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**MECHANISM FOR THE ETHICAL REVIEW  
AND ONGOING OVERSIGHT OF MULTICENTRE PROJECTS**

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## SUMMARY

In substance, the multicentre mechanism presented herein concerns all research projects carried out in more than one institution, whether the institution is part of the health and social services network or a university with a minister-designated research ethics board (REB) that has formally undertaken to comply with this mechanism. After receiving scientific approval for a research project, the coordinating principal researcher—the person in charge of coordinating the activities of researchers in centers taking part in a multicentre project—must submit the file to a main REB for review. This REB is selected according to two basic requirements. First, the REB must be competent, i.e., it must meet the requirements of Article 21 of the Civil Code of Québec as well as other normative requirements, including the working conditions and operating rules for REBs laid down by the minister or the Ministry, and it must have recognized expertise and experience in the project research area. In addition, the REB must be tied to an institution where the mechanism applies. According to the ground rules, when these two requirements have been met, the coordinating principal researcher must submit the project to the REB of his/her home institution. When the ground rules do not apply, the researcher must submit the project to the REB of one of the concerned institutions where research subjects will be recruited or, failing that, find an REB that meets the two basic requirements.

The research project must be submitted concurrently to the main and local REBs for ethical review, as well as to the authorities designated by the concerned institutions for the site-specific assessment (feasibility and suitability). These two reviews are conducted simultaneously.

Each local REB conducts a preliminary project review focusing mainly on local considerations. This review can occur in a full or select committee, provided the REB meets the three-week deadline. Each local committee forwards any comments to the main REB. This is a crucial step that can affect the main REB's decision. This review provides an opportunity to make the REB aware of local considerations, such as the particular needs of research subjects recruited in the institution, as well as any scientific or ethical issues of particular concern.

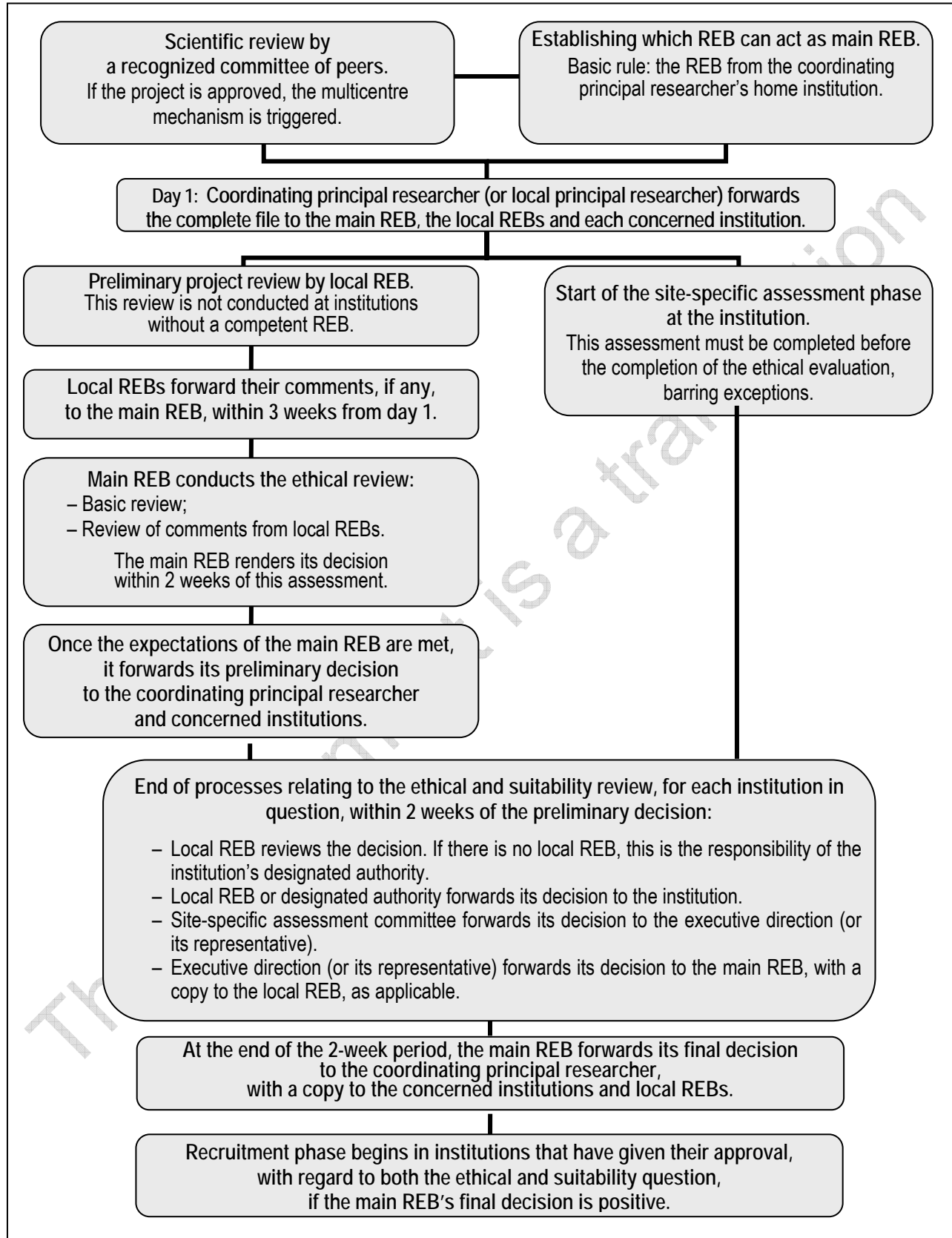
The main REB is responsible for compiling the comments it receives and adding them to the evaluation file. It then conducts the ethical review in a full committee. This review is similar to that for other types of projects, except that the committee must also consider the comments received. The multicentre mechanism encourages dialog with local REBs, since the ultimate decision must be supported by all REBs or at least most of them. When the main REB is satisfied, it issues its positive preliminary decision within two weeks of the meeting.

On receiving the preliminary decision, the local REBs and institutions without an REB have two weeks to notify the main REB of their decisions regarding the ethics and suitability of the project. Subsequently, the main REB issues its final decision. If it is positive, the research project can begin. The coordinating principal researcher is then required to comply with the terms set down by the main REB regarding ongoing project oversight. This REB also assumes responsibility for passive ongoing oversight and liaises with the concerned institutions.

Lastly, the proposed mechanism includes special terms for registering projects, dealing with complaints and allegations of breach of ethics, identifying research subjects, and ensuring REB accountability.

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## MULTICENTRE MECHANISM SUMMARY



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## Overview

The ethical review and ongoing oversight of a multicentre project—a single project that is carried out in a number of institutions—has been a stumbling block for many years, both for researchers and research ethics boards (REB). The recent survey on the *Plan d'action ministériel en éthique de la recherche et en intégrité scientifique*<sup>1</sup> (Ministerial Action Plan on Research Ethics and Scientific Integrity) revealed that researchers find it difficult to deal with the lack of uniformity in REB procedural methods and decisions, and fear this will delay or put a halt to research. REB chairs felt limited in their ability to modify multicentre projects and reported sometimes feeling pressure from researchers. In addition, both researchers and REB chairs mentioned the considerable human and financial costs tied to the ethical review of this type of project.

There are many ethical considerations tied to this issue. At least five of them—each with its share of thorny questions—have captured the attention of Ministère de la Santé et des Services sociaux. The first concerns the principle of justice, i.e., the unfair distribution of resources in a system where researchers with means have an advantage over those with less funding, and unequal treatment such as the protection of research subjects (ethical double standard). The second consideration is related to the principle of beneficence. Feeling that the system in place limits the benefits of research, researchers become demotivated and delay or even stop research. The third involves the principle of nonmaleficence. There is a greater chance that research subjects will be less protected against risk, and some doubt REB competence due to irregular decisions and the lack of an overall vision of the project and its possible effects on research subjects while underway. The fourth consideration is related to the principle of autonomy of the research subject, i.e., double standards with respect to consent forms and the information they contain, and questions regarding the validity of informed consent. The fifth and final consideration concerns the principle of popular representativeness, of which REBs are one ramification: REBs are unable to fully play their role of protecting subjects due to the increasing level of competence and advanced expertise required to evaluate multicentre projects—qualifications few REBs have. In addition, REB independence is restricted by the lack of a counterbalancing power that would ensure implementation of REB decisions, and there is no longer an overall vision of project ethics.

In view of the above, the Ministry has taken steps, including consultations with various stakeholders in the industry,<sup>2</sup> with a view to establishing a specific mechanism for the ethical review and ongoing oversight of multicentre projects. The mechanism has three objectives: ensure better protection of research subjects, ensure better use of human and financial resources, and streamline the current process for multicentre research. In November 2007 the Ministry announced the introduction of the mechanism, which was followed by a project demonstration phase and numerous training sessions intended for all stakeholders likely to be affected by the mechanism. This period provided an opportunity to improve the initial document in response to observations, comments and questions that were raised, resulting in this updated version. The Ministry would like to thank all those who helped to enrich this document.

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1. Sonya Auvy, *Le Plan d'action ministériel en éthique de la recherche et en intégrité scientifique: une entreprise insensée ?*, p. 46–49 and 163–165. Investigation report produced for the Unité de l'éthique, 2006, XXI, 274 p., [Online], < <http://ethique.msss.gouv.qc.ca/site/138.0.0.1.0.0.phtml> >, consulted January 15, 2007.

2. See Appendix 3.

## 1 Definitions

- 1.1 *Central REB*: The minister's research ethics board.
- 1.2 *Local REB*: Research ethics board that performs its duties in the institution where a research project will be partially or fully carried out, and that will conduct the preliminary project review if its status allows it, as per Article 21 of the Civil Code of Québec. Alternatively, an REB acting for an institution, e.g., under a delegation agreement or pooling arrangement.
- 1.3 *Main REB*: Central or local research ethics board that acts as the main authority for a number of institutions and is tasked with evaluating multicentre research projects and ensuring ongoing oversight. This board is also in charge of liaising with local REBs and, as the case may be, the concerned institutions.
- 1.4 *Local researcher*: Any person responsible for partially or fully carrying out a research project within an institution. The local researcher reports to the coordinating principal researcher and local principal researcher, as the case may be. He/she may act as local principal researcher.
- 1.5 *Coordinating principal researcher*: Person who coordinates a research project in Québec for the purposes of the multicentre mechanism. The coordinating principal researcher is the only point of contact with the main REB. He/she reports to the main REB and concerned institutions regarding project progress as well as the adherence of local researchers and the research team to the responsibilities assigned in implementing the mechanism. To act as coordinating principal researcher, the researcher must reside in Québec or carry out most of his/her professional activities in the province (residency criteria). The coordinating principal researcher may be a local principal researcher. The designation of the coordinating principal researcher varies according to the project's funding source:
  - 1.5.1 *Research project funded by private enterprise*: the coordinating principal researcher is designated by the sponsor, who must ensure that this person respects the residency criteria mentioned above;
  - 1.5.2 *Project funded by a public or private organization within the framework of a cooperative group*: the coordinating principal researcher is designated by the organization, which must ensure that this person respects the residency criteria mentioned above;
  - 1.5.3 *Other research project funded by a public or private organization*: the coordinating principal researcher is that person to whom the grant has been issued, or a designated representative, if the former does not meet the residency criteria as mentioned above;
  - 1.5.4 *Research project not included in any of the previous categories*: the coordinating principal researcher is the project's principal researcher, or a designated representative, if the former does not meet the residency criteria as mentioned above.
- 1.6 *Local principal researcher*: Local researcher who acts as the team leader at a concerned institution. The principal researcher reports to the institution and the coordinating principal researcher. He/she may also act as coordinating principal researcher.
- 1.7 *Site-specific assessment committee*: Ad hoc or standing committee whose members are qualified to evaluate the feasibility of a project in a concerned institution. The committee may consist of one or more bodies or persons designated by the concerned institution (e.g., finance department, professional services branch, pharmacy).

- 1.8 *Scientific committee*: Committee of peers tasked with evaluating a research project with respect to its scientific rigor or validity.
- 1.9 *Institution*: Institution in the meaning of the *Act respecting health services and social services* or, as the case may be, a university with a minister-designated research ethics board that has formally undertaken to comply with the multicentre mechanism.
- 1.10 *Concerned institution*: Institution where a research project will be partially or fully carried out.
- 1.11 *Institution not having an REB*: institution not having an REB or whose REB cannot make a decision because it does not meet the requirements set forth in Article 21 of the Civil Code of Québec.
- 1.12 *Site-specific assessment*: Review by a site-specific assessment committee that pertains mainly to the administrative feasibility of the research project.
- 1.13 *Preliminary project review*: Ethical review during which a local REB evaluates the project, particularly with regard to local considerations.
- 1.14 *Multicentre project*: A single research project carried out in more than one institution.
- 1.15 *Sponsor*: A natural or legal person, a private or public institution or organization in charge of funding a research project subject to Health Canada rules. The definition includes an organization or person that the sponsor has contracted to perform one or more tasks or functions tied to the research project.
- 1.16 *Research*: Must be understood broadly to include any research activity in the health and social services domain that involves the participation of research subjects, whether the research is basic, clinical, epidemiological, genetic, psychosocial, observational, or of another nature. A research activity includes both research projects and research banks.
- 1.17 *Research subject*: Must be understood broadly to include living persons (e.g., users, relations, stakeholders), cadavers, human remains, biological material, body fluids, embryos, fetuses, and personal information and data arising from biological material of human origin.
- 1.18 *Therapy*: Must be understood broadly to include, in particular, any medication, service, care, or treatment.

#### Examples of the Concept of "Researcher"

- A Québec researcher has received a research grant from a Québec agency. The project requires the support of two researchers per concerned institution. The researcher works in one of the concerned institutions.
  - Coordinating principal researcher: The person to whom the granting agency has granted funding.
  - Local principal researcher: Will be appointed by the coordinating principal researcher in each concerned institution, since more than one researcher will work on the project at each institution. One of them could be the coordinating principal researcher.
  - Local researchers: will be appointed by the coordinating principal researcher.
- A Québec researcher has received a research grant from a Canadian agency. The project is limited to reviewing the files of users of some twenty institutions.
  - Coordinating principal researcher: The person to whom the granting agency has granted funding.
  - Local principal researcher: Not applicable.
- An Alberta researcher has received a grant from a federal agency to carry out a project on health determinants across Canada. Two Québec public network institutions will be approached. There will be no local principal researcher in the concerned institutions.
  - Coordinating principal researcher: the Alberta researcher must find a researcher who meets the residency criteria, and who will act as coordinating principal researcher for the purpose of implementing the mechanism.
  - Local principal researcher: Not applicable.

- A promoter plans to carry out a research project in a number of institutions in the network as well as the private sector.
  - Coordinating principal researcher: Must be appointed by the sponsor.
  - Local principal researcher: Must be appointed by the sponsor in each institution where the project will be carried out. The coordinating principal researcher may also serve in this capacity in his/her home institution.
  - Local researcher: Must be appointed by the sponsor when there is more than one researcher in a concerned institution.
- A pharmaceutical company is currently conducting clinical trials in France, the United States, and Alberta. It wishes to add ten centers in Québec—two private ones and eight health and social services network institutions.
  - Coordinating principal researcher: Must be appointed by the sponsor for the eight network institutions.
  - Local principal researcher: Must be appointed by the sponsor in each of the eight public institutions.
  - Local researcher: Must be appointed by the sponsor when there is more than one researcher in a public institution.

## 2 Mechanism scope

The mechanism applies to research conducted partially or fully in more than one institution in Québec, in the meaning of the terms *research* and *institution* indicated herein. In no way does it affect delegation agreements between various institutions covered by the multicentre mechanism.

### Examples of Mechanism Scope

- A pharmaceutical company is currently conducting clinical trials in France, the United States, and Alberta. It wishes to add ten centers in Québec—two private ones and eight health and social services network institutions.
  - Mechanism scope: The company must obtain the ethical approvals required to carry out its project in the two private centers. The multicentre mechanism applies to the eight public network institutions.
- A funded researcher plans to carry out a project on health determinants across Canada. A single center will take part in Québec.
  - Mechanism scope: The mechanism is not applicable, as the project will be carried out in only one Québec institution.
- A funded researcher plans to carry out a project on intravenous drug users in fifteen centers in Canada. In Québec, three public network institutions and three private centers will be approached.
  - Mechanism scope: The mechanism applies only to the three network institutions. The researcher must obtain the ethical approvals required to carry out his/her project in the other Québec centers and those located elsewhere in Canada.
- A Canadian researcher was approached by a sponsor to take part in a research project being carried out in the United States and Spain. The sponsor plans to carry out the project in Alberta (two institutions) and Québec (one institution).
  - Mechanism scope: The mechanism is not applicable, as the project will be carried out in only one center in Québec.
- A Canadian researcher was approached by a sponsor to take part in a research project being carried out in the United States and Spain. The sponsor plans to carry out the project in Alberta (two institutions) and Québec (three institutions, including two private clinics).
  - Mechanism scope: The mechanism is not applicable, as the project will be carried out in only one institution in Québec subject to the Ministry jurisdiction.
- A Canadian researcher was approached by a sponsor to take part in a research project being carried out in the United States and Spain. The sponsor plans to carry out the project in Alberta (two institutions) and Québec (three institutions, including one private clinic).
  - Mechanism scope: The mechanism applies only to the two network institutions. The researcher must obtain the ethical approvals required to carry out his/her project in the other Québec center and the centers located elsewhere in Canada.
- A researcher at Université du Québec à Chicoutimi plans to conduct research in a number of university institutions, none of which has a designated REB.
  - Mechanism scope: The mechanism is not applicable, as the project will not be carried out in universities with a designated REB.
- A Québec university researcher plans to conduct research in five health and social services network institutions. The university has a minister-designated REB but has not undertaken to comply with the multicentre mechanism.
  - Mechanism scope: The researcher must obtain the approval of the university's REB, as the university has not undertaken to comply with the multicentre mechanism. However, this mechanism applies for the five network institutions.

- A researcher is affiliated with a health and social services network institution having signed a delegation agreement that gives an REB affiliated with another network institution the authority to assess the project. The researcher wants to conduct a research project at his/her institution and four other network institutions that are not part of the delegation agreement.
  - Mechanism scope: The mechanism is applicable. The REB set to act as primary authority is the REB designated under the agreement since it is affiliated with a network institution and can thus act on behalf of REBs from other network institutions.
- A researcher is affiliated with a health and social services network institution having signed a delegation agreement that gives an REB affiliated with another network institution the authority to assess the project. The researcher wants to conduct a research project at his/her institution and four other network institutions that are also part of the delegation agreement.
  - Mechanism scope: The mechanism is not applicable, as all the institutions concerned by the project are covered by the delegation agreement.
- A researcher affiliated with a health and social services network institution wants to conduct research at three health and social services network institutions that have a delegation agreement. The REB authorized to assess the project under the agreement is affiliated with an institution not covered by the multicentre mechanism.
  - Mechanism scope: The mechanism is not applicable, as the project will only be conducted in institutions covered by the delegation agreement. However, if during the course of the project the researcher decided to expand the research to other institutions not included in the agreement, the REB that initially approved the project could not act as the primary decision-maker since it is not covered by the mechanism. Special provisions are provided for in this case (see Section 3.5.3).
- A researcher affiliated with a health and social services network institution wants to conduct research at five health and social services network institutions, three of which have a delegation agreement. The REB authorized to assess the project under the agreement is affiliated with an institution not covered by the multicentre mechanism.
  - Mechanism scope: The mechanism applies because the REB designated by the agreement to assess the project cannot act for the two other institutions involved in the project.

### 3 Establishing which REB can act as the main REB

#### *Basic requirements*

3.1 To act in the capacity of main REB, all REBs must satisfy two established basic requirements: The REB must be competent and tied to an institution where the mechanism applies. Competence implies that the REB meets the requirements of the Civil Code of Québec<sup>3</sup> as well as other normative requirements that apply,<sup>4</sup> including the working conditions and operating procedures for REBs laid down by the minister or the Ministry. It is also measured by the main REB's expertise and experience in the project research field.

#### *Ground rules*

3.2 The REB of the coordinating principal researcher's home institution is competent to act as a main authority, provided that it meets the requirements of Section 3.1. The researcher's home institution should be understood here as:

3.2.1 The institution the researcher is affiliated with, i.e., the institution that granted a research certificate (e.g., research privilege, research field of practice, research permit)<sup>5</sup>

3.2.2 The institution where the researcher partially or fully practices his/her profession

3.2.3 The recognized research center of an institution the researcher is affiliated with

3. We are referring here to designation requirements according to the profile of the research subjects to be approached. For projects that involve minors, disabled persons, or persons with a sudden disability, the competent main REB must be one of the designated REBs.

4. For example, a research project funded by National Institutes of Health (NIH) may require review by the REB of an institution covered by a U.S. Federalwide Assurance if the institution did not state in its application that the REBs were subject to the Ministry multicentre mechanism.

5. Institutions can decide that this research certificate is automatic for university professors.

- 3.2.4 In the event that the coordinating principal researcher has more than one home institution whose REB meets the requirements of Section 3.1, the REB of the concerned institution where research subjects will be recruited should be given priority. If it has more than one REB, the coordinating principal researcher is free to choose from among them

*Exception to the rule*

3.3 If the ground rules in Section 3.2 do not apply,<sup>6</sup> the REB that is competent to act as a main authority is the first one to meet a criterion below, in the order presented:

- 3.3.1 The REB in one of the concerned institutions where research subjects will be recruited, provided this REB meets the basic requirements of Section 3.1
- 3.3.2 Any REB that meets the basic requirements of Section 3.1 or the central REB.

*Application acceptance or rejection*

3.4 The institution is required to accept applications from principal researchers who submit research projects for ethical review when the criteria of sections 3.2 (home institution) and 3.3.1 (recruitment location) are met; as per Section 3.3.2, it can accept or refuse, unless it is the central REB, in which case it is obliged to accept the application.

*Research project that becomes multicentre while underway*

3.5 In the event a research project conducted in an institution becomes multicentre while underway, the authorized main REB is the one that initially approved the project, and the coordinating principal researcher is the person who initially submitted the request, subject to the following.

- 3.5.1 When the researcher who submitted the original request does not meet the residency criteria, a coordinating principal researcher must then be assigned as per the terms outlined in sections 1.5.1 to 1.5.4.
- 3.5.2 The researcher who submitted the original request can refuse to act as coordinating principal researcher when the project is funded by private enterprise or subsidized by a public or private organization within the framework of a cooperative group; the sponsor or organization must then assign a researcher who will act as coordinating principal researcher in implementing the mechanism. For other types of projects, the researcher who submitted the original request is obligated to act as coordinating principal researcher if he/she meets the residency criteria.
- 3.5.3 The REB that initially approved the project must meet the basic requirements outlined in Section 3.1. When these requirements are not met, the researcher who originally submitted the request, or the newly appointed coordinating principal researcher, as the case may be, must contact a qualified REB to act as the primary authority, as per the criteria in sections 3.2 or 3.3, whichever presides. Acceptance or refusal of the request is subject to the regulation provided for in Section 3.4. Costs associated with the ethical review process—both for the REB that acts as main authority and for the local REBs—are those stipulated in Section 14. However, they are deducted from the amount already received by the REB that initially approved the project.

*REB fields of competence*

3.6 For the purposes of this section, REBs must notify the Ministry at least once a year of the research fields and methods in which they have expertise and experience. This declaration will be made using the annual online report form issued by the Ministry.

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6. This could be the case, for example, if the REB of the coordinating principal researcher's home institution was not deemed competent.

### Establishing which REB can act as the main REB

- The competent REB is the REB affiliated with the home institution of the coordinating principal researcher, provided that
  - It is designated, if the project involves minors, persons of full age who are incapable of giving consent, or persons of full age who suddenly become incapable
  - It has recognized expertise and experience in the project research field
- When the coordinating principal researcher is affiliated with more than one home institution whose REBs meet the above criteria, the researcher must then submit his/her project
  - To the REB of the concerned institution where research subjects will be recruited
  - To the REB of any of the concerned institutions, when subjects are recruited in more than one institution
- When neither of the above situations applies, the competent REB is the first one to meet a criterion below, in the order presented:
  - The REB of one of the concerned institutions where research subjects will be recruited, provided the REB has recognized expertise and experience in the project research field and meets legislative and normative requirements
  - Any other REB reporting to the Ministry that is recognized for its expertise and experience in the project research field and meets legislative and normative requirements
  - The Central REB.

### Some examples that illustrate how an REB is chosen to act as the main REB

#### Example 1

- Research project in rehabilitation, with persons of full age who are capable of giving consent
- Home institution of coordinating principal researcher: ABC Rehabilitation Institute (health and social services network)
- Rehabilitation Institute profile: Rehabilitation mission, designated REB, recognized expertise and experience in this research field
- Recruitment location for research subjects: Five network institutions, each with a designated REB

Criterion 1: Home institution	The researcher should submit the project to the REB of his/her home institution.
Criteria 2 and 3:	Not applicable

#### Example 2

- Research project in obstetrics, conducted in only one center in Québec, already approved by the REB at ABC Hospital of Québec City.
- Home institution of principal researcher: ABC Hospital of Québec City.
- The promoter wishes to add two network institutions that have a competent REB.
- The researcher who initially made the request refused to act as coordinating principal researcher.

Criterion 1: Home institution	The REB of ABC Hospital of Québec City shall act as main REB since it meets the basic requirements.
Criteria 2 and 3:	Not applicable

#### Example 3

- Research project in epidemiology
- Home institution of (coordinating) principal researcher: A Québec university with a designated REB
- University profile: Educational institution that has not undertaken to comply with the Ministry mechanism and whose REB has recognized expertise and experience in this research field
- Recruitment location for research subjects: Five health and social services network institutions, only three of which have recognized expertise and experience in this research field

Criterion 1: Home institution	The basic rule does not apply since the main researcher is affiliated with an institution that has not adhered to the mechanism.
Criterion 2: Recruitment location for subjects	After having been approved by the REB of the university with which the main researcher is affiliated, the project shall be submitted to one of the three REBs that meet the basic requirements, which must then act as main REB for the five institutions.
Criterion 3:	Not applicable

#### Example 4

- Research project on child abuse
- Home institution of (coordinating) principal researcher: Québec university whose REB is not designated
- University profile: educational institution; the university has made an agreement with a designated REB from the health and social services network, which evaluates its researchers projects.
- Recruitment location for research subjects: Ten Québec hospital emergency rooms; the REBs of these hospitals are designated and have expertise in this field; the designated REB acting for the university has expertise in this field, but subjects will not be recruited in the institutions to which it is affiliated.

Criterion 1: Home institution	The principal researcher (coordinator) shall submit his/her project to the designated REB from the health and social services network institution with which his/her university entered into an agreement. If the agreement permits, this REB could act as the main REB for all network institutions involved in the project.
Criterion 2: Recruitment location for subjects	If the agreement does not allow the REB from the institution with which the university entered into an agreement to act as main REB, the project shall be submitted to an REB at one of the concerned institutions that meets the basic requirements, and which will then act as the primary authority for the ten institutions.
Criterion 3:	Not applicable

#### Example 5

- Research project in geriatrics, with people suffering from Alzheimer's
- Home institution of coordinating principal researcher: ABC Hospital of Rimouski
- ABC Hospital profile: general mission; REB not designated; recognized expertise and experience in the field
- Recruitment location for research subjects: ABC Hospital and two other institutions located in Rivière-du-Loup and Lévis; both have recognized expertise and experience in this research field; the Rivière-du-Loup REB is not designated, and the Lévis REB is designated

Criterion 1: Home institution	The coordinating principal researcher cannot contact the REB of his/her home institution, as Article 21 of the Civil Code of Québec stipulates that the REB must be designated in the event of research conducted with persons who are incapable of giving consent.
Criterion 2: Recruitment location for subjects	The coordinating principal researcher should contact the REB of the Lévis institution, as it alone is designated.
Criterion 3:	Not applicable

#### Example 6

- Research project in obstetrics
- Home institution of coordinating principal researcher: ABC Hospital of Québec City
- ABC Hospital profile: general mission, no obstetrics department, REB not designated
- Recruitment location for research subjects: Hôpital de Shawinigan and Hôpital de Trois-Rivières; both institutions have an obstetrics department but no REB

Criterion 1: Home institution	The coordinating principal researcher cannot contact the REB of his/her institution, as this REB does not have recognized obstetrics expertise or experience.
Criterion 2: Recruitment location for subjects	The coordinating principal researcher should contact either of the concerned institutions, as both have an obstetrics department. However, since there is no local REB, this criterion cannot be applied.
Criterion 3: Recognized field of expertise and experience	The coordinating principal researcher has two options: choose the REB of an institution with recognized expertise and experience in obstetrics, but which may refuse to act as main REB; or submit his/her project to the central REB, which shall be obliged to act as the main REB.

## 4 Actions prior to ethical review by the main REB

### *Graduate or postgraduate student project*

- 4.1 Any project carried out by a graduate or postgraduate student must undergo an ethical review by the REB of his/her university, unless the REB is not designated and therefore not qualified to conduct this review. In such cases the student can take advantage of the multicentre mechanism if permitted by the university or, failing that, contact the central REB.

*Scientific review*

4.2 In order for the multicentre mechanism to get underway, the coordinating principal researcher must submit his/her project for peer review and approval by a recognized scientific committee, i.e.,

- 4.2.1 The scientific committee of the coordinating principal researcher's home institution
- 4.2.2 The scientific committee of an institution whose research center receives funding from a Québec or federal granting agency
- 4.2.3 The scientific committee of a Québec or federal granting agency, or of an agency recognized by one of the two
- 4.2.4 The scientific committee of a university (e.g., program committee, thesis committee)
- 4.2.5 The scientific committee of an organization that is recognized either by a member state of the Organization for Economic Cooperation and Development (OECD)—such as Institut national de la santé et de la recherche médicale (INSERM) in France or the National Institutes of Health (NIH) in the United States—or by one of these recognized organizations

*Forwarding of file to the main REB*

4.3 Once the research project has been approved by a recognized scientific committee, the coordinating principal researcher submits it to the competent main REB (see Section 3.4). The researcher sends the REB the requested number of copies of the complete file in the required format. This file consists of at least the following:

- 4.3.1 The project review application form, issued by the Ministry, dated and signed<sup>7</sup>
- 4.3.2 The review report of the scientific committee that approved the project, containing the committee's contact information and its decision, as well as its questions, concerns, and comments
- 4.3.3 A letter containing the name and contact information of local REB chairs or, in the absence of an REB, the name and contact information of the concerned institutions as well as the coordinating principal researcher's pledge to notify said REBs and institutions of the name and contact information of the main REB
- 4.3.4 A project summary, using language that is as nontechnical as possible<sup>8</sup>
- 4.3.5 The proposed research protocol (clearly identified as such and dated), as well as supporting documentation and appendixes
- 4.3.6 When research concerns a product under study (such as a medication, a natural health product, or a medical device), a summary of all tolerance, pharmacological, pharmaceutical, and toxicological data published on the product under review, as well as a summary of clinical experience regarding this product to date (e.g., recent investigator's brochure, no-objection letter from Health Canada<sup>9</sup>)
- 4.3.7 A document detailing the coordinating principal researcher's qualifications for carrying out the project, if not already known by the institution or REB (e.g., résumé, research certificate, research privilege or field of practice, proof of right to practice issued by a professional corporation)
- 4.3.8 A list of all steps taken with other REBs with a view to securing project approval as well as a list of any significant previous decisions (e.g., negative decision or request

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7. This form contains a section asking researchers to list their current research activities and a pledge to comply with the ethical standards applicable to the project. These activities and pledge are therefore not part of the documents that constitute the complete file.

8. While the project review application form issued by the Ministry can be used instead of a summary, certain REBs still require a summary. For this reason, the Ministry mentions it in Section 4.3.

9. This document must be submitted prior to final approval by the main REB.

for project modification) by other REBs or regulatory authorities regarding the same project (in Canada) and the list of any changes made to the research project following these decisions. Reasons must be provided for any previous negative decisions

- 4.3.9 Questionnaires and other documents for subjects to be approached or their authorized third parties that will be completed or used in the project
- 4.3.10 Documents used in recruiting subjects (e.g., ad, online notice, telephone protocol), including those containing details on reimbursement of fees incurred or access to care or services
- 4.3.11 A description of any ethical difficulties inherent to the project, if not already included in the protocol
- 4.3.12 As applicable, provisions regarding compensation in the event of loss and third party liability insurance coverage, if not included in the protocol
- 4.3.13 The fact sheet (clearly identified as such and dated) and all information for subjects to be approached, written in languages they understand and in other languages, if necessary
- 4.3.14 The consent form (clearly identified as such and dated), written in languages understood by the subjects to be approached and in other languages, if necessary
- 4.3.15 The relevant sections of the budget and the sponsor/institution/researcher agreement that may have an incidence on the ethics of the project,<sup>10</sup> for each of the institutions involved,<sup>11</sup> (e.g.: those that concern the methods of payment, those that permit the examination of existing or possible conflicts of interest—institutional or individual—and those that provide insight into researcher freedoms regarding the dissemination of results);
- 4.3.16 A list of proposed methods for ongoing ethical oversight, if not included in the protocol
- 4.3.17 Any other document required by the main REB

*Forwarding of file to institutions*

4.4 The coordinating principal researcher must submit the file to the designated authorities for each of the institutions concerned at the same time he/she submits it to the main REB for a site-specific assessment review (see Section 5) and, in the absence of the REB, for a review of the preliminary decision rendered by the main REB (see Section 9.1). The coordinating principal researcher sends the institutions as many copies of the project as they request. Although this task may be delegated to the local researcher, the coordinating principal researcher is still responsible for ensuring that this task is completed within the required timeframe.

*Forwarding of file to local REBs*

4.5 The coordinating principal researcher must submit three copies of the file to each of the competent local REBs,<sup>12</sup> on the same day it is sent to the main REB. He/she does not have to complete other forms or provide any other documents, as the case would be in the event there was no multicentre mechanism. The letter that accompanies the file must indicate that the request deals with the preliminary assessment and that the project was submitted to a main REB; it must contain the coordinates of the main REB and all relevant information that

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10. To learn more about this subject, please refer to the *Note de clarification relative à l'examen, par le comité d'éthique de la recherche, des parties pertinentes du budget et de l'entente promoteur – établissement – chercheur* produced by Ministère de la Santé et des Services sociaux, available online at the following address: <<http://ethique.msss.gouv.qc.ca>>.

11. Preliminary versions of these documents can be used, but the final versions must be submitted to the main REB for final approval.

12. The local REB must meet the formal requirements covering REB status. Thus, when the project comes under Article 21 of the Civil Code of Québec, the REB must be designated to be able to conduct the preliminary assessment of the project; if not designated, the researcher is not obligated to submit the file. The institution is then deemed not to have a local REB, with regard to the multicentre mechanism.

concerns the institution in question (e.g.: number of subjects approached, department to handle recruitment). Although this task may be delegated to the local researcher, the coordinating principal researcher is still responsible for ensuring that this task is completed within the required timeframe.

#### Actions Prior to Review by the Main REB

- For research projects by a graduate student (masters and doctorate level degrees), ethical review and approval by the REB of the student's university, barring exceptions
- Preliminary project approval by a recognized scientific committee
- Establishing which REB can act as the main REB.
- Same-day submission:
  - To the main REB: the number of copies of the complete file requested;
  - To the REB of each institution concerned for preliminary review: three copies of the complete file;
  - To the authorities designated by each of the institutions, for a site-specific assessment review and, in the absence of the REB, for a review of the preliminary decision rendered by the main REB: the number of copies of the complete file requested by each institution.

## 5 Site-specific assessment

### *Assessment content*

5.1 On receipt of an application from the coordinating principal researcher or local principal researcher, as the case may be, the concerned institution forwards the file to its site-specific assessment committee for analysis of the project. This committee reviews the following aspects:

- 5.1.1 The availability of the institution's facilities, equipment, and human resources required by the project
- 5.1.2 The suitability of the local research environment for the proposed project
- 5.1.3 The project's financial aspects and any effect on the institution's budget
- 5.1.4 How medication, if any, is to be managed
- 5.1.5 Whether or not the project is in harmony with the institution's policy directions.

### *Decision*

5.2 The site-specific assessment committee can issue one of three decisions, which must be substantiated and in writing:

- 5.2.1 The project can take place in the institution, and no changes are required
- 5.2.2 The project can take place in the institution, if changes are made
- 5.2.3 The project cannot take place in the institution for practical reasons (e.g., unavailable equipment, unsuitable local research environment, medication management problem, incompatibility with institution's policy directions)

5.3 The site-specific assessment committee can ask that changes be made to the research project that will be valid only for the institution, provided they do not affect the integrity of the research project design or result in less protection for research subjects that will be recruited at this institution and are deemed essential to carrying out the project in this institution.

### *Deadline*

5.4 The site-specific assessment committee must render its decision within two weeks of receipt of the preliminary decision by the main REB, barring exceptions.

*Reporting the institution's decision to the main and local REBs*

5.5 The main REB and local REB, if any, must be informed of the institution's decision regarding project suitability when this decision is handed down after the deadline provided in Section 5.4, for the purposes of ongoing project oversight.

#### Purpose of the Site-Specific Assessment

The review looks at

- The availability of the institution's facilities, medical equipment, and human resources required by the project
- The suitability of the local research environment for the proposed project
- Financial aspects and any effect on the institution's budget
- Medication management methods
- The possibility of a tie-in between the project and the institution's goals.

## 6 Preliminary review by the local REB

*Review content*

6.1 The local REB conducts a **preliminary review of the research project**. It must inform the main REB of any concerns arising from the scientific or ethical review, as well as any aspects tied to local considerations, among which,

- 6.1.1 The skills and qualifications of local researchers, as the case may be, as well as their ability to carry out the project given the number of research projects in which they are currently involved (e.g., suitability of planned project management procedures)
- 6.1.2 The value of the project to the local community and the institution's research subjects, particularly the absence of unfair or excessive recruitment and the suitability of procedures for approaching subjects
- 6.1.3 The suitability of documents for the institution's research subjects and, as the case may be, the value of translating these documents (e.g., in Italian) or adapting them to subjects (e.g., in Braille)
- 6.1.4 Ongoing oversight means in effect in the institution in addition to the basic means.

*Review procedure*

6.2 The local REB may conduct its preliminary review in a select committee (expedited review) or a full committee, provided it meets the deadline provided in Section 6.3. When review is conducted by a select committee, this committee's observations and findings must be forwarded to all members of the local REB.

*Deadline for forwarding comments*

6.3 If the need arises, the local REB must forward any comments and explanations to the main REB in writing within three weeks of the date on which the researcher submitted the file,<sup>13</sup> failing which the main REB will understand that the local REB has no comment.

*Minutes*

6.4 A summary of the preliminary review must be included in the local REB's minutes.

#### Preliminary Review by the Local REB

- Review in a select or full committee, provided the deadline is met
- Basic ethical review focusing on local considerations, among which,
  - The skills and qualifications of local researchers, as the case may be
  - The value of the project to the institution's research subjects and the community
  - Documents for subjects recruited in the institution
  - Ongoing project oversight means used in the institution
- The local REB has three weeks from the date the researcher submits the project to forward its comments to the main REB.

13. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter L1 issued by the Ministry.

## 7 Ethical review by the main REB

### *Compilation of comments from local REBs*

7.1 The main REB compiles comments from the local REBs and includes them in the file forwarded to its members for the ethical review. It may contact the chair of the local REB for more information or to discuss any other subject if it considers it appropriate or if the local REB requests it.

### *Forwarding the file to the members*

7.2 Members of the main REB have at least two weeks to examine the file unless they accept a shorter time limit. Comments from the local REBs must be forwarded to committee members as soon as possible, and by the start of the project assessment meeting, at latest. The main REB must add the research project to the agenda of the meeting following the end of the preliminary examination process, unless this interferes with the deadline given to members for analyzing the file or if the agenda does not allow the addition of new items, in which case the research project should be put on the following meeting's agenda and evaluated at that time.

### *Primary review*

7.3 A primary ethical review of the research project must be done in full committee.

### *Content of the primary review*

7.4 In its primary review, the main REB must

- 7.4.1 Ensure that the scientific aspects of the project are ethically acceptable
- 7.4.2 Ensure that the coordinating principal researcher and the research team have the necessary competence to carry out the project, including by checking the number of current projects under the responsibility of the researcher and whether management procedures for these projects are appropriate
- 7.4.3 Ensure that the project is justifiable from the standpoint of its impact on the community—the individuals and population who will take part in the research project—and the potential benefits they may gain from the results. The main REB must be satisfied on the following points in particular:
  - 7.3.1.1 Affordable access to the test therapy if proven to be effective for the people for which it was intended
  - 7.3.1.2 How the research results will be conveyed to the research subjects and the community that took part
- 7.4.4 Check that the criteria used to recruit research subjects are ethical and whether the subjects are members of a vulnerable or unfairly excluded group
- 7.4.5 Determine whether the risk/benefit ratio for the subjects is positive
  - In the case of projects involving **persons of full age who are capable of giving consent**: by checking whether the risk incurred is not disproportionate to the benefit that can reasonably be anticipated from the project
  - In the case of **minors or persons of full age who are incapable of giving consent**: by making sure that the project has the potential to produce benefit to the person's health—when the activity concerns only that individual—or has the potential to produce results capable of conferring benefit to other persons in the same age category or having the same disease or handicap—when the activity concerns many subjects
- 7.4.6 Ensure that privacy and confidentiality mechanisms are appropriate
- 7.4.7 Ensure that methods used to recruit research subjects are appropriate (e.g., classified or Internet ads)

- 7.4.8 Ensure that consent mechanisms are appropriate (e.g., consent form, other documents intended for subjects approached)
- 7.4.9 Ensure that ethical obligations regarding integrity have been complied with, particularly by checking whether a conflict of loyalty or a conflict of interest—real or apparent—, or a possibility thereof, exists and whether mechanisms for the dissemination of research results have been planned
- 7.4.10 Determine appropriate means for ongoing oversight of project ethics (see Section 11)

7.5 The main REB must also review the comments made by local REBs and take them into account in its decision.

#### Ethical Review by Main REB

- Basic review usually conducted by every REB, and a review of local considerations in the light of the comments.
- Review of any other element brought to its attention.

## 8 Letter of notification of the main REB's preliminary decision

*Search for acceptable compromise*

8.1 When the local REBs' comments are rejected by the main REB on the grounds of ethical considerations, the chair of the main REB must make an effort to find a compromise that is acceptable to the local REB before rendering a final decision. To do this, he/she must contact the chair of the local REB. If they cannot come to an agreement, the main REB's chair will contact those of all the REBs of the concerned institutions to discuss the matter (e.g., conference call, videoconferencing). If no agreement is reached, the preliminary decision of the main REB prevails, but the local REB has the right to refuse that the project take place in its institution (see Section 9.2).

*Nature of preliminary decisions by the main REB*

8.2 Decisions rendered by main REBs within the multicentre mechanism must be substantiated. Only preliminary decisions (positive or negative) are submitted for approval to local REBs and concerned institutions where there are no REBs. Any other decisions are nevertheless brought to the attention of local REBs so that they can follow the progress of the file. The main REB can render any one of the following preliminary decisions:

- Approve the project as it stands
- Approve the project subject to certain modifications by the coordinating principal researcher
- Approve the project after a deferred decision, the coordinating principal researcher having satisfactorily answered the REB's questions or clarified certain points
- Approve the project because the coordinating principal researcher's arguments have convinced the REB to reconsider its decision
- Reject the project, either because the coordinating principal researcher did not make the required modifications or because he/she did not provide satisfactory responses to the questions or clarifications requested by the REB, or because the committee rejected the researcher's arguments

A positive preliminary decision by the main REB can include special conditions that apply to a particular concerned institution, but the nature of these conditions must not compromise the integrity of the research project design or result in less protection for research subjects that will be recruited at this institution.

*Positive preliminary decision after approval of the project as it stands*

8.3 If the main REB approves the project as is, it sends a letter notifying the coordinating principal researcher of its **positive preliminary decision**,<sup>14</sup> with copies to all the local REBs and concerned institutions where there are no REBs. This letter must include on the names of the local REBs that provided comments, and if necessary, be accompanied by documents in which they request purely administrative changes.

*Positive preliminary decision after a conditional approval of the project*

8.4 If the main REB approves the project with modifications, it sends a letter<sup>15</sup> notifying the coordinating principal researcher of its decision, with copies to the local REBs. The coordinating principal researcher must submit his/her modifications as quickly as possible to the main REB, and send a copy of the new document, in which the modifications are clearly indicated, to the main REB and all the local REBs concurrently.

8.5 The main REB can evaluate the researcher's modifications in full or select committee, depending on their nature.<sup>16</sup>

8.6 The procedure set out in sections 8.4 and 8.5 applies until the main REB's requests are satisfied, unless the coordinating principal researcher indicates to the committee that the modifications cannot be made, in which case the procedure set out in sections 8.10 and 8.11 apply. Once the main REB's requests have been met, the procedure set out in 8.3 applies. The letter announcing the main REB's **positive preliminary decision** must be accompanied by the new, approved versions of the documents, if any.

*Positive preliminary decision after an initially deferred decision*

8.7 If the main REB cannot render a decision on the project, it sends a letter notifying the coordinating principal researcher of its deferred decision,<sup>17</sup> with copies to the local REBs. The coordinating principal researcher must provide the REB with the requested answers and clarifications as quickly as possible. The researcher must send a copy of the answers and clarifications, as well as any new version of the document with the modifications clearly indicated, to all the local REBs at the same time as the main REB. The local REBs have a week to forward their comments, if any, to the chair of the main REB.

8.8 The main REB can evaluate the researcher's answers or clarifications in a regularly scheduled meeting or in select committee, depending on the nature of the grounds on which its decision was delayed.<sup>18</sup>

8.9 The procedure set out in sections 8.7 and 8.8 apply until the requests of the main REB are satisfied, unless the committee decides to reject the project, in which case the procedure set out in sections 8.10 and 8.11 apply. When the requests of the main REB are satisfied, the procedure in Section 8.3 applies. The letter announcing the **positive preliminary decision** of the main REB must be accompanied by the new, approved version of the documents, if any.

*Positive preliminary decision after a reconsideration of the project*

8.10 If the main REB accepts the arguments of the coordinating principal researcher after reconsidering the project, it should apply the most appropriate procedure leading to a positive preliminary decision.

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14. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter P4 issued by the Ministry.

15. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter P1 issued by the Ministry.

16. When the modifications requested by the REB are of a subjective nature, they must be reviewed in full committee. Other modifications can be evaluated by the select committee, even if they concern a project subject to Article 21 of the Civil Code of Québec.

17. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter P2 issued by the Ministry.

18. When the requested clarifications are of a subjective nature, they must be reviewed in full committee. Other modifications can be evaluated by the select committee, even if they concern a project subject to Article 21 of the Civil Code of Québec.

*Negative preliminary decision after a project is rejected*

8.11 If the main REB intends to reject a project, it must notify the coordinating principal researcher of its decision in writing<sup>19</sup> and give the latter the chance to state his or her position. It must send a copy of its decision to the local REBs.

8.12 The main REB cannot render a negative preliminary decision before the deadline given to the coordinating principal researcher for putting forward his or her arguments. If the main REB maintains its negative decision—because the coordinating principal researcher has not provided any arguments, or his/her arguments have been rejected—the committee must send a letter to the coordinating principal researcher notifying him/her of its **negative preliminary decision**,<sup>20</sup> with copies to the local REBs and concerned institutions where there are no REBs. The letter announcing the negative preliminary decision by the main REB must mention the comments of the local REBs and be accompanied by any documents in which the REBs had requested purely administrative changes. A copy of the letter must be sent to the Ministry.

*Time limit*

8.13 Decisions rendered in full committee by the main REB must be handed down no later than two weeks after the meeting. Those made by select committee must be announced at the first opportunity.

*Minutes*

8.14 The minutes of the main REB must allow any person who consults them to be fully aware of the committee's work. They must therefore include a list of the documents examined, describe the various steps in the committee's reasoning—including the dilemmas encountered and the differing opinions of committee members—and include the grounds for the decision. The nature of the information recorded in the minutes must comply with the requirements set out by the Ministry for this purpose.

Preliminary Decision by the Main REB

- The main REB must consider the comments of the local REBs. In the event it rejects a local REB's comments, the chair of the main REB must contact the chair of the REB in question to try and find an acceptable compromise. If they still disagree, the chairs of all the local REBs are consulted. If the disagreement is not resolved, the decision of the main REB's chair prevails, but the local REB can refuse to allow the project to take place in its institution.
- Decisions rendered by the main REB within the multicentre mechanism must be substantiated. Only preliminary decisions (positive or negative) are submitted for approval to the local REBs and the concerned institutions where there are no REBs. Any other decisions, if any, must nevertheless be brought to the attention of local REBs so that they can monitor progress of the file.
- The main REB notifies the coordinating principal researcher of its preliminary positive decision, with copies to all the local REBs and, as the case may be, to concerned institutions where there are no REBs.
- Project approved (without conditions, conditional on modifications, or after deferred approval) → start of the final phase of the ethical review process. The decision may be subject to special conditions that apply to a particular concerned institution, but the nature of these conditions must not compromise the integrity of the research project design or result in less protection for research subjects that will be recruited in this institution.
- Project approved (without conditions, upon receipt of modifications or after deferred approval) → start of the final phase of the ethical review process. The decision may be subject to special conditions that apply to a particular concerned institution, but the nature of these conditions must not compromise the integrity of the research project design
- Project rejected → a copy of the letter must be sent to the Ministry.

19. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter P3 issued by the Ministry.

20. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter P5 issued by the Ministry.

## 9 End of the ethical review and decision by the concerned institution

### *Review of preliminary decision rendered by the main REB*

- 9.1 Upon receipt of the preliminary decision rendered by the main REB, the local REB or the authority appointed by the concerned institution without an REB reviews the following points:
- 9.1.1 Whether the decision is appropriate in the light of the comments, if any;
  - 9.1.2 As the case may be, whether the local researchers have the qualifications and capacity to carry out the project given the current number of projects in which they are involved (e.g., whether project management procedures are appropriate);
  - 9.1.3 Whether purely administrative changes are needed to the documents intended for the institution's research subjects (e.g., addition of the resource person's name and contact information) and, if necessary, whether documents must be translated or be presented in a more appropriate format for the research subjects.

### *Final decision of the local REB*

- 9.2 The local REB must notify the institution of its final decision by the deadline stated in Section 9.4. Its decision, which must be justified in writing,<sup>21</sup> can be of three types:
- 9.2.1 The REB approves the main REB's decision and makes no purely administrative modifications
  - 9.2.2 The REB approves the decision but calls for purely administrative modifications
  - 9.2.3 The REB does not approve the main REB's decision because the latter does not take into account the scientific or ethical issues brought to the attention of the main REB; consequently the project cannot take place in the institution. To invoke these grounds, the REB of a concerned institution must have forwarded its comments to the main REB during the preliminary review process before the set deadline. If the local REB does not agree with the decision rendered by the main REB, it must send a copy of its decision to the Ministry

### *Decision by the authority designated by the institution*

- 9.3 The authority designated by the concerned institution where there is no REB must notify the institution of his/her decision by the deadline stated in Section 9.4. The decision, which must be justified in writing, can be of three types:
- 9.3.1. The decision is positive and requires no purely administrative changes, and the authority thus recommends that the institution endorse the main REB's decision
  - 9.3.2 The decision is positive but calls for purely administrative changes, and the authority thus recommends that the institution endorse the decision of the main REB
  - 9.3.3. The decision is negative on scientific or ethical grounds, and the authority thus recommends that the institution not endorse the main REB's decision. When the authority designated by the institution renders a negative decision, the institution must send a copy of the decision to the Ministry

### *Decision by the institution*

- 9.4 The concerned institution<sup>22</sup> must inform the main REB of its decision within two weeks of the latter's preliminary decision. The institution's letter<sup>23</sup> must be accompanied by the local REB's decision, if a local REB exists, and any documents to which purely administrative changes were made. The coordinating principal researcher, and as the case may be, the

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21. At a minimum, the letter must contain the aspects mentioned in the explanatory model of reply letter L2 issued by the Ministry.

22. For the purposes of implementing the mechanism, the authority authorized to speak on behalf of the institution is the executive direction or another authority duly mandated for this purpose. The duly mandated authority must not be subject to apparent, real or potential conflicts of interest. Ideally, it should neither be the research centre nor the REB. The authority must be duly appointed in writing by the institution's executive director or board of directors.

23. At a minimum, the letter must contain the aspects mentioned in one of the Ministry's L3 and L4 explanatory models of reply letter.

local principal researcher must receive copies. If the decision is positive, the institution must say explicitly in its letter that it endorses the local REB's decision or, in the absence of an REB, the main REB's decision. By endorsing the positive decision of the local REB or designated authority, the institution assumes complete responsibility for the execution of the project on its premises. In this sense, it is directly accountable for it.

*Final decision of the main REB*

9.5 After expiry of the deadline for concerned institutions to pronounce on the preliminary decision it has rendered, the main REB drafts a letter with its final decision. The letter, which must state the decision of each concerned institution, is sent to the coordinating principal researcher, with copies to the local REBs, or in the absence of a local REB, to the concerned institutions. It must be accompanied by any new version of the approved documents showing purely administrative changes requested by the local REBs and concerned institutions where there are no REBs that had not made their opinions known at the time the REB rendered its preliminary decision. If a concerned institution cannot forward its decision to the main REB by the set deadline due to exceptional circumstances beyond its control, it must notify the latter. Barring such exceptional circumstances, the main REB must not delay sending the letter containing its final decision. It can, however, send a second letter to this particular concerned institution.

*Special conditions for certain institutions*

9.6 The final decision of the main REB can be made subject to special conditions for particular institutions, but the nature of these conditions must not compromise the integrity of the research project design or result in less protection for research subjects that will be recruited at this institution.

*Binding nature of a positive decision by the main REB*

9.7 The decision by the main REB is binding and executable from the moment it has written its final approval letter, subject to the institution's decision (see sections 5.5 and 9.4). All final positive decisions by the main REB shall remain in effect for one year beginning on the date they were rendered.

*Appealing the main REB's final decision*

9.8 The main REB's final decision cannot be reversed by another REB. The coordinating principal researcher can, however, appeal the decision (see Section 10).

*Notification of the Ministry*

9.9 If the main REB renders a final negative decision, it must send a copy of the decision to the Ministry.

**End of the Ethical Review Process and Decision by Concerned Institution**

- The ethical review process must be completed no later than two weeks after the project's preliminary approval letter is received from the main REB.
- Upon receipt of the preliminary decision rendered by the main REB, the local REB or the authority designated by an institution with no REB reviews it and renders its own decision, which is then forwarded to the authority of the competent institution (executive direction or the authority duly mandated for this purpose). The Ministry must also receive a copy if the decision is negative.
- The institution notifies the main REB of its final decision.
- The main REB writes a letter with its final decision after the two-week deadline. The decision can be made subject to special conditions applying to a particular concerned institution, but the nature of these conditions must not compromise in any way the integrity of the research project design or result in less protection for research subjects that will be recruited at this institution.
- The Ministry must be notified of a negative decision rendered by the local REB, by an authority designated by the institution, or by the main

## 10 Appeal of a decision rendered by a main REB

### *Preliminary step*

10.1 Before appealing a decision rendered by a main REB, the coordinating principal researcher must ask the committee to review its decision. If its decision remains unchanged, the researcher may then appeal to the minister's central REB or, if the latter is party to the decision, to an REB designated by the Ministry.

### *Requirements for an REB to act as an appeal authority*

10.2 The requirements for an REB to act as an appeal authority are those set out in the *Normes relatives à l'appel des décisions des comités d'éthique de la recherche* (standards pertaining to the appeal of research ethics committee decisions) issued by the Ministry.

### *Grounds of appeal*

10.3 The grounds a coordinating principal researcher may invoke for appealing a decision rendered<sup>24</sup> by the main REB are the following:

- The decision contravened a procedural requirement and is therefore invalid (see Appendix 1).
- The decision violated a principle of natural justice (see Appendix 1).

### *Appeal deadline*

10.4 The coordinating principal researcher has thirty days to appeal from the date the main REB completes its review of its initial decision.

### *Filing an appeal*

10.5 Appeals must be filed in writing to the appeal REB. They must include a brief description of the grounds for the appeal as well as the complete file submitted to the main REB, including any related paperwork (e.g., correspondence, review decision). The coordinating principal researcher may also include any attachments he or she feels will help demonstrate the appeal's admissibility.

10.6 Upon receipt of the application, the appeal REB checks to make sure it is complete and informs the main REB, local REBs, and concerned institutions with no REBs that it has received an appeal application. The main REB has two weeks to forward to the appeal REB a copy of any committee minutes that concern the pending application as well as any other documentation it deems appropriate for determining whether or not the appeal is admissible.

10.7 The appeal REB has two weeks from receipt of the appeal application to inform the coordinating principal researcher, the main REB, local REBs, and concerned institutions with no REBs of the date it will determine whether the application is admissible.

### *Determining appeal admissibility*

10.8 The appeal REB must determine whether the appeal is admissible within thirty days of receipt from the main REB of the documentation referred to in Section 10.5.

10.9 The appeal REB must meet with the coordinating principal researcher and the chair of the main REB if either so requests. The latter may delegate another member of the research team or the REB to represent them. At the request of the parties, the appeal REB must collect testimony from the witnesses when determining whether the appeal is admissible.

10.10 For the appeal to be admissible, the appeal REB must conclude that the decision was invalidated by failure to meet a procedural requirement or that it violated a principle of

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24. It could be an appeal of a negative decision or of conditions imposed by the REB for approving the project.

natural justice, and that consequently the research activity did not receive the treatment it should have in the circumstances.

- 10.11 The appeal REB has two weeks following the meeting to forward its decision to the coordinating principal researcher, the main REB, local REBs, and concerned institutions with no REBs.

*Appeal application deemed admissible*

- 10.12 Once the appeal application has been deemed admissible, the appeal REB notifies the coordinating principal researcher, the main REB, local REBs, and concerned institutions with no REBs of the date it will reexamine the ethics of the research activity.

- 10.13 The appeal REB must reexamine the ethics of the research project within thirty days of the decision on appeal admissibility. It must offer the coordinating principal researcher the opportunity to answer its questions, if any. It can also draw on outside experts as it deems necessary.

- 10.14 The appeal REB must render its decision within two weeks of the meeting. A copy of the decision must be forwarded to the coordinating principal researcher, the main REB, local REBs, and concerned institutions with no REBs.

- 10.15 The appeal REB's decision is final and binding on all parties that had originally accepted the main REB's decision and had not refused the project in their institution for feasibility reasons. It also applies to local REBs that had not originally accepted the REB's decision. Institutions that for whatever reason had not yet pronounced on the project's feasibility at the time that the appeal was launched may still refuse the project for this reason, even if the appeal REB renders a positive decision. The management and ongoing oversight of the research activity is the responsibility of the main REB.

*Appeal application deemed inadmissible*

- 10.16 When the appeal REB concludes that there was nothing irregular about the main REB's decision and that it did not violate a principle of natural justice, the coordinating principal researcher's mandate ends. The project can then be submitted to each of the local REBs consulted under the multicentre mechanism to have it completely examined in full committee, unless the institution in question has already notified the main REB that it cannot proceed with the project for reasons of feasibility.<sup>25</sup> It cannot, however, be submitted to the appeal REB for the institution associated with the main REB since the latter's decision was ruled in order on appeal. The application must be presented to the REB by the principal researcher for the project at the institution, or if there is none, by the principal researcher. The rules for examining nonmulticentre projects then apply. Thus, if an REB renders a positive decision, the activity may take place at the institution it oversees. If the REB renders a negative decision, the researcher may turn to the institution's appeal REB, as per the appeal process set out by the Ministry.

*Appeal application record-keeping*

- 10.17 Appeal files compiled by appeal REBs must be kept in confidential files at their offices, according to the rules set by the minister or the Ministry, as the case may be.
- 10.18 The appeal REB must forward a copy of the complete file to the main REB. The main REB and local REBs must include in the files of all appealed research projects all related documents forwarded by the appeal REB.

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25. The Ministry's decision to override the multicentre mechanism is due to the fact that the main REB's decision can have major consequences if, although ethically justified, it prevents the project from going ahead in many regions, if not all of Québec, even though local REBs could, on the basis of the same information available to the main REB, render positive decisions that are just as ethically justifiable. If the multicentre mechanism allows local REBs to reject positive decisions by the main REB, it must also allow them to reject negative ones.

*Notification of the Ministry*

10.19 The appeal REB must notify the Ministry of all appeal applications at the time of their receipt and specify the names of the institutions concerned. It must also notify it of what followup the application received.

*REB accountability*

10.20 Appeal REBs must list the appeal applications they received and note how they were handled in their annual reports to their supervisory authorities.

10.21 The main REB must indicate in its annual report to its administrative authority which of its decisions were appealed and how these appeals were handled, and if designated, it must do the same in its annual report to the minister. When the main REB is not designated, it must send a letter to the Ministry no later than June 1 each year notifying it of the decisions that were appealed during the fiscal year ending that March 31.

10.22 The local REB's annual report to its administrative authority must mention whenever a main REB's decision has been appealed to an appeal REB as well as how the appeal was handled. This information must also appear in its annual report to the minister if the REB is designated.

*Costs*

10.23 Appeal costs are assumed by the main REB's administrative authority when the appeal REB rules that the application is admissible, and by the coordinating principal researcher in the opposite case.

**Appeal of a Decision Rendered by a Main REB**

- Before appealing a decision rendered by a main REB, the coordinating principal researcher must ask the committee to review its decision. If its decision remains unchanged, the researcher may then appeal to the minister's central REB or, if the latter is party to the decision, to an REB designated by the Ministry.
- The grounds a coordinating principal researcher may invoke for appealing a decision rendered by the main REB are the following:
  - The decision contravened a procedural requirement and is therefore invalid or beyond the REB's jurisdiction (see Appendix 1).
  - The decision violated a principle of natural justice (see Appendix 1).
- The coordinating principal researcher has thirty days to appeal from the date the main REB completes its review of its initial decision.
- The appeal REB must rule whether the appeal is admissible. If it deems the appeal admissible, it reexamines the ethics of the research project; if it deems it inadmissible, the mandate of the coordinating principal researcher ends. The project can then be submitted to each of the local REBs consulted under the multicentre mechanism to have it completely examined in full committee, unless the institution in question has already notified the main REB that it cannot proceed with the project for reasons of feasibility. It cannot, however, be submitted to the appeal REB for the institution associated with the main REB since the latter's decision was ruled in order on appeal. The Ministry's decision to override the multicentre mechanism is due to the fact that the main REB's decision can have major consequences if, although ethically justified, it prevents the project from going ahead in many regions, if not all of Québec, even though local REBs could, on the basis of the same information available to the main REB, render positive decisions that are just as ethically justifiable. If the multicentre mechanism allows local REBs to reject positive decisions by the main REB, it must also allow them not to reject negative ones. The application must be presented to the REB by the principal researcher for the project in the institution, or if there is none, by the principal researcher. The rules for examining nonmulticentre projects then apply. Thus, if an REB renders a positive decision, the activity may take place in the institution it oversees. If the REB renders a negative decision, the researcher may turn to the institution's appeal REB, as per the appeal process set out by the Ministry.
- The appeal REB must notify the Ministry of all appeal applications at the time of their receipt and specify the names of the institutions concerned. It must also notify it of what follow-up the application received.
- Special accountability measures are provided for in the section on REB accountability.
- Appeal costs are assumed by the main REB's administrative authority when the appeal REB rules that the application is admissible, and by the coordinating principal researcher in the opposite case.

## 11 Ongoing oversight of research projects

### *Compliance with standards*

11.1 Ongoing oversight of research projects must comply with existing standards, especially regarding REB notifications and REB application review procedures.<sup>26</sup> Forms are provided by the Ministry (see Appendix 2) for compliance with Section 11.5.

### *Duties of coordinating principal researcher*

11.2 The coordinating principal researcher is responsible for communications regarding ongoing oversight. He or she must remind local researchers of their duty to immediately forward all information bearing on project ethics so that it may be forwarded to the main REB and local REBs in a timely manner.

### *Role of main REB*

11.3 The main REB is responsible for passive oversight of research projects. It is not required to transmit requests it receives in this regard to local REBs for review and approval, subject to sections 11.4, 11.8.2, 11.8.3 and 11.8.4. The main REB liaises with concerned institutions or REBs by forwarding copies of decisions it has rendered.

11.4 Notwithstanding Section 11.3, the coordinating principal researcher must quickly inform local REBs or concerned institutions of any urgent situation of direct concern to them.

### *Basic oversight means*

11.5 The main REB determines the means of ongoing oversight it deems appropriate in the case at hand and requests that the coordinating principal researcher meet the following minimum requirements:

- 11.5.1 Ensure that research subject identification terms and conditions are observed
- 11.5.2 Submit to the main REB for prior approval any research project modifications other than administrative ones, except modifications required to eliminate immediate dangers to research subjects. In such cases, the REB must be notified as soon as possible
- 11.5.3 Notify the main REB as soon as possible of any serious adverse event or serious adverse drug reaction that could be related to experimental medication or a natural health product or, as the case may be, any accident related to a project procedure, and specifically identify the events involving the concerned institution and notify the local REB of them, or the concerned institution if there is no REB
- 11.5.4 Notify the main REB as soon as possible of any new information likely to affect the ethics of the research project or influence a research subject's decision to take part in the project
- 11.5.5 Inform the main REB as soon as possible of any suspension or revocation of project authorization by a funding or regulatory agency
- 11.5.6 Inform the main REB as soon as possible of any noted modifications to clinical equipoise in light of data gathered
- 11.5.7 Inform the main REB as soon as possible of any problem noted by a third party during an internal or external monitoring or audit activity and likely to challenge either the ethics of the project or the REB's decision<sup>27</sup>
- 11.5.8 Provide the main REB as soon as possible with a report on any temporary or permanent premature interruption of the project at any or all sites, indicating the nature and reasons for this interruption and the repercussions it will have on the research subjects, if any

26. Applications on project oversight under Article 21 of the Civil Code of Québec can be evaluated by a select committee if appropriate.

27. This also covers any deviation from protocol liable to impact on either the ethics of the project, or the decision of the main REB.

- 11.5.9 Provide the main REB with an annual report stating the progress of the research work
- 11.5.10 Provide the main REB as soon as possible with a final report stating the research results<sup>28</sup>
- 11.5.11 Appropriately conserve research-related documents for the purposes of ongoing oversight

*Other ongoing oversight means*

- 11.6 The main REB may require the creation of an independent data-monitoring committee, which will assess data and provide the main REB with a report for the purposes of Section 11.5.3.
- 11.7 When the main REB has established methods for active ongoing oversight, they apply to all institutions involved. The REB is responsible for ensuring these methods are implemented. Methods halted at the request of a concerned institution only apply to that institution, which must ensure they are implemented.

*Adding a local researcher, institution or sub-study*

- 11.8 When a modification request concerns the addition of a local researcher, the addition of one or more participating institutions or the addition of a sub-study to the project's main theme, the request is subject to the following conditions:
  - 11.8.1 When the request concerns the **addition of a local researcher**, the main REB informs the local REB (or designated authority in the case of an institution having no REB) within two weeks of the request, which then has two weeks to deliver their decision to the main REB. Eligible costs are those related to the ongoing oversight.
  - 11.8.2 When the request concerns the addition of one or more participating institutions to a **multicentre project in progress**, the coordinating principal researcher must submit the complete file, including the original review application form, to all local REBs concerned for preliminary review; to the authorities designated by each of the institutions having no REB, for review of the final decision made by the main REB; and to the authorities designated by each of the institutions, for site-specific project assessment. The process applying to the initial request gets under way, with such modifications as the circumstances require. Fees claimable by the local REB are those relating to the preliminary assessment.
  - 11.8.3 When the request concerns the addition of one or more participating institutions to a **research project that becomes multicentre or becomes subject to the multicentre mechanism**,<sup>29</sup> the person acting as coordinating principal researcher must complete the project review application form issued by the Ministry. The process used is the same as that indicated in Section 11.8.2, unless the REB that initially approved the request does not meet the basic requirements (see Section 3.1) and it is necessary, because of this, to contact an REB as main REB, which will not already reviewed the project as a full committee (see Section 3.5.2). In this event, such a request is no longer governed by the ongoing oversight of the project; it is considered a new request. In all cases, costs claimed by the local REB are those relating to the preliminary assessment.
  - 11.8.4 When the request concerns the **addition of a sub-study**, the coordinating principal researcher must forward the relevant documentation to the main REB and to the

28. For the purposes of the mechanism, the deadline for approval renewal is calculated as of the date the final decision was rendered by the main REB, and not the date of the meeting at which the REB made its preliminary decision.

29. For example, this could be the case for a research project carried out at several institutions bound by a delegation agreement and to which the multicentre mechanism did not apply. The decision to conduct it in other institutions not bound by this agreement would make the mechanism applicable to the project.

local REBs concerned, for a preliminary assessment of the sub-study, and to each of the institution's designated authorities, for a sub-study site-specific assessment. The process applying to the initial request gets under way, with such modifications as the circumstances require. Expenses claimable by all REBs are those relating to the ongoing oversight.

*Deadline for review of applications involving ongoing oversight*

11.9 Notwithstanding the cases set out of Section 11.8, the main REB must examine every project modification application within thirty-five days. For other applications subject to Section 11.5, it must proceed with caution and according to the standards in effect. When an application entails the modification of a project-related document, the main REB must remind the coordinating principal researcher to send local REBs the new document and an annotated copy of the former version clearly showing the changes made.

*Feedback to institution*

11.10 The main REB must quickly provide the local REB, or the concerned institution if there is no REB, with any information likely to challenge its initial acceptance.

11.11 An institution with no REB must quickly inform the proper authority of any correspondence from the main REB that refers to ongoing oversight and has an impact on aspects pertaining to its jurisdiction.

*Feedback to main REB*

11.12 A concerned institution and, as the case may be, a local REB, must quickly provide the main REB with any information likely to change its final decision, e.g., allegations of a breach of ethics. The main REB must then notify the coordinating principal researcher of such information.

*Powers of the main REB*

11.13 The main REB may take any measures it deems appropriate, further to information likely to change its final decision, without prejudice to measures that local REBs and concerned institutions would like to take. It must quickly inform the coordinating principal researcher, local REBs, and concerned institutions of such measures.

11.14 When the local REB or concerned institution has taken special measures as a result of information likely to change its decision or that of the main REB, the main REB must be informed of these measures as soon as possible such that it can notify the coordinating principal researcher of such measures.

**Ongoing Oversight of a Research Project**

- The coordinating principal researcher must report on the actions of the local principal researchers and the research team members and is responsible for submitting applications involving ongoing oversight.
- The main REB determines the ongoing oversight means (at least the basic passive means), assumes responsibility for them, and must comply with the regulatory requirements that apply to the research project.
- The main REB is also responsible for liaising with concerned institutions and local REBs.
- Local REBs and concerned institutions with no REB must quickly provide the main REB with any information likely to change its final decision, and vice versa. The main REB, local REBs, and concerned institutions may all take any measures they deem appropriate.

## 12 Link between the multicentre mechanism and certain measures of the ministerial action plan related to research ethics

Measures of the ministerial action plan that involve research ethics and any special provisions that apply to REBs apply to multicentre research projects. The following measures must, however, be adapted with a view to applying the present mechanism.

### *Project register*

12.1 Multicentre research projects assessed under the new mechanism must be entered on a list of approved projects or the institution's project register, as the case may be. The terms and conditions differ, however, according to whether or not there is an REB at the institution and whether the REB acted as a main or local REB.

12.1.1 **An institution with no REB or project register** must keep a list of research projects approved by a main REB, specifying a) the nature and date of the decision it rendered and b) the name of the main REB and the nature and date of the final decision.

12.1.2 **An institution with an REB that acted as a local REB** must enter in its project register a) a notation that the project underwent a multicentre review, b) the date the REB performed the preliminary review and the nature and date of the decision rendered, c) the nature and date of the decision rendered by the institution, d) the name of the main REB and the nature and date of the final decision rendered, and e) all information required for any other research projects approved by the REB.

12.1.3 **An institution whose REB acted as the main REB** must enter in its project register a) a notation that the project underwent a multicentre review, b) the names of the concerned institutions that either rejected or endorsed the decision of their REB or the main REB, c) any special provision that applies to a concerned institution, and d) all information required for any other research projects approved by the REB.

### *Complaints and breaches of ethics*

12.2 Complaints and breaches of ethics must be dealt with by each concerned institution, according to the procedure in its regulatory framework. The institution must nevertheless inform the main REB as soon as possible of any inquiries that are opened. The main REB may take any temporary measures it deems appropriate without prejudice to measures the institution may wish to take.

12.3 When a complaint or breach of ethics is well founded, the institution must inform the main REB, which may take any measures it deems appropriate without prejudice to measures the institution may wish to take.

### *Research subject identification mechanism*

12.4 The research subject identification mechanism must be either a centralized directory or a list of recruited research subjects that the researcher is obliged to maintain and update. When an institution has no REB, only the second identification mechanism is allowed. A research subject can only be listed in one identification mechanism. If the institution has a centralized directory, it must only register the name of research subjects who have been recruited on site.

12.5 The institution must provide the main REB with the research subject identification method it has adopted, so that this REB can then inform the coordinating principal researcher following a positive final decision.

- 12.5.1 In a letter outlining its final decision, the main REB must advise the institution to address all requests pertaining to research subject identification method to it.
- 12.5.2 The main REB forwards the institutions' requests for research subject identification to the coordinating principal researcher. If local principal researchers participate in the project, the coordinating principal researcher is responsible for ensuring that the requests from the main REB on this matter are handled by the local principal researcher from the requesting institution. When these requests have been carried out, the coordinating principal researcher informs the main REB.

*REB accountability*

- 12.6 In their annual report to the board of directors, the Ministry and, as required, the minister, the local REBs of concerned institutions and the main REB must give an account of the multicentre research projects for which they conducted ethical reviews or performed ongoing oversight. Reporting to the Ministry and, as required, the minister is done using the online report form produced by the Ministry.

**Links with Certain Measures of the Ministerial Action Plan on Research Ethics**

- **Research project register:** Multicentre research projects assessed under the mechanism must be entered in the list of approved projects or the institution's project register, as the case may be. The terms and conditions differ, however, depending on whether or not the institution has an REB and whether the REB acted as a main or local REB.
- **Complaints and breaches of ethics:** The procedure in effect at the institution where the complaint or breach of ethics allegation was lodged is the one used. The main REB must nevertheless be informed as soon as possible of any inquiries that are opened and must also be informed of their results when the complaint or breach of ethics is well founded. It may take any temporary or permanent measures it deems appropriate without prejudice to measures the institution may wish to take.
- **Research subject identification:** The institution must provide the main REB with the research subject identification methods it has adopted, so that the REB can then inform the coordinating principal researcher in the event of a positive final decision. In a letter outlining its final decision, the main REB must advise the institution to address all requests pertaining to research subject identification mechanism requests to it. The main REB forwards the institutions' requests for research subject identification to the coordinating principal researcher. If local principal researchers participate in the project, the coordinating principal researcher is responsible for ensuring that the requests from the main REB on this matter are handled by the local principal researcher from the requesting institution. When these requests have been carried out, the coordinating principal researcher informs the main REB.
- **REB accountability:** In their annual report to the board of directors, the Ministry and, as required, the minister, the local REBs of concerned institutions and the main REB must give an account of the multicentre research projects for which they conducted ethical reviews or performed ongoing oversight. Reporting to the Ministry and, as required, the minister, is done using the online report form produced by the Ministry

**13 Liaison between REBs**

The Ministry will strongly encourage initiatives from those involved in the process that promote dialog; lead to model contracts governing relations between sponsors, researchers, and institutions; and standardize REB operating procedures or requirements and the content of the ethical review in order to resolve any problems with the multicentre mechanism.

**14 Funding of the multicentre mechanism**

Funding of the multicentre mechanism takes into account the varying circumstances of researchers. The Ministry would point out, however, that the following amounts illustrate the actual costs associated with the ethical review and ongoing oversight of a multicentre research

project. It would also add that the mechanism is much more economical than the method currently used for multicentre research project ethical review and oversight, particularly by easing the burden on local REBs, which will no longer be required to assess such projects in full committee.

*Nature of projects to which costs are attached*

14.1 Amounts required for the multicentre mechanism apply to research projects currently governed by the ministerial circular entitled *Contribution de l'entreprise privée dans le cadre d'activités de recherche découlant d'un octroi de recherche* (Private business contributions to research activities pursuant to a research grant). They also apply to research projects funded by Fonds de la recherche en santé du Québec for which costs relating to the ethical review were provided for in the application.

*Costs relating to main REB services*

14.2 The following amounts must be paid to the host institution of the main REB:

- A fixed amount of \$5,000 in compensation for the ethical review in conjunction with up to ten institutions, plus \$200 for each additional institution
- An amount established according to the user/payer principle as compensation for ongoing oversight of the project, in conjunction with the concerned institutions

*Costs relating to local REB services*

14.3 The following amounts must be paid to the host institution of the local REB:

- A fixed amount of \$850 in compensation for the preliminary review
- An amount established according to the user/payer principle as compensation for requests relating to ongoing oversight that would require the services of the local REB.

*Costs relating to the site-specific assessment*

14.4 The site-specific assessment is funded from the amounts received under the ministerial circular entitled *Contribution de l'entreprise privée dans le cadre d'activités de recherche découlant d'un octroi de recherche* (Private business contributions to research activities pursuant to a research grant).

**Funding**

- Projects for which amounts must be charged for multicentre mechanism application purposes:
  - Research projects currently subject to the ministerial circular entitled *Contribution de l'entreprise privée dans le cadre d'activités de recherche découlant d'un octroi de recherche* (Private business contributions to research activities pursuant to a research grant).
  - Research projects funded by Fonds de la recherche en santé du Québec for which costs relating to the ethical review were provided for in the application.
- Host institution of the main REB:
  - Ethical review by the main REB in conjunction with up to ten institutions: \$5,000, plus \$200 per additional institution
  - Ongoing oversight in conjunction with the concerned institutions: amount determined by the institution according to the user/payer principle
- Concerned institution with an REB:
  - \$850 to cover the costs of carrying out the preliminary review (see Section 6 and sections 11.8.2 and 11.8.3) ;
  - An amount established by the institution according to the user/payer principle as compensation for ongoing oversight of the project, requiring the services of the local REB (in particular, see sections 11.4, 11.8.1 and 11.8.4).
- The costs of the site-specific assessment are paid from sums received under the ministerial circular.

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## Appendix 1: Examples of grounds of appeal

### Examples of procedural breaches that render the REB's decisions invalid:

- The main REB reviewed the application without having the expertise required to do so and without drawing on outside experts.
- The main REB exceeded its jurisdiction through misunderstanding, ignorance, or erroneous application of an ethical standard (e.g., it refused the use of a placebo in a situation where the three Canadian research councils allow it).
- The main REB exceeded its jurisdiction by contravening legislation.
- The main REB reached its decision without a quorum.
- The main REB reviewed the application in select committee instead of full committee, as it was required to.
- The main REB reviewed a research activity that was under the jurisdiction of a designated REB, whereas it was not designated.

### Examples of violations of principles of natural justice:

- The main REB refused to hear testimony from the researcher.
  - Reminder: Researchers must have the opportunity to learn the facts that may be detrimental to them and to present their points of view.
- The main REB was not honest and impartial in its judgment of the application.
  - Reminder: The REB's decision must be reached by individuals presenting basic guarantees of neutrality toward the researcher. This includes
    - Lack of financial interest
    - Absence of intellectual bias or prejudice, including prejudice resulting from personal relations between an REB member and one of the interested parties (e.g., previous animosity or competition between a member and the applicant), an REB member's social or professional associations (e.g., an REB member conceals the fact that he or she belongs or belonged to another REB opposed to the application), or an REB member's behavior during the decision-making process (e.g., a member demonstrates partiality during the meeting)
- The main REB turned down the researcher's application without taking into account the entire content of the file or all the arguments put forward.
  - Reminder: The REB must make its decision on the basis of a detailed proposal, which means that all members must have access to all documentation. Turning down an application without having consulted the complete file constitutes a miscarriage of justice.
- The main REB did not give reasons for its decision.
  - Reminder: The REB must give reasons for its decisions so that the researcher understands why the committee turned down the application.

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## Appendix 2: Documentation pertaining to the multicentre mechanism

The Ministry has prepared a number of explanatory documents in consideration of the multicentre mechanism, including

- A guide for researchers
- A guide for general management at health and social services institutions
- A guide for REBs
- Frequently asked questions
- Sample response letters for use by any main REB, indicating what must be included in such letters
- Sample response letters for use by any local REB or general management at health and social services institutions, indicating what must be included in such letters

The following forms must be used when applying the mechanism:

- *Formulaire de demande d'évaluation d'un projet multicentrique* (Multicentre project review application form) (formulaire M-ÉVAL-2008);
- *Formulaire de demande d'approbation d'une modification à un projet multicentrique* (Multicentre project modification approval application form) (formulaire M-MOD-2008) ;
- *Formulaire de demande d'approbation d'une modification à un projet multicentrique portant sur l'ajout d'un établissement, d'un chercheur local ou d'une sous-étude* (Multicentre project modification approval application form for adding an institution, local researcher, or sub-study) (formulaire M-AJOUT-2008) ;
- *Formulaire de demande de renouvellement annuel de l'approbation d'un projet multicentrique par un REB* (Annual renewal application form for multicentre project approval by an REB) (formulaire M-REN-2008) ;
- *Formulaire de notification d'un nouveau renseignement ou d'une modification de l'équilibre clinique concernant un projet multicentrique* (Notification form for new information or changes in clinical equipoise concerning a multicentre project) (formulaire M-NR-2008) ;
- *Formulaire de notification de la fin d'un projet multicentrique* (Multicentre project termination notification form) (formulaire M-FIN-2008) ;
- *Formulaire de notification d'un accident survenu au cours d'un projet multicentrique* (Notification form for accidents related to multicentre project procedures) (formulaire M-ACC-2008) ;
- *Formulaire de notification d'une activité de surveillance ou de vérification menée par un tiers au cours de laquelle un problème susceptible de remettre en cause l'éthicité d'un projet multicentrique a été constaté* (Notification form for monitoring or audit activities led by a third party during which a problem likely to call into question the ethics of a multicentre project was noted) (formulaire M-AUDIT-2008) ;
- *Formulaire de notification d'une déviation au protocole de recherche susceptible de remettre en cause l'éthicité d'un projet de recherche* (Notification form for deviations from protocol liable to impact on the ethics of the project) (formulaire M-DÉV-2008) ;
- *Formulaire de notification de l'interruption temporaire ou de la reprise d'un projet multicentrique* (Notification form for the temporary interruption of a multicentre project) (formulaire M-INTP-2008) ;

- *Formulaire de notification d'un incident thérapeutique ou d'une réaction indésirable graves survenus au cours d'un projet multicentrique se déroulant dans un établissement auquel s'applique le mécanisme multicentrique* (Notification form for serious adverse reactions that occurred during a multicentre project at an institution to which the multicentre mechanism applies) (formulaire M-RIG-M-2008) ;
- *Formulaire de notification d'un incident thérapeutique ou d'une réaction indésirable graves survenus au cours d'un projet multicentrique se déroulant dans un site autre que ceux auxquels s'applique le mécanisme multicentrique* (Notification form for serious adverse reactions that occurred during a multicentre project at a site other than those to which the multicentre mechanism applies) (formulaire M-RIG-NM-2008).

These documents are available online at <http://ethique.msss.gouv.qc.ca>.

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### Appendix 3: Consultations conducted

December 19, 2006, to January 19, 2007	First written consultation conducted among all REBs on the Ministry de la Santé et des Services sociaux list and other research community actors
January 30, 2007	First work meeting with a group of targeted actors (35 people): <ul style="list-style-type: none"> <li>• REB chairs (The Ministry network, universities with designated REBs, Central Research Ethics Committee, and the private sector)</li> <li>• Ministerial partners (Ministry de l'Éducation, du Loisir et du Sport and Ministry du Développement économique, de l'Innovation et de l'Exportation)</li> <li>• Representatives of Québec research funds</li> <li>• Researchers</li> <li>• Representatives of Canada's Research-Based Pharmaceutical Companies (R<sub>x</sub>&amp;D) and Association québécoise de recherche clinique (AQRC)</li> </ul>
February 14 to March 30, 2007	Second written consultation conducted among all REBs on the Ministry list and other research community actors
March 23, 2007	Bilateral meeting with the research committee of Conférence des recteurs et des principaux des universités du Québec (CREPUQ)
April 4, 2007	Bilateral meeting with Ministry du Développement économique, de l'Innovation et de l'Exportation
April 16, 2007	Bilateral meeting with AQRC and R <sub>x</sub> &D
April 17, 2007	Second work meeting with the group of targeted actors present on January 30, 2007
April 26, 2007	Bilateral meeting with representatives of the Faculty of Medicine at Université de Montréal
June 1, 2007	Bilateral meeting with AQRC members
June 4, 2007	Bilateral meeting with R <sub>x</sub> &D members
June 8, 2007	Bilateral meeting with the CREPUQ university research ethics subcommittee
June 29, 2007	Bilateral meeting with the CREPUQ university research ethics subcommittee
July 27, 2007	Bilateral meeting with representatives of the Cavendish, Montagne, Bordeaux-Cartierville, and Jeanne-Mance health and social services centers