

# Clinical Trials in Quebec: Criteria for Differentiating between “Direct Research Costs” and “Insured Services”

This statement proposes criteria to facilitate a non-arbitrary determination of the qualification of the following items as “**direct research costs**”:

- Drugs and other products, including medical devices, used in a research project (the “**Products**”);
- Procedures required under a protocol (the “**Procedures**”);
- Treatment of participants in the event of adverse events, medical conditions, or injuries caused or exacerbated by their participation in a research project (each, a “**Injury**”).

**Meeting only one of the criteria listed in the table below** is sufficient for a cost to constitute a “direct research cost” subject to the requirements imposed by applicable laws. The fact that a Product or Procedure may or may not be used in as part of the standard of care, as well as for research purposes, does not affect its qualification as a “direct research cost” when it is determined that one of the criteria set out below has been met.

The purpose of this statement is to establish a common definition of “direct research costs,” applicable regardless of the source of funding for the study.

Regarding reimbursement terms:

- For research trials involving a private sponsor, the sponsor is responsible for reimbursing the direct costs of the research.
- For academic trials, the responsible investigator, the institution, and the pharmacy will agree on the terms and conditions for reimbursement of these costs.

This statement is intended as a reference, information, and support tool for health and social services institutions (**HSSIs**) and sponsors/contract research organizations (**Sponsors/CROs**). It is not intended to be a legal opinion and/or interpretation that is binding on Sponsors/CROs and HSSIs or that limits the scope of application of the *Manuel de gestion financière (Financial Management Manual)* and applicable guidelines.

COST TYPE	CRITERIA
<b>Products</b>	
<b>Acquisition Costs</b>	<ol style="list-style-type: none"> <li>1) The Product is included as an investigational product in the protocol that is part of the regulatory submission to Health Canada (e.g., no objection letter).</li> <li>2) It is a Product or a specific formulation of a Product for the treatment(s) being studied or any other concomitant product, the administration, dosage, or choice of which, as required by the research project documentation, differs from what would have been done as part of the services offered by the HSSI.</li> <li>3) The Product or a specific formulation is required by the research project documentation <b>AND</b>:               <ol style="list-style-type: none"> <li>a. Is not on the list of the RAMQ in HSSIs or of the HSSI; <b>OR</b></li> <li>b. Is acquired specifically for use in the research project, even if it has not been used (e.g., an expired Product or inventory remaining at the end of the project).<sup>1</sup></li> </ol> </li> <li>4) The Product is necessary to prevent or treat an adverse event resulting from the treatment being studied, as <u>required</u> by the research project documentation or according to the investigator’s clinical judgment.</li> </ol>

<sup>1</sup> **Note:** From a sound inventory and resource management perspective, the health institution may, where possible, return to its inventory Products covered by criterion 3b) that have not been used in the project or are about to expire. These Products may then be used as part of insured services. This practice reduces waste and limits the costs charged to the sponsor, which will not be billed for an unused or expired Product when it has been properly recovered. If the Product cannot be reused in insured services, it will be billed to the sponsor and then destroyed or returned according to the agreed terms.

COST TYPE	CRITERIA
<b>Other Costs</b> (management, preparation, etc.)	<ol style="list-style-type: none"> <li>5) Any action that must be performed by the pharmacy department and that is directly related to a research project is considered a “direct research cost” (e.g., administrative or Product management costs, time required for reconstitution), even if the cost of acquiring the Product is not a “direct research cost.”</li> <li>6) Costs other than those related to Products may constitute “direct research costs” (e.g., treatment of an Injury reported as an adverse event caused by the Product or another Injury caused by the Product or by participation in the study).</li> </ol>
<b>Procedures</b>	
<b>Procedure Costs</b>	<ol style="list-style-type: none"> <li>1) Infrastructure which are (i) dedicated to or used for HSSI’s or third-party’s research; (ii) employed, financed and/or otherwise paid for by HSSI (e.g., private infrastructure from external suppliers); and (iii) used to perform the Procedure or to meet the requirements of a protocol.</li> <li>2) The frequency with which the Procedure is performed differs from that which would have been observed in the patient's trajectory of care.</li> <li>3) The Procedure described in the research project documentation is a modification or addition to a standard HSSI practice, as determined by the HSSI, and results in additional costs.</li> <li>4) The specific Procedure (prophylaxis or other) is necessary to prevent or treat an adverse event arising from the treatment being studied, as <u>required</u> by the research project documentation or according to the investigator's clinical judgment.</li> </ol>
<b>Other Costs</b>	<ol style="list-style-type: none"> <li>5) Costs of Procedures, or arising from Procedures, that are required to diagnose and treat an Injury (e.g., treatment of an Injury that is reported as an adverse event caused by the Product or another Injury caused by the Product or by participation in the study).</li> </ol>

## Appendix 1 – Legislative Context

This context is provided for informational purposes to support the criteria set out to differentiate between “direct research costs” and “insured services.” This context is intended to serve as a reference, information, and support tool for HSSIs and Sponsors/CROs.

1. **Context:** In Quebec, HSSIs and their investigators, as well as sponsors and CROs, are required to comply with applicable federal and provincial laws, including research guidelines and directives, the Financial Management Manual, and relevant ministerial directives and, where applicable, ethical and professional conduct rules (the “**Applicable Laws**”), which set out various mandatory rules. For example:

2.1 **Article 1474 of the *Civil Code of Québec***, which is of public order, provides that no person may exclude or limit their liability for a bodily or moral injury caused to another person.

➔ This rule applies in particular in the event of an Injury suffered by a participant. Thus, a sponsor cannot limit its liability unless the Injury is solely caused by a HSSI’s or investigator’s wrongful act or omission. Therefore, a failure on the part of a HSSI or an investigator that did not cause such Injury cannot limit the sponsor’s liability. Similarly, a participant’s failure to comply with the protocol cannot exempt the sponsor from liability, as the participant is not bound by contractual obligations (of result or otherwise) and takes part in the research project without consideration, in a disinterested manner and subject to compensation in the event of an Injury.

➔ The Financial Management Manual (Appendix 1H) and ministerial directive 2023-015 list that “hospitalization costs, ambulatory surgery and ambulatory medical services costs, and outpatient costs incurred by the research project” may be direct research costs if they are specifically incurred for the purpose of carrying out a research project and can be identified easily and non-arbitrarily. Where applicable, the sponsor must bear the costs, which are subject to an additional contribution of 30%.

2.2 **Articles 2883 and 2884 of the *Civil Code of Québec***, which are of public order, confirm that it is not possible to agree on a limitation period other than that provided by law or to waive the limitation period in advance.

➔ As a result, a sponsor cannot limit its liability if a HSSI or an investigator fails to notify it of a claim within ten (10) days or by stipulating that any claim must be made no later than one year after the end of the project.

2.3 **Articles 10 and subsequent of the *Civil Code of Québec*** distinguish between the concept of “medical care” required or not required by the health status, and “participation in research.” This distinction is also found in the Financial Management Manual, ministerial directives, and other Applicable Laws. However, the law defines these two concepts broadly, so that they may overlap:

- The term “care” refers to any type of examination, specimen taking, treatment, or act of a medical, psychological, or social nature, whether or not required by the physical or mental health status, as well as prior lodging facility; and
- The term “research” refers to any process aimed at developing knowledge through a structured study or systematic investigation.

Therefore, it is not so much the type of act or Product that matters, but rather the context in which it is used or the reason for its use. For example, and in accordance with Applicable Laws, a HSSI:

- may only use its operating budget to provide insured services, i.e., health and social services provided as part of its mission;
- may carry out ancillary activities (*‘activités accessoires’*) to the services it provides (e.g., research and teaching), provided that these ancillary activities are self-financed;

(**Note.** The direct costs of self-financed research include, in particular: (1) drugs, except those provided free of charge by a pharmaceutical company for the purpose of carrying out the project; (2) the costs of acquiring materials, except where they are graciously provided by the contracting company or company; (3) hospitalization costs, ambulatory surgery and ambulatory medical services costs, and outpatient costs incurred by the research project; and (4) all other direct costs incurred by the research project.)

- must maintain a balanced budget at all times.

Otherwise, an HSSI will be in breach of the accounting and legal rules applicable to it.

- 2.4 The **general health insurance plan** guarantees the payment, for every eligible person, to the extent provided for in the law, of the cost of:
- medications listed on the List of Medications (for HSSI, the RAMQ List of Medications (outpatient) and HSSI List of Medications) that are provided in Quebec by a pharmacist on prescription from an authorized professional, as well as related pharmaceutical services; and
  - services and medications specified by regulation, which are included in the List of Medications (subject to very limited exceptions, e.g., for exception patients) and which are provided as part of the activities of a HSSI.
- ➔ Thus, the public plan does not cover costs and expenses *directly* incurred by a research project. In the event that Products (e.g., if they are included on the List of Medications) or acts (e.g., the diagnosis or treatment of an Injury) are submitted to the public plan in violation of the above, various remedies and measures may be taken (e.g., by the RAMQ).
- 2.5 The **Food and Drug Regulations** prohibit the sale of drugs intended for clinical trials unless this is done in accordance with these regulations. These regulations require, among other things, that authorization be obtained and that the sponsor submit a statement specifying, among other things, that the project will be conducted in accordance with good clinical practices, which require, among other things, that:
- the sponsor provides insurance or legally and financially indemnifies the HSSI and the investigator against any claims related to the project, except those arising from their negligence or professional misconduct; and
  - the sponsor's policies and procedures address the costs in the event of an Injury, which must comply with Applicable Laws.
- 2.6 **The procurement** of drugs and other products by HSSIs is highly regulated, both by legal provisions, including the *Act respecting contracts by public bodies* and the *Act respecting prescription drug insurance*, and by contractual provisions, including those set out in contracts entered into through calls for tenders. Under these requirements, a HSSI cannot enter into contracts by mutual agreement (i.e., without going through a call for tenders) if their value exceeds the threshold set out in the law and/or HSSI policies. Such contracts must then be entered into by specific HSSI bodies (other than those involved in research).
- ➔ Thus, a HSSI cannot be required to repurchase or bear the acquisition costs of Products initially obtained as part of a research project.
- 2.7 The **Financial Management Manual (Appendix 1H) and ministerial directive 2023-015** confirm that direct research costs refer to costs “specifically incurred for conducting a research project,” which includes fees, salaries, employment benefits, and other employment-related costs, including the annual variation in accrued costs for various salary components (vacation, sick leave, etc., and related employment-related costs) to carry out and coordinate the research project, as well as supplies, equipment maintenance, use, and access costs, and licensing costs.
- ➔ Thus, the costs incurred at the pharmacy level constitute direct research expenses, including, in particular, the time spent by professionals involved in Product management (such as receiving, storing, handling, and preparing Products) and in coordinating the research project, the equipment and supplies used, and the software required.

Failure to comply with these Applicable Laws, including those referred to in sections 2.1 to 2.7, may result in administrative and financial penalties, in addition to giving rise to civil and other remedies.