THE HUMAN VARIOME PROJECT

sharing data · reducing disease

an NGO Official Partner of UNESCO

MINUTES

International Scientific Advisory Committee Meeting
Thursday 22 May, 2014
1430 – 1630 hrs Paris, France.

MEMBERS

Garry Cutting (Co-chair, USA)
John Burn (Co-chair, UK)
Richard Cotton (HVP Scientific Director, Australia)
Raymond Dalgleish (UK)
Johan den Dunnen (The Netherlands)
Marc Greenblatt (President HGVS, USA)
Finlay Macrae (Australia)
Ming Qi (China)
Raj Ramesar (South Africa)
Peter Taschner (The Netherlands)
Mauno Vihinen (Sweden)
Michael Watson (USA)
Martina Witsch-Baumgartner (Austria)
Non-voting members
Arleen Auerbach (USA)
Qasim Ayub (UK)
Collet Dandra (South Africa)
Dhavendra Kumar (UK)
Augusto Rojas-Martinez (Mexico)
Heidi Rehm (USA)
Aida Falcon de Vargas (Venezuela)
Tom Weber (USA)

Apologies
Stephen Lam (President IFHG, Hong Kong)
Donna Maglott (USA)
Non-voting members
Mireille Claustres (France)
Mona Omar El Ruby (Egypt)
Ada Hamosh (USA)
Rita Ines Noher de Halac (Argentina)
Katsushi Tokunaga (Japan)

ICO Staff
Heather Howard (HVPI Operations Manager)
Timothy D. Smith (HVPI Communications Officer)
Helen Robinson (HVPI Liaison Officer for WHO)

AGENDA

1. **Welcome to new members**

   Garry Cutting welcomed the new non-voting members to the Committee and outlined the process of monthly teleconferences through which the Committee meets.

2. **Apologies**

   Apologies from those listed above were noted.

3. **Confirmation of minutes of previous meeting**

   The minutes of the previous meeting were confirmed.

4. **Issues arising from previous meeting**

   a. ***Establishment of an Ethics Committee – Garry Cutting/John Burn***

      Garry Cutting and John Burn led a discussion about how the Human Variome Project should deal with ethical issues. The Committee acknowledged that there were a number of committees from various organisations

operating internationally that dealt with these issues and that there was perhaps not a need to create another committee but to ensure that existing committees worked together. Members of the Committee noted the HUGO ethics committee—led by Ruth Chadwick and which had been agreeable in the past to working with the Project on ethical issues—and the Ethics Working Group of the Global Alliance for Genomics and Health (GA4GH)—which had recently called for comment on a draft international code of conduct. Helen Robinson reported that WHO views ethics within the field of genetics and genomics as very important and that the draft work plan for the new international programme on genetics, genomics and public health recognised two areas of ethics: issues relating to privacy, consent and conflict of interest, and issue relating to equity of access to health services.

John Burn suggested that a way to start to "operationalise" these discussions around ethics would be to write to the GA4GH Ethics Working Group and ask them to consider appointing a Human Variome Project representative, and perhaps a representative from HUGO as well. In doing so, the Project would consider endorsing them as the lead agent on issues relating to ethics and policy, and in return, the GA4GH would endorse the Human Variome Project as a supplier of high quality, clinically relevant data via the efforts of the Project's members and the databases they curate. The Committee noted that current members of this group may not be fully aware of issues facing database curators and clinicians. The Committee further noted that the involvement of industry groups and private, for-profit organisations in the GA4GH raises the possibility of conflicts of interest and this might impact on the Project's relationships with UNESCO and WHO. However the Committee also noted that industry involvement cannot be completely avoided, nor is it desirable to do so, but that all relationships need to be transparent and open.

The joint BRCA Challenge project (see Item 8.b) being undertaken between the Human Variome Project and GA4GH could also provide another avenue to further "operationalise" issues in this space as these issues will be encountered in the conduct of the project.

The Committee also noted that a truly representative ethics committee would require broader representation beyond North America and Western Europe. The Committee felt that the Project had a lot to offer in this area through the Project's relationships with countries in Africa, South America and South East Asia and China.

John Burn undertook to write to the GA4GH on behalf of the Committee and as co-chair of the joint Human Variome Project/GA4GH BRCA Challenge about the issues raised in the Committee's discussions and to further explore how the GA4GH and the Project will work together towards and international collaborative stance.

ACTION:	John Burn to draft a letter to the GA4GH and send to the Committee for comment

5. ISAC Priorities for 2014-2016 – Helen Robinson

The Committee considered a draft document prepared by the ICO that summarised discussions on this issue to date. As a result of this consideration and further discussion within the Committee, the document (see Attachment A) has been updated.

a. Haemoglobinopathies Initiative

Raj Ramesar noted that the Human Variome Project would be well served to undertake a flagship project, like the BRCA Challenge, that dealt specifically with a large health problem in low- and middle-income countries that relates to genetics and genomics. He suggested that a focus of such a project could be sickle-cell disease and other haemoglobinopathies and that it should be approached from a public health perspective. It was further suggested by the Committee that this could be expanded to include malaria, which would open up support from groups working with infectious diseases. Garry Cutting noted that there already exists a very good database on haemoglobinopathies (HBVar) curated by Ross Hardison and others, but that the Human Variome Project could make supporting the expansion of this database, especially through the inclusion of clinical correlates to the existing molecular data, part of a truly global effort to really understand these diseases. He suggested that the initiative could follow the model of InSiGHT and CFTR2 and develop the structures needed to collect data on patients with haemoglobinopathies globally and provide this data to the HBVar database. It was also noted that Sir David Weatherall and Doug Higgs should be approached for their advice. Raj Ramesar commented that this would generate a lot of interest within African countries and assist with engaging them in the work of the Project. Peter Taschner suggested that this initiative could be given to the International Confederation of Countries Advisory Council as a project that they can use to assist in the development of collaborations inside and between countries.

6. Standards Development & Recommended Systems Status

a. AP06-2013: Diagnostic Grade VCF Specification – Activity Proposal

The Committee reconsidered an Activity Proposal to propose a 'diagnostic grade' VCF file specification. The Committee felt that this activity would be better handled by the Global Alliance, and resolved to write to the Global Alliance Data Working Group, which had already expressed interest in a similar activity, to propose a joint activity.

ACTION:	ICO to write to GA4GH Data Working Group

b. AP08-2014: Minimum content of a country specific database – Activity Proposal

The Committee considered an Activity Proposal to specify minimum content requirements for a country specific database. The Committee resolved to appoint the International Confederation of Countries Advisory Council (ICCAC) as Sponsoring Council for this activity. The Committee directed the ICCAC to ensure that any Working Group chartered to undertake this activity work closely with the existing Working Group developing minimum content requirements for gene/disease specific databases.

c. Variation Ontology – Recommended Systems Status

The Committee considered an application for Recommended Systems Status for the Variation Ontology. The Committee resolved to send the application for peer review.

d. Café Variome – Recommended Systems Status

The Committee considered an application for Recommended Systems Status for Café Variome. The Committee resolved to send the application for peer review.

7. Scientific Director's Report

Richard Cotton reported that the Project, with the assistance of Johan den Dunnen and Rolf Sijmons had negotiated an agreement with BMJ to publish mutation reports. He congratulated the work of Zilfalil bin Alwi and others involved in the establishment of the South East Asian Regional Node. Finally, he thanked John Burn for representing the Project as part of a UNESCO delegation to the government of Nigeria in Abuja for discussions regarding the establishment of a regional centre for sub-Saharan Africa.

8. Other matters

a. Voting in Advisory Council Chair Elections – Raymond Dalgleish

This matter was carried over to the next meeting.

b. Human Variome Project/GA4GH BRCA Challenge

John Burn updated the Committee on the progress being made towards planning the joint BRCA Challenge—an international initiative of the Human Variome Project and the Global Alliance for Genomics and Health to collect BRCA1 & BRCA2 variants globally. The Committee noted the discussions that were held during dedicated satellite meeting of HVP5 on 19 May 2014 and the agreement that was made to enable submission of BRCA variants to either ClinVar or LOVD/EBI, each of which would mirror the data held in the other database. An expert review committee (ENIGMA) would then be convened to develop consensus pathogenicity interpretations based on the submitted data.

Richard Cotton moved that the Committee officially endorse this project. The Committee unanimously resolved to endorse the project.

c. World Health Organisation

Helen Robinson updated the Committee on the Project's relationship with WHO. The WHO secretariat in Geneva is drafting a work plan for the newly established global programme on genetics, genomics and public health. This work plan will include joint activities with the Human Variome Project to establish a global evidence base for genomic medicine and will culminate towards presenting a resolution to the World Health Assembly in 2017 or 2018.

9. 2014 ISAC Meetings

- 31 July
- 28 August
- 25 September
- 21 October (in person at ASHG)
- 27 November
- 18 December

HVP - ISAC PRIORITIES FOR 2014 – 2016

1. Introduction

This document takes the agreement of HVP members in 2012 to use HVP5, the 5th Biennial Meeting of the HVP, as a point to check progress and adjust strategies of HVP's Project Roadmap of 2012-2016. It is also an opportunity to think beyond 2016 and what might be possible to achieve by 2020. Much has changed since discussions in 2012 – HVP's activities have grown considerably, there is greater interest and involvement in international data sharing in many quarters, and there have been numerous innovations in the bio-molecular field to name but a few things.

Appendix A contains the relevant background material from the 2012 – 2016 Roadmap for reference.

2. Moving forward to 2016 and beyond

In October 2013, in preparation for HVP5, each of the three official bodies of the HVP were asked to consider their past achievements and future priorities. These discussions have led to the proposal for one overarching document that integrates all of the overall priorities but that also allocates responsibilities and activities to the relevant people linked to each of the three committees and councils in a rationale manner. This will both help simplify, align and improve co-ordination between the three - ISAC, ICCAC and G&DC.

ISAC PRIORITIES FOR 2014 – 2016

During the period 2014 – 2016, HVP will focus on one overarching goal that links all of its activities:

Promoting the storage, curation and sharing variation data derived from genome sequencing so that it can be increasingly used as medically or clinically actionable information in all countries of the world

This will be done in manner that ensures that:

1. ***There is measurable growth in the quality and quantity of curated databases over time***
2. ***The storage, curation and sharing of variation information is financially and ethically sustainable beyond any single individual***
3. ***Developing countries in particular are able to benefit from these advances.***

3. How this will be achieved

This will be achieved through two major activities to be pursued between 2014 and the time for the next major HVP strategic review in 2016[1]:

1) **BRCA Challenge** – Working with the Global Alliance for Genomics and Health to bring together various stakeholder groups operating internationally and within countries to establish a common breast cancer genetic variant data initiative that enables international data collection and interpretation to support improved clinical services across the world. The BRCA Challenge it will address cross-linking of information across existing databases, standardized curation processes and collaborations with existing national and regional efforts.
2) **Global Genomic Haemoglobinopathies Initiative** – aimed at drawing together countries, particularly low and middle income countries, to work cooperatively to apply the latest genomic and genetic knowledge to the task of reducing the burden of disease associated with these genetic diseases. This initiative will build capacity to store and share quality data and strengthen the necessary governance required to support internationally consistent and responsible health service delivery.

The ISAC will oversee each of these activities and will work through the ICCAC and G/DSDBAC to achieve results. As well, each of the three bodies will have a small number of additional tasks designed to both integrate into these two activities as well as strengthen the overall work of HVP and its members.

4. Actions and Tasks for ISAC

SPECIFIC ACTION AREAS	TASKS	TIME/RESPONSIBILITIES
Promote Data Curation role in consistently defining and assessing the quality of data to be used in clinical services	1. Identify 'good quality' databases that are well curated and adhere to international standards and use them to define and promote good practice for sustainable databases	HVP to work with other groups including ACMG to clarify and define role of database curation in international data sharing; also ClinVar and ClinGen
	2. Monitor the merging and harmonization of current databases into larger more operational groups	ISAC with ICCAC
	3. Agree and promote the use of standardized nomenclature for variation information.	working already group established

[1] In preparation for HVP6 at UNESCO in Paris

Identify means for long term financing of 'good quality' sustainable databases	1. Gather information to know more about users of current databases	
	2. Identifying resources to research the economics and financing, particularly cost-benefit analyses, of genomic medicine that could be used to present the business case for data sharing between countries to governments and funders	
	3. Develop a model for self-funding of DNA diagnostics based on sharing of information on genes, variants and phenotypes that reach an agreed standard of quality	
Phenotype – define the major challenges/barriers impacting on progress in this area	Establish international group to start work on this and agree TORs	Peter Robinson and IRDiRC, GA4GH?
Work with journals to facilitate and promote submission of key variant data prior to publication	Publish a list of journals who assist on HVP's web site and promote these to HVP authors	ISAC with G&DC - on-going
Ethical practice – ensure that all databases and activities associated with HVP are compliant and active in meeting their ethical, legal and social responsibilities	Map ethical, legal and other regulatory requirements in regions of world to identify mechanisms for promoting data sharing across borders	ISAC, ICCAC (below) and G&DC with assistance of UNESCO and WHO
	Develop guidelines to assist HVP database comply	
Equity	Develop strategy for progressively addressing a range of issues related to equity and its measures in HVP activities	ISAC with ICCAC and G&DC with assistance of UNESCO and WHO
Education – on the basis of agreed HVP standards and practices identify and deliver training course/s in conjunction with various national and regional, international meetings	Develop plan that includes information on target audiences, topic areas, potential trainers opportunities, evaluation and funding model	ISAC with ICCAC and G&DC as appropriate

5. Actions and Tasks for ICCAC

ACTIONS	TASKS	TIME/RESPONSIBILITIES
Horizon 2020	Prepare an application for funding for appropriate grant	Group of interested EU countries plus non-EU as

	area	appropriate; Chair ICCAC to oversee
Continue the global coverage by increasing number of HVP Country Nodes by targeting those countries publishing information, particularly in developing countries	Develop minimum standards for HVP CN, including minimum budget advice	
	Move HVP CNs closer to their national and regional HG societies	
	Develop process for moving from Interim to Full status	Publish process by mid-2015; implement by end of 2016
	Improve the quality of HVP CN activities by providing assistance with governance, management, nomenclature, standards, and ethical practice	ICO through ICCAC
Continue to map and report on variation storage and data sharing activities globally	Prepare and publish report of world-wide activities of HVP C Nodes	Report due end of 2016; include section on ethical practice
Encourage regional clusters of HVP CN to work together to harmonize efforts, share experiences	ASEAN group African group RALGH group EU group?	Explore feasibility and then define resource requirements and identify sources of support

6. Actions and Tasks for G&DC

ACTIONS	TASKS	TIME/RESPONSIBILITIES
Recruit more curators of gene/disease databases	Identify existing curators of multiple databases	
Define best practice standards for database curators		By end of 2015
Address ethics and other regulatory issues	develop a series of scenarios to assist curators to monitor practices and exchange knowledge on these matters	on-going; with assistance of ICO, WHO and UNESCO

APPENDIX A

Background from 2012 – 2016 Roadmap

The 2012-2016 Roadmap contains the following guidance – see pp. 4-5.

The Human Variome Project is an international consortium of researchers and healthcare professionals who are working towards a common vision: a world where the availability of and access to genetic variation information is not an impediment to diagnosis or treatment. The aim of the HVP is to ensure that all information on genetic variation can be collected, curated, interpreted and shared freely and openly. This will lead to speedier, better and cheaper diagnosis or treatment of genetic disorders and better insight into the causes, severity and effect of common disease.

The HVP has four roles:

1. To establish and maintain standards, systems and infrastructure necessary for the worldwide collection, curation interpretation and sharing of information across the genome
2. To advocate and promote ethical behavior in the field of medical genetics and genomics
3. To share knowledge about our genome and its function in determining health
4. To assist individuals and nations build their capacity to address genetic aspects of individual and global health

The Roadmap set some 'goals' to be achieved by 2016 –

- A spectrum of HVP Standards and Guidelines, developed through the Project's Standards development process and communicated via a Solution Blueprint, that fully describe the technical and administrative aspects of developing, operating and maintaining the various components of the Global Collection Architecture
- A process of accreditation for HVP data repository infrastructure – HVP Country Nodes and Gene and Disease databases
- High quality, complete and accredited gene/disease specific databases for at least 3 00 genes with work underway for a further 5 000 to be completed by 2022
- HVP Country Nodes in over 40 countries sharing information with international gene/disease specific databases
- An organizational framework that supports members to behave ethically
- An education and training strategy that provides a range of professional development and educational programs for HVP consortium members
- Training programs and knowledge sharing initiatives designed to build capacity around medical genetics and genomics in low- and middle-income countries

Are these relevant today for HVP and 2016?