THE HUMAN VARIOME PROJECT

sharing data · reducing disease

an NGO Official Partner of UNESCO

MINUTES

Interim Scientific Advisory Committee Meeting
Thursday 28th February, 2013
By GoToMeeting

ATTENDEES

Garry Cutting (Chair, USA)
John Burn (Alt Chair, UK)
Arleen Auerbach (USA)
Mona El Ruby (Egypt)
Johan den Dunnen (The Netherlands)
Marc Greenblatt (President HGVS, USA)
Mauno Vihinen (Sweden)
Richard Cotton (HVP Scientific Director, Australia)

Heather Howard (HVPI Operations Manager)
Tim Smith (HVPI Communications Officer)

Apologies
Ming Qi (Head China Node Partnership, China)
Aida Falcon de Vargas (Venezuela)
Mireille Claustres (France)
Richard Gibbs (USA)
Yoichi Matsubara (Japan)
Finlay Macrae (Australia)
Gert-Jan van Ommen (The Netherlands)
Stephen Lam (President IFHG, Hong Kong)

AGENDA

1. **Welcome**

   Garry Cutting welcomed everyone to the meeting.

2. **Confirmation of minutes of previous meeting**

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

3. **Issues arising from previous meeting**

   a) Establishment of an Ethics Committee

   Garry Cutting was unable to do this before the meeting and has undertaken to speak to some people regarding the establishment of the committee and report back to the next meeting.

ACTION:	Garry Cutting will report back to the next meeting

   b) Working Group Initiation

   Tim Smith confirmed that the Working groups have been initiated and the Chairs (listed under Item 6) have accepted their roles.

c) Editors Recommendation "Ensuring the Open and Free Sharing of Published Variant Data"– Tim Smith

The document was made available to the Consortium for comment. No adverse comments were received. The ISAC agreed that the statement be posted on the HVP Website and sent out to Editors of Genetics Journals.

d) Database Quality Interest Group

The paper submitted by Mauno Vihinen (see Attachment A) reporting on the work of the Database Quality Interest Group was discussed. The Committee requested more time to consider the report and will send comments directly to Mauno Vihinen. It was suggested that the paper could form the basis of an Activity Proposal.

ACTION:	Members to send comments on Variant Database Quality Assessment paper to Mauno Vihinen by 15 March, 2013.

e) HVP statement in line with ACMG statement

As there was little time to read and comment on the statement the ISAC requested an additional week to make comments. It will then made available to the Consortium for their comments before being made public.

f) EuroGenTest Meeting report

Timothy Smith and Mauno Vihinen updated the Committee on the outcome of the EuroGenTest Workshop in Manchester in January, "The challenge of getting clinical data into databases." The Workshop was well attended by participants from Europe and the US, including representatives from ICCG, ClinVar, UK-based diagnostic labs, LOVD, DMUDB, DECIPHER, GEN2PEHN, and both Human Variome Project International and the HVP Australian Node. The participants were hoping to generate some guidelines around clinical data submission, but as the day progressed it became more apparent that the output of the workshop would be a publication outlining the state of the art and a vision for the future. The Human Variome Project's Global Collection Architecture was presented and the participants agreed that it was a good working model for complete global collection. The presentations from the Workshop can be viewed at: http://www.ngrl.org.uk/Manchester/publications.

4. Applications for Recommended System Status

g) Application for Recommended System Status– HGVS variation nomenclature

h) Application for Recommended System Status - Mutalyzer

i) Application for Recommended System Status - LOVD

Timothy Smith thanked those members of the Committee who suggested reviewers for these applications. The International Coordinating Office is in the process of contacting potential reviewers and will continue to update the Committee as to progress.

5. Activity Proposals

None received since the last meeting.

6. ISAC Sponsored Working Groups

j) Assigning Pathogenicity to a Genetic Variant – Chair – Marc Greenblatt

k) Minimal content for a gene variant database – Chair – Peter Tashner

l) Sequence Variant Description Committee - Chair - Johan den Dunnen

A progress report from each Chair was requested for the next meeting

ACTION:	ICO to request reports from the Chairs for the next meeting 28th March, 2013

7. Scientific Directors Report

The Scientific Director's (see Attachment B) report was discussed.

8. Meetings and Events

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

IRDiRC Meetings: 2 meetings are being held from the 16th to the 19th April in Dublin. Garry Cutting and Gert-Jan van Ommen have been invited to the first, main IRDiRC meeting and will let the committee know if he is able to attend. Timothy Smith and several other Human Variome Project Consortium members have been invited to attend the second RD-SymPathI Workshop.

9. Other matters

John Burn advised the Committee of several matters:

- Corresponding with the UK Genetic Testing Network exploring the option of making submission to DMuDB a requirement of licensing for UK diagnostic laboratories.
- Is now a member of the UK Genomics Board overseeing the recently announced "100,000 Genomes Project"
- Will be speaking to the Wellcome Trust in the coming weeks about the Human Variome Project
- Has had preliminary discussions with RD-Connect—may be some funding available for a European office to assist the work of the Melbourne-based ICO

Richard Cotton raised the subject of the Human Variome Project setting up a method of publishing short reports of genetic variants. Some preliminary discussions with the BMJ have occurred and they are open to the idea. He requested that the Committee start thinking about who might be approached to serve as Editor for such an initiative.

ACTION:	Richard Cotton to report further at the next meeting.

10. 2013 ISAC Meetings

March – Thursday 28th
May – Thursday 9th
June face to face meetings will be held at UNESCO in Paris 6, 7 & 10th June, 2013
Scientific Advisory Council Meeting - 6th June, 2013.
International Confederation of Countries Advisory Council Meeting - 7th 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 – Thursday 25th
August – Thursday 22nd
September – Thursday 26th
October – Face to Face ASHG Boston Wednesday 23rd
November – Thursday 21st
December – Thursday 12th

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VARIANT DATABASE QUALITY ASSESSMENT

Computer science and IT communities have discussed and developed criteria for database platform/system quality, however, there are no widely accepted systematic criteria and evaluation systems. Each domain has developed its own. Closest to this field comes BioDBcore, which has developed core attributes of biological databases. However, it is not a quality scheme.

The criteria described in computer science and information technology quality papers are more suitable to assess database platforms (e.g. DMuDB, LOVD, MUTbase, UMD etc.) than for variant database content. For some platforms, there might be little difference due to limited customization and flexibility. Even in the same installation using the latest version of LOVD, one gene variant database might be of much better quality than another depending on the curator(s). This leads to one division of quality assessment areas: separation of the platform evaluation from the database content evaluation. The advantage would be that the number of different platforms is much smaller than the number of variant databases. This would reduce redundancy and if deviations from the standard platform settings are indicated separately, they would stand out. The database content evaluation will have most impact from the (clinical) user perspective.

The database administrator or manager could provide the technical information. This kind of self-assessment or –evaluation would save time for the quality evaluators. For example technical details could be easily collected in this way. For popular platforms like LOVD scripts could be made to automatically collect a number of facts.

The quality evaluation is divided to four areas. The basic principle is to have a simple system, which still can provide a good overview of the quality. There could be overall ranking in the style of hotels with stars, which could then be broken down to individual scores. As main evaluation areas can be considered:

- Data quality
- Technical quality
- Accessibility
- Timeliness

The goal is to capture the major issues pertinent to quality. On the other hand the quality assessment should be simple for the database users to comprehend and apply. Each of the quality areas is divided into a number of quality evaluation areas.

The goal of this group composed of John Hancock, Andrew Devereau, Peter Taschner and Mauno Vihinen has been to get the project started. HVP needs to decide on the quality criteria and on how the quality evaluation will be implemented. In this document we have concentrated on the evaluation criteria and left the details of implementation to the future.

Objectivity of the evaluation is important and it makes the evaluation easier.

The four quality evaluation criteria can be divided into more specific items:

Data quality
Database scope and purpose
Contents (patient data, if so, how much, fulfillment of minimal requirements)
Completeness
Coverage
Accuracy, error rate
Consistency (language, spelling, reference sequences) - type of curation

Integration to other resources
Use of standards (gene names, reference sequences, variation nomenclature, data models, ontologies …)
Date stamps
Authority, curatorial team competence
Contact details
Use of references
Data collection, sources
Definition of pathogenicity
What kind of data (e.g. NGS data, SNVs)
Range of numerical values
Correct units
No data lost when inputted
Consents, privacy
Ethical issues
Public/nonpublic data

Technical quality
Database management system, suitability
Speed of access
Quality control measures implemented
Use of automatic steps (e.g. HGVS names with Mutalyzer)
How corrections made
Reliability (uptime)
Version history
Functional links
Use on different browsers
Data security (operating system, backups, firewall)

Accessibility
Design
Readability
User friendly, logical interface
Navigation
Language, correctness
Ease of use
Consistency on the site
Interactivity
Available freely, is registration required
How to contact
Help, support, tutorials
Documentation (purpose, scope, motivation, copyright, disclaimer, database policy, data items, annotation guidelines)
Searchability (search engine/possibilities)
Downloadability of data/search results
Format(s) of output (for further analyses)
Graphics (use, clarity etc)
Contacts to community, support groups etc
Other modes of access, esp. web services access

Timeliness
Update frequency - including whether it is currently being maintained
Currency of updates (how new data included)

Versioning policy (are old versions available?)

Relevant references

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Scriver CR, Nowacki PM, Lehväslaiho H. 1999. Guidelines and recommendations for content, structure, and deployment of mutation databases. Hum Mut 13:344-350.

Scriver CR. 2000. Guidelines and recommendations for content, structure, and deployment of mutation databases: II. Journey in progress. Hum Mut 15:13-15.

Vihinen M, den Dunnen JT, Dalgleish R, Cotton RGH. 2012. Guidelines for establishing locus specific databases. Hum Mutat 33:298-305.

Human Variome Project - Scientific Directors Report – February, 2013

a) Consortium Members

There are currently 1011 Consortium Members from 72 Countries

b) New & Potential Country Nodes

There are no new Nodes to report since our last meeting.

c) Database Selection Sub-Committee

A draft of the "Process for establishing and assisting International Gene/Disease Specific Databases (LSDB's) by China" has been reviewed by the sub-committee and the changes have been recirculated it is due to be finalised within the next month.

d) Countries Development Program

The applications from Austria and Belgium have been sent to the panels for review. The panel for the application by Belgium and the Congo has now come back with a positive review and the funding documents will now be drawn up. No other application has reached the point of being put to a panel this should happen in the next month. Other countries and regions are still in the process of putting forward applications.

e) Country Council (ICCAC)

A meeting of the ICCAC was held on the 19th February the minutes of which will be available on the website when confirmed. A meeting is now scheduled for every 2 months. The baseline survey has been sent to 42 countries and 11 replies have been received to date. We are still following up on some outstanding reports which have been promised. The report will be finalised over the next few months and will be presented in Paris.

f) Gene/Disease Database Council (G/DSDAC)

A meeting was held on the 13th February, 2013 with Raymond Dalgleish the Chair of the G/DSAC (minutes of this meeting will be available on the HVP website when confirmed) and a full meeting is scheduled to take place on the 3rd April with meetings to follow every 2 months. The council currently has 1 Working Group under its purview "Disclaimer Statement on LSDB websites" and is working towards increasing the membership with a new mail out to known non HVP databases is underway.

g) UNESCO

Work is continuing on the Meetings to be held in Paris surrounding the celebrations of the discovery of DNA and the Mapping of the Genome to be held 5 – 10th June, 2013 together with our scheduled committee and council meetings.

h) World Health Organisation

Telephone interviews have started to consult on what future role the WHO may play in the future of Global Genetic Healthcare. Larger group consultancy's will be held at the HUGO, Mutation Detection and ESHG meetings.

i) Meetings and Events

Some other meetings at which the HVP will be involved during 2013

- BioVision – Lyon, France, 24-26th March – Invitation to present HVP.
- 6th International Biocuration Conference, Churchill College, Cambridge, UK, April 7-10. Richard Cotton Invited speaker.
- IRDiRC Meeting – Dublin, Ireland – Garry Cutting invited to attend
- IRDiRC 'RD-SymPathI Meeting – Dublin, Ireland – R Cotton on organising committee and Tim Smith attending other HVP members invited.
- 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).
- Mutation Detection 2013 – Lake Louise, Canada, 22nd – 26th April, Sessions on HVP topics
- Human Variome Project Workshop/Session at Human Genome Meeting/ International Congress of Genetics 2013, Singapore, April 16. R. Cotton and T Smith
- 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, 6th June, 2013.
- HVP International Confederation of Countries Advisory Council Meeting, UNESCO Headquarters, Paris, France, June 7th.
- HVP Gene/ Disease Specific Advisory Council Meeting, UNESCO Headquarters, Paris, France, June 7th.
- UNESCO Headquarters, Paris, France, June 10th, 2013 - 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).
- Human Genome Variation Society: Clinical Applications of Next Generation Sequencing, ESHG Satellite meeting, Paris, France, June 8. HVP Co-Organizer
- ESHG, 8th – 11th June, 2013, Paris –
    - Booth
    - WHO Consultancy
- OESO 12th World Conference on Cancers of the Oesophagus, UNESCO Headquarters, Paris, France, August 27-30. R Cotton – Co President.
- InSiGHT Annual Meeting – Cairns Australia – 25th 28th August includes Joint HVP day - T. Smith speaker
- Human Genome Variation Society: Clinical Applications of Next Generation Sequencing, ASHG Satellite meeting, Boston 22nd October - HVP Co-Organizer
- ASHG, 22nd – 26th October, 2013, Boston –

- Booth
- ISAC Meeting
- Editors Interest Group Meeting,
- WHO/HVP consultation