



1. Purpose

The purpose of this SOP is to outline the process for filing a Clinical Trial Application with Health Canada.

2. Responsibilities

Sponsor: The Sponsor is responsible for filing a Clinical Trial Application with Health Canada and adhering to Division 5 Food and Drug Regulations.

3. Procedures

3.1 Investigator initiated clinical trials involving humans conducted in Canada are governed by Division 5 of the Health Canada Food and Drugs Regulations.

Clinical Trial Application (CTA)

3.2 Clinical Trial Applications (CTAs) are required from sponsors for:

- 3.2.1 All Phase I-III clinical trials involving an investigational product;
- 3.2.2 Comparative bioavailability studies;
- 3.2.3 Clinical trials involving marketed products, where the proposed use of the product is outside the parameters of the approved Notice of Compliance or Drug Identification Number.

3.3 Phase IV clinical trials are not subject to CTA filing requirements with Health Canada.

3.4 The Sponsor may request and attend a pre-CTA consultation meeting with Health Canada, if desired.

3.5 Prior to the initiation of a clinical trial in Canada, sponsors must file a Clinical Trial Application (CTA) with Health Canada. Refer to www.hc-sc.gc.ca for the current CTA and associated guidance document. (Usually the CTA submission occurs after funding for the project has been secured and either prior to or simultaneously with the Research Ethics Board submissions).

3.6 Main documents required for preparation of a CTA submission include:

- 3.6.1 Drug Submission Application Form
- 3.6.2 Protocol
- 3.6.3 Protocol Synopsis
- 3.6.4 Informed Consent Form
- 3.6.5 Research Ethics Board Attestation Form, or equivalent
- 3.6.6 Qualified Investigator's Undertaking Form
- 3.6.7 Investigator's Brochure or Product Monograph or Chemistry Manufacturing Control (CMC) information

3.6.7.1 For Investigator-initiated CTAs, the Chemistry Manufacturing Control information may be obtained by either by (1) a letter of cross-reference which allows Health



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- Canada to access the CMC information from a previously approved application; or
 - (2) a letter from the drug manufacturer granting access to the Drug Master File; or
 - (3) Full CMC information provided by the manufacturer for inclusion in the CTA.
- 3.7 The CTA is evaluated by Health Canada, any deficiencies will be identified and reported to the sponsor within 30 days. If no deficiency is identified, Health Canada will forward the sponsor a No Objection Letter (NOL) within 30 days.
- 3.8 The Sponsor may begin study initiation activities once the Health Canada No Objection Letter (NOL) has been received.
- 3.9 The NOL and all other submission documentation and correspondence should be filed with the study regulatory documentation.
- 3.10 Complete and submit a completed Clinical Trial Site Information Form for each research site. Ensure the Health Canada control number and trial start date information are included on the form.

Health Canada Screening

- 3.11 Health Canada reviews the CTA, and if any deficiencies are identified, Health Canada will inform the Sponsor within 30 days of the submission.
- 3.12 Minor issues with documentation or deficiencies with the CTA will be addressed with the Sponsor by either:
- 3.12.1 A Screening Rejection Letter (itemizing deficiencies/significant information lacking from the CTA submission, resubmitted information will be considered “new” and be assigned a new control number).
 - 3.12.2 A Request for Clarification, sent via fax (a response is required within 2 calendar days).
- 3.13 Health Canada will forward an acknowledgment letter to the Sponsor to indicate that screening of the CTA is complete, and the review process has commenced.
- 3.14 If applicable, Health Canada will forward the Sponsor any queries regarding the CTA. The Sponsor should respond within 2 calendar days to maintain the 30-day review period.

Clinical Trial Application Amendment (CTA-A)

- 3.15 Changes to a clinical trial with an existing NOL, should be submitted to Health Canada on the CTA Amendment (CTA-A) form for approval. Refer to www.hc-sc.gc.ca for the current CAT-A form and associated guidance document.
- 3.16 The sponsor should initiate a CTA-A when an amendment to the protocol:
- 3.16.1 Affects the selection, eligibility criteria, follow-up or withdrawal of the trial participant;
 - 3.16.2 Affects the evaluation of the clinical efficacy of the investigational product;
 - 3.16.3 Alter the risk to the health of a trial participant;
 - 3.16.4 Affects the investigational product safety assessment;
 - 3.16.5 Extends or decreases the duration of the trial;



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- 3.16.6 An amendment to existing information regarding investigational product chemistry and manufacturing affects the safety or quality of the product.
- 3.17 Health Canada should approve the CTA-A before the sponsor implements any modifications to the clinical trial.
- 3.17.1 If the sponsor immediately initiates one or more amendments because the clinical trial or investigational product poses a significant risk to the trial participants, he/she may do so without waiting for Health Canada approval. However the sponsor should provide Health Canada with the required information within 15 days of implementation of the amendments.
- 3.18 The CTA-A is evaluated by Health Canada, any deficiencies will be identified and reported to the sponsor within 30 days. If no deficiency is identified, Health Canada will forward the sponsor a No Objection Letter (NOL) within 30 days.

Investigator Brochure Updates

- 3.19 Submit an updated Investigator's Brochure (IB) as a Notification, unless included as part of a planned CTA-A.
- 3.20 Include a summary of the changes for ease of review and evaluation.

CTA Records and Documentation

- 3.21 The sponsor should maintain complete and accurate records to preserve all clinical trial related information to demonstrate compliance with regulations.
- 3.22 Clinical trial records should be maintained for a period of 25 years.

Other Health Canada Documentation

- 3.23 Health Canada documentation concerning participating clinical trial sites includes:
- 3.23.1 **Clinical Trial Site Information** form (required as part of the CTA). This form should be completed for each participating clinical trial site and submitted to Health Canada prior to initiation of trial activities at the site. This form provides details concerning the clinical site, qualified investigator and affiliated research ethics board.
- 3.23.2 **Research Ethics Board Attestation** form. The local research ethics boards may use the research ethics board attestation form or create a similar form that certifies that their activities and procedures meet regulatory requirements. This form should be completed for each participating site and is to be provided to Health Canada only upon request.
- 3.23.3 **Qualified Investigator Undertaking** form. The qualified investigators at the local sites should complete this form to certify they are qualified to undertake the responsibilities. This form is to be provided to Health Canada only upon their request.
- 3.24 For studies involving international sites, unless otherwise requested by Health Canada, non-Canadian sites are exempt from completing the documents outlined in 3.13.1-3.13.3.



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3.25 If further information regarding Health Canada requirements, or interpretation of their requirements, is required contact the Office of Clinical Trials, Therapeutic Products Directorate: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/clini/cta_contact_information-eng.php.

4. References

- 4.1 Notice: Release of New Guidance for Clinical Trial Sponsors: Clinical Trial Applications. Health Canada, date: 2003-06-25 (www.hc-sc.gc.ca).
- 4.2 Food and Drug Regulations, Division 5: Drugs for Clinical Trials Involving Human Subjects.
- 4.3 Network of Networks Standard Operating Procedures for Clinical Research ([N₂ organization](#)).