SUMMARY

Statement of Principles

R M G A

on the Return of Research Results and Incidental Findings

This pamphlet provides an overview of the RMGA *Statement of Principles on the Return of Research Results and Incidental Findings.*

The entire document is available on the RMGA website at the following address:

http://www.rmga.qc.ca

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GLOSSARY

Scientific validity: Capacity of a test to measure the characteristic it is designed to identify. In particular, this concept includes the capacity that the test will be positive if the genetic characteristic is present (analytical sensitivity), and negative if it is absent (analytical specificity).[1] ("Scientific validity" is also called "analytical validity").

Biobank: An organized collection of human biological material and associated information, stored for one or more research purposes.[2]

Clinical utility: The value of the results in guiding the participant's choices regarding prevention or therapeutic strategies.[3] The assessment of the utility requires consideration of the benefits but also of the potential risks associated with the knowledge of the result or intervention.

Generally, the criteria considered for determining the clinical utility of a result may be grouped in two broad categories[4]:

1) Criteria concerning the result:

a) the "service rendered" by the latter (in particular the value of the result to determine the possible medical measures in terms of prevention or treatment); and

b) the context in which the result is offered (availability of treatment or prevention strategy);

2) Criteria relating to the participant: the measure of the clinical utility of a result may vary from one participant to another (depending on the participant's situation). Social and cultural aspects should also be taken into account.[5]

[1] Adapted from: Council of Europe, *Explanatory Report – Additional Protocol to the Convention on Human Rights and Biomedecine, concerning Genetic Testing for Health Purposes,* 2008, at art 5, s 48.

[2] Public Population Project in Genomics and Society (P3G), Lexicon, online: http://p3g.org/biobank-lexicon#b.

[3] Council of Europe, supra note 1 at art 5, s 57.

[4] *Ibid.*

[5] Adapted from: *Ibid.*

Clinical validity:

Measurement of the accuracy with which a test identifies or predicts a clinical condition. It is defined in terms of clinical specificity, sensitivity and predictive value.[6]

General research results:

Aggregated results concerning a group or cohort of persons. The expression "general results" will be used hereinafter.

Human biological materials:

Tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, and other body fluids (whether or not obtained pre or post mortem). The term also includes materials related to human reproduction, including embryos, fetuses, fetal tissues and human reproductive materials.[7]

Incidental findings:

Unanticipated discoveries that are outside of the research objectives but that are relevant to the individual participant.[8]

Individual research results:

Results which concern an individual participant discovered during the course of research. The expression "individual results" will be used hereinafter.

In the context of the present Statement, "individual results" do not include:

- Existing personal information used during research (e.g. medical records).

[6] Adapted from: *Ibid.*

[7] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans,* December 2010 [TCPS 2], at glossary.

[8] Adapted from: *Ibid.*

GENERAL PRINCIPLES: Principles 1 to 4

DECIDING WHICH RESULTS TO RETURN

PRINCIPLE 1 GENERAL RESULTS

General research results **should be** made easily accessible to the scientific community, to research participants, and to the general population.

PRINCIPLE 2 INDIVIDUAL RESULTS AND INCIDENTAL FINDINGS THAT SHOULD BE OFFERED

Individual results and incidental findings **should be** offered to participants when:

1) they are material[9], i.e. when the following conditions are met:

1.1) they meet generally accepted criteria of scientific[10] and clinical validity[11] (criteria which are widely recognised by the medical community);

1.2) they have clinical utility[12] for the participant, i.e.:

-the benefits associated with the communication of the results outweigh the risks;

- prevention or treatment is available; and

- individual, familial and social factors were considered;

2) exceptions and additional considerations related to the research context have been weighed;

3) REB approval has been obtained;

4) the participant has consented to the return of results; and

5) the research result has been confirmed.

[9] Note that according to the TCPS 2, material incidental findings are those "that have been interpreted as having significant welfare implications for the participant, whether health-related, psychological or social," and that must be returned to participants (*ibid* at art 3.4).

[10] Among the common characteristics of evidentiary requirements for reviewing the scientific validity of a result, (also called "analytical validity") a researcher could assess measures such as precision, reliability, accuracy, sensitivity, and specificity of the result. However, the accuracy of the result should not be confirmed until the researcher ensures that the other conditions are met. In this way, only results that could be communicated to the participant will be confirmed, and clinical laboratory services will not be wasted.

[11] Refers to both the "analytical validity" and "clinical validity" (see the Glossary for more details).

[12] Refer to the definition of clinical utility in the glossary.

PRINCIPLE 3 INDIVIDUAL RESULTS AND INCIDENTAL FINDINGS THAT MAY BE OFFERED

Individual results and incidental findings that are not compliant with the criteria set out in Principle 2 may be offered to participants (i.e. *at the researcher's discretion*) when:

1) they meet generally accepted criteria of scientific and clinical validity;

2) the benefits of return surpasses the risks;

3) REB approval has been obtained;

4) the participant consented to the return; and

5) the research result has been confirmed.

PRINCIPLE 4 INDIVIDUAL RESULTS AND INCIDENTAL FINDINGS THAT HAVE IMPLICATIONS FOR FAMILY MEMBERS

It is possible that individual results and incidental findings have implications for the participant's BIOLOGICAL RELATIVES. Under certain circumstances, these results may be returned (i.e. *at the researcher's discretion*) to family members when:

1) they meet the generally accepted criteria of scientific and clinical validity;

2) the benefits of the return outweigh the risks;

3) REB approval has been obtained;

4) the research result has been confirmed;

5) the participant agrees to share the result with biological relatives; and

6) the biological relatives concerned agree to receive the results.

EXCEPTIONS - Principles 5 to 7

It is impossible to apply a single approach to all research contexts. It is particularly important to consider the specific circumstances of participants. The vulnerability of participants is a crucial element and leads to certain categories of exceptions.

PRINCIPLE 5 MINORS

Individual results and incidental findings concerning a MINOR should be returned when all the following conditions are met:

1. they meet the generally accepted criteria of scientific and clinical validity;
2. they have significant implications for the health of the minor;
3. effective treatment or prevention is available and should be initiated **during childhood or adolescence;**
4. REB approval has been obtained; and
5. the research result has been confirmed.

Under these circumstances, the parents should not refuse the return of results. A refusal to receive this category of result could be considered medical neglect.

PRINCIPLE 6 MINORS

Individual results and incidental findings concerning the future adult health of a MINOR **should not be offered.**

However, in **exceptional circumstances,** this principle may be outweighed and results may be returned to the minor's parent when the following conditions are met:

1) the results meet the generally accepted criteria of scientific and clinical validity;

2) the results are important for the immediate health of a parent or adult-aged sibling, considering:

- the probability of the risk occurring (for the parent or adult-aged sibling) is high;
- the consequences for the parent's or adult-aged sibling health is serious;
- treatment or an effective method of prevention is available;

3) REB approval has been obtained;

4) the results have been confirmed;

5) parental consent has been obtained; and

6) when possible and appropriate, the assent of the minor participant is obtained.

LEGALLY INCAPACITATED ADULTS

Québec civil law anticipates that the rules related to the minor's exercise of civil rights also apply to adults under legal guardianship or trust, taking into account the necessary adaptations.[13] In the same way, the principles and procedures indicated in the section addressing paediatric research apply to research with incapacitated adult participants, with necessary adaptations.

PRINCIPLE 7 DECEASED PARTICIPANTS

Individual results and incidental findings should be returned POST-MORTEM to members of the family when:

1) they meet generally accepted criteria of scientific and clinical validity;

2) they have significant implications for family members;

3) the participant has previously consented that they be transmitted to family members;

4) REB approval has been obtained;

5) the family (i.e. the persons directly affected by the results) have consented; and

6) the research result has been confirmed.

[13] *Civil Code of Québec*, L.R.Q. c. C-1991, s. 266.

ADDITIONAL CONSIDERATIONS RELATED TO THE RESEARCH CONTEXT – Principles 8 to 10

It is impossible to apply a single approach to all research contexts. Therefore, it is important to take certain contextual elements into consideration to determine if an individual result or incidental finding should be returned to the participant.

The principles set out below are not exhaustive. They should be considered in addition to Principles 1 to 7 where applicable.

PRINCIPLE 8 BIOBANKS

When biological samples or medical/genetic data are deposited in a BIOBANK for future use, the question of research results management and return should be addressed in the biobank's management policy, and more specifically in the agreement for the transfer of medical/genetic data or biological material.

PRINCIPLE 9 POPULATION-BASED RESEARCH

In POPULATION-BASED RESEARCH, some elements linked to the research context could render the return of individual results and incidental findings impossible or unreasonable.

The following elements may be considered in such an assessment and to request a REB waiver concerning the communication of research results:

1) the scope of research objectives;

2) the number of participants involved;

3) the nature or duration of the relationship between the researcher and the participants, especially:

   a) the number of meetings between the participant and the researcher;

   b) whether these meetings took place with the researcher himself or other personnel;

   c) the duration of the participant's involvement in the project;

   d) whether the researcher is also the participant's treating physician; and

4) whether the data or samples are readily accessible to the researcher.

PRINCIPLE 10 LONGITUDINAL RESEARCH

In LONGITUDINAL RESEARCH, the nature of the relationship between the researcher and the participant could modify expectations for the return of research results. For example, expectations of communication of research results could be intensified if a participant was regularly recontacted.

To judge the nature of the relationship between researcher and participant, the following factors may be considered:

1) number of participants involved in the research;

2) the number of encounters between the researcher and the participant;

3) whether these encounters took place with the researcher himself or other personnel;

4) the duration of the participant's involvement in the project; and

5) whether the researcher is also the participant's treating physician.