussed; Multiplex assay focus (microarray, RT-PCR), analytical controls focused, assay independent vs. analyte specific. This document is not intended to address analyte specific controls which are integrated into an assay for analyte-specific intended use. There was discussion on breaking it out to address specific issues in cancer, infectious disease, acquired disease- e.g. deal with quantification, copy number.

Issue of document size was raised; this could be a rather lengthy publication. A series of monographs was suggested as an alternative. Agreed to form working groups and more fully develop outlines for each section and then determine if there is too much content for a single document. If so then determine organization of subject matter for monographs and approach journal editor, pitch concept of an introductory/overview article followed by a series of monographs.

Next Steps: Form manuscript working group. Define document scope. Please email Janet Warrington if you are interested in participating in this project and include sections of the document (see outline below) or manner in which you wish to contribute.

DRAFT OUTLINE (Thanks to David Barton/EuroGentest for contributions to the outline.)

Working title: Recommendations for the characterization and qualification of analytical performance controls for DNA based genetic tests

The purpose of this paper is to provide recommendations regarding technical/analytical performance controls for DNA based genetic tests, including qualification/selection criteria, characterization, and metrics. The type and amount of control information furnished in the test report is also addressed.

1. Introduction

DNA based genetic tests history and state of the art: an international perspective.

The need for standardization and acknowledgement of the multiple efforts underway

Analytical/technical performance versus analyte performance.

A. (David Barton/Ireland, Orna Dreazan/Israel, Dr Nobori/JBA/Japan, Jean Amos Wilson/USA, others)

2. Nomenclature

Harmonized terminology, what's the same and what's different

A.(Philippe Corbisier/Belgium, Orna Dreazen/Israel, Roberta Madej/USA, /ISO, others)

3. Existing guidelines/standards for RM development and what's needed, and what would be ideal.

A. (Philippe Corbisier/Belgium, Orna Dreazen/Israel, Roberta Madej/USA, /ISO, others)

4. **Recommended selection/qualification criteria**

Expand on each of these desired characteristics and provide examples:

Fit for purpose, independently confirmed, stability, homogeneous, renewable and accessible, traceable, safety, purity, concentration, complexity (similarity to sample), discussion of super/meta/synthetic versus biological.

A. (Els Dequeker/Belgium, Drs Noburi or Kuwa / Japan, Janet Warrington/USA, Jean A Wilson/USA, N.K.Ganguly/India, others)

5. **Characterization of controls**

Recommended methods of characterizing control material including integrity, quantification, evaluation pre and post extraction, amplification, labeling, pooling etc.

A. (Mike Zoccoli/USA, Elaine Gray, Paul Metcalfe/UK, Detlef Niese/Switzerland, Harry Hanon/USA, Peter Barker/USA, Marc Salit/USA, Helen Parkes/UK, Maria Dusinska/Slovak Republic, Ming Qi/China, Vince Vilker/USA)

6. **Use of controls in genetic tests; recommendations**

Control measurement recommendations;

What to measure, when to measure, how to measure

A. (Rob Elles/UK, Elettra Ronchii/OECD-France, Ishwar Verma/India, Vicky Pratt/USA, Jean-Jacques Cassimain/Belgium, Jorge Sequeiros/Portugal, Milan Macek/Czech Republic, Marc Salit/NIST, Helen White/UK Wessex, Maria Chan/USA others)

7. **Reporting. Control report content; what to report; context of information, accessibility, language and metrics, harmonization, how much is enough, what is too little.**

Comments on privacy and information protection

A. (Philippe Corbisier/Belgium, Orna Dreazen/Israel, Ira Lubin/USA, Dr Noburi, Dr Kuwa /Japan, Yeyang Su/China, Elaine Gray, Paul Metcalfe/UK, N.K.Ganguly/India others)

8. **Common sources of error, issues**

A. (Uwe Scherf/USA, Roberta Madej/USA, Ed Liu/Singapore, David Barton/Ireland, Els Dequeker/Belgium, Yan Cao/China, Yoshiki Uyama/Japan, N.K.Ganguly/India, others)

9. **Access to shared controls and control information**

Initiatives to share control information (databases) access to shared materials

A. (Joe Boone/USA , Helen Parkes/UK , Philippe Corbisier/David Barton, Elettra Ronchii/suggest someone? Dr Kuwa, Dr Noburi/Japan, Helen White/UK Wessex, Maria Chan/USA others)

10. **Summary and Next Steps**

A. (Janet Warrington/USA, David Barton/Ireland, others)

B. Invitations in progress, not confirmed

Note: Bob Williamson has offered to act as a reviewer and editor for us.

Next steps: Please contact Janet if you are willing to help draft portions of the manuscript or would like to contribute by reviewing drafts.

2. **IMCLGS web site update** (www.imclgs.org). It has been suggested that we find a non-commercial site for the website to avoid any perceived conflict of interest.

a. Background: One outcome of May 2005 meeting was to set up a website to facilitate info exchange in the active global stds dev community. In order to avoid having to raise money charge members etc Affymetrix offered to host it. We don't filter info and have set this up as a separate site but understand there may be reluctance from some of Affymetrix' competitors to post info.

b. Challenge has been support. Janet has approached (Ray Woosley)CPATH/FDA , IFCC (Philippe Corbisier), and the NIH (NHGRI/F.Collins, NCI/A. Barker)

c. Preference expressed for an international site such as IFCC vs a government hosted site. Phillippe and Francois following up with Heinz Schimmel and IFCC Molec Dx Comm to determine if IFCC could host it.

d. What else should we be linked to -- Posting? (Info from LGC, EurogenTest, IQLM, descriptions of OECD activities, CLSI - "trying to raise awareness")

3. **Proposal to hold meetings to discuss recommendations for qualifying algorithms for DNA based tests and leading to development of recommendations for qualification of computational algorithms for clinical genetic tests.**

1. Build consensus among the international community of stakeholders on how to qualify (select) computational algorithms developed/used for multiplexed clinical genetic tests
2. Produce a recommendations document on the qualification and characterization of computational algorithms for clinical genetic tests

4. **Propose hosting three meetings over the period of 2006 and 2007, one each in USA, Singapore and the EU to meet with key stakeholders, share experience with current processes, discuss local initiatives and propose recommendations for inclusion in the document.**

a. The first meeting in the US in 2006 would be organizational as well as providing US based leaders the opportunity to share experiences with current processes, discuss initiatives and suggest recommendations. This meeting could happen as a satellite meeting to a related meeting or simply be a stand alone meeting. If a stand-alone meeting, probably hold it in Atlanta or Washington DC to facilitate participation of key federal-employee stakeholders.

b. The second meeting would be focused on genetic testing in Pan Asia, current status of algorithm qualification, lessons learned, and recommendations. Envision this as a satellite meeting to the AACR 100th anniversary meeting in Singapore. Ed Liu has offered to co-chair if we have it there. I can call Dan Von Hoff to pitch it- if this sounds like a good plan.

c. The third meeting would take place in the European Union and include presentations of current state of the art in the EU, obtain recommendations and compare and contrast with recommendations suggested at the two previous meetings. Location TBD perhaps this could be a satellite meeting to an OECD Biotechnology Working Group meeting. Would Elettra Ronchii, David Barton, Rob Elles, Philippe Corbisier, Heinz Schimmel, Els Dequeker consider co-chairing (TBD)?

- d. Desirable to have a consistent core of participants at all 3 meetings. The planning committee could propose a meeting structure that would make sense, not be overly burdensome.
- e. Volunteers for planning committee- good balance of key folks-global representation.
- f. Meeting size: JW might be able manage maybe hotel and meals for ~50 people. If interest in larger meetings would need to find additional sponsors.
- g. Next steps. Form planning committee

5. New business - Proposal to change the name of the IMCLGS.

- a. Background: IMCLGS, International Meeting of Clinical and Laboratory Genomic Standards, was named by the meeting planning committee to describe the May 2005 Paris meeting.
- b. To better represent ongoing efforts it has been suggested that we simplify the name to Clinical and Laboratory Genetic and Genomic Standards (CLGGS.org)
- c. Next steps. Query IMCLGS membership, if consensus then work with dba to transition name, logo, web address etc.