PUBLIC POPULATION PROJECT IN GENOMICS (P^3G)

IWG 3 on Ethics, Governance and Public Engagement

MINUTES of the IWG 3 session of the 3rd annual meeting of the Members of P^3G, held at the Delta Centre Ville Hotel, room "Verriere B", in Montréal, Province of Québec, Canada, on **May 20th, 2007 at 13:00 (EDT) – 17:00 (GMT).**

ATTENDEES:

Bartha Maria Knoppers (Université de Montréal, Canada)
Jane Kaye (University of Oxford, UK)
Steve Benteau (PTRG, Memorial University of Newfoundland, Canada)
Denis Bilodeau (Genome Quebec, Canada)
Angela Brand (German Center for Public Health Genomics (DZPHG), Germany)
Anne Cambon-Thomsen (INSERM U 558, University of Toulouse III, France)
Theresea Chow (Singapore Tissue Network, Singapore)
Alejandra Contreras (INMEGEN, Mexico)
Iiro Eerola (European Commission DG Research, Belgium)
Jesus Karol Estrada (INMEGEN, Mexico)
Renate Gertz (University of Edinburgh, Generation Scotland, UK)
Andrew Hicks (Genetics Resource Centre, Faroe Islands)
Adrienne Hunt (UK Biobank Ethics and Governance Council, UK)
Kazuto Kato (Institute for Research in Humanities, Kyoto University)
Joost Keers (University Medical Centre Groningen, Netherlands)
Janis Klovins (Latvian Biomedical Research and Study Center, Latvia)
Renee Langlois (Statistics Canada, Canada)
Cesar Lara (INMEGEN, Mexico)
Stephanie Lazor (CRDP Université de Montréal, Canada)
Juha Muilu (Institute for Moleculard Medicine Finland, University of Finland)
Daryl Pullman (Memorial University/CHIR Institute of Genetics, Canada)
Susan Wallace (CRDP Université de Montréal, Canada)
Wendy Wolf (Nugene Project, USA)

1. Tour-de-table

2. Agenda

Dr Knoppers welcomed the members and thanked Dr Kaye for stepping in for Alastair Kent to serve as Chair. She then outlined the agenda for the meeting:

(1) Discuss change to principle 1 of the P^3G Charter of Fundamental Principles
(2) Introduce methodology for the generic consent form process
(3) Discuss changes to the generic consent form
(4) On Day 2, discuss COREs, ethics questionnaire topics for Phase II, and P^3G intellectual property policy

3. P^3G Charter of Fundamental Principles

The 'Promoting Harmonization of Epidemiological Biobanks in Europe' (PHOEBE) group raised the question that one line of the P^3G Charter of Fundamental Principles read "P^3G will optimize the benefits of collaborative, publicly funded research for the benefit of all."

At the P^{3}G annual general meeting, it was proposed that this line be edited to read, "benefits of collaborative research," as projects could involve private companies as well as public and therefore it is no longer appropriate to concentrate on only publicly funded research. IWG3 members were asked to confirm that they were comfortable with this change.

The IWG3 members noted:

- P^{3}G is public; the public aspect of it is captured in the title
- privately sponsored population genomics research should also follow these principles
- publicly funded research came from looking at P^{3}G documentation; 'public' in P^{3}G was more about public good than publicly funded research (open to discussion); others have said public means calling upon members of the public (open-call to the public)

After discussion it was agreed that the change should be made and that PHOEBE should be thanked for bringing the suggested change to the attention of P^{3}G.

4. Generic Consent Forms

Dr Wallace introduced the methodology used to create the generic consent form and information sheet. She thanked those who had submitted them.

-14 member biobanks sent in their information sheets and consent forms. Some were sent afterward the analysis was completed and were not included; in total, the generic documents drew from 12 information sheets and 11 consent forms

- The analysis focused on 5 key clauses (access, commercialization, confidentiality, consent, and governance) to get a sense of what the different groups were trying to say
- Some clauses included an 'OR' because there was an option, ex., a large collection/research project (general) vs. specific problem
- Generic materials were created by the Policymaking Core of the CRDP using clauses from the members' materials, but these clauses were anonymized
- Clauses were chosen that were common to all the studies, but also items were included that were specific to some studies in order to promote discussion.

Dr Wallace was asked if she knew how the original consent materials were written; she did not. She was also asked if the generic forms could be used by this group. Dr Knoppers responded positively and noted that there would be a background article on this process that could pick up on the compatibility of the generic consent form and regional nuances (legislation, etc.)

The members were asked to think of the relationship between the information sheet and the consent form. What things are missing and what needs to be included?

After an extensive discussion (see Annex 1 for a detailed list of the proposed changes), Dr Wallace was charged with revising the generic information sheet based on the members' comments and circulating it for further comment. It was decided to delay consideration of the generic consent form until after the generic information sheet was revised and discussed further. At this point the meeting was adjourned for the evening.

[Opening of Day 2 discussions]

5. Administrative news

Dr Knoppers opened the second day of the IWG3 meeting with some administrative news. The next P^{3}G meeting will be held the afternoon of 22 October and the morning of 23 October 2007, just prior to the American Society of Human Genetics meeting in San Diego, California. The next annual general meeting of P^{3}G may be in Berlin, July 2008. The epidemiologists will have a working group meeting in York, UK in September 2007 to discuss the generic dataset.

6. Funding

Several potential applications for funding with European colleagues were introduced by P^{3}G members:
- ASSIST will be a program to bring together current knowledge of standards in biobanking, from start-up to decommissioning. New standards will be pinpointed and developed. There will be a manual and website. (FP7)
- ENGAGE – from genomics to translational medicine (FP7)
- Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) is a proposed pan-European project to coordinate and harmonise existing biomolecular resource infrastructures for biobanking (ESHRI programme)
- Network of Networks – public health genomics core (more information will be available at the October meeting)

7. Ethics questionnaire topics for Phase II

The IWG3 members were asked to look at the Phase I questions in the ethics and governance section of the P^{3}G questionnaire and the responding Phase 1 results (downloaded from the P^{3}G website). The group discussed possible changes for Phase II of the questionnaire. The questions will be redrafted reflecting the suggested changes and sent to members for further discussion. (See Annex 2 for proposed changes)

8. P^{3}G intellectual property policy

The IWG3 members were asked to review P^{3}G's intellectual property policy, as taken from the P^{3}G funding application. It was decided that the important points were in the draft but it needed to be reworked and simplified, using bullet points to make it clearer. Dr Wallace agreed to redraft it and send it out for members' review.

9. Adjournment

Dr Kaye thanked the members for their hard work over the last two days. At this point the meeting was adjourned.

ANNEX 1 – Proposed changes to the generic information sheet (agenda item 4)

The changes noted below were suggested through discussions of the working group at their May 2007 meeting. Numbering refers to the numbers on the generic information sheet.

General notes:

-General format note: do we want to set it up as a question? How did you get my name or say we got your name by [style question as opposed to content]

-a good idea to get experts to review the style for clarity (a crystal mark about patient information)

*software available to determine level of education needed

-Access to consent form from P3G:

-set up in a way of obligatory requirements; then optional ones (specification), like legislation requires … etc.

-want to make it as user friendly for everyone

*also remember the world is not unilingual English

Section specific notes:

3. Introduction/Overview of Project – 3.1 Aim

"set up a gene bank"

-focus rather on the biological aspect (why say 'gene'?); restricting it to 'gene' bank is too narrow and does not correspond to reality – DNA is more than gene banks

-what is the terminology that should be used? An interesting question considering the definition of the lexicon of gene is extremely restrictive

-'establish a biobank' instead of 'set up a gene bank'

-must remember to use language that is understandable to the common person: 'gene' might be better than 'bio', the latter perhaps is too broad

-CHANGE: gene bank is out

'OR' (the two options)

-the first option should mention genes but [CHANGE] "A bank of biological samples and data" is better

-second option is too broad; should add something more specific about the research

-the OR is questionable: seem to complement each other; could come up with a paragraph that combines the two

[Side Note]

-how many banks mention use of data, access of data from researchers outside the country? About half mentioned this

-also a q. of where does this information belong, the info sheet or consent form?

-for P3G it is important to say explicitly re: access that will be used by others in other questions

<u>3.2 Number of People</u>

-CHANGE: "this research requires"

-OR is a choice: the difference is in the randomization and in lifestyle

-if first bit is comprehensive, can lose the second clause

3.3 Duration of the Study
-could collapse Number of People and Duration of the study; less is more; if our aim is clear and comprehensive, the rest can be rather streamlined
-or put 'random selection' from 3.2 in another section

-should there be a section about recruitment, i.e. how did the information come about?
-CHANGE: 3.4 Method of Recruitment/ Rationale of recruitment
*don't write up a clause; rather indicate PFI

[Other]
-Destruction of information
*did not go into storage; q. of whether we want to go past 5 sections we looked at

4. Governance
4.1 Organization/Support
-contact information; currently under 12.2 (don't put names)
-if doing a guide, put institution rather than Professor so and so b/c Professors might change
***should also be communicated in storage section or governance and custodianship of that it is an institutional project (samples, etc. belong to the institution; not the professor/etc) b/c there have been instances of samples, etc., being taken when Professor takes new post

4.2 Funding
-CHANGE: replace 'not-for-profit' with 'this research is'

4.3 Oversight
-'population genetics' is broad; change to 'population genomics' or remove it completely b/c it is going to be too confusing to the ordinary person
-CHANGE: stop after 'all applicable norms' or 'the study of populations'
-the oversight body is a safeguard of the public interest
-CHANGE: 'this project' is better than 'this research' (in order to minimize confusion)

4.4 Approval
-take out accreditation b/c indicates a process for institutions, not project
-accredited suggests having gone through appropriate research approval programs; 'recognized' might be better (broader than accreditation or certification)
-Is it a research committee or any other committee? The research ethics committee seems more appropriate but this is not reality - it is broader
-Government projects need government body; second option meets concern
-CHANGE: remove 'committee' and replace with 'Name of governance body'
-CHANGE: 'Project name, has received approval from…… recognized by (governing body, government) if applicable'

4.5 Legislation
-CartaGene has to put in that data is protected by Loi des Statistiques Act – obliged to mention the act protects over and above normal confidentiality
-CHANGE: in agreement that legislation will be optional

5. What will happen to you?

-CHANGE: new heading: ‘Recruitment’; b/c existing is a change in style – we need to think about the style

5.1 Invitation
-CHANGE: ‘asked to participate in [Project]’ - omit purpose of study
-understand vs. be aware: ethics committees say can’t say that do not understand vs. be aware; understand what participation involves, not the complex science
-CHANGE: invitation section (5.1) should be before #3, before name of the project and introduction
-re: ‘please take the time to read’: Mexico uses a cartoon (comic book) and Japan has pictograms; we could have pictures next to it
    -only people that can read can participate? Need pictures – consent form has translation and systems clauses but info sheet needs pictures
*should seriously recommend that this is a very limited tool – clauses are just indicative of areas that need to be addressed
-interesting to get a collection of these visual media – but we would lose anonymity
-related topic is the way the information is explained to the participant; in Japan, there are medical coordinators MCs that work in hospitals to explain the procedure
Pt – we should be focusing on the context as well – best practice in terms of actually seeking consent depends on the process of consent (what Susan and I have done was only substance)
-Australia has independent people; in Japan, usually nurses employed by persons

5.2 is what is required
-CHANGE: new heading ‘Requirements’
-‘reading’ needs to be addressed
-e-health questionnaires
-CHANGE: ‘sample (eg. Blood/urine/hair/saliva)’ or ‘biological sample’
-the amount needs to be specific (to consider REC concern about touching)
*add immortalization if applicable – culture your DNA (cell culture and storage); do you then have to talk about duplication…? Describe method instead
-how much information do we suggest they put in there?
-CHANGE: Provide a sample [Amount] and [future uses]
*RECs will review it; we just have to make sure we have the necessary elements that they need to think about
-we should be less restrictive or we risk setting an international standard
-CHANGE: Could say it is a sample, and the amount, and future uses (cell culture and storage) and then clauses that have been accepted by REC as examples
-Or options:
    (1) keep them as is/preserve as is
    (2) change them
    (3) immortalize them/manipulate or transform them
*amplification – grey area re: change and amplification
-would rather not put statement in about growing DNA – could put ‘describe method’
-CHANGE: questionnaire include all PFIs
-‘to allow staff to perform basic clinical measurements, including [PFI]’ - leave it open or give guidance to mention invasive ones? No change: leave it.

‘If applicable’
-CHANGE: remove these two issues from this section; they should be incorporated elsewhere – they are very important clauses

(1)
-what is going to happen if I lose capacity or die has to be in another section; maybe confidentiality is better section
-CHANGE: take-out us
-re: medical records, who will have access (one way or two way)? Current sentence is too broad
-'for permission to access your health records now and in the future' *Patriot Act – court order, etc. in 9.2
-'if you die': information about death, possible cause of death (Iceland); or breast-cancer study 10,000 women in 1994 not possible b/c died, study could have gone ahead if had consent
-can change latter part of this clause to something broader, e.g. add cause of death
-could be viewed as extension of withdrawal of consent: because you die or lose capacity, want permission for other REC approved research
-about access but also future storage/access

(2) follow-up research
-must be a separate point that only applies to some projects
-would be for the project to re-contact you; not just anyone
-CHANGE: 'the Project (UK Biobank) could re-contact you … for their own aims, or because new research project requires…'

6. Risks
-broken up into blood and information (physiological and psychological risks)
(1) blood – seems silly, does not fulfill ethical purpose, but perhaps legal; maybe leave this
-CHANGE: cut 'at the injection…temporary'
(2) the questionnaire - maybe should be with 5.2 section re: questionnaire
-CHANGE: begin at 'If you do not wish to answer a question' (cut previous sentence)
*risk of linkage of the sample and the person; this is a risk to researchers
(3) CHANGE: cut anxiety line
(4) confidentiality
-leave confidentiality risks to confidentiality section
*a sentence at the beginning of confidentiality should be about the sources of data (building of a profile)
-information leaks – private information risks
-linkage under the risks (can be mistakes)
-should maybe put confidentiality before risks; and a one line repetition of confidentiality risks in risks section
-or put confidentiality after risks, and benefits before risks
*REC board for Memorial spends more time on the consent form than information form

7. Benefits
-CHANGE: 'Project is intended to benefit'
-CHANGE: 'Participation is not expected to provide you with any direct individual benefits. However, you can choose to receive your clinical measurements'
*should clinical measurements be part of consent?
-Communication of results to third parties – GP (results separated from communication)
*some projects are releasing results of number of white blood cells, etc.
*some results sent to you on the spot or later
-whole second paragraph should be under feedback

-OR clear it up so that communication of results is re: benefit to the individual; need to differentiate between research results and individual measurements, etc. in section 10. Communication of research results
-vaccination of carriers: West Nile Virus and a T.O. biobank – if carrier status known; what is the duty of care on biobanks– to feedback re: harm to participants – notice of abnormalcy to notify physician; but more basic – will biobank over time become more active for public health initiatives – can't envisage all of that for our purposes
-in the long-term, this knowledge will lead to …. Will have to come up with a policy when they will start to use it for policy
-CHANGE: remove population health – will contribute to public health (stop there); include sharing with physician

8. Confidentiality
-CHANGE: new heading 'Project Confidentiality'
-qualify who this applies to – who is given access
-linked in the database; part of the research is to be able to link part of the research data – so identifiable
*what is personal medical information (name, medical records, or DNA)
-say samples cannot reveal who you are (but DNA identifies you)
-CHANGE: 'Collected data are stored in a database where identifying information cannot be traced. To do this, we will:'
-within the information available from the project; the individuals cannot be traced
-CHANGE: remove 'traced' and replaced with 'released'
-CHANGE: remove decoding step (whole paragraph)

9. Access by Others
*really external confidentiality
<u>9.1 Access by researchers</u>
-CHANGE: 'Before release' (replace transfer)
-CHANGE: the data **and/or** samples
-will give researchers access; researchers will not be able to identify you as an individual

<u>9.1.2 Requirement for scientific/ethical review</u>
-CHANGE: should precede 9.1 because applies to all access

<u>9.1.3 International/commercial access</u>
-no access to identify you line is repetitive
-CHANGE: may collaborate (remove 'will'
-CHANGE: remove last sentence

<u>9.1.4 Return of samples/data</u>
*return of data/samples is particular to public infrastructures; leave it
-another of the benefits

<u>9.2 Access for other than research purposes</u>
-depends what country you live in – jurisdictionally based (must flag this out)

10. Communication of Research Results
-CHANGE: move/merge with benefits
-CHANGE: 'General research results will be made available to participants and other interested people at [website and/or newsletter]'

11. Commercialization
11.1 compensation
-CHANGE: section should be in a separate section

11.2 Ownership/renunciation of rights over samples
-CHANGE: delete the heading – put under 11. Commercialization
-do participants have any property rights?
-CHANGE: 'all rights in their samples and data' (remove property)
-legal owner and custodian/guardian
-CHANGE: 'blank has been set up as the legal guardian….transfer'
-CHANGE: 'In signing the consent form, you will not derive any personal financial'
-CHANGE: just remove the second sentence
-benefit sharing – if there is going to be commercial gain, are we going to require a portion to be returned to the public good
-there needs to be a line about giving the broader picture – if there are any profits; but double-edged sword – resource but profit
-the resource may however require a return of such future benefits to the resource; don't want them to be commercialized but want them to benefit from
*will need perhaps to go back to this after a further draft (re; benefit sharing)
* benefit sharing undoes the gift
-'…also supports the resource'
***in aim of the project, should say that it is a resource
-need to look at this in terms of P3G fundamental principles as well – to get clarity about where those duties lie

12. Withdrawal
12.1 Withdrawal procedures
-CHANGE: 'this will be overseen by [body]' (replace 'audited')

12.2 Degrees of Withdrawal
-although it may not be possible to trace all distributed samples and data
-will stop downloading further info but existing one will be anonymized (anonimization will be added to degree of withdrawal)

ANNEX 2 – Proposed changes to the Ethics and Governance section of the P^{3}G questionnaire (agenda item 5)

The changes noted below were suggested through discussions of the working group at their May 2007 meeting. Numbering refers to the numbers on the P3G questionnaire.

3.1.1 Confidentiality
- remove 'double coded' after 'coded'
- pluralize the word 'code' as in 'identification by a code(s)'
- add after 'identify participant' the words 'by the study'
- delete subquestion 'Do you forsee anonymization…' after 'Coded'
- delete 'Nominative information…'
- delete subquestion 'Do you forsee anonymization…' after 'Nominative information…'

3.1.2 Authorized uses/Restrictions on use
- change title to 'Consent'
- change first question 'Generic consent…' to 'Is broad consent provided by participants for future uses?'
- delete 'Specify [ ]'
- add question 'Will internal future uses of the data require additional ethics approval?'
Is the above question in the right place?
- delete question 'Please provide a short description…'

3.1.3 Elements of the consent process
- add '☐ ☐ Participant's authorization to access their administrative health records
- delete 'Limited' in 'Limited duration of…'
- under 'Individual results returned to participants', add 3 yes/no subquestions:
  - ☐ ☐ Initial assessment results (physical measures)
  - ☐ ☐ Genotype results
  - ☐ ☐ Results that show an individual risk
- after 'Results that show…' subquestion, add 'If yes, specify how' with brackets
- add ☐ ☐ 'General research results returned to participants
- delete 'If needed, please provide…'

3.2.1 Access to data and samples
- delete 'With respect to the study governance rules,' in first sentence
- after yes/no boxes, add:

If yes,

Yes no

☐ ☐ Private
☐ ☐ Public
☐ ☐ International
If yes, ☐ ☐ With local researcher?
☐ ☐ Court order
☐ ☐ Insurers
Specify: [ ]
☐ ☐ Employers
Specify: [ ]
☐ ☐ With written agreement
☐ ☐ Other family members

-add ‘What kind of data samples can third parties have access to?’
☐ Anonymized
☐ Coded

yes no
-add ‘☐ ☐ Will external research use require prior outside/local ethics committee approval?

yes no
- add ‘☐ ☐ Must results be returned to the database?
If yes,
☐ If validated
☐ When published
☐ If study is completed
☐ Others Specify: [ ]

yes no
- add ‘☐ ☐ Must samples be returned to the database?
*Were there any subcategories with this question?

yes no
- add ‘☐ ☐ Is commercialization foreseen?
If yes, will IP be distributed to:
☐ The resource/biobank only
☐ Shared with the biobank
☐ Third party exclusive

yes no
- add ‘☐ ☐ Is mandatory licensing foreseen?
If yes:
yes no
☐ ☐ Nonexclusive

<u>3.2.2 Legislative Framework</u>
- delete ‘(s)’ from ‘legislation(s)’
- add before ‘Is there specific legislation governing biobanks…’,
yes no
☐ ☐ ‘Is there specific legislation governing research involving human beings in your country?’

<u>3.2.3 Ethics Review</u>
- change ‘overall project’ to ‘biobank’
- delete ‘Organization(s) responsible…’
* should this section by moved elsewhere in questionnaire?