

Canadian College of Medical Geneticists Canadian Association of Genetic Counsellors

Joint Statement on the Process of Informed Consent for Genetic Research

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1. Introduction

This document has been developed and endorsed by the Canadian College of Medical Geneticists (CCMG) and the Canadian Association of Genetic Counsellors (CAGC) with the financial support of Health Canada. The CCMG and the CAGC are the Canadian certifying bodies for Medical Geneticists and Genetic Counsellors, respectively. Together with provincial and federal government authorities and other professional bodies, the CCMG and CAGC play an important role in establishing standards for the provision of genetic services in both research and clinical contexts in Canada.

The CCMG and CAGC both strive to foster a culture of ethical behavior in the field of medical genetics. The essence of the process of informed consent is to maintain the rights and welfare of research participants and to protect research participants' personal autonomy. Both the CCMG and the CAGC believe that a non-coercive approach to recruitment of research participants is necessary for an ethically responsible process of informed consent.

2. Scope

This document outlines the key considerations in ensuring participants enter into research studies voluntarily and have a reasonable understanding of the nature of the research, their role in the study, and the risks and benefits at the individual and population levels. This document highlights the importance of dialogue and interaction in the process of informed consent for genetic research. The Tri-Council Policy Statement: *Ethical Conduct for Research Involving Humans*¹ provides over-arching guidance for any research involving humans, but the CCMG and CAGC believe that more detailed guidance is needed specifically related to human genetic research.

The recommendations outlined herein are relevant to all of the members of the CCMG and the CAGC, and should serve as guidance to the broader community involved in genetic research. This would include, but is not limited to: medical professionals within and outside the genetics community, researchers from other fields performing research with a human genetic component, the ethics community (including Research Ethics Boards), the legal community, professional licensing bodies, professional organizations, funding agencies, governmental organizations, policy makers, industry stakeholders, patient advocacy groups and the research participants themselves.

Research is a critical step in advancing knowledge and it is recognized that many families wish to participate in research in order to increase the understanding of a disease that affects their family. The consent process should demonstrate an effort on the part of the researchers to clearly and accurately inform the participants of the breadth and potential implications of the research. The process of consent should be designed in such a way as to protect the rights and welfare of the

participants but should not be so cumbersome as to unduly impede the research initiative. A balance must be maintained between the interests of the researcher and those of the participants. Independent parties such as institutional REBs should review the informed consent process for genetic research studies to ensure that consent is being achieved in the most appropriate manner possible.

Over time, the nature of research and the relationship between researchers and research participants may evolve. Acceptable practices in the current environment may not apply to future research; requiring refinement and/or redefinition of this statement to both protect the participants and sustain a productive and innovative research community. It is the expectation that this statement will evolve and will be reviewed regularly to ensure its applicability.

3. Guiding Principles in the present research context:

- i. Non-coercion– The principle of non-coercion refers to the professional’s responsibility to present information in a way that does not allow his or her personal biases to influence a potential research participant’s decision whether or not to be involved in the research
- ii. Autonomy – The principle of autonomy refers to an individual’s right to make decisions and independent choices
- iii. Beneficence – The principle of beneficence refers to the professional’s responsibility to act in a way that reflects the best interest of others,
- iv. Nonmaleficence – The principle of nonmaleficence refers to doing no harm
- v. Justice – The principle of justice refers to treating all individuals equitably

4. Nature of Genetic Research

The impact of participating in research reaches beyond the benefits and risks to the individual participant. In genetic research, the results may have significance for the individual, their relatives (including offspring and family members extending over numerous generations), and other similar individuals/families. As with other areas of biomedical research, there is the potential for infringement of privacy² that may inappropriately affect medical care or insurability for the participant and their family members. Similarly, there is the potential to discover information relevant to a particular cultural or ethnic group that subsequently may be inappropriately used to discriminate against members of such groups.

5. Genetic Research

For the purposes of this document, genetic research is defined as any research involving the analysis of human genetic material and may include analysis of DNA, RNA, proteins and metabolites, as well as the assessment of detailed family history where the intent is to collect and evaluate information about the heritability of human disease, including studies of a qualitative nature. Genetic research includes the discovery of previously unknown genes or gene functions and studies where information obtained could be generalized to a sub-section of the population based on genotype and/or characteristics within a family. Genetic research also includes advancing our understanding of genetic conditions and the interaction between genes and external factors such as diet (nutrigenomics), drugs (pharmacogenomics) and exercise.

It should be recognized that the process of informed consent at the individual and population level varies with the nature of the research and the study population. Attempts have been made to take this variability into account in creating this document.

6. Genetic Counselling

Because of the intricacies and sensitivities involved in the process of informed consent relating to medical genetic research, it would be ideal for the individuals supervising the consent process be certified genetics professionals (certified geneticists and/or genetic counselors). Certified genetics professionals have training specific to the medical, scientific and psychosocial aspects of genetic diseases and genetic testing and are often best able to assess and inform participants of information that could be of significant impact to them. When this is not feasible, the professionals responsible for the consent process should have a thorough understanding of the basic principles upon which this document was based. The professionals responsible for obtaining consent from participants have the role of accurately and effectively educating potential research participants about the study in a non-coercive manner.

7. Process of Consent

Consenting to participate in a research project is a process during which the study participant learns sufficient details of the project such that they can give their free and expressed consent. *The key component of the consent process is the dialogue between the researcher (or delegate) and the participant.* It is this giving and receiving of information that forms the basis of true “informed” consent. The emphasis, therefore, must be on imparting critical information to the participant, rather than on simply obtaining a signature at the bottom of a consent form.

Ideally, the consent dialogue should occur face to face; however, if this cannot be achieved, this should not be a barrier to participation provided that a satisfactory dialogue can take place by other means. Throughout the consent process, every effort should be made to remove communication barriers by using plain language and culturally appropriate translation services.

Upon completion of the consent dialogue, the research participant should be provided with a written information sheet that clearly and succinctly explains the key elements discussed. However, in no way can this written summary replace the dialogue that is necessary for true informed consent. It should be noted that long, complicated consent forms can be off-putting to research participants and should be avoided if at all possible.

The CCMG and CAGC believe that the following key elements, which are consistent with the Tri-Council Policy Statement: *Ethical Conduct for Research Involving Humans*¹, should be considered and discussed during the process of informed consent for genetic research:

i. Basic Description of the Research Project

The dialogue should begin with a basic description of the scope of the research project. This may include discussion of: the goals of the project, the research question, the importance of the research and expected results, including whether the results could affect the health care decisions of the participants or their families. The rationale for research participant selection and the number of participants involved in the study may be described along with a timeframe for the project. General contact information for the researchers and contact information of an impartial party, often

the Chair of the institutional Research Ethics Board, should be provided in the written information sheet.

ii. Potential risks and benefits

There should be a discussion of known significant potential risks and benefits to the individual. This may include, but may not be limited to: potential issues related to impact on medical care/diagnosis, privacy and confidentiality, social impacts (e.g. stigmatization, discrimination), cultural or community concerns, and limitations of the study (e.g. what the study will reveal, what it will not reveal, including the potential for difficult to interpret results). It should be clear to the potential participant that declining to participate or withdraw at any time will not affect his/her care in any way.

iii. Inclusion of children, persons with intellectual disability, and other vulnerable groups in research studies

Ideally, all research participants should be capable of giving their own free, informed and express consent to participate. However, it is understood that there will be instances in which the inclusion of children and/or those with intellectual disability is necessary in order to answer critical research questions. In keeping with Article 5.3 of the *Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans* and with Article 8 of the *UNESCO International Declaration on Human Genetic Data*, such individuals should only be included in research that has the potential to be beneficial to themselves as individuals or to the group that they represent^{1,3}.

When research studies include children, wherever possible, an attempt should be made to gain the assent of the children to participate⁴. The possibility of doing so will depend, of course, on both the ages of the children involved and their intellectual capacity to understand the research in question. Otherwise, consent from a parent or legal guardian is required.

When research projects involve the participation of Aboriginal populations, there are additional considerations related to ensuring that the research is carried out in a way that respects the cultures and values of the communities involved⁵.

iv. Withdrawal from the study

Research participants should understand that they are free to withdraw their consent to participate at any time without repercussions⁶. The manner of withdrawal and any limitations in the withdrawal process should be discussed with the participant in advance (e.g., can they request: return of information or samples, destruction, anonymization, transfer to a third party, etc.) When applicable, during the withdrawal process the researcher should clarify the manner with which specimens should be withdrawn; ethnic or cultural requirements should be adhered to by the researcher¹.

In the course of the consent dialogue, the degree to which withdrawal is possible must be clear. In some instances, it may be possible to discard all specimens or delete data associated with that participant. Participants must understand that full withdrawal may not be possible if identifiers have been removed or if study results have been published prior to participant withdrawal. As indicated in Article 9(c) of the *UNESCO International Declaration on Human Genetic Data*³,

“If not irretrievably unlinked, the data and biological samples should be dealt with in accordance with the wishes of the person. If the person’s wishes cannot be determined or are not feasible or are unsafe, the data and biological samples should either be irretrievably unlinked or destroyed”.

v. Privacy and Confidentiality

Research participants should be assured that privacy and confidentiality would be protected to the greatest possible extent. Every reasonable effort should be made to maintain privacy and avoid a breach of confidentiality except where required by law, such as the “duty to warn” provision in the Personal Information Protection and Electronic Documents Act (PIPEDA)⁷ which protects an individuals’ confidentiality except when there is “*significant risk of substantial harm to others*”.

Although it may be technically possible to determine the source of an anonymous specimen using forensic DNA methods, professional and ethical standards of genetic researchers do not support the use of any technology to re-identify anonymous specimens. For studies using “anonymous” specimen collections, research participants should be aware of which identifiers may remain attached to specimens (e.g. gender, age, clinical information). In the case of rare diseases or in small communities, this information may be sufficient to identify participants; consideration should be given to this possibility and when applicable, potential participants informed.

Where projects involve the recruitment of multiple family members and results are disclosed, care should be taken while disclosing a participant’s results to ensure that no inference is made concerning a relative’s results, recognizing that avoiding this may not always be possible. Participants should be made aware that since personal genetic information is confidential, the researchers cannot share it with other family members without their consent, and that the “burden” of voluntary dissemination of results rests with the participant him/herself.

vi. Conflict of interest

Known conflicts of interest should be declared to the research participant including those related to funding sources and reimbursement related to the recruitment of research participants. Conflicts of interest should be managed or avoided so as not to affect the judgment of the researcher. A researcher with a conflict of interest should take steps to ensure that recruitment of study participants be conducted by another professional free of conflicted interests to avoid any suggestion of coercion, bias or untoward behaviour on the researcher’s part.

vii. Disclosure of results

Research participants should be informed at the outset if the results from the study will be disclosed and, if so, in what manner (e.g. individually to each participant or collectively as a study group through publication or another means). As indicated in section 7(v) above, researchers must take care to protect the privacy and confidentiality of individual participants in the course of results disclosure. Researchers should ensure that participants do not have unrealistic expectations with respect to disclosure of results. For example, a realistic estimate of the timeframe should be communicated to the participant. Ideally, participants should have the option to decline to be informed of study results at the time of enrollment or at any time during the study.

It is recommended that for all studies in which results will be disclosed, genetic counselling should be a component of the informed consent process. The counselling provided should be appropriate

to the clinical impact of the study. It should be provided at a level of depth and by staff with a level of training and expertise that is appropriate for the complexity of the information being explained⁶.

Clinically Significant Results: It is recommended that any clinically-significant laboratory results ascertained through a research laboratory and disclosed to the research participant be validated in an accredited clinical diagnostic laboratory to ensure that appropriate quality assurance measures have been followed^{8,9}. Accredited clinical diagnostic laboratories that offer confirmation of research findings can be identified using online databases such as GeneTests.org¹⁰.

Unexpected Results: Genetic research is unique in that there is the potential to obtain information about individuals or families that was unanticipated. In addition, it is possible that in the course of studying one disease, a researcher may discover that an individual, family or community is at increased risk for another, possibly unrelated, disorder. If individual results are to be disclosed, research participants should be made aware of the possibility that unexpected results could be obtained and should be informed of policy with regards to disclosure of such results in the context of significant health implications for the individual and/or his family⁹. Prior consent should be obtained with regard to the research participant's wish to be informed of these unanticipated results.

viii. Consent to future research use

Prior to participation in a genetic research project, when applicable, participants should be asked to provide consent for future use that includes as much detail as possible⁶.

ix. Re-contacting study participants

The process of informed consent should include a discussion of whether a research participant would be willing to be re-contacted to obtain additional specimens for the current study, to participate in future studies, or to be informed of new significant genetic discoveries. The research participant should have the option of agreeing or disagreeing to future contact and be informed that the onus will be on the participant to maintain contact information.

x. Commercial use

Research participants should be made aware of any foreseeable commercial uses or benefits of the research in which they are participating. If there is intention to use specimen collections from the study for commercial gain on the part of the researcher or the researcher's institution, this must be communicated to the research participants.

xi. DNA, Cell line & Tissue banking issues

When biological materials such as DNA, cell lines and tissue are collected, the nature and use of the specimens must be discussed. Information provided may include but is not limited to: use, specimen identification (unique identifiers or anonymous), location and duration of storage, security, custodianship, and disposal. Researchers should be aware of potential culturally sensitive issues with respect to disposal of specimens¹.

Use of Existing Collections of Biological Materials

Subject to local REB approval requirements, existing collections of biological materials may be used for additional research in circumstances such as:

- a) Consent is obtained from each individual.

Or

- b) The specimens are anonymous and irretrievably unlinked from the source. As indicated in section 7(v) above, consideration must be given to what information remains linked to specimens and whether this information may identify individuals, especially in the case of rare diseases or small communities.

Xii. Storage, Access to and Disposal of Information

Research participants should be made aware of how information related to the study will be stored, who will have access to the information, how it will be transmitted between researchers or between research centres, how long the information will be stored upon completion of the study and the manner in which the information will be disposed ¹.

8. Conclusions

Research is a critical component of our understanding of the biological basis of disease. Genetic research has unique components that must be considered in designing a study to ensure that participants have all access to all of the information they need to make a truly informed decision to participate in a particular research project. The present document, prepared by the Canadian College of Medical Geneticists and Canadian Association of Genetic Counsellors, endeavours to outline the key components of the informed consent process for genetic research to act as a guide for all parties involved in such research.

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References:

1. Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans http://www.ncehr-cnerh.org/english/code_2/ Accessed May 30, 2008
2. Lunshof, JE, Chadwick, R, Vorhaus, DB, Church, GM (2008). From privacy to open consent. *Nature Reviews Genetics* 9:406-11
3. UNESCO International Declaration on Human Genetic Data http://portal.unesco.org/en/ev.php-URL_ID=17720&URL_DO=DO_TOPIC&URL_SECTION=201.html Accessed May 30, 2008
4. Wendler, DS (2006). Assent in paediatric research: theoretical and practical considerations. *J Med Ethics* 32(4):229-34
5. Arbour, L, Cook, D (2006). DNA on Loan: Issues to consider when carrying out genetic research with Aboriginal families and communities. *Community Genet* 9:153-60

6. Caulfield, TM, McGuire, AL, Cho, M *et al.* (2008). Research Ethics Recommendations for Whole Genome Research: Consensus Statement. *PloS Biology* 6(3):430-5
7. Personal Information Protection and Electronic Documents Act (PIPEDA)
http://www.privcom.gc.ca/legislation/02_06_01_01_e.asp Accessed May 30, 2008
8. OECD Guidelines for Quality Assurance in Molecular Genetic Testing
<http://www.oecd.org/dataoecd/43/6/38839788.pdf> Accessed May 30, 2008
9. McGuire, AL, Caulfield, T, Cho, MK (2008). Research ethics and the challenge of whole genome sequencing. *Nature Reviews Genetics* 9:152-6
10. GENETests www.genetests.org