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# MINUTES

Interim Scientific Advisory Committee Meeting  
Monday 17<sup>th</sup> December, 2012  
By Skype

## ATTENDEES

Garry Cutting (Chair, USA)	Mona El Ruby (Egypt)
Arleen Auerbach (USA)	Mauno Vihinen (Sweden)
John Burn (UK)	Richard Cotton (HVP Scientific Director, Australia)
Mireille Claustres (France)	
Marc Greenblatt (President HGVS, USA)	Heather Howard (HVPI Operations Manager)
Finlay Macrae (Australia)	Tim Smith (HVPI Communications Officer)

## Apologies

Johan den Dunnen (The Netherlands)  
Aida Falcon de Vargas (Venezuela)  
Richard Gibbs (USA)  
Yoichi Matsubara (Japan)  
Gert-Jan van Ommen (The Netherlands)  
Ming Qi (Head China Node Partnership, China)  
Stephen Lam (President IFHG, Hong Kong)

## AGENDA

### 1. Welcome

In the absence of Garry Cutting, Richard Cotton welcomed everyone to the meeting. Marc Greenblatt left the call after checking that the Skype link worked due to unforeseen circumstances.

### 2. Confirmation of minutes of previous meeting

The acceptance of the minutes was moved by Richard Cotton. Motion passed unanimously.

### 3. Issues arising from previous meeting

#### a. Establishment of an Ethics Committee

Heather Howard reported that the ICO has not had the opportunity to make any progress on this matter. This will be rectified in the New Year and a report made to the next meeting of this Committee.

b. Process for the granting of Warrants of Recommendation

Heather Howard reported that this process had also been delayed and as such there was nothing to report. A draft process document will be circulated prior to the next meeting of this Committee.

c. Establishment of HVP China Country Development Program selection committees

Garry Cutting joined the conference call and assumed the chair.

Heather Howard reported that the office would be putting forward two applications (leads: Austria and Belgium) for consideration by selection panels. She thanked ISAC members for volunteering to serve on the panels and informed them that they will be contacted by the office in the coming week.

d. Working Group Charters

Timothy Smith reminded the Committee that the previous meeting proposed creating two Working Groups to undertake the activities specified in AP02-2012: Assigning Pathogenicity to a Genetic Variant and AP03-2012: Minimal content for gene variant databases (LSDBs). The Committee must now officially charter these Working Groups. The ICO has prepared draft charters for discussion.

Richard Cotton proposed that members submit comments on the draft charters via email to Timothy Smith ([tim@variome.org](mailto:tim@variome.org)) by the 30<sup>th</sup> of December, which the ICO will then collate and circulate to the Committee for sign off via email.

Mauno Vihinen noted that, in relation to establishing minimum content requirements for gene/disease specific database, the Gen2Phen project had already done some work in this area and should be involved in this activity. He also noted that there is some overlap between this activity and the database accreditation activity that he is currently drafting an Activity Proposal on. Timothy Smith suggested that, as the ICO noted in its comments on the Activity Proposal, the proposed scope is very broad and may need to be constrained to remove the overlap. The charter could also specifically instruct the Working Group to work closely with the anticipated Database Quality Working Group.

Richard Cotton asked Mauno Vihinen if he would be willing to chair the minimum content Working Group. Mauno Vihinen noted that the Activity Proposal came from Leiden and there was interest there. Arleen Auerbach indicated she was willing to be involved in the Working Group.

**ACTION:** Committee Members to submit comments on the draft charters to the ICO by December 30

e. Alternate Chair

Richard Cotton nominated Arleen Auerbach. Arleen Auerbach nominated Mauno Vihinen. Arleen Auerbach and Mauno Vihinen were elected as alternate chairs.

#### 4. Applications for Warrants

a. Application for Warrant of Recommendation – HGVS variation nomenclature (Peter Taschner)

b. Application for Warrant of Recommendation - Mutalyzer (Peter Taschner)

c. Application for Warrant of Recommendation - LOVD (Peter Taschner)

The Committee noted that the applications were still current, but deferred making a decision until the ICO has prepared a process for assessing applications on which the Committee has agreed.

## 5. Activity Proposals

### a. Sequence Variant Description Committee (Johan den Dunnen)

The Committee noted the ICO's comment that the proposed Activity did not fit within the Project's Standards Development Process in that it called for the creation of a standing committee to deal with nomenclature issues. The Committee also noted that it was very important for the Project to be proactive in the nomenclature space. Mauno Vihinen mentioned that he had identified several issues with the current nomenclature guidelines. Garry Cutting noted that variant nomenclature is a broad issue and is important to a lot of people and groups. He requested that Johan den Dunnen provide the Committee with more information about how the proposed committee would be run and who would be represented on it. The Committee members recognized that it was important for cytogeneticists via the American Society of Cytogenetics or the International Standards for Cytogenomic Arrays (ISCA) Consortium lead by David Ledbetter to be represented, as well as the Decipher Consortium. Mona El Ruby requested that clinical geneticists be represented on the committee. Garry Cutting concurred, noting that he had observed pushback from clinical geneticists in the past when nomenclature had changed as it made it difficult to provide information to their patients. Mauno Vihinen suggested that the Committee may need sub-groups for different disciplines. Richard Cotton requested that David Cooper from the HGMD be approached as well.

Heather Howard suggested that the ISAC charter a Working Group to perform the first part of the proposed activity: review and extend existing nomenclature guidelines, and simultaneously, that Working Group would make some recommendations to the ISAC about how the Committee would be managed into the future.

**ACTION:** ISAC to act as Sponsoring Council for a Working Group to review and extend nomenclature guidelines and provide advice to the Committee about how nomenclature should be managed into the future. The ICO to draft a charter for the working group and circulate to the Committee with the draft charters discussed previously

## 6. Scientific Directors Report

The Scientific Director's (attached) report was tabled.

Garry Cutting requested more information on the relationship between the Human Variome Project and WHO. Heather Howard and Timothy Smith updated the Committee on the outcomes of the two consultation sessions run in San Francisco and Malaysia. All the participants were supportive on WHO/HVP/PHG Foundation undertaking a join project in 2013 to establish the need for and feasibility of a WHO run global programme on genetics and genomics. The project would consist of a series of consultations via interviews, events and surveys, both inside and outside of WHO. The resulting report would be given to WHO for a decision on whether to implement a global programme on genetics and genomics, most likely in 2014.

## 7. Meetings and Events

The Committee noted the proposed schedule of meetings and events in the Scientific Director's report.

## 8. Strategy for collection and storage of large datasets

Richard Cotton updated the Committee on the free online publication of the Emory labs molecular dataset. He further reported that the HVP Australian Node was moving ahead with plans to begin collecting whole-exome and

whole-genome data within Australia. John Burn updated the Committee on the UK's recent commitment of £100 million to set up high-throughput whole-genome diagnostic pipelines, most likely storing the data at EBI. The Committee noted that they need to begin considering how the Human Variome Project will approach the issue of collecting and storing WGS data and how prepared the current collection architecture is for this eventuality.

Garry Cutting noted that storing whole-genome sequences is a massive undertaking and that a better option may be to store only the variant data (VCF data). John Burn endorsed this idea on advice from his bioinformaticians. He also noted that however it is handled, it will result in a huge influx of data into gene/disease specific databases. Finlay Macrae informed the Committee that the curator of the InSiGHT database is taking up a part-time appointment in the diagnostic service at Victorian Clinical Genetics Service DNA lab to explore how WGS data can be presented to consumers, stored and shared including with the InSiGHT database, and how it fits with the entire HVP system more broadly. Mauno Vihinen cautioned the Committee that data quality will be a problem that needs to be addressed, as will the fact that the majority of variants generated during diagnostic WGS will not have clear disease relevance. Richard Cotton noted that NCBI and EBI are already working on pipelines and systems for handling this data and perhaps the role of the Human Variome Project is to help propagate their solutions to the community.

John Burn updated the Committee on a conversation that he had recently with Johan den Dunnen and expressed his concern that Johan's funding for continued development of LOVD will soon end. He urged the Committee to consider how this work can be supported.

## 9. Other matters

### **IrDiRC Representation on the ISAC**

Richard Cotton asked the Committee if there was support for asking two representatives from IrDiRC to sit on the ISAC, nominally Seglolenne Ayme (Europe) and Kym Boycott (US/Canada). John Burn recommended that the HVP first approach IrDiRC to establish better how the two groups could work together and if having representation from each group on the other's advisory committee was the best way to achieve that.

**ACTION:** International Coordinating Office to correspond with IrDiRC about further collaboration

### **The United States of America**

Garry Cutting update the Committee on recent developments in the US, namely Heidi Rehm and others involved in collating variant data from testing laboratories expressing interest in working with international groups, particularly the Human Variome Project. He noted that this could be construed as the Human Variome Project gaining recognition in the US for its potential role in coordination of variant data at the international level.

### **EuroGenTest and Patient Organisations**

Mireille Claustres asked the Committee to consider further engagement with EuroGenTest and patient organizations. Richard Cotton informed the Committee that he has spoken with EuroGenTest in the past and they are generally supportive. He promised to do further work on the matter to explore ways to engage further.

**ACTION:** Richard Cotton to explore further engagement with EuroGenTest

### **Incidental Findings during WGS**

Mireille Claustres asked the Committee for opinions on the issue of disclosure of incidental findings discovered during whole-genome and whole-exome sequencing. Richard Cotton spoke of guidelines currently being developed in The Netherlands. He suspected that many other groups were working on guidelines as well. Garry Cutting mentioned that the American College of Medical Genetics were. He also noted that it is a bit like a Hydra at the moment, with many different heads; once it's all bubbled to the top, there will be a need to achieve consensus.

John Burn expanded on Richard Cotton's information about guidelines in The Netherlands, noting that the way they are proceeding is for an independent clinically-oriented team to determine how much information to give to the clinician dealing with the patient. By doing so, they provide the clinician with a buffer and prevent them from knowing information that they should not be passing on to the patient. Arleen Auerbach noted that this issue is best handled at the national level and that the Human Variome Project should be abreast of the issue but that it should not be an Human Variome Project activity. It was suggested that the Human Variome Project may have a role in keeping people informed of how each country is approaching the issue. John Burn noted that HVP Country Nodes will want to be involved in the issue as it will impact on database content.

#### **10. 2013 ISAC Meetings**

- January – Monday 21st
- February – Monday 25th
- March – Monday 25th
- May – Monday 6th
- June face to face meetings will be held at UNESCO in Paris 5-7th June, 2013
  - Scientific Advisory Council Meeting - 5th June, 2013.
  - International Confederation of Countries Advisory Council Meeting - 6th June, 2013
  - Gene/Disease Specific Advisory Council Meeting – 7th June, 2013
  - UNESCO Ambassadors Information Seminar – 10th June, 2013 followed by a Cocktail Party in the evening.
- July – Monday 29th
- August – Monday 19th
- September – Monday 30th
- October – Face to Face ASHG Boston 23rd
- November – Monday – 25th
- December – Monday 16th

The proposed dates and times for future meetings were noted. Garry Cutting will poll members for a better day than Mondays. He thanked everyone for making the call and promised to investigate better options than Skype for the future.

## Scientific Directors Report – December, 2012

### a. Consortium Members

There are currently 998 Consortium Members from 72 Countries

### b. New & Potential Country Nodes

There are no new Nodes to report since our last meeting however there are a number of countries who have indicated to the ICO that they will be forming a Node in the New Year; these are India, France, Philippines, Brunei and Brazil.

### c. Database Selection Sub-Committee

I am pleased to report that a draft of the “Process for establishing and assisting International Gene/Disease Specific Databases (LSDB’s) by China” has been sent to the sub-committee for review

### d. Countries Development Program

This program currently has applications from Austria, Belgium, Malaysia, and Kuwait. Two have reached the point of consideration for funding. The others are still undergoing the review process. Some other countries and regions are still in the process of putting forward an application.

### e. Country Council

A survey has been sent to all 16 HVP Nodes and 25 other countries to establish a base line of what is offered in Genetics within each country. This will be finalised early next year when a report will be completed.

### f. Gene/Disease Database Council

The council currently has 1 Working Group under its purview “Disclaimer Statement on LSDB websites” and is working towards increasing the membership. It is expected that relevant interest groups and activity proposals will be developed next year.

### g. UNESCO

We have strengthened our ties with UNESCO by supporting a person on a part-time basis within the Basic Sciences Division to work on raising the profile of the HVP activities to UNESCO delegations. They will also be working on the organisation of the celebrations around the discovery of DNA to be held in June together with our scheduled meetings.

### h. World Health Organisation

The preliminary consultations to establish if we should proceed with the joint project investigating the need and feasibility of a WHO global programme on genetics and genomics were carried out in San Francisco and Kuala Lumpur. We are pleased to report that the overwhelming majority of participants agreed that the project should go ahead and that it is critical that WHO plays a role in the future of Global Genetic Healthcare.

### i. Meetings and Events

The ICO held a satellite meeting on the topic of “Establishing a Country Node” at the 10<sup>th</sup> APCHG in Malaysia, as well as WHO consultation meeting and a Booth. There was considerable interest in establishing Country Nodes from some of the delegates.

Some other meetings at which the HVP will be involved

- 6th International Biocuration Conference, Churchill College, Cambridge, UK, April 7-10. Richard Cotton Invited speaker.
- Human Variome Project Workshop/Session at Human Genome Meeting/ International Congress of Genetics 2013, Singapore, April 16. R. Cotton and T Smith
- Health Informatics Society of Australasia (HISA) Big Data 2013 Conference – “Big Data: addressing the challenges of the data deluge in health”, Rydges Melbourne, Australia, April 18-19. R Cotton Organizer (member of Scientific Program Committee).
- 12th International Symposium on Mutation in The Genome (International Mutation Detection Meeting), Lake Louise, Canada, April 22-26 R Cotton Organiser
- HVP Scientific Advisory Committee Meeting  
UNESCO Headquarters, Paris, France, June 5.
- HVP International Confederation of Countries Advisory Council Meeting, UNESCO Headquarters, Paris, France, June 6.
- HVP Gene/ Disease Specific Advisory Council Meeting, UNESCO Headquarters, Paris, France, June 7.
- UNESCO/HVP Celebration of the discovery of DNA (60 years), the completion of the sequencing of the Genome (10 years) and the UNESCO declaration on Genetics (10 years).  
UNESCO Headquarters, Paris, France, June 10
- Human Genome Variation Society: Clinical Applications of Next Generation Sequencing, ESHG Satellite meeting, Paris, France, June 8. HVP Co-Organizer
- OESO 12th World Conference on Cancers of the Oesophagus, UNESCO Headquarters, Paris, France, August 27-30. R Cotton - President.
- InSiGHT Annual Meeting – Cairns Australia – 28th 31st August includes Joint HVP day - T. Smith speaker