INESSS
LE SAVOIR PREND FORME

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Guide to Submitting an Application to INESSS for Innovative Non-Pharmaceutical Technologies for Access to the Health and Social Services System

A publication by the Institut national d'excellence en santé et en services sociaux (INESSS)

Direction de l'évaluation des médicaments et des technologies à des fins de remboursement

Québec

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Preamble

The work carried out by the Directorate of Drug and Technology Assessment for Reimbursement (DER) will lead to the publication of a recommendation regarding access to the health and social services system. The innovative non-pharmaceutical technologies covered by this guide are those that have reached a sufficient level of maturity to consider their deployment—that is, their widespread adoption across all eligible settings or populations (Figure 1). This guide therefore applies to innovative non-pharmaceutical technologies approved by Health Canada.

The DER accepts only evaluation mandates for innovative non-pharmaceutical technologies assigned to it by the Ministry of Health and Social Services (MSSS). At the request of the MSSS, the DER may also issue a call for expressions of interest to innovators for evaluation mandates covering a range of innovations.

For all other types of applications, including digital applications with or without artificial intelligence (AI), artificial intelligence systems using deep learning, or innovations not approved by Health Canada, please contact us at ITDM@inesss.qc.ca to learn about the applicable procedures.

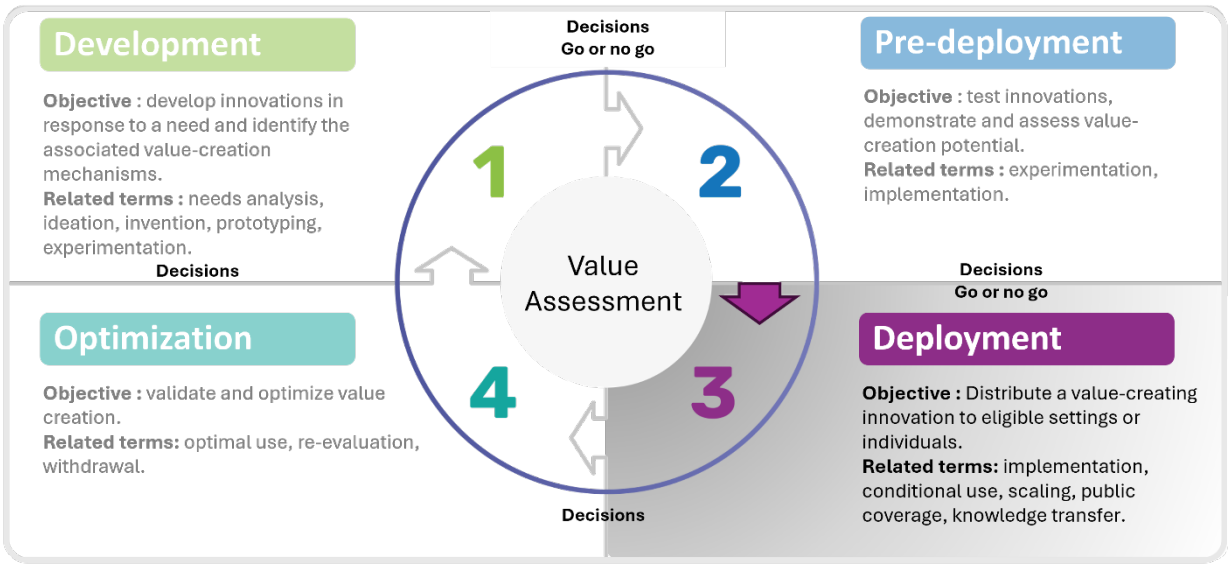


Figure 1 Innovation Life Cycle[1]

[1] Innovation lexicon https://www.inesss.qc.ca/fileadmin/doc/INESSS/DocuMetho/INESSS_Innovation_Lexicon.pdf

The following are not covered by this submission guide:

- Non-pharmaceutical innovations not intended for deployment across all eligible settings or individuals;
- Medical devices directly related to the administration of a drug or health products intended for evaluation for inclusion on the *Drug List* or the *Drug List—Institutions.* These must be submitted in accordance with the procedures described under the section " *Request for Registration on* the Drug *List* - Presciption medications" and " *Request for Registration on* the Drug *List* - Medical devices";
- Laboratory and genomic tests for inclusion in *the Quebec Directory and the system for measuring clinical laboratory procedures*. These must be the subject of an evaluation application in accordance with the procedures and process described under the topic "Medical Biology and Genomics".

General Instructions

This document, drafted and published by the DER, provides the information necessary to prepare an application for the evaluation of a non-pharmaceutical innovation for the purpose of gaining access to the health and social services system. In this guide, you will find the required documents, the terminology used, and the specific requirements for an application to evaluate a non-pharmaceutical innovative technology.

ASSESSMENT PROCESS

The evaluation of innovative non-pharmaceutical technologies is part of the Institute's evaluation process as described in its Statement of Principles for the Framework for Assessing the Value of Interventions . Further information on the policy and guidelines that guide INESSS's work is also available on its website.

The guide for submitting an application to INESSS for innovative non-pharmaceutical technologies for access to the health and social services system is intended to provide specific information regarding an application for the evaluation of an innovative non-pharmaceutical technology.

Submitted applications must comply with the content, format, and structure specified in this submission guide. If you have any questions, please contact the INESSS DER by email at ITDM@INESSS.qc.ca.

The information contained in the application submitted to INESSS is treated as confidential.

In preparation for submission, **create an evaluation submission package** and add the required documents to it. Organize the documents into subfolders according to the different aspects of the evaluation (administrative, population-based, clinical, organizational, economic, environmental, ethical, other). Please refer to sections 1 through 6 of this guide. An example of a submission folder structure is provided in Appendix IV;

The ITDM form found on the website under the "Submit an application for evaluation" sub-section of the Non-pharmaceutical Innovations topic serves as a checklist to ensure that all required documents are included in the application. A written justification is required for any missing documents. The completed ITDM form must also be submitted along with the other documents in the application.

The DER has implemented an electronic submission solution using a secure platform. Please request the secure link in advance, specifying the desired date, by emailing ITDM@inesss.qc.ca .

IMPORTANT

Only complete applications will be deemed admissible.

An innovator who wishes to submit new documents during the evaluation process (e.g., a new publication or a clinical study manuscript not included in the file) must submit a written request to ITDM@inesss.qc.ca. Depending on the nature of the information, the evaluation timeline may be adjusted. Please note that no new information will be accepted once the recommendation has been submitted to the Minister, effective as of the date the recommendation is placed under moratorium.

1 ADMINISTRATIVE SECTION

The documents required for the administrative component are described in this section. Upon submission, they must be grouped into a subfolder named “Administrative Component.”

☐ Cover Letter

Prepare a cover letter for the application, which must be written in French. The following information must be included:

- A brief description of the subject of the evaluation;
- Contact information for the person responsible for the case on behalf of the innovator. The contact information for a second person may be included, if desired;
- Identification, if applicable, of the consultant authorized to communicate with INESSS regarding the application.

☐ Form: “Application for Evaluation of a Non-Pharmaceutical Innovation”

Complete the form “Application for Evaluation of a Non-Pharmaceutical Innovation”, available on the INESSS website under the “Non-Pharmaceutical Innovation” topic (sub-section “Submit an application for evaluation”).

Here is the information needed to complete the form:

A) Description of the innovation

- Select the type of innovation from the options provided. If the type of innovation is not available in the list, please notify us by email at ITDM@inesss.qc.ca ;
- Select the purpose of the innovation from the options provided;
- Enter the trade name and trademark of the innovation (sometimes, an innovation may have several commonly used names);
- Describe the innovation: How does the innovation work? Provide one or more photos showing the various components of the innovation. What components are essential for the innovation to function properly, including, if applicable, diagrams summarizing the algorithms used? Specify whether any external elements are required (another device, IT platform, etc.).
- Identify the developer or promoter of the innovation, as well as their field of activity;
- Identify the target user(s) from the options provided. If the target users are not listed, please notify us by email at ITDM@inesss.qc.ca ;
- Identify the product(s), technology(ies), medication(s), intervention methods, and organizational models that the innovation is intended to replace. Indicate what the current practice is;

- Indicate whether one or more similar innovations are currently available or under development;
- Indicate the status in other provinces, territories, or countries.

B) Health Canada-Approved Use

- List the use(s) recognized by Health Canada.

C) Use Requested for INESSS Evaluation

- List the use(s) requested from INESSS. Does the use requested from INESSS differ from that recognized by Health Canada?

D) Submitted selling price

- Indicate the selling price for Quebec.

E) Applicant's contact information and certification

- Enter the applicant's full contact information (name, address, email, phone number).
- Sign and date the certification stating that all information provided complies with the conditions to which the applicant has committed. Include the contact information of the person signing the certification. If this form is subsequently amended by the innovator, it must be signed and dated again. This certification may be signed by any authorized person, at the discretion of the innovators.

☐ Medical Device Licence Issued by Health Canada

Include this document in the submission file. It is issued by the Medical Devices Directorate of Health Canada's Therapeutic Products Directorate pursuant to section 36 of the Medical Devices Regulations.

For any other product that has not been the subject of a medical device licence, please contact INESSS at ITDM@inesss.qc.ca.

☐ Authorization to Share Information

Use the letter template Authorization to Share Information available on the INESSS website under the Non-pharmaceutical Innovations topic (sub-section "Submit an application for evaluation"). This document authorizes INESSS to share the information included in the application (one-way sharing) with Health Canada, the Canadian Drug Agency (CDA-AMC), and the Quebec Ministry of Health and Social Services. Please note that this document does not authorize Health Canada or CDA-AMC to share information with INESSS.

☐ **“Summary Description of the Application” Form**

Use and complete the most recent version of the “Summary Description of the Application” form, available on the INESSS website (sub-section “Submit an Application for Evaluation”). This document provides a summary of the entire submission package.

2 POPULATIONAL DIMENSION[2]

Provide a document presenting the elements related to this dimension in the form of a text with appropriate bibliographic references, titled “Explanatory Document—Populational Dimension.” Upon submission, it must be placed in a subfolder titled “Populational Dimension.”

☐ Explanatory Document

- Provide evidence-based explanations that concisely outline the factors related to the health condition or issue and its consequences. The information presented in this section should enable INESSS to understand how the non-pharmaceutical innovation can contribute to improved health and well-being for the population as a whole, with a focus on equity (i.e., addressing significant health and well-being needs of the population and being accessible to all who need it).

Information to Include (if applicable)	Details
The severity of the health condition or issue addressed by the innovation	Describe the health condition or issue addressed by the innovation: • The natural progression of the condition, symptoms (if applicable). • The impact of the severity of the condition or problem on mortality, morbidity, and quality of life. • The burden of the condition or problem on the target population.
The target population	Describe the population in Quebec targeted by the innovation (as specified). • Proportion of the population that could have access to the innovation. • Characteristics of the target population: size, gender, age, subpopulations most affected, etc.
Comparator(s)	• Define the current practice in Quebec. • Indicate and justify the choice of comparator(s) (other relevant options available). • Identify the benefits and limitations of the relevant available options.
The extent of the partially met or unmet need	• Describe the unmet need and its significance. • Specify the potential role of the innovation within the care pathway. • Identify the anticipated benefit(s) of the innovation in relation to its intended purpose.

[2] More information on INESSS’s ethical principles and foundations, as well as its policies, guidelines, and processes—including definitions of terminology—can be found on the institute’s website at: https://www.inesss.qc.ca/metho-et-veille/demarche.html

Information to Include (if applicable)	Details
Accessibility[3]	Describe how the innovation will be made available in a timely manner to all those who could benefit from it. • Specify the services offered to affected individuals (through training, patient support, etc.). • Identify the professionals or practitioners who will serve as the interface between the user and the innovation. • Specify how people outside urban areas will have access to the innovation.

☐ Other Documents

- Create an “Other Documents” subfolder if it is necessary to provide additional documents relevant to the evaluation. This is not a requirement of INESSS.

[3] Take into account the social determinants of health, where relevant.

3 CLINICAL DIMENSION[4]

The documents to be provided for the clinical dimension are described in this section. Upon submission, they must be grouped into a subfolder named “Clinical Dimension.”

The materials provided must enable INESSS to understand how the innovation improves the health and well-being of users and their family members or caregivers, while respecting their individual contexts and values. The objective is to provide health and well-being outcomes in terms of efficacy, safety, quality of life, and the experience of care and services for people living with a condition and their family members or caregivers.

☐ Published clinical studies or manuscripts submitted for publication

- Submit at least one randomized, controlled trial that has been published or is available as a manuscript for publication. If no such study is available, please explain why;
- When a clinical study available as a manuscript for publication is submitted with the application, it is the innovator’s responsibility to provide the approximate expected publication date and to forward the official publication as soon as possible.
- In the absence of a study directly comparing the innovation with the most relevant comparator(s), one or more indirect comparisons (Appendix I), whether published or unpublished, must be submitted;
- The following are not eligible:
  - general narrative or editorial-style articles, or author opinions;
  - documents and publications written in a language other than French or English;
  - letters of recommendation from experts;
  - preclinical studies (except for Class I and II devices, as defined by Health Canada).
- Name publication files by including: the title of the document (usually the name of the study), the first author’s name, and the year of publication.

[4] Further information on INESSS’s ethical principles and foundations, as well as its policies, guidelines, and processes—including definitions of terminology—can be found on the institute’s website at: https://www.inesss.qc.ca/metho-et-veille/demarche.html

Example:

1. Study title,_First author's name_Year
2. Study title_First author's name_Year
3. Etc.

- From among the submitted studies, select the most relevant ones—up to a maximum of five—and describe them by filling out the corresponding boxes in the clinical section of the "Summary Description of the Application" form available on the INESSS website under the Non-pharmaceutical Innovations topic (sub-section "Submit an application for evaluation").
- Provide the *Clinical Study Report (*CSR*)* for the main clinical studies that have been published or are available as a manuscript for publication, if applicable. Please create a subfolder named "Clinical Study Report."

Real-World Data

To support the evaluation—whether during an initial evaluation or a reevaluation—you may submit results from real-world studies. Please note that submitting this type of data does not replace the requirement to submit at least one clinical study that has been published or is available as a manuscript for publication.

Additional details regarding the information required when submitting real-world evidence are provided in Appendix II.

☐ Appendices, supplements, errata, or editorials

- Provide the appendices and supplements for all primary clinical studies.
- Provide only errata and editorials related to published primary clinical studies.
- Please clearly identify the documents and place them in a subfolder named "Other Publications."

☐ Posters, abstracts, or oral presentations related to the submitted primary studies

- Submit posters, abstracts, or oral presentations related to the submitted primary studies. Such supporting documents may be submitted only if they are associated with published primary clinical studies (or available as a manuscript for publication). For example, these may include data on quality of life or study extension.
- Please clearly identify the study to which the documents relate and place them in a subfolder named "Posters or Abstracts." Posters and conference abstracts related

to studies that have never been published or that are in manuscript form will not be accepted.

☐ List of clinical studies, published or unpublished, including those currently in progress

- Provide a list of the clinical studies submitted in the application, along with their official or expected publication dates. The following information should be included:
  - start and end dates of the studies;
  - complete references;
  - articles associated with each study;
  - any other relevant information.
- Other publications may be included in the application, such as documents describing the scales and questionnaires used in clinical trials, their validity, and the relevant guidelines.

☐ Health Canada Summary Basis of Decision (class III and IV only)

- Submit the summary of Health Canada's reasons for decision explaining why Health Canada authorized the sale of certain medical devices in Canada at the time of the medical device licence application[5]. If this report is not available at the time of submission, submit it as soon as possible during the review process once it becomes available.
- Include the content of Health Canada's requests for clarification *(Clarimail)*. A summary of the questions and answers may also be submitted.

☐ User Guide

- Submit the official French version of the user guide or, if the French version is not yet available, the English version. In the latter case, submit the French version as soon as possible.
- It is the innovator's responsibility to notify INESSS as soon as possible whenever there is a relevant change to the user guide.

☐ Data Demonstrating the Precision and Accuracy of Results

- Submit the data—whether published or unpublished—reporting the test results corresponding to the applicable ISO standards for these devices, if applicable.

[5] Innovators should contact Health Canada to obtain a copy of this document if they do not already have one.

4 ORGANIZATIONAL DIMENSION[6]

Provide a document presenting the elements related to this dimension in the form of a text with appropriate bibliographic references, titled “Explanatory Document – Organizational Dimension.” Upon submission, it must be placed in a subfolder titled “Organizational Dimension.”

☐ Explanatory Document

- Provide the information necessary to assess the effects of implementing the innovation within Quebec’s health and social services system.
- The information provided by the innovator must enable INESSS to understand how the innovation fits into the organizational context of health and social services in a way that helps strengthen the health and social services system. It must be presented in the form of a text in a document titled “Explanatory Document – Organizational Dimension.”

Elements to Include (if applicable)	Details

The human and material resources required for the implementation and maintenance of the innovation.	These elements may be derived from pilot projects, the innovator’s assumptions, international experiences or implementations, evaluations of similar innovations, etc.
	• Specify whether the innovation requires modifications to the facilities and equipment of the Quebec healthcare network.
	  - If so, explain how (for example, reducing the space required, eliminating step X, integrating the innovation’s alarms into the central care station, etc.).
	• Specify whether the innovation requires staff to use specific equipment (smartphone, tablet, etc.).
	  - If so, does the innovation integrate well with other resources that require the same type of equipment?
	• Indicate the administrative or legislative procedures required for the successful

The learning curve for professionals and/or users (if applicable). *For example, in terms of training and user follow-up procedures.*	
The innovation’s impact on resource allocation. *For example, hospital, medical, and professional resources, or productivity.*	

[6] Further information on INESSS’s ethical principles and foundations, as well as its policies, guidelines, and processes—including definitions of terminology—can be found on the institute’s website at: https://www.inesss.qc.ca/metho-et-veille/demarche.html

	implementation of the innovation within the healthcare network.
	• Specify whether a major reorganization of care and services will be necessary.
	  - If so, what would be the extent of the impact on staff in terms of time, techniques, and the number of people required?
	  - Specify whether professional training is necessary, whether the involvement of other professionals is required (type and number), whether external staff must be mobilized, or whether changes to the care pathway are anticipated.
	• Describe the services offered by the innovator in terms of training, user support services/programs, technical support, and maintenance and/or patient care.
	• Position the innovation within the care and service pathway.
	• Specify whether the innovation is a more user-friendly option.
	• Indicate the potential benefits of the innovation for the organization of care or the health and social services network (reduction of waitlists, increased geographic accessibility, alleviation of the burden on healthcare staff, etc.).

Integration of the innovation into the optimal management or monitoring of the condition	• Are there any practice guidelines, standards, etc., regarding patient follow-up in the context targeted by the innovation? • Does the innovation ensure the continuation of best practices adopted in Quebec? Please explain. • Are there any implementation evaluation data from other jurisdictions?

☐ Other Documents

- Create a subfolder named “Other Documents” if it is necessary to provide additional documents relevant to the evaluation. This is not a requirement of INESSS.

5 ECONOMIC DIMENSION[7]

The documents to be provided for the economic dimension are described in this section. Upon submission, they must be grouped into a subfolder named “Economic Dimension.”

☐ Costs

This document summarizes, in a table, the unit price, the cost of use, or the cost associated with the use of the innovation under evaluation and its comparators.

Important Information to Provide	Details
• Prices and costs (in CAD) for all components of the innovation and its comparators.	• The purchase, rental, or licensing price per unit. If the innovation cannot be defined by a purchase price (such as a procedure, intervention, or program), then an estimate of the human and material resources required to implement it must be provided. • An overview of all costs, including the components necessary for using the innovation. For example, accessories, installation, maintenance, or servicing. • These costs are compared on a common basis or over a common period, such as per cycle, per month, per injection, per treatment, per kilocalorie, per cm^2, etc.
• Characteristics specific to the innovation	• Characteristics of use: - Is it a single-use device? - Will it be reused by multiple people? - What is the expected lifespan of the innovation? • Payment terms regarding the price: - Would the costs of purchasing the innovation be paid as a lump sum each month? - Are there other factors that affect the purchase price or the cost of using the innovation?

- Complete the cost table in the “Summary Description of the Application” form available on the INESSS website under the Non-pharmaceutical Innovations topic (sub-section “Submit an Application for evaluation”).

[7] Further information on INESSS’s ethical principles and foundations, as well as its policies, guidelines, and processes—including the guidelines for the economic evaluation of health and social services interventions and the Glossary of Terms Used in Pharmacoeconomics—can be found on the institute’s website at: https://www.inesss.qc.ca/metho-et-veille/demarche/nos-politiques-lignes-directrices-et-processus.html

- Use the INESSS standard values for weight and body surface area documented in Appendix III. Otherwise, provide an explanation justifying the deviation.

☐ Efficiency Analysis

- Submit at least one efficiency model, based on a published or unpublished study. The purpose of this analysis is to evaluate the efficiency of the intervention under study.
- The study's primary analysis must focus on a relevant comparator and must constitute a standard of care established in clinical practice in Quebec. The preferred comparator is the one that will potentially be replaced or displaced by the innovation being evaluated. This comparator must be the same as the one presented in the requirements for the populational and clinical dimensions.
- Scenario analyses using other relevant comparators may accompany this analysis.
- Provide a functional Excel spreadsheet containing the model, calculations, and results of the economic analysis. If applicable, the embedded macros required for the analysis should be accessible without restriction. Additionally, the spreadsheet must be self-contained and free of all external links (e.g., source of a variable, reference within a macro). INESSS reserves the right to reject an analysis based on another platform.
- Complete the section on the description of the economic study in the "Summary Description of the Application" form available on the INESSS website under the Non-pharmaceutical Innovations topic (sub-section "Submit an application for evaluation").

Special Cases

- *Cost-Consequence Analysis* – If a cost-consequence analysis is submitted and the explanation provided is deemed insufficient to justify the absence of a cost-utility, cost-effectiveness, or cost-reduction analysis, INESSS may request an acceptable cost estimate.
- *Standard Values* – Use the INESSS standard values for weight and body surface area documented in Appendix III. Otherwise, provide an explanation justifying the deviation.
- If it is not possible to provide a cost-utility analysis for the subject of the evaluation, an explanation must be provided to justify its absence.

The elements listed below must be clearly explained and supported in the submitted analysis or in the explanation provided:

- type of analysis;
- objective, context, and target population;

- comparator;
- perspective;
- sources of inputs;
- time horizon and discount rate;
- outcome measure and implications of uncertainty.

☐ Budget Impact Analysis

- Provide a budget impact analysis. The purpose of this analysis is to estimate the effect of the changes anticipated by public coverage of an innovation on the budget of the Ministry of Health and Social Services. These changes between the *status quo* scenario and the public coverage scenario may result in additional costs or cost reductions (savings). The elements listed below must be clearly explained and supported in the submitted analysis.
- Provide a functional Excel spreadsheet containing the calculations and results. Where applicable, the embedded macros required for the analysis should be accessible without restriction. Additionally, the file must be self-contained and free of any external links (e.g., source of a variable, reference within a macro). All references cited and used to support the analysis's assumptions must be listed.
- Complete the table of key assumptions for the budget impact analysis results in the "Summary Description of the Application" form available on the INESSS website under the Non-pharmaceutical Innovations topic (sub-section "Submit an application for evaluation").

The elements listed below must be clearly explained and supported in the submitted study:

- the target population for the innovation being evaluated;
- the time horizon, discount rate, and perspective;
- market size, methodological approaches, and projections;
- market shares and their sources;
- the estimated market shares for the innovation under evaluation and their sources;
    - If the innovation is already funded by other governments in Canada or elsewhere in the world, please provide the estimated (in Quebec) or actual (in other jurisdictions) market shares for the target population.
- the costs of the innovation, its comparators, and the costs associated with treating the targeted medical condition;
- deterministic sensitivity analyses as well as supplementary analyses, where relevant.

The results of the budget impact analysis must be presented in 12-month periods and for the total number of years, from the perspective of the Ministry of Health and Social Services. At a minimum, three types of results must be highlighted in a table:

- Gross budget impact: corresponds to expenditures related to the acquisition of the innovation, regardless of the consequences on other expenditures. In the case of combination therapy, this impact must be broken down.
- Market uptake: corresponds to the anticipated number of distinct patients treated with the evaluated innovation or the anticipated number of units used.
- Net budget impact: corresponds to the budgetary impact, i.e., the difference between the current situation and the actual situation, taking public coverage into account.
- Use the INESSS standard values for weight and body surface area documented in Appendix III. Otherwise, provide the reasons justifying the deviation.

6 ETHICAL AND ENVIRONMENTAL ASPECTS - OPTIONAL

The inclusion of ethical and environmental considerations in the submission guidelines is part of an effort to support the evolution of practices and promote continuous improvement. These are cross-cutting aspects that complement the multidimensional approach to value assessment. Submitting documentation related to these two areas is optional but may enable INESSS to identify potential courses of action related to these two areas.

To submit materials related to ethical and environmental aspects, provide a document (optional) in the form of a text with appropriate bibliographic references and titled “Explanatory Document—Ethical and Environmental Considerations.” Upon submission, it must be placed in a subfolder titled “Ethical and Environmental Considerations.”

Ethical Considerations

The items suggested in this table are provided for guidance only and do not constitute an exhaustive list; other ethical considerations may apply to certain evaluation subjects.

Items to Include (if applicable)	Details
Autonomy and Consent	• Explain how the innovation or its use respects the autonomy of users and those who benefit from it. • Indicate how the free and informed consent of users and those who benefit from the innovation is obtained.
Justice and Equity	• Describe the laws, rules, principles, and standards of Quebec society that apply to the innovation and the measures put in place to comply with them. • Specify whether the innovation helps address issues of inequity. • Explain how the innovation affects the distribution of resources within Quebec society.
Privacy and Data Confidentiality	• Outline the measures put in place to ensure the protection and confidentiality of data used in innovation.

Environmental Considerations

Items to include (if applicable)	Details
Sustainability	• Provide the information necessary to assess the lifespan of the innovation and its various components. • Indicate where the various components of the innovation are manufactured.
Energy Consumption	• Describe the energy consumption required to ensure the innovation functions properly for each use or over a given time period (day, month, year).

	• Specify the energy source (electricity, solar cells, lithium batteries—rechargeable or non-rechargeable, etc.).
Carbon Footprint	• Specify whether the use of the innovation results in greenhouse gas emissions. • Specify whether the innovation requires the use of a cloud data center. • Provide, if available, data on the carbon footprint associated with the manufacturing of the innovation.
Waste Management	• Identify the types of waste generated by the use of the innovation and specify whether they can be recycled or reused. • Describe how the innovation's components are managed throughout its life cycle (reuse, refurbishment, repair, recycling, disposal, etc.). • Indicate whether the use of the innovation involves the release of harmful, toxic, or hazardous materials.
Resource Use	• Indicate the resources required for the manufacture or use of the innovation (land, wood, water, minerals, metals, fossil fuels, etc.).

APPENDIX I

Methodological aspects regarding indirect comparisons

In the case of an unpublished indirect comparison, provide the complete report of that comparison. It is desirable that:

- The rationale and objectives of the indirect comparison be explicitly stated and justified
- A systematic review justifying the comprehensiveness and relevance of the selected studies, the comparability of their characteristics, the identification of the selected interventions, the feasibility of the indirect comparison, and the appropriateness of the chosen method
- The network of interventions be presented and justified
- The results of the assessment of the validity conditions of the indirect comparison be explicitly presented
    - Homogeneity within each comparison in the network
    - Transitivity
    - Consistency, where applicable.
- The methods used to perform the statistical analyses should be justified (primary and sensitivity analyses)
- Heterogeneity among studies evaluating the same comparison should be quantified, explored, and explained through subgroup analysis or meta-regression.
- The results of the primary analyses should be presented in the form of text, figures, and tables
- The results of sensitivity analyses should be presented to demonstrate the robustness of the selected results.
- Methodological limitations and their impact on the selected results should be explicitly described.
- An interpretive conclusion regarding the results selected for the indirect comparison should be presented in a nuanced manner, taking into account the described methodological limitations.
    - For informational purposes, upon publication of the opinion, INESSS's analysis and assessment of the indirect comparison will be published. However, quantitative data will be redacted.
- In the case of a published indirect comparison, provide the publication and its supplements.

If an indirect comparison would be relevant but is impossible to conduct, provide an explanation documenting the factors that justify the inability to perform such a comparison. If, during the evaluation, INESSS determines that the explanation provided is insufficient, a request may be made to the innovator to obtain such a comparison.

APPENDIX II

Real-World Data

The following are examples of characteristics common to real-world data.

Data Sources
Records
Data collected as part of a randomized pragmatic trial
Medical-administrative databases
Electronic medical records
Billing database

Methodological approaches	
Observational designs	Experimental designs
Cohort studies	Cluster-Randomized Trials
Case-control studies	Non-randomized comparative studies
Before-and-after studies	

Real-world studies can provide additional information to pivotal clinical trials or shed light on uncertainties and concerns that exist or were raised by INESSS during a previous evaluation.

Along with these studies, the following items must be submitted:

- A description of the context for submitting real-world evidence;
    - A clear justification of the need to use real-world data and how the evidence compares to other submitted studies;
- A report including the following information, as applicable, based on the study protocols and data sources:
    - the research question;
    - the target population and its representativeness relative to the Quebec population;
    - the data source used;
    - a description and definition of key elements—such as measures of exposure and outcomes, and potential confounding factors;
    - inclusion and exclusion criteria;

    - the characteristics of the included patients;
    - the methodology describing how the data were collected, processed, transformed, and matched, if applicable;
    - the statistical plan;
    - sources of potential bias and how these biases were mitigated.

If certain information cannot be provided, a justification is required.

- Study protocol, whether published or unpublished, if available.

APPENDIX III

Standard values for weight and body surface area adoptedd by INESSS

Where applicable and by convention, the weight and body surface area indicated below must be used. Different values may be used provided justification is provided.

Target population	Body weight[a]	Body surface area[a]
Women/Men	76 kg	1.85 m^2
Women only	69 kg	1.72 m^2
Men only	84 kg	1.98 m^2
Infants and young children	On a case-by-case basis, depending on the medical condition, age at diagnosis, and the timing of treatment initiation.	

a Although other characteristics of individuals exposed to the treatment influence the estimation of these average values, only age and sex were considered. These averages are estimated using Quebec-specific microdata from the Canadian Community Health Survey (CCHS) – Nutrition 2015.

APPENDIX IV

Folder Structure of an application

The following folder structure is a simplified example of an electronic file submitted to INESSS for evaluation. Please avoid creating multiple nested subfolders.

1- **Administrative Section**
   a. Cover Letter
   b. Form *Application for Evaluation of a Non-Pharmaceutical Innovation*
   c. Medical Device Licence
   d. *Information Sharing Authorization* Form
   e. Form: *Summary Description of the Application*

2- **Population-Based Dimension**
   a. Explanatory Document for the Population Dimension

3- **Clinical Aspect**
   a. Published Clinical Studies
      i. Study AB003_Caron et al. 2024
      ii. Study AB002_Caron et al. 2022
      iii. Study AB001_Caron et al. 2021
      iv. Study CD002_Caron et al. 2019
      v. Study CD001_Caron et al. 2018
      vi. Full Clinical Study Report (CSR) for the pivotal study
         1. CSR_Study AB003
         2. CSR_Study AB003_Statistical Analysis Plan (SAP)
      vii. Indirect comparison
      viii. Other relevant publications (if applicable)
   b. Appendices, supplements, errata, or editorials
   c. Posters, abstracts, or oral presentations related to the main studies
      i. Caron 2022
      ii. Caron 2021
   d. List of published and unpublished clinical studies
   e. Clinical Executive Summary
   f. Health Canada Summary Basis of Decision (Class III or IV only)
   g. User Guide

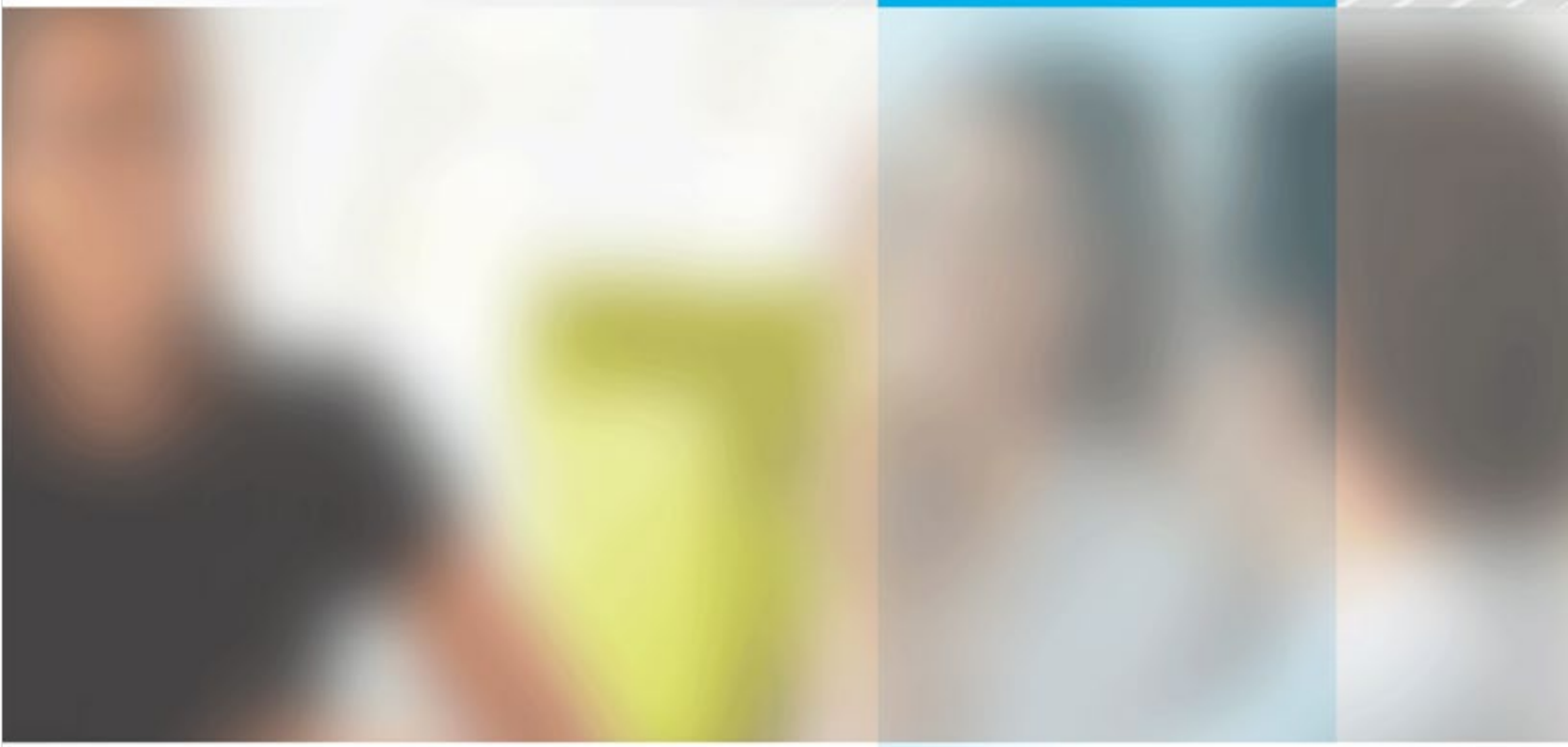
4- **Organizational Dimension**
   a. Explanatory document for the organizational dimension

5- **Economic Dimension**
   a. Costs
   b. Economic Study
      i. Analysis.pdf
      ii. PE.xls spreadsheet
      iii. PE References
   c. Budget Impact Analysis

i. Budgetary Impact.pdf
ii. Budgetary Impact.xls

6- Ethical and Environmental Aspects

a. Explanatory Document on Ethical and Environmental Aspects



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