Health Canada Santé Canada

Guidance on expanded access clinical trials

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Canada

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Foreword

Guidance documents provide assistance to industry and health care providers on how to comply with governing statutes and regulations. They also provide guidance to Health Canada staff on how mandates and objectives should be met fairly, consistently and effectively.

Guidance documents are administrative, not legal, instruments. This means that flexibility can be applied. However, to be acceptable, alternate approaches to the principles and practices described in this document should be supported by adequate justification. They should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As always, Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, to help Health Canada adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read along with the relevant sections of the Food and Drug Regulations and other applicable policy and guidance documents.

This document may be updated in the future to align with any future changes made to the Food and Drugs Act or its regulations.

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1 Overview

1.1 Purpose, scope and application

The *Food and Drug Regulations* (the Regulations), made under the authority of the *Food and Drugs Act* (Act), govern the sale and importation of drugs for use in human clinical trials in Canada, including expanded access clinical trials. This guidance document explains the regulatory requirements for expanded access clinical trials. These requirements are supported by Part C, Division 5 of the Regulations, which pertain to drugs for clinical trials involving human participants.

This guidance document is meant for **sponsors**, health care providers and potential participants who are interested in, involved in, or participating in expanded access clinical trials involving sites in Canada.

- **For potential participants, this document:**
    - provides information to support access to **investigational drugs** through an expanded access clinical trial when appropriate
- **For sponsors and health care providers, this document:**
    - provides supplemental information on the requirements to conduct an expanded access clinical trial in Canada
    - clarifies the application and post-authorization requirements
    - outlines procedures for obtaining authorization for expanded access clinical trials in Canada

Sponsors should also consult other relevant policy and guidance documents, such as:

- Guidance document for clinical trial sponsors: Clinical trial applications
- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2022)

1.2 What is an expanded access clinical trial

In Canada, an **expanded access clinical trial** is a type of clinical trial that provides access to investigational drugs that have the potential to treat people living with medical conditions who do not qualify for other clinical trials or are not able to participate in one. “Investigational drugs” are pharmaceutical, biologic, and radiopharmaceutical drugs for human use that are tested or studied in a clinical trial. Please note that clinical trials involving natural health products, veterinary drugs, and medical devices are excluded from the scope of this guidance document.

When appropriate, expanded access clinical trials can utilize more flexible protocols and a decentralized model to facilitate access for a larger, potentially more diverse population of participants, in more accessible settings.

Expanded access clinical trials can sometimes help to facilitate access to drugs before they have been authorized for sale by Health Canada, with adequate justification of expected benefits versus risks to participants. This could include, for example, but not limited to: drugs for some mental health disorders or serious or life-threatening conditions where authorized alternatives may be limited for certain patients.

Since it is a type of clinical trial, an expanded access clinical trial intends to:

- discover or verify the clinical, pharmacological, and pharmacodynamic effects of the drug
- identify any **adverse events** resulting from the drug
- study the absorption, distribution, metabolism, and excretion of the drug **and/or**
- assess the drug's safety or efficacy

1.3 Key points

Since expanded access clinical trials are a type of clinical trial under Part C, Division 5 of the Regulations, they require the completion of a clinical trial application (CTA), for review by Health Canada. In their applications, sponsors must provide evidence from previous studies to demonstrate that the proposed use of the investigational drug would not endanger the health and safety of participants.

CTAs for expanded access clinical trials follow the same review processes and timelines as other clinical trials, as outlined in C.05.006 of the Regulations. Currently, this includes a review period of about 30 days from the date of receipt of the complete application. Our scientists and physicians review applications to assess whether:

- the risks in using the drug in the trial are considered and would not endanger health and safety
- the best interests of those taking part in the trial have been considered, including that drugs are used in the right way for the participants being studied
- the goals of the trial can be met

All CTAs are assessed on a case-by-case basis.

Learn more about the CTA process.

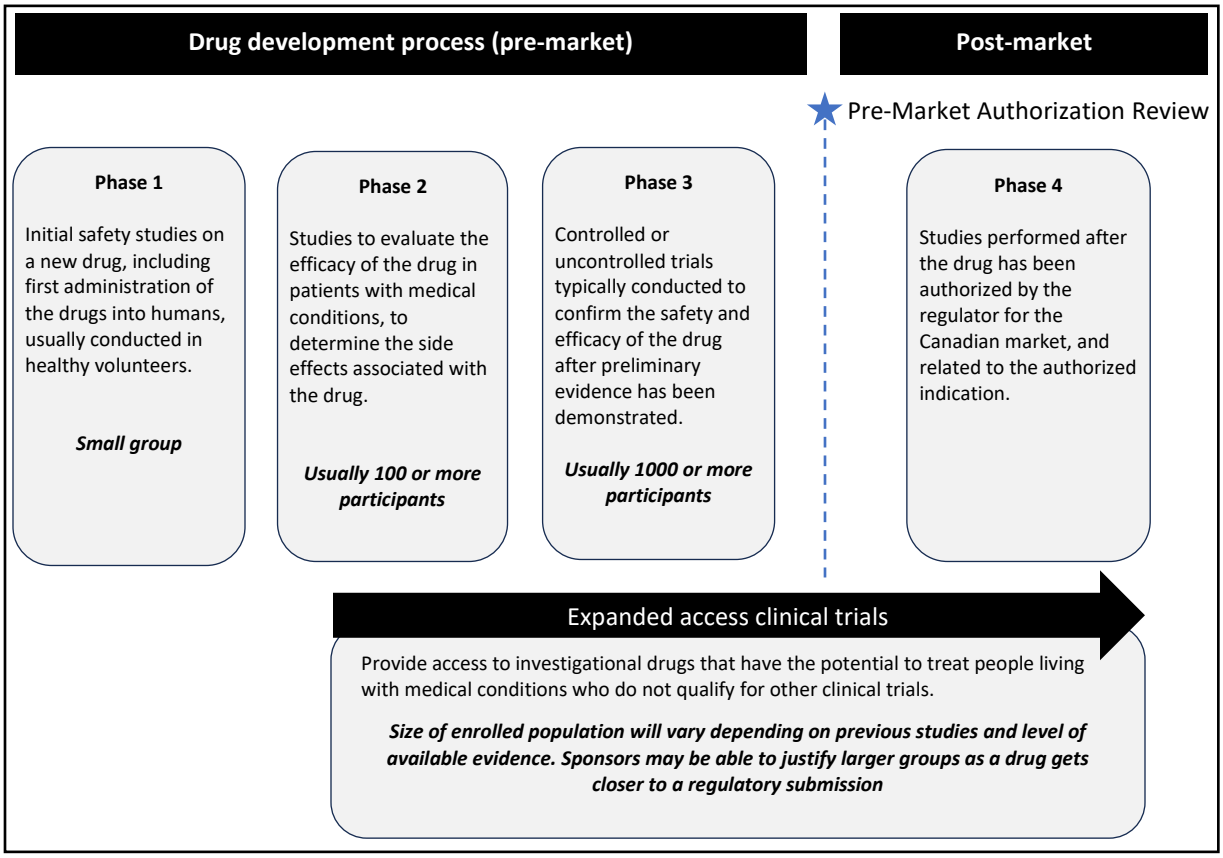
Using the clinical trials framework to provide expanded access in Canada enables access to investigational drugs while providing safeguards and requirements to protect the health and safety of participants. As stated in C.05.010 of the Regulations, sponsors must ensure that an expanded access clinical trial is conducted in accordance with **good clinical practices**. The rights, safety and well-being of participants are to be protected in accordance with these principles.

Please refer to the International Council for Harmonisation's E6 guideline for good clinical practice to learn more about some of the participant protection mechanisms in clinical trials, as well as the E19 guideline to learn more about safety monitoring and safety data collection.

1.4 Background

As development of the drug progresses, the goal of late-phase (phases 2 and 3) clinical trials is usually to gather evidence that meets the standards required by drug regulators (Figure 1).

Figure 1: Types of clinical trials



Late-phase clinical trials aim to show a statistically conclusive effect on a specific outcome of interest by setting specific criteria for who can and cannot participate.

These controls help protect the safety of participants and make it more likely that the results will lead to reliable and useful findings. But this also means that not everyone will get to participate in a clinical trial if:

- they do not meet the eligibility criteria (the requirements that must be met in order for a person to be included in the study)
- their disease has progressed too far
- they live too far from study sites
- there are no available clinical trials, or ongoing trials are either not recruiting or are in the process of closing

In such cases, potential participants might be able to receive investigational drugs through an expanded access clinical trial. Expanded access clinical trials provide access to investigational drugs that have the potential to treat people living with medical conditions who do not qualify for other clinical trials or are not able to participate in one. They can be designed to facilitate access for a larger, potentially more diverse population of participants, in more accessible settings.

As with other clinical trials, the sale or importation of a drug for an expanded access clinical trial is authorized under Part C, Division 5 of the Regulations. Sponsors of expanded access clinical trials must protect participants in accordance with ethical, medical and quality standards of the clinical trials framework.

Sponsors may propose an expanded access clinical trial before or after market authorization. However, an expanded access clinical trial should only be conducted for drugs that are being (or have been) actively studied in Canada or other countries. A prior clinical trial is not required to have been conducted in Canada.

There must be a strong rationale for initiating an expanded access clinical trial that provides access to a drug before it has been authorized for sale by Health Canada. For example, an expanded access clinical trial could enable access to a drug for a specified population or new indication while a regulatory submission is under review by Health Canada. As part of their rationale, sponsors may refer, for example, to the severity of the condition, lack of available alternatives, or possible increased benefits or decreased risks compared to existing authorized products.

Other examples of when a sponsor may find it useful to conduct an expanded access clinical trial:

- when a sponsor wants to open an arm of an international expanded access program in Canada
- when a traditional clinical trial is unavailable in Canada but there is evidence from international studies to support investigation of and access to the drug in Canada
- when a sponsor wants to study the effects of a drug in a broader, more diverse population (can be before or after market authorization)
- when a sponsor wants to study the long-term effects of a drug in conditions more aligned with the real world

To conduct an expanded access clinical trial, sponsors are expected to provide evidence from other studies in the CTA. This information can help demonstrate that the investigational drug will not endanger the health and safety of participants, and may be beneficial in treating the specific disorder in the population being studied.

Expanded access clinical trials also require an **investigator's brochure** specific to the investigational product proposed for this type of trial.

Learn more about the type of information that should be submitted in a CTA.

1.4.1 Comparisons to the Special Access Program and other types of clinical trials

Expanded access clinical trials are distinct and separate from Health Canada's Special Access Program (SAP). Through the SAP, health care professionals may request access to drugs that are not currently authorized for sale in Canada to treat individual patients with serious or life-threatening conditions. Access to these drugs may be considered when conventional therapies have failed, are unsuitable, or are unavailable. Unlike expanded access clinical trials, which have overarching research objectives, SAP is a patient-focused program that provides exceptional access to unauthorized drugs for individual patients in emergency medical situations.

Learn more about SAP and its requirements.

Please note that expanded access clinical trials are not meant to restrict access to other programs or avenues like SAP. SAP is intended for patients in emergency medical situations. Expanded access clinical trials could be helpful for groups of patients looking for longer-term treatment options for serious but not immediately life-threatening conditions, or where other approved alternatives exist.

Expanded access clinical trials are also different from other types of clinical trials, such as extension studies, open-label individual patient clinical trials, and seeding trials:

- **Extension studies**: In contrast to expanded access clinical trials that allow for the recruitment of new participants who may not have participated in any prior clinical trials, extension studies (also known as extended trials) are associated with a particular prior trial. Extension studies are typically designed to allow participants of a prior trial to continue receiving the drug in a second related study and the sponsor can investigate long-term outcomes. They can allow participants to continue accessing an investigational drug after a prior trial is completed and closed. This can be important in situations where discontinuing access to the investigational drug may adversely affect participants.
- **Open-label individual patient (OLIP) clinical trials**: An OLIP clinical trial (also sometimes referred to as a "single patient study") is a type of clinical trial designed for individual participants only. These trials provide access to an unauthorized drug for a participant suffering from a serious or life-threatening condition. In contrast, expanded access clinical trials:
    - can be designed for a broader, expanded population of participants,
    - may be a better option for managing exceptional access for large groups of participants, **and**
    - may generate more useful evidence given the larger sample size.
- **Seeding/marketing trials**: Seeding trials are more common in the United States, and have been described as clinical trials designed to promote the use of recently approved drug therapies among health care providers. They are typically designed to fulfill marketing objectives and are unlikely to generate scientific evidence. Unlike seeding trials, which occur after market authorization, expanded access clinical trials can occur during the drug development process and must include research objectives. Because seeding trials occur after market authorization, they do not require a clinical trial application to be submitted to Health Canada, as long as the purpose and condition of use align with the market authorization.

While public-facing guidance does not currently exist on the above types of clinical trials, all clinical trials with unauthorized drugs must follow the same procedures and requirements outlined in Part C, Division 5 of the Regulations. For more information on these requirements, please see the guidance document for clinical trial sponsors: clinical trial applications. Individuals interested in learning more about the different types of clinical trials can reach out to the Office of Clinical Trials at Health Canada (see contact information).

1.5 Expanded access clinical trials: Special considerations

As expanded access clinical trials provide access to unauthorized drugs to a broader group of potential participants, they carry unique risks compared to other types of clinical trials.

Sponsors should ensure that expanded access clinical trials do not:

- expose a broader participant population to unjustified risks associated with investigational drugs
    - These investigational drugs have not yet undergone regulatory review for market authorization by Health Canada. For this reason, their efficacy and safety have not been fully evaluated. Sponsors should provide evidence from completed or ongoing clinical trials or other studies to demonstrate that benefit of the investigational drug in a proposed expanded population outweighs possible risks to the health and safety of participants. Sponsors should also continue to monitor the health and safety of participants as the trial progresses.

- impede the clinical development of the drug in Canada
    - There is a risk that these types of trials could divert participants or supply from a confirmatory clinical trial (a trial that generates statistically conclusive evidence of the drug's efficacy and safety). Sponsors should assess and explain how providing the drug in an expanded access clinical trial could potentially interfere with clinical development in Canada.
- enable broad market access prior to market authorization
    - Broad market access to a drug should only occur after Health Canada has reviewed the drug's safety, efficacy and quality evidence and authorized its sale in Canada. Sponsor **protocols** should define the Canadian participant population, timelines for bringing the drug to market, and how access will be limited to those in exceptional need.

Sponsors of expanded access clinical trials must meet all applicable regulatory requirements in their CTA and provide specific information in their protocol on these potential risks. See the section on addressing unique risks for more information.

2 Information for potential participants

2.1 General considerations

Clinical trials are investigations that help advance medical knowledge, to try and find out whether a drug is safe and effective in humans for a specific disease or condition. They are essential to develop scientific evidence about a therapeutic product that can potentially improve the quality of life for people living with a disease or condition.

For more information on clinical trials generally, please visit Health Canada's website:

- Clinical trials and drug safety - Canada.ca

While clinical trials may provide access to an investigational drug for some participants, their main purpose is to answer a specific scientific/research question. To achieve this objective, clinical trials should be rigorously designed with appropriate measures. For example, to participate in a traditional clinical trial, a potential participant may be required to live near the trial site or only have one condition or disease. These trials may also result in some participants receiving a **placebo**. Strict controls typically result in certain potential participants being excluded from a clinical trial or from receiving the drug as part of a trial. Therefore, participation in a clinical trial does not always result in a participant gaining access to the investigational drug.

Expanded access clinical trials facilitate access to investigational drugs for people living with medical conditions who cannot participate in other clinical trials; they may allow for a wider and more diverse range of participants in more accessible settings. In general, expanded access clinical trials have broader research objectives, such as studying long-term safety and effectiveness in more diverse populations. They can aim to gather information about rare side effects that may only become evident in an expanded participant population.

Despite the expanded eligibility criteria, it's possible that some people may still not be considered eligible to participate in an expanded access clinical trial.

2.2 Benefits and risks

After considering treatment options that are available on the market, people with medical conditions may choose to explore investigational drugs as potential treatments for their condition.

Investigational drugs used in expanded access clinical trials come with possible benefits and risks. In general, there is less information about the efficacy and safety of an investigational drug compared to a drug that Health Canada has reviewed and authorized for sale.

Evidence to demonstrate a drug's safety and efficacy can vary depending on whether it's in the early or later phase of development. The drug may ultimately prove to be of no benefit to a particular participant or may be associated with unexpected and serious adverse effects. For a variety of reasons, only some drugs that begin clinical trials are eventually granted market authorization.

Potential participants who wish to enrol in an expanded access clinical trial to gain access to an investigational drug should be informed of the risks and potential benefits by the trial **sponsor**. The *Food and Drug Regulations* require clear communication to potential participants about the health and safety risks and potential but unconfirmed benefits. Potential participants must give their informed consent before they can participate in a trial.

Learn more:

- Informed consent
- Clinical trials and drug safety

2.3 How sponsors initiate expanded access clinical trials

There is no requirement for a drug manufacturer to provide access to their investigational drug through an expanded access clinical trial. Health Canada cannot compel a drug manufacturer to do so.

Sponsors (often the drug manufacturer) may initiate expanded access clinical trials when there is an identified need for people living with medical conditions who are unable to participate in ongoing clinical trials. Sponsors would then develop a **protocol** that outlines the investigational plan. This plan would include criteria for participant eligibility, treatment administration, monitoring outcomes and participant safety, and collecting data. The sponsor would then submit this protocol to Health Canada for review by filing a clinical trial application (CTA).

Health Canada reviews CTAs for expanded access clinical trials like any other clinical trial. The information is reviewed to make sure that:

- the investigational drug will be used in a safe way for the proposed participants **and**
- any health and safety risks associated with the drug will be addressed appropriately

Health Canada also reviews evidence provided by the sponsor from previous clinical trials or other studies. The sponsor must demonstrate that the proposed use of the investigational drug in an expanded population will not endanger the health and safety of participants. Sponsors of expanded access clinical trials are expected to also provide specific information in their CTA that will allow Health Canada to thoroughly assess the unique risks of the trial in an expanded population.

This could affect how sponsors define participant eligibility. For example:

Potential participants may be:

- required to be diagnosed with a certain condition to be included
- required to have tried other available alternatives or
- excluded based on safety reasons (for example, potentially dangerous interactions with other drugs)

Potential participants who qualify for an ongoing confirmatory clinical trial may:

- not be permitted to enrol in an expanded access clinical trial
- be invited to enrol in an ongoing confirmatory clinical trial instead of an expanded access clinical trial

If the CTA meets regulatory requirements and is deemed acceptable, Health Canada issues a No Objection Letter to the sponsor within the review period of 30 days. The clinical trial site must also be approved by a **research ethics board** (REB), and the Clinical Trial Site Information (CTSI) form filed with Health Canada, before the sponsor can begin enrolling participants at the site.

2.4 Finding, joining and participating in a clinical trial

2.4.1 How to find a trial

Individuals can search Health Canada's Clinical Trials Database for information about ongoing, pending, and closed clinical trials that have met regulatory requirements. This includes the status of any clinical trial for a certain medical condition or a specific drug product.

Potential participants may find a clinical trial for their condition by searching for a specific drug or searching for their medical condition. If an individual wants to specifically look for an expanded access clinical trial, they can type the word “expanded” into the protocol title box under the search criteria (sponsors are asked to include the words “expanded access” in their protocol title to help potential participants identify the type of trial).

Many hospitals, health charities, patient organizations and other not-for-profit organizations such as provincial clinical trial organizations also have links to clinical trials or “finders” on their websites. Potential participants are encouraged to utilize these websites in addition to the Clinical Trials Database to search for available clinical trials.

Health Canada does not sponsor or design clinical trials, and the Clinical Trials Database is not a recruitment tool. Individuals who want more information on clinical trials found in the database should contact the clinical trial sponsor and speak to a health care provider (if possible).

If there isn't a clinical trial available in Canada for a specific drug or condition, individuals could contact a drug manufacturer or other potential sponsor to ask them to consider initiating one. Health Canada cannot compel a sponsor to come forward with a clinical trial application.

2.4.2 Joining a trial

If an individual finds a pending or ongoing clinical trial that interests them, they may contact the sponsor directly to start the screening and enrolment process. The sponsor of the clinical trial should also be contacted for more information about a trial's objectives, participant enrolment criteria, potential clinical trial sites and to confirm the status of the trial. If contact information for the sponsor is not provided on the Clinical Trials Database, individuals may need to find the information through the sponsor’s website.

A sponsor sets out the eligibility criteria for enrolling in an expanded access clinical trial.

Potential participants may be excluded due to potential safety risks posed by existing conditions or dangerous interactions with other drugs, or if they have not tried other available treatments. Sponsors establish these criteria to mitigate the risks posed by the investigational drug.

After a potential participant has contacted the sponsor of the expanded access clinical trial, they may be screened for enrolment. The sponsor makes the final determination on who is enrolled in an expanded access clinical trial, based on the eligibility criteria.

If there is a confirmatory clinical trial going on at the same time as the expanded access clinical trial for the same drug and medical condition, sponsors may encourage potential participants to enrol in the ongoing confirmatory clinical trial first, before they can be considered for enrolment in the expanded access clinical trial. Enrolment in a different clinical trial instead of the expanded access clinical trial could still potentially give participants access to the investigational drug.

2.4.3 Giving informed consent

Sponsors are expected to obtain informed consent from potential participants who are deemed eligible for an expanded access clinical trial.

In the clinical trial context, ‘informed consent’ means that a potential participant is willing to participate in a specific trial, after having been fully informed about the trial and given the opportunity to ask questions. The process of obtaining consent for a clinical trial usually involves a face-to-face meeting or communication between the **Qualified Investigator** (or other authorized individuals) and the potential participant.

In some cases, the sponsor may be able to justify conducting the informed consent process through a virtual meeting platform. This should take place in real-time and face-to-face, using both audio and video.

Sponsors should ensure potential participants:

- are fully informed of all aspects of the trial that are relevant to their decision on whether to participate, including potential indemnity coverage if they are harmed during the trial
    - this is documented in an informed consent form (developed by the sponsor and reviewed and authorized by a research ethics board)
- know who to contact if they have questions about the research or how to end their participation in the clinical trial
- have a 24-hour contact number or know who to contact if they experience a research-related injury (for example: local health care provider, Qualified Investigator, research personnel)
- know who will have access to their personal health information collected during the study and how it will be collected, stored, and used
- have a written record of their informed consent, which the Qualified Investigator should also retain

In addition to the above information, sponsors should answer any questions potential participants may have about participating in the clinical trial before they agree to participate.

Potential participants are encouraged to consult with a health care provider (if possible) and/or someone they trust to carefully consider and weigh the:

- potential benefits and risks of an unapproved investigational drug **and**
- possible harms and inconveniences of participating in a clinical trial

3 Information for sponsors and health care providers

3.1 General considerations

Drug manufacturers: Drug manufacturers who want to market their drug in Canada must first file an appropriate drug submission for their product. Drug manufacturers can decide to provide (or not) potential access to investigational drugs through an expanded access clinical trial.

Who can sponsor an expanded access clinical trial: The *Food and Drug Regulations* (the Regulations) define a sponsor as "an individual, corporate body, institution or organization that conducts a clinical trial". The sponsor is not required to be the drug manufacturer; however, a manufacturer would always be involved in an expanded access clinical trial, at the very least as the supplier of the investigational drug.

Sponsors of expanded access clinical trials may have, but are not required to have, conducted a prior clinical trial for the chosen investigational drug.

Benefits of running an expanded access clinical trial: In addition to providing participants with access to investigational drugs, these trials may help sponsors:

- develop a better understanding of long-term safety, tolerability and rare adverse events, to support proactive safety labelling
- generate complementary data and evidence in settings more aligned with the real-world

For more information, see the section below on Evidence generation and data reliability.

Risks of expanded access clinical trials: Expanded access clinical trials should not displace, affect or discourage confirmatory clinical trials from taking place, as confirmatory trials generally aim to generate evidence required for market authorization. For example, sponsors should not:

- divert the supply of investigational drugs to an expanded access clinical trial to the detriment of a confirmatory clinical trial
- make it difficult to recruit participants in a confirmatory trial (the use of controls and possible placebos may sway participants towards expanded access clinical trials instead) **or**
- use evidence from expanded access clinical trials to supplement ambiguous data obtained through confirmatory clinical trials

For these reasons, sponsors must account for how they plan to continue any planned or ongoing confirmatory trials as part of their clinical trial application. This is described in the Addressing unique risks section.

Patient-focused drug development: Health Canada supports the International Council for Harmonisation's Reflection Paper on Patient-Focused Drug Development. Where possible, sponsors should involve participants, family members, or caregivers in the design and conduct of expanded access clinical trials.

Indigenous participation: Sponsors of expanded access clinical trials should carefully consider how to adapt trial protocols to enable Indigenous participation. For example, sponsors should consider:

- training and education requirements for Indigenous Peoples who are involved in organizing expanded access clinical trials and non-Indigenous sponsors looking to work with Indigenous Peoples and communities
- indemnity coverage for Indigenous people who are already disadvantaged by inequities in the health care system

- seeking and obtaining prior approval through local and territorial groups before undertaking research on Indigenous land or with Indigenous participants **and**
- how personal health data can be properly collected, stored, and used

For more information on conducting research with Indigenous peoples:

- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2022) – Chapter 9: Research Involving the First Nations, Inuit, and Métis Peoples of Canada

3.2 Authorizing an expanded access clinical trial

Expanded access clinical trials can be initiated when a sponsor submits a clinical trial application (CTA) or an amendment (CTA-A) to an existing clinical trial and receives a No Objection Letter, pursuant to section C.05.006 or C.05.008 of the Regulations, respectively.

In cases where an international expanded access program is seeking to open an arm in Canada, they would need to be opened in Canada as expanded access clinical trials, and sponsors would need to submit a new CTA or CTA-A. For more information, see the section on how to open arms of international expanded access programs in Canada.

As stated in the Regulations, sponsors of all clinical trials are expected to provide information and documents as part of their CTA or CTA-A. This information must be sufficient for Health Canada to assess the risks and benefits of the drug and the trial.

Sponsors of expanded access clinical trials are expected to provide in their CTA or CTA-A evidence from previous studies to demonstrate that use of the investigational drug is justified:

- for expanded access
- in an expanded study population

These previous studies may be conducted by the same or other sponsors.

Sponsors are expected to submit robust evidence in their CTA or CTA-A; however, it is recognized that the amount of evidence available for reference in the CTA may depend on the population under study. For example, evidence may be limited in certain areas that are more challenging to investigate, such as in the areas of rare diseases and paediatrics.

A CTA for an expanded access clinical trial is the same as a CTA for any other clinical trial, and is typically composed of three parts (modules):

- Module 1 - contains administrative and clinical information about the proposed trial
- Module 2 - contains Quality (Chemistry and Manufacturing) summaries about the drug product(s) to be used in the proposed trial, **and**
- Module 3 - contains additional supporting Quality information

A CTA-A would mostly contain Module 1 information, but any changes to the quality information would require additional Module 2 and 3 information as well.

To learn more about the different modules of information in a CTA and CTA-A, consult the guidance on submitting clinical trial applications.

If the CTA or CTA-A meets regulatory requirements and is deemed acceptable, Health Canada issues a No Objection Letter to the sponsor within the review period of 30 days. The clinical trial site must also be approved by a **research ethics board** (REB), and the Clinical Trial Site Information (CTSI) form filed with Health Canada, before the sponsor can begin enrolling participants at the site.

More information on CTSI forms:

- Section 2.7.3 of the guidance on clinical trial applications
- Instructions for completing a CTSI form

A qualified investigator requiring a controlled substance for research purposes, which includes administration to humans in an expanded access clinical trial, must also receive an authorization from Health Canada's Office of Controlled Substances. This occurs after a No Objection Letter for the expanded access clinical trial or sub-study has been issued by Health Canada. More information on launching an expanded access clinical trial with controlled substances can be found in this section.

3.2.1 Considerations for filing a clinical trial application or amendment

Whether the sponsor should submit a CTA or a CTA-A will depend on the situation and context for the expanded access clinical trial.

Scenario A: In cases where there is no ongoing clinical trial in Canada for the chosen investigational drug and indication

In this case, sponsors of the expanded access clinical trial would be required to submit a **new CTA**. The requirements for a new CTA are outlined in the Regulations, as well as in the guidance document on CTAs.

Scenario B: In cases where a prior clinical trial exists for the drug and indication, but is/was led by a different sponsor

In this case, sponsors of the new expanded access clinical trial would be required to submit a **new CTA**, but could seek authority to cross-reference their application with the Drug Master File of the prior clinical trial. Cross-referencing could support the new sponsor's CTA, and may allow the new sponsor to reference additional information and analysis produced by the other clinical trial. See the section in the guidance on CTAs on cross-referencing a Drug Master File and the section below on Quality Requirements.

Scenario C: In cases where the sponsor is conducting an ongoing clinical trial and wants to open a new expanded access clinical trial or add-on an expanded access sub-study

There may be benefits for sponsors to open an expanded access clinical trial through a **new CTA**, including better transparency for potential participants and searchability in clinical trial databases.

There are situations where a sponsor may be able to add an expanded access sub-study to an existing trial by filing a **CTA-A**. The eligibility to add an expanded access sub-study by way of amendment would depend on the similarities between the proposed expanded access sub-study and the ongoing clinical trial.

Special considerations for submitting a CTA-A under this scenario:

- Sponsors proposing an expanded access sub-study to an existing trial should amend the existing trial title by adding the words "… with an expanded access sub-study" at the end. This will make expanded access clinical trials more easily findable and searchable for potential participants.
- Sponsors are strongly encouraged to indicate in advance their intention to add-on an expanded access sub-study at a later date, but it is not a requirement. Expanded access sub-studies added on after-the-fact could still be approved.
- Expanded access sub-studies can have different timelines, additional participants, and different inclusion/exclusion criteria than the main study. However, the expanded access sub-study should fall within a similar clinical context as the main study.
- In their CTA-A, sponsors would need to outline their expanded access sub-study by amending the existing protocol **or** by adding a new annex or Canadian-specific addendum to the protocol.

- For clinical trials involving controlled substances under the *Controlled Drugs and Substances Act*, section 56 exemptions are issued to a qualified investigator based on the location, practitioner, substance, and quantity. If the expanded access sub-study proposes new locations or practitioners than the main clinical trial, new exemptions may need to be sought to access the controlled substances. Please see the section on controlled substances for more information.

Health Canada may suggest that the sponsor submit a new CTA instead of an amendment to an existing trial if Health Canada finds that the scope for a proposed expanded access sub-study is very different than that of the original trial. Changes in population may not result in the need for a new CTA, as one of the features of an expanded access clinical trial is to provide access to investigational drugs to people that cannot participate in other clinical trials. However, if the clinical context differs significantly, for example if the sponsor wants to change the drug, indication, or dosage, this would be considered a significant change in scope and may require a new CTA.

Find more guidance on filing a CTA-A.

3.2.2 How to open arms of international expanded access programs in Canada

"Expanded access" works differently in many countries. For example, the United States (U.S.) expanded access program is run as a multi-tier access program for individuals and groups. It offers a potential pathway for patients with a serious or immediately life-threatening condition to gain access to an unauthorized drug for treatment outside of clinical trials when no comparable or satisfactory alternative options exist.

Canada's Special Access Program is similar to the individual-level tier of the U.S. program. However, Canada's Special Access Program does not currently include tiers for group-level access.

Under current regulations, at this time, group-level "expanded access" to a drug in Canada can only be obtained though expanded access clinical trials. As such, anyone looking to open an arm of an international expanded access program in Canada for multiple patients would need to do so as an expanded access clinical trial. They would need to file a clinical trial application with Health Canada and obtain a No Objection Letter.

3.2.3 Trial titles and protocols

Sponsors should clearly identify expanded access clinical trials by naming their trial protocol accordingly, by including the words "expanded access" in the title. For example: "An expanded access protocol for the treatment of [insert condition] with [insert drug]…"

Sponsors proposing an expanded access sub-study to an existing trial (as an amendment, via a CTA-A) should add "… with an expanded access sub-study" to the end of the existing trial title. Doing so will enable potential participants to find and search for expanded access trials in Canada.

Sponsors of expanded access clinical trials (or sub-studies of existing trials) should identify that they are offering expanded access in their cover letter.

In some cases, Health Canada may conclude that a clinical trial, originally not identified as an expanded access clinical trial in the CTA, does indeed fit the definition of an expanded access clinical trial. Health Canada will then suggest to the sponsor that the trial should be identified as such, for transparency and consistency.

Sponsors are encouraged to align their trial protocols with the principles outlined in the International Council for Harmonisation's M11 guideline (Clinical electronic structured harmonised protocol), which promotes structured, harmonized protocol content, and clear documentation of deviations and rationale. Aligning with these principles will support transparency, improve regulatory review efficiency, and help maintain trial integrity.

Expanded access clinical trials may be associated with unique risks, which Health Canada evaluates during a review of a CTA or CTA-A. As described in the section on special considerations, sponsors should ensure that expanded access clinical trials do not:

- expose a broader participant population to unjustified risks associated with investigational drugs
- impede clinical development of the drug in Canada
- enable broad market access to the drug prior to market authorization

Sponsors should include information in their CTA or CTA-A on how they propose to address these 3 risks, as relevant. For example, to mitigate the risk of impeding clinical development, sponsors are encouraged to review other planned or ongoing clinical trials through the Clinical Trials Database or other registries to determine if the proposed expanded access clinical trial could potentially impede the clinical development of the drug in Canada.

3.2.4 Addressing unique risks related to expanded access clinical trials

A CTA or CTA-A for an expanded access clinical trial should contain sufficient information and evidence for Health Canada to assess the unique risks of the expanded access clinical trial.

Table 1 gives examples of information a sponsor may consider submitting as part of the annex to the protocol in a CTA, or an annex or addendum to the protocol submitted as part of a CTA-A. The examples demonstrate that the study incorporates proposed risk mitigation measures into the trial design.

Every CTA or CTA-A is assessed on a case-by-case basis.

Table 1: Examples of information and evidence to include

Risk to be addressed	Potential information and evidence to include
Expose a broader participant population to unjustified risks associated with investigational drugs	For example, a defined population of participants is expected to significantly benefit from treatment with the investigational drug because… • the condition is serious, life-threatening or debilitating • there is an unmet medical need • the drug presents a significant increase in efficacy or a significant decrease in risk in relation to an existing drug marketed in Canada • participation is restricted to eligibility criteria commensurate with identified risks from previous clinical trials with the investigational drug
Impede clinical development of the drug	For example: • information on the sponsor's ongoing or planned confirmatory clinical trials to support a potential, future drug submission • if the sponsor is conducting a traditional clinical trial at the same time: plans, for example as defined in the trial or expanded access protocol, to complete enrolment in the sponsor's ongoing phase 1 to 3 clinical trials before the launch of an expanded access clinical trial (may include potential participant screening and triaging by the Qualified Investigator) • high-level information on ongoing or planned clinical trials from other sponsors (found through the Clinical Trials Database) that

Risk to be addressed	Potential information and evidence to include
	may be similar to the expanded access clinical trial in question, and how they may differ • defined inclusion criteria for expanded access clinical trials based on participant exclusion from other ongoing trials, as supported by evidence
Enable broad market access to the drug prior to market authorization	For example: • tentative projected timeline to bring the proposed drug to market in Canada • proposed sunset date for the expanded access clinical trial • proposed size of Canadian participant population, and how access to the drug will be limited to those in medical need who will likely benefit from access • information on how the drug is potentially transitioning from access under the Special Access Program to access under an expanded access clinical trial

3.2.5 Ongoing risk monitoring and reporting

As with any clinical trial, Health Canada is to be notified of any changes to the health and safety of participants through the established reporting of serious adverse reactions. For further information, follow the instructions for the reporting of Adverse Drug Reactions (ADRs) in clinical trials.

As outlined in Table 1 above, expanded access clinical trials also come with unique associated risks, which are not static. The risks depend on context and will evolve depending on how drug development progresses, and other factors. This means that a risk may not exist when Health Canada first reviews a CTA or CTA-A, or when the expanded access clinical trial starts, but it could develop afterwards.

Ad-hoc events could trigger Health Canada to review these ongoing risks. For example:

- if Health Canada becomes aware of an ongoing confirmatory clinical trial in Canada that resembles the expanded access clinical trial
- if the sponsor cancels its plans for bringing the drug to market

To be able to assess the safety and evolving risks of an ongoing expanded access clinical trial, Health Canada **may** request additional information or updates from the sponsor after the trial begins. A commitment may be included in the No Objection Letter to ensure the sponsor is aware of this possibility.

For example, sponsors could be asked to provide the following information:

- number of participants enrolled since the last update and total number since the expanded access clinical trial began
- number of individuals who are administering the drug on behalf of the Qualified Investigator (if applicable) since the last update and total number since the expanded access clinical trial began
- any new evidence regarding the safety and efficacy of the investigational drug in the expanded population
- status of the sponsor's planned, ongoing or completed confirmatory trials since the last update, or other commitments made in the expanded access CTA or CTA-A related to the clinical development of the drug in Canada

- updates on any other commitments made in the expanded access CTA or CTA-A, including proposed milestones for potentially bringing the drug to market

This process of ongoing risk oversight and monitoring aligns with international standards, as outlined in the International Council for Harmonisation's E6 guideline on good clinical practice.

Health Canada may suspend the authorization to sell a drug for the purposes of a clinical trial if there are reasonable grounds to believe that information submitted about the trial is false or misleading (there may be other grounds to suspend). The ability to suspend is outlined in section C.05.016(1) of the regulations.

3.2.6 Annual updates to the investigator's brochure

Due to the ongoing and evolving risks of expanded access clinical trials outlined above, sponsors of such trials are expected to file their annual updates to the Investigator's Brochure as a Notification (CTA-N).

For more information on updates to the Investigator's Brochure:

- Section 2.8.5 of the guidance on clinical trial applications
- Appendix A of the E6R3 guideline on good clinical practices

3.2.7 Quality requirements

Chemistry and manufacturing requirements for expanded access clinical trials are the same as for all clinical trials. The scope and detail of information submitted to support the quality portion of a CTA should be sufficient to adequately assess the drug's characteristics.

For applications that cross-reference a Drug Master File, where chemistry and manufacturing information is referenced, sponsors are still required to complete the appropriate Quality Overall Summary (QOS) template (Module 2, [2.3]) including the introduction and any sections not covered by the letter of access.

The information contained in the investigator's brochure must be specific to the investigational drug used in the expanded access clinical trial. A literature-based investigator's brochure would likely not be appropriate for an expanded access clinical trial, given the need to characterize the investigational drug being provided to an expanded population of participants.

In addition, quality requirements should generally meet the standard for a phase 3 clinical trial, given the broad participant population that may receive the investigational drug.

For information on quality requirements, consult the following guidance document and notice:

- Quality (chemistry and manufacturing) guidance: Clinical trial applications (CTAs) for pharmaceuticals
- Quality requirements for investigational biologic drugs used in clinical trials: Notice to clinical trial sponsors

3.3 Transparency, equity and fairness

Sponsors are strongly encouraged to register their clinical trials with an international registry that is acceptable by the World Health Organization, to:

- be transparent about clinical trial information **and**
- show equity and fairness of access for participants

Registering a clinical trial can help sponsors attract a larger amount of potential participants, and it can also help potential participants find and determine treatment options.

An example of an acceptable registry is the clinical trial registry operated by the National Institutes of Health in the United States.

Sponsors can register their trial once they have received the No Objection Letter from Health Canada.

Learn more:

- Clinical Trials Database
- Draft guidance on the registration of clinical trials and public disclosure of results

Please note that trial registration may be required if the sponsor is subject to an *Agreement on the Administration of Agency Grants and Awards by Research Institutions.* For more information, consult the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2022).

Information made public by sponsors (for example, through a website) regarding the trial should include contact information to enable potential participants or their health care providers to contact the trial sponsor about enrolment. Trial information should be accessible and written in a way that potential participants can understand.

Sponsors should consider how they convey information about expanded access clinical trials with investigational drugs that have not been authorized for sale by Health Canada. Sections 9(1) and 20(1) of the *Food and Drugs Act* (Act) prohibit advertising any drug or device in a manner that is:

- false, misleading or deceptive **or**
- likely to create an erroneous impression regarding its character, value, quantity, composition, merit, design, construction, performance, intended use or safety

The act defines "advertisement" as "including any representation by any means whatever for the purpose of promoting directly or indirectly the sale or disposal of any food, drug, cosmetic or device." Health Canada will rely, as a general principle, on the ordinary meaning of "promote," which is to encourage or incite the sale of a health product.

For more information, consult:

- Guidance on distinction between advertising and other activities for health products

Sponsors should be clear and transparent regarding the trial's purpose, objectives, and potential risks and benefits. The expectations of participants should be managed carefully by sponsors throughout the trial to avoid any potential misconceptions regarding the safety and efficacy of the drug.

3.4 Decentralization: Delegating activities outside of the clinical trial site

There is growing recognition for the need for flexible clinical trial models that facilitate easier and more diverse participation. In Canada, many people live outside urban areas and away from major clinical research networks. This can make it difficult to recruit people from rural or remote areas who face logistical or financial challenges, impacting the ability of potential participants to access investigational drugs that may provide benefits. Flexible clinical trial models can help facilitate the participation of underrepresented or equity-deserving groups in clinical trials.

Sponsors can choose to adopt a decentralized model for any type of clinical trial. However, in confirmatory clinical trials, not being able to go to a clinical trial site may pose challenges with standardized evaluation of the participant and reliability of the collected data.

In expanded access clinical trials, the emphasis is on providing promising drugs to participants in need and including as diverse a participant population as possible. For this reason, sponsors could consider adopting a decentralized clinical trial model, where a qualified investigator would oversee clinical trial activities that are administered on their behalf by individuals in different physical locations. This means clinical trial activities could be conducted outside of the main location of the clinical trial site, such as in smaller communities or distinctions-based Indigenous communities.

The clinical trial site where the Qualified Investigator is located must be identified in a CTSI form submitted to Health Canada. However, additional physical locations where clinical trial activities are conducted by other individuals under the supervision of the Qualified Investigator (such as a physician's office, a pharmacy, or the participant's home) are not considered additional clinical trial sites. As such, additional locations do not require the completion of CTSI forms or additional REB approvals.

Even though they don't require separate CTSI forms or REB approval, all locations where clinical trial activities occur, including distant locations, are considered extensions of the main clinical trial site. With the exception of a participant's home, these locations may be inspected as part of a clinical trial site inspection, especially if the drug is going to be stored there.

Regardless of whether the location is inspected, appropriate safeguards must be put in place to ensure the drug is stored, transported, and administered safely and securely.

With appropriate risk-based safeguards for participants, local health care providers, who may be located in a variety of locations, may be involved in drug administration, safety monitoring or other trial-related activities. Risk-based monitoring should take into account treatment complexity, participant safety and individual competencies. Local providers could, for example, already be providing health care to the participant (such as their family doctor).

Sponsors could also consider delegating activities to contract research organizations or other service providers, usually through recorded agreements.

Sponsors and individuals involved in trial activities may discuss and negotiate the terms of agreements in advance of launching an expanded access clinical trial. For example, this includes negotiating:

- any differences in local treatment practices/standards and the protocol for the expanded access clinical trial
- any sort of financial compensation for clinical trial activities undertaken on behalf of the sponsor or Qualified Investigator

Regardless of the model proposed, all clinical trial activities remain under the supervision of the Qualified Investigator. The Qualified Investigator is ultimately responsible for medical decisions taken as part of the trial at all locations associated with their clinical trial site.

3.5 Health care provider participation

Health care providers who undertake or are involved in activities on behalf of the Qualified Investigator (such as administering the investigational drug, monitoring participants and collecting data) are conducting clinical trial activities.

Health care providers who are involved in expanded access clinical trial activities could verify that their roles, responsibilities and liabilities are specified in an agreement (such as the clinical trial protocol or through additional contracts), or otherwise adequately overseen by the Qualified Investigator.

Additional CTSI forms and additional REB approval are not required for physical locations that are added to an existing clinical trial site. An example would be adding a health care provider's office where the health care provider conducts activities related to the clinical trial on behalf of the Qualified Investigator.

These activities must be clearly defined in the trial protocol and may be appropriately recorded in the trial's delegation log. Ultimately, the qualified investigator is responsible for medical decisions taken in relation to trial activities, wherever those activities have occurred.

Health care providers connected to a different institution than the Qualified Investigator should be aware of local and institutional policies and requirements that may apply to their activities at their institution. In other

words, health care providers may have additional responsibilities under a local or institutional research ethics board.

Health care providers who have the legal ability to sponsor an expanded access clinical trial in Canada could offer to sponsor an expanded access clinical trial or to open a new clinical trial site as part of an existing expanded access clinical trial. The manufacturer may consider requests to supply the investigational drug for an expanded access clinical trial or an additional clinical trial site, but there's no legal requirement for the manufacturer to do so.

3.6 Evidence generation and data reliability

New drug submissions require substantial evidence that is typically generated from confirmatory (phase 3) clinical trials. While the evidence generated in an expanded access clinical trial may not be sufficient to support a final drug submission on its own, these trials may be designed to collect long-term safety or tolerability data that can be used to *complement* results from confirmatory clinical trials in a final drug submission. Data generated in an expanded access clinical trial can characterize effects such as rare adverse reactions or longer-term outcomes that may only appear in larger, more diverse populations over time.

Evidence generated from expanded access clinical trials should never be used to supplement ambiguous or inconclusive data from other more rigorous, controlled clinical trials since this can affect the perceived efficacy and safety of the drug. If using evidence from expanded access clinical trials to complement results from confirmatory trials in a final drug submission, sponsors should clearly specify the research question answered, how the data was collected and analyzed, and any limitations.

While following specific patient populations in a highly specialized environment facilitates the collection of high quality controlled data, it can also limit its generalizability in real world settings. Depending on the research protocol proposed by the sponsor, expanded access clinical trials may be able to generate evidence on treatment use of the investigational drug in a more generalized setting that is closer to real-world conditions (e.g., in a doctor’s office). As a result, sponsors may wish to treat the data collected in an expanded access clinical trial similarly to **real-world data**.

Many health system stakeholders are integrating **real-world evidence** into their decision-making. This includes Health Canada, Canada's Drug Agency (CDA) and the Institut national d'excellence en santé et en services sociaux (in Quebec).

Health Canada acknowledges that real-world evidence has the potential to provide valuable support in areas outside of controlled clinical trials, and continues to explore ways to improve Canada’s ability to leverage real-world evidence throughout the drug product lifecycle. Real-world data can provide useful information for the enhancement of more robust decision-making with respect to safety and efficacy, as well as utilization and treatment patterns. Also, real-world evidence has the potential to be a powerful tool when making decisions about access. However, it does come with challenges, including the potential for bias (e.g. confounding), and issues that may impact the robustness of the findings. As such, careful consideration is required when using real-world evidence to support regulatory decisions.

Sponsors may wish to review the following publication by Health Canada for more information on data collection methods and how research protocols should be designed to ensure the high quality of real-world evidence:

- Elements of real world data/evidence quality throughout the prescription drug product life cycle

The following guidance by Health Canada and CDA lays the foundation for using real-world evidence in regulatory approval and health technology assessments:

- Guidance for Reporting Real-World Evidence | CDA-AMC

Results from an expanded access clinical trial could affect the final product label/monograph, or require changes to an existing product label/monograph. This will depend on the strength of the evidence. For example, a finding of serious adverse reactions could change the product monograph by narrowing the indication or adding a black box warning. Depending on the results, drug manufacturers could be subject to terms and conditions imposed by Health Canada, such as the requirement to conduct post-market studies to monitor the long-term safety and effectiveness of the drug.

3.7 Expanded access clinical trials with controlled substances

Expanded access clinical trials are regulated under Part C, Division 5 of the *Food and Drug Regulations*. However, sponsors who wish to conduct a trial with a controlled substance listed in Schedules I to V of the *Controlled Drugs and Substances Act* (CDSA) must also comply with the CDSA's requirements.

Under the CDSA, all activities with controlled substances, including the sale, import, export, production, transportation and possession of controlled substances, are prohibited unless authorized under its regulations or by exemption. Possession is only prohibited for controlled substances listed in Schedules I, II and III to the CDSA.

A practitioner (usually the Qualified Investigator) requiring a controlled substance for research purposes, which includes administration to humans in an expanded access clinical trial, must receive an exemption from Health Canada. This is done by submitting a separate application for an exemption to the Office of Controlled Substances, after a No Objection Letter for the expanded access clinical trial has been issued by Health Canada.

Applications to perform research with a controlled substance that is a restricted drug listed in the schedule to Part J of the *Food and Drug Regulations* require additional supporting documents. Upon receipt of an application, the Office of Controlled Substances will identify any additional supporting documents required.

Prior to granting an exemption for research with controlled substances, Health Canada confirms that:

- there is a record of handling
- the risk of diversion in transit is reasonably addressed
- the risk of diversion at the clinical trial site or associated locations is reasonably addressed

Investigational drugs that are controlled substances must be provided by a licensed dealer who is authorized to conduct regulated activities with the substance under the CDSA.

If the authorized manufacturer is located outside of Canada, a CDSA-licensed dealer must import the substance. The licensed dealer must obtain an import permit from Health Canada. Only licensed dealers can apply for import permits.

Exemptions for research with controlled substances are specific to the location, practitioner, substance, and quantity of the drug in a clinical trial. This means that if a sponsor proposes an expanded access sub-study to an existing trial and proposes different or additional locations or practitioners, new exemptions may be required for new practitioners administering the drug and for new sites where the drug is stored.

A sponsor should consider the following when designing the trial protocol:

- To reduce the number of exemptions required, sponsors are advised to plan in advance for expanded access sub-studies with controlled substances, so that all potential storage locations, practitioners

and quantities are identified in a single exemption application. As long as the drug is stored solely in already-identified locations, only one exemption may be required.

- Typically, exemptions are issued to the Qualified Investigator of a clinical trial site, who would be responsible for safeguarding, transporting, and administering the drug. However, in a decentralized trial, other individuals (such as family doctors) could be authorized to conduct activities on behalf of the Qualified Investigator, including drug administration and storage. In this case, the Qualified Investigator would have two options with regards to the exemption:
    - The Qualified Investigator would hold the exemption, but other individuals could be authorized under the exemption to administer a specific amount of the drug to participants. These authorized individuals would be expected to follow, and would be bound by, the terms and conditions in the exemption. The storage address for each remote site would need to be identified, and if the drug is to be transported to a participant's home, then the drug would need to be safeguarded during transport. In this approach, the Qualified Investigator would hold ultimate responsibility, not only for the drug they are personally handling, but also the drug that the delegated individual would be handling, including storage and security. The Qualified Investigator would need to accept responsibility for all activities undertaken on its behalf as part of the trial.
    - If the Qualified Investigator is not willing to be responsible for all activities undertaken on their behalf, then each individual involved in trial activities with a controlled substance would need their own exemption. In this case, they would have the same responsibilities and requirements as the Qualified Investigator with regards to the exemption, and would have a set amount of the drug authorized to them. This individual would be ultimately responsible for all activities in the exemption, and not the Qualified Investigator. This individual would be responsible for maintaining the exemption (renewing, etc.), independently from the Qualified Investigator.

Learn more about the application process for clinical trials with controlled substances:

- Controlled substances

To apply to use a controlled substance for clinical trials (must be completed by the practitioner seeking the exemption):

- Application form

Researchers should familiarize themselves with all Health Canada notices to stakeholders on the requirements for conducting clinical research with specific controlled substances.

Researchers interested in conducting an expanded access clinical trial with a controlled substance should contact the Office of Controlled Substances to obtain information on associated requirements. See contact information below.

Health Canada also conducts compliance and enforcement activities for all activities involving controlled substances and precursors under the CDSA and its regulations. This includes activities conducted in clinical trials. Compliance monitoring and enforcement helps to support the legitimate use of controlled substances, while reducing the risk of diversion.

For information on the principles that Health Canada follows when monitoring compliance and enforcement of controlled substances, visit:

- Compliance and enforcement policy for controlled substances and precursors (CS-POL-001)

4 Contact information

For questions regarding this guidance document:

Bureau of Policy, Science and International Programs
Pharmaceutical Drugs Directorate
Health Products and Food Branch
Health Canada
1600 Scott St, Holland Cross - Tower B
Address Locator: 3106B
Ottawa ON K1A 0K9
Email: policy_bureau_enquiries@hc-sc.gc.ca

For questions about clinical trials involving pharmaceutical drugs:

Office of Clinical Trials
Pharmaceutical Drugs Directorate
Health Products and Food Branch
Health Canada
1600 Scott St, Holland Cross – Tower B
Address locator: 3105A
Ottawa ON K1A 0K9
Email: OCT_BEC_Enquiries_Enquetes@hc-sc.gc.ca

For questions about clinical trials involving biologic or radiopharmaceutical drugs:

Office of Regulatory Affairs
Biologic and Radiopharmaceutical Drugs Directorate
Health Products and Food Branch
Health Canada
100 Eglantine Driveway
Ottawa ON K1A 0K9
Email: brdd.ora@hc-sc.gc.ca

For questions about conducting an expanded access clinical trial with a controlled substance, or about the exemption process:

Office of Controlled Substances
Controlled Substances and Cannabis Branch
Health Canada
161 Goldenrod Drwy
Address locator: 0300B
Ottawa ON K1A 0K9
Email: exemption@hc-sc.gc.ca

5 Glossary

5.1 Definitions specific to this guidance

Expanded access clinical trial: A type of clinical trial that provides access to investigational drugs that have the potential to treat people living with medical conditions who do not qualify for other clinical trials or are not able to participate in one.

Investigational drugs: Pharmaceutical, biologic, and radiopharmaceutical drugs for human use that are tested or studied in a clinical trial.

5.2 Definitions adapted from the Food and Drug Regulations

Note: These definitions are subject to change should the definitions change in the Food and Drug Regulations.

Adverse events: Any adverse occurrence in the health of a clinical trial participant who is administered a drug, that may or may not be caused by the administration of the drug, and includes an adverse drug reaction.

Good clinical practices: Generally accepted clinical practices that are designed to ensure the protection of the rights, safety and well-being of clinical trial participants and other persons, and the good clinical practices referred to in section C.05.010.

Investigator's brochure: A document containing the preclinical and clinical data on the drug.

Protocol: A document that describes the objectives, design, methodology, statistical considerations and organization of a clinical trial.

Qualified investigator: Person responsible to the sponsor for the conduct of the clinical trial at a clinical trial site, who is entitled to provide health care under the laws of the province where that clinical trial is located.

Research ethics board: A body not affiliated with the sponsor (made up of researchers, people with specific expertise, and community members), and whose principal mandate is to approve the initiation of, and conduct periodic reviews of, biomedical research involving human participants in order to ensure the protection of their rights, safety and well-being.

Sponsor(s): An individual, corporate body, institution or organization that conducts a clinical trial.

5.3 Definitions taken from other Health Canada (HC) sources

Placebo: A control treatment that does not contain the medicinal ingredient that is given to a group of trial participants. (Taken from Clinical Trials Database definitions.)

Real-world data: data relating to patient status and/or the delivery of health care routinely collected from a variety of sources. (Taken from HC publication on elements of real-world data/evidence quality throughout the prescription drug product life cycle.)

Real-world evidence: evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of real-world data. (Taken from HC publication on elements of real-world data/evidence quality throughout the prescription drug product life cycle.)