A P3G generic access agreement for population genomic studies

To the Editor:

The Public Population Project in Genomics and Society (P3G) is a not-for-profit consortium that provides the international research community with access to the expertise, resources and innovative tools for the harmonization of health and social sciences research (http://www.p3gconsortium.org/). The Generic Access Agreement (GAA; **Supplementary Note**) is a tool P3G has developed for use by population genomic studies (also often called biobanks or resources). Over the past decade, in anticipation of expanding demand for access by researchers and industry, large population studies collecting DNA samples worldwide have been developing access principles and policies to ensure ethical and legal access procedures to their resources that respect participant consent (**Table 1**). These access policies are now being operationalized into agreements that clearly stipulate the obligations of researchers and institutions who wish to access these resources. The access agreement is typically the final step in the access request process, following the submission and successful review of an application for access[1].

This P3G GAA attempts to address both the sharing of data and the sharing of materials (that is, biospecimens). All studies named in **Table 1** provide data, and some may additionally allow access to the biological samples themselves, under certain conditions. Although many aspects of access apply uniformly between data and materials, certain considerations are unique to materials, such as their limited and depletable nature. Our proposed GAA aims to foster some level of uniformity of access by addressing both data and materials together.

Access agreements must be drafted clearly, so that researchers and their institutions are aware not only of their obligations, but also that "the border between acceptable and unacceptable conduct be clearly delineated and predictable…"[2]. Explicit sanctions are important in order to respond effectively to any breach. These sanctions must be balanced—harsh enough to deter abuse by researchers and yet not to discourage access.

We have surveyed available literature, policies and access agreements in an attempt to identify access norms, which have been captured by the GAA. Its utility, however, extends beyond suggesting best practices, as it also aims to enhance international harmonization of access procedures. Researchers should not encounter a completely different access procedure each time they apply for access to a study. Mindful of national and cultural heterogeneity, the GAA seeks to promote scientific knowledge as a common good that should be shared, with appropriate protections in place. The adoption of this unique tool will hopefully improve transparency and interoperability in the sharing of data and samples.

It is problematic for population studies to simply rely on existing agreements. First, substantial heterogeneity exists between studies, and existing access agreements often reflect peculiarities. The GAA seeks to harmonize the core conditions that should be considered by all population studies. Second,

Table 1 Existing agreements, related policies and guidelines reviewed

Organization	Document	Version/date
Avon Longitudinal Study of Parents and Children	Management and policy	Version 3.0, December 2011
Avon Longitudinal Study of Parents and Children	Access policy and material transfer agreement	Version 4.1, October 2012
CARTaGENE	Access agreement	NA
Canadian Partnership for Tomorrow Project	Data access policy	March 2012
Electronic Medical Records and Genomics Network Generation Scotland	Data use agreement management, access and publications policy	Version 4.3, March 2010
International Cancer Genome Consortium	Data access agreement goals	August 1, 2009
International Cancer Genome Consortium	Structure, policies and guidelines	April 2008
National Cancer Research Institute	Samples and data for research; template for access policy development	June 2009
P3G Ethics and Policymaking Core	Material and data access agreements, core elements	2008
P3G Ethics and Policymaking Core	Model consent form	February 2011
The Cancer Genome Atlas	Data use certification agreement	March 1, 2010
The Cancer Genome Atlas	Human subjects protection and data access policies	NA
UK Biobank	Access procedures; application and review	Version 1.0, November 8, 2011
UK Biobank	Material transfer agreement for data and/or samples	November 8, 2011
The Wellcome Trust Case-Control Consortium	Data access agreement	Version 18, June 2010
The Wellcome Trust Case-Control Consortium	Access policy; access to genotype data	Version 1, July 2009

NA, not available.

existing agreements are often limited to data and rarely address the use of and access to samples. Third, existing access agreements tend to be conceived in highly legalistic terms. This drafting approach is problematic because it lacks the clarity needed to communicate clear and understandable expectations to researchers as to their commitments. The GAA not only offers a principled analysis of the content of access agreements, but also provides explicit clauses to promote comprehensibility among researchers.

It is essential that these agreements are not developed in isolation. Harmonization, at the current implementation stage of population studies, will reinforce international data and sample sharing norms, promote equitable procedures and improve researcher familiarity with simplified access procedures. Ultimately, some agreement on core bioethical principles[3] and the procedures accompanying them will foster an equitable and transparent playing field across population studies and foster their translation into genomic medicine.

The GAA has drawn on a variety of sources. A selection of existing data or material access agreements among P3G members was reviewed to determine common elements. Access-related documents from population studies—such as publication policies, intellectual property policies and consent forms—were also reviewed to ensure coherent integration. General principles were drawn from existing P3G resources developed to encourage harmonization in access[4–7]. The sources reviewed are listed in **Table 1**.

From the results of our review, a provisional GAA was drafted by the legal team at the Centre of Genomics and Policy of McGill University in Canada. The draft agreement was then circulated for two iterations of comments and revisions among the P3G International Steering Committee[8]. The resulting version of the agreement was then discussed and approved by the consensus of both the International Steering Committee and the Board of the P3G.

A few drafting principles were adopted in the preparation of this document: first, brevity; second, use of clear and simple language (as such agreements will often be read by scientists and administrators with limited legal training); and third, limiting of the template to essential elements so as to encourage uniform treatment of access applications, reduce time for negotiation between the study administrators and researchers, and allow customization for local needs and laws.

Certain issues arose in the drafting of this document. There was uncertainty concerning the commensurability of procedures for access to data and access to samples. Initially, the team developed a list of "special considerations for samples." Although samples require unique treatment for their quality, security, liability and disposal upon termination, we found that they could largely be integrated under general conditions used in the GAA.

Extensive discussion also went into the intellectual property terms. Our definition of 'invention' was drawn from the European Parliament and Council's Directive on biotechnological inventions[9]. The discussion reflected the tension between incentivizing research by allowing limited patent protection of inventions and promoting the valorization of the resource by allowing future research to build on the findings of past research. The final solution is to protect the potential for downstream patentability while reserving a robust, open license for future use and sublicense. Thus, protection for downstream inventions is explicitly recognized, with reference to international directives that were judged to offer the best balance of the interests. Finally, certain types of conditions mentioned in existing access agreements were not included. The most common reasons were that these conditions were either overly technical and legalistic or too specific to a certain type of study to merit inclusion in a generic access agreement.

The success of population studies will depend on their ability to adequately balance promotion and regulation of access. Research will suffer if the conditions of access are too strict; participants will suffer if they are too liberal. The GAA aims to strike this essential balance, to ensure equitable and clear conditions of access for population studies. Its successful adoption by the member institutions of P3G will help to establish an international standard for access to population studies. Their effective translation into population health will hopefully be enhanced and promoted.

Note: The Generic Access Agreement is available in the online version of the paper (doi:10.1038/nbt.2567).

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The International Steering Committee of P3G dedicates this article to the late David Cox—a co-author, visionary scientist and friend.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

Bartha Maria Knoppers[1], Rex L Chisholm[2], Jane Kaye[3] and David Cox[4,18] (on behalf of the P3G International Steering Committee), Adrian Thorogood[5] (ad hoc member; academic secretary), Paul Burton[6] (Chair), Anthony J Brookes[7], Isabel Fortier[8], Pat Goodwin[9], Jennifer R Harris[10], Kristian Hveem[11], Alistair Kent[12], Julian Little[13], Peter H J Riegman[14], Samuli Ripatti[15,16] & Ronald P Stolk[17] (P3G International Steering Committee)

[1]Centre of Genomics and Policy, McGill University, Montreal, Quebec, Canada. [2]Department of Cell and Molecular Biology, Northwestern University, Chicago, Illinois, USA. [3]HeLEX-Centre for Health, Law and Emerging Technologies, University of Oxford, Oxford, UK. [4]Pfizer, New York, New York, USA. [5]Centre of Genomics and Policy, McGill University, Montreal, Quebec, Canada. [6]Department of Health Sciences, University of Leicester, Leicester, UK. [7]Department of Genetics, University of Leicester, Leicester, UK. [8]McGill University Health Center, Montreal, Quebec, Canada. [9]C3 Collaborating for Health, London, UK. [10]The Norwegian Institute of Public Health, Oslo, Norway. [11]Department of Genetics, Norwegian University of Science and Technology, Trondheim, Norway. [12]Genetic Alliance UK, London, UK. [13]Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Ontario, Canada. [14]Erasmus Medical Center, Rotterdam, Netherlands. [15]Institute for Molecular Medicine Finland (FIMM), Hjelt Institute, University of Helsinki, Helsinki, Finland. [16]Wellcome Trust Sanger Institute, Hinxton, UK. [17]Department of Clinical Epidemiology, University of Groningen, Groningen, Netherlands. [18]Deceased.
e-mail: bartha.knoppers@mcgill.ca

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The P3G "Generic Access Agreement" is a template for use by those involved in prospective, longitudinal population genomics studies and is inspired by approaches found amongst P3G members (www.p3gconsortium.org); WTCCC (www.wtccc.org.uk); EMERGE (www.genome.gov/27540473); ICGC (www.icgc.org); UK Biobank (www.ukbiobank.ac.uk); NIH (cancergenome.nih.gov); and CPTP (www.partnershipfortomorrow.ca). This document has also been developed in conformity with the suggested principles and procedures of the "Data Sharing Code of Conduct for International Genomic Research" and the European Commission's report *Biobanks for Europe*. The Agreement integrates conditions for access to biological materials along with those for data access.

This Agreement is offered as a template to assist or inform researchers seeking access to population studies, and is not intended to be proscriptive. It is designed to indicate the elements that may be considered when creating consents, accompanying access procedures, and governance structures. Each study will necessarily need to include or delete elements according to its aims, cultural and ethical norms, and national legislation or policy. We hope this Agreement will provide a starting point and a useful guide.

Letterhead of (Population Genomics Study)

ACCESS AGREEMENT
[Name of Resource/Biobank/Study]*
(*collectively referred to below as "Study")

DEFINITIONS

"Applicable Law" means the laws specified by the parties, in the section entitled **Choice of Law**.
"Applicants" refers together to the applicant institution and the principal investigator of the Approved Research Project, both of whom have signed and accepted the Access Agreement.
"Approved Research Project" means the research project with appropriate institutional and ethics approvals that seeks to access Data and Materials.
"Data" means the data supplied to the Applicants for the Approved Research Project.
"Effective Date" means [insert date].
"Inventions" means findings that are new, involve an inventive step and are susceptible of industrial application.
"Participant Identifiable Information" means any information whatsoever that identifies, or could identify, Research Participants.
"Research Participants" means individuals (living or dead) who have contributed their Data or Materials.
"Materials" means the biological tissues or samples supplied to the Applicants for the Approved Research Project.

PARTIES TO THE ACCESS AGREEMENT

Name of Study: _____

Applicant Institution: _____

Principal Investigator Name(s):_____

1. GENERAL

The Applicants agree that the use of the Data and Materials under this Access Agreement is limited to the scope of the Approved Research Project and complies with Applicable Law and ethics approvals.

The Applicants agree to respect the policies of [Study] with respect to the handling, storage and use of its Data and Materials. These policies include [e.x. Participant Consent Forms, and Study Access, IP and Publications Policies], and are available [give web address or include as Annex]. The Applicants will be responsible for the training and conduct of all research personnel involved with the Approved Research Project. The Access Agreement is effective upon execution and receipt of a signed copy by all parties.

2. DELIVERY – TIMETABLE AND CONFIRMATION OF RECEIPT

[Study] will deliver the following Data and Materials to the Applicants: [insert description of Data and Materials to be delivered]. The Data and Materials will be delivered to the following address: [insert delivery address]. [Study] will use reasonable efforts to deliver the Data and Materials within [insert number] days of the Effective Date.

3. PRIVACY, CONFIDENTIALITY, AND IDENTIFIABILITY

The Data and Materials provided to the Applicants have been [coded or anonymized – (provide description of data treatment here)]. If the Applicants inadvertently receive Participant Identifiable Information, they will take all reasonable and appropriate steps to protect the privacy and confidentiality of such information. This may require immediate destruction of the information on request of [Study]. The Applicants agree to make no intentional attempt to re-identify Research Participants through linkage of Data, or otherwise. The Applicants will immediately report any identification of Research Participants to [Study].

The Applicants will not transfer any of the Data and Materials obtained, or any information derived therefrom, to third parties, except with the approval or on the request of [Study].

4. SECURITY

The Applicants will adhere to the security protocol outlined [in the Study Access Application], and employ all reasonable efforts to prevent unauthorized access to the Data and Materials in their custody.

5. LIMITS ON LIABILITY

[Study] will not be liable for damages related to the provision of Data and Materials to the Applicants. This includes but is not limited to damages in relation to inaccuracies, lack of comprehensiveness, or use of the Data and Materials, or any delay or break in supply by [Study].

The Applicants acknowledge that [Study] makes no guarantee that the Materials are free of contamination from viruses, latent viral genomes, or other infectious agents. The Applicants agree to treat the Materials as if they were not free from contamination, to assure appropriate biosafety training to research personnel, and to implement appropriate biohazard containment measures.

6. INTELLECTUAL PROPERTY

The Applicants must not make IP claims on Materials or Data derived directly from [Study]. However, the importance of downstream Inventions made with [Study] Materials and Data is recognised; patents on such Inventions are permitted. In doing so, the Applicants agree to implement licensing policies that will not obstruct further research.

The Applicants will own all results, data, and inventions which arise under the Research Project. The Applicants do however grant to [Study] a perpetual, non-cancellable, royalty-free, worldwide license, with right to sublicense, to use study results for all purposes.

7. RESULTS AND PUBLICATION

Upon completion of the Approved Research Project, the Applicants will send to [Study] [reports, enriched data, etc.]. The Applicants must endeavour to publish results in an academic journal or in an open access database. The Applicants agree to acknowledge [Study] in any publication or presentation on work derived in whole or in part from the Data and Materials and to supply [Study] with a copy or web address of any publication.

8. REPORTING A BREACH

If the Applicants become aware that the terms of the Access Agreement have been breached, they will promptly notify [Study] of such breach. The Applicants will provide to [Study] in a timely manner any material information relating to the breach, including the date and nature of the event, remedial measures taken, and plans to avoid further or future breach. In the case of a breach please contact: [Study Contact Name and Info].

9. TERMINATION

[Study] has the right to terminate this Access Agreement upon material breach of any term of the Access Agreement by the Applicants. The Applicants may terminate this Access Agreement at any time with immediate effect by providing written notice to [Study] of the termination.

Upon termination, the Applicants agree to destroy all copies of Data except as required by publication practices or Applicable Law, and to destroy [or return forthwith] all Materials. The Applicants will send written confirmation to [Study] detailing the destruction of the Data and Materials.

10. MISCELLANEOUS

Duration of Agreement/Procedure for Renewal: (Insert local clause)
Choice of Law: This Access Agreement shall be construed in accordance with the laws of [insert jurisdiction].
Representations and Warranties: (Insert local clause)
Force Majeure: (Insert local clause)
Authority and Compliance: (Insert local clause)
Assignment: (Insert local clause)
Severability: (Insert local clause)
No Partnership or Employment Relationship: Nothing in this Access Agreement creates a partnership or employment relationship between the Parties.

[*These conditions may be modified to allow for the specific needs of population studies, and negotiation between the parties.]

APPLICANT SIGNATURE(S): [etc]
DATE: