Health Canada Santé Canada

Canada

CAPRA Webinar

June 11, 2020

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Overview

Health Canada is aware of the impact of the pandemic on the conduct of clinical trials, including the need for:

- participants to self-isolate
- deployment of healthcare personnel involved in clinical trials to other duties during this public health emergency, resulting in delays in completing certain tasks.

Pre-CTA Meetings

- **Are there any changes to the pre-CTA process at this time**?
  - COVID-19 requests
    - Given priority
    - At time of requesting COVID-19 meeting, submit copies of slide deck, briefing documents and questions
    - Prior to pre-CTA, Health Canada reviews this information
    - Based on information submitted, advanced feedback maybe provided to sponsor
    - If advanced feedback provided, pre-CTA meeting to focus on sponsor's response to questions
  - For None COVID-19 requests
    - No change in the process

Application Process

- Health Canada prioritizes the review of clinical trial applications designed to investigate the diagnosis, treatment and/or prevention of COVID-19.
  - 14 days internal target date for COVID-19 review
  - IR responses requested within 24 hour of issuance
- Sponsors may continue to file other CTA and CTA amendments according to Health Canada guidance.
- During the course of a CTA review, if sponsors are unable to respond to an Information Request (IR) within specified time lines, consider withdrawing the submission without prejudice and refiling when the information is available.

Application process

- Normal procedure
  - Sponsor mails CD to Health Canada
- COVID-19 variation
  - Sponsor can email application to Health Canada in non-eCTD electronic only format

- Both TPD and BRDD are accepting COVID-19 related CTAs via email.
  - BRDD: hc.brdd.cta-dec.dmbr.sc@canada.ca
  - TPD: hc.oct.smd-dgp.bec.sc@canada.ca

- If your CTA(-A) is larger than 20 megabytes, the CTA(-A) may be split and sent under separate emails (e.g. one email for Module 1, and one email for Module 2/3). The subject line of the emails should clearly link to one another (e.g. “Email 1 of 2: CTA(-A), [Product Name], [Protocol Number]”).

Consent Process

- Written consent not always possible at time
- Electronic consent
  - remote written informed consent;
  - Documentation of process
  - When feasible, written re-confirmation of informed consent from participant

- Non-written informed consent (verbal)
  - Obtained through reading the contents of the informed consent form to the trial participant
  - Receive the individual's informed consent before a witness,
  - Attestation by the witness that the consent was given
  - Documentation of process
  - When feasible, written re-confirmation of informed consent from participant.

Participants Affected with COVID-19

- The ongoing safety of trial participants is primary concern
- Sponsors decide whether
  - the study is to placed on hold (i.e. not administering the investigational product until the participant has recovered)
  - whether the participant's involvement in the study is to be discontinued.
- All participants affected by a COVID19 related study disruption should be documented by unique participant identifier, site and a description of how the individual's participation was altered.
- Study participants need to be informed of any risks/changes to the study and monitoring plan that could impact on their wellbeing.

Getting Investigational Product to Participant

- Can ship clinical trial investigational products (IP) from Canadian sites directly to participants.
  - Applies to all product formulations (e.g. tablets, injectables).
  - Applies to drugs that a subject could take on their own
  - Transport, handle and store done in a manner that mitigates the risk of exposure to temperatures outside labelled storage conditions.
  - Verify that the investigational drug has been received by the participant
  - Accurate documentation of the process in the participant's study record

Clinical Trial Visits

- Need to evaluate alternative methods for safety assessment if participants not be able to come to the investigational sites as specified in the study protocol.
  - Example: phone contact, virtual visits via telemedicine or alternative care sites, alternative locations for imaging studies/laboratory tests
- If alternative monitoring is done,
  - need documentation that captures
    - why it was done;
    - the method used to collect the information;
    - what data was collected;
    - who provided the information;
    - how the source of the information was verified
  - **Study protocol amendments not needed.**
  - May create issues of confidentially related to participant's medical records (Electronic Health Record).
  - Participants need to consent to any identifiers leaving the original site

Virtual visits

- **Clinical trial site**
  - The location where a qualified investigator (QI) conducts or monitors clinical trial activities.
  - Sponsor notifies Health Canada when clinical trial site received REB approval and opens for recruitment
- **Satellites**
  - Distant of the clinical trial site
  - QI delegates to qualified person specified trial activities at satellite
  - QI responsible for activities occurring at satellite
  - Does not require individual REB for each satellite or Health Canada notification when trial opens.
  - Process does not need to document in study protocol; but rather in clinical trial site SOPs

Putting a Study on Hold

- Halting recruitment / temporarily halting the trial may be required.
- Document reason for halting recruitment / temporarily halting trial in study records
- Notify Health Canada as clinical trial notifications (CTA-N).

Protocol Deviations

- The clinical trial site(s) should have a system in place to identify, document, assess and report all protocol deviations to the sponsor and REB
- Document deviations to facilitate future analysis of the study findings.
  - Define and identify the protocol deviations to be reported. Consider methods to prevent protocol deviations and document the reasons for any protocol deviations.
- Unless the deviations place participants at risk, not required to report deviation to Health Canada.
- Consider submitting at regular intervals a cumulative list of deviations occurring in a particular study, rather than individual notifications

The Interim Order

- Concepts of the Interim Order have leveraged elements from the forthcoming broader Clinical Trials Modernization Initiative
- Under subsection 30.1(1) of the *Food and Drugs Act* (FDA), the Minister may make an interim order if the Minister believes that immediate action is required to deal with a significant risk, direct or indirect, to health, safety or the environment.
- Purpose:
  - To support the initiation of clinical trials by increasing efficiencies and reducing the administrative burden of certain requirements, while also maintaining standards designed to safeguard the health and safety of clinical trial subjects.
- Enabled by powers in the *Budget Implementation Act, 2019.*
- These powers will be brought into force at the same time the Interim Order takes effect
- Will be in effect only for a period of one year from the date it is made
- A Governor-in-Council regulation needs to be made within a year to continue these exemptions.

Changes under Interim Order

	Part C, Division 5	IO
HC REVIEW, AUTHORIZATION Scope of what is authorized	Authorization applies to the investigational product – authority beyond that is reliant on voluntary compliance. No ability to add terms and conditions	**Authorization applies to both the COVID-19 drug or medical device and the trial itself.** **Ability to add or amend terms and conditions on the authorization at any point.**

Changes under Interim Order

	Part C, Division 5	IO
Requirements proportional to risk	"One size" fits all requirements for novel and marketed drugs being studied off label. 2019 Interim policy introduced to reduce requirements for non-investigational off label uses of marketed drugs in clinical trials.	**Introduces a risk-based approach for drug trials.** **Trials involving new uses of marketed drugs for COVID-19 may benefit from reduced application requirements and exemptions for labelling, and some record-keeping requirements**.

Changes under Interim Order

	Part C, Division 5	IO
POST-AUTHORIZATIONMID TRIAL	Requires all post-authorization changes be submitted to Health Canada as either an amendment for authorization or as notification	**Facilitates changes within the course of a clinical trial involving a COVID-19 drug or medical device by requiring HC approval for only significant changes to an authorized trial.** **Non-significant changes would not need to be submitted to HC.**

Changes under Interim Order

	Part C, Division 5	IO
Who can conduct a trial	Qualified Investigator **must** be qualified physician or dentist.	**Enables broader range of regulated health care professionals (e.g. nurse practitioners, midwives) to conduct the trial as qualified Investigators**

Changes under Interim Order

	Part C, Division 5	IO
POST-AUTHORIZATIONMID TRIAL	Requires all post-authorization changes be submitted to Health Canada as either an amendment for authorization or as notification	**Facilitates changes within the course of a clinical trial involving a COVID-19 drug or medical device by requiring HC approval for only significant changes to an authorized trial.** **Non-significant changes would not need to be submitted to HC.**

Changes under Interim Order

	Part C, Division 5	IO
COMPLIANCE AND ENFORCEMENT	Authority to suspend or cancel a clinical trial site or the whole trial. No ability to allow arms of the trial to continue	**Allows Health Canada to suspend or cancel a part or the entire trial**

Thank you

- A Notice to clinical trial sponsors for the Management of clinical trials during the COVID-19 pandemic was published online on March 23, 2020 and can be found on the Health Canada website at the following address: www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/announcements/management-clinical-trials-during-covid-19-pandemic.html.
- For any questions related to clinical trial applications (CTA), please contact:
  - For pharmaceutical drugs: Therapeutic Products Directorate (TPD) at hc.oct.enquiries-requetes.bec.sc@canada.ca.
  - For biologics and radiopharmaceuticals: Biologic and Radiopharmaceutical Drugs Directorate (BRDD) at hc.brdd.ora.sc@canada.ca.