CTA and CTA-A Review Template

Referenced SOPs: *N2 SOP 002, N2 SOP 018*

All UofC-sponsored investigator-initiated, clinical trials that require Health Canada approval must be submitted to Quality Assurance and Regulatory Compliance Office for review. The office will review all the study-related documentation from a regulatory perspective before approving the HC 3011 form for signature by the Associate Vice-President Research (Health).

The following checklist will assist you in ensuring that your study documents are ready for review by the QA and Regulatory Compliance Office.

Please include this completed checklist when submitting your CTA to the QA and Regulatory Compliance Office for review.

Click here to access: Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications

At the end of this document are three appendices that you may find helpful:

- **APPENDIX A** – GCP Required Protocol Elements (Page 9)
- **APPENDIX B** – GCP Required Elements of Consent (Page 16)
- **APPENDIX C** – Cover Letter Template (Page 17)

The QA reviewer's comments and feedback starts on page 19.

Study Information

Study Title:

REB Study Number:

Qualified Investigator (QI):

Individual handling the regulatory submission:

Role:

☐ Qualified Investigator ☐ Coordinator

☐ Program Manager ☐ Other

Protocol

The following elements need to be present as per Good Clinical Practice (GCP) requirements – GCP 6. (Refer to Appendix A at the end of the document).

- ☐ Date and version number in either the header or footer
- ☐ There is a statement that the study will be conducted in accordance with GCP and Food and Drug Regulations Division 5 Part C or other applicable regulations (e.g., NHP).
- ☐ There is a section explaining plans for a Data Safety Monitoring Board (DSMB). If no Data Safety Monitoring Board will be set up, reasons for why this is not deemed necessary should be provided.
  - **Note:** A more detailed DMSB charter, terms of reference and guidance documents should be created for your essential documents. Templates for these documents may be obtained by contacting UC QA staff.
- ☐ Monitoring methods by the coordinating centre are discussed.
  - **recommended**: do not include a very detailed monitoring plan in the protocol as this is subject to modifications.
- ☐ If this is a multi-site study, serious Adverse Events (SAE) reporting to the study Sponsor is described including definitions of SAEs and reporting timelines.
- ☐ Adverse Drug Reactions (ADR) reporting to Sponsor Health Canada is described including the definition of reportable ADRs and reporting timelines.
- ☐ The Protocol Safety and Efficacy Assessment Template form (PSEAT) is included and consistent with the study protocol. Note: the PSEAT is only required for an initial CTA.
- ☐ A statistician has been consulted.
  - **Note**: It is highly recommended to obtain the input from a statistician.

Consent

- ☐ All elements as per GCP requirements are present – refer to the CHREB template.
  - Refer to Appendix B for GCP 4.8.10 complete list of required elements.
- ☐ The version date of the document is noted in the header or footer.
- ☐ The risk section is consistent with the Product Monograph (PM)/ Investigator Brochure (IB).

Alternative Forms of Consent are included (if applicable):

- ☐ Assent form
- ☐ Deferred Consent form
- ☐ E-Consent form
- ☐ Surrogate consent form
- ☐ Verbal consent form

Health Canada Form 3011

Drug Submission Application
Guidance for completing the Drug Submission Application Form HC3011

- [ ] All study **drugs** not marketed in Canada and all **drugs** marketed in Canada that are used outside the approved indications, route, and dose or with non-approved dosage form are listed on the HC 3011. Ensure the current version of the HC 3011 form is used.
- [ ] • **Note**: It is highly recommended to use the MS Word version rather than the Smart-Form PDF, which can pose issues when collecting electronic signatures. The form can be converted to PDF once completed.
- [ ] Check the Health Canada product database for the most recent and up-to-date product monograph (if unsure you can verify with the AHS Research Pharmacy (pharmacy.research@albertahealthservices.ca), regarding the formulation to be used, e.g. 10mg/ml).
- [ ] Check if the drug supply is imported or available in Canada. Note: products marketed/approved in Canada, but imported from another country for the trial (e.g., international collaboration), should be included in the CTA or CTA-A
- [ ] The plans for using drug brands are outlined. *From CTA Guidance: For a clinical trial submission please enter the name of the investigational product, and where there is more than one investigational product, all of them should be captured and a separate Part 2 should be completed for each one of them. (Note: an investigational product corresponds to a product involved in the conduct of a clinical trial. It could be a product not available in Canada, a product in development or a product already approved in Canada but used outside the approved indication.)*
  - **Note**: If different brands will be used at participating study sites, all the brand names used are listed.
- [ ] All brands and strengths that could be used in the trial are listed (All Product Monographs/ Investigator Brochures to be provided). This may happen if the protocol states that the study sites will use the products as available through their respective hospital pharmacies.
- [ ] Applicable schedule(s) are assigned accurately (check Health Canada Drug product database).
  - **Schedule C** (radiopharmaceuticals)
  - **Schedule D** (biologicals) to the Food and Drugs Act,
  - **Schedule F** (prescription drugs) to the Food and Drug Regulations and please identify if the product falls under the Controlled Drugs and Substances Act *(CDSA).*
- [ ] The University of Calgary and the Qualified Investigator are identified as the study sponsor (Section A, #11. Governors of the University of Calgary / Dr. Jane Smith).
- [ ] As per #17 – a Qualified Investigator is listed as the contact for the sponsor
- [ ] An appropriate contact is listed for this regulatory submission.
  - **Note**: the contact can be a CRO, the Qualified Investigator or a research manager.
- [ ] Box #53 related submissions are referenced e.g., a CTA preceding a CTA-A.
- [ ] If the pharmaceutical company you are dealing with makes you aware of any related submissions using the IP, they should be listed in box 53.

☐ Part 2 Drug Product Formulation Information is complete, and the list of the active ingredients and strength is accurate.

- **Note**: it is recommended to ask the research pharmacy to verify this section of the HC3011 form.

☐ Information regarding animal sources and nanomaterials is provided and accurate.

- **Note**: it is recommended to ask the research pharmacy to verify this section of the HC3011 form.

☐ Boxes #61 to #68 are complete and accurate.

- **Note**: cross-check with the protocol and the Product Monograph. It is recommended to ask the research pharmacy to verify this section of the HC3011 form.

☐ The proposed indication is accurate.

- **Note**: cross-check with the protocol.

☐ All other boxes are complete and accurate.

☐ Boxes #75 - #81 indicate Qualified Investigator as signing authority with proper title and contact information.

I, the undersigned, certify that the information and material included in this drug submission application is accurate and complete[5].

75. Name of Authorized Signing Official	76. Signature	77. Date
Qualified Investigator's name	Signature	YYYY MM DD
78. Title Enter full title (e.g. Associate Professor, Dept. of ___)	79. Telephone No. 403-123-4567	80. Fax No.
81. Name of Company to which the Authorized Signing Official Belongs		

Appendix 1: Template Authorization for a Third Part to import the New Drug Described in this Clinical Trial Application or Amendment

☐ "Not applicable" if no study product is imported or the University of Calgary is the sole importer.

OR

☐ If the study product(s) will be imported by each Canadian center (e.g., multicenter trial with a central supply by a US pharmacy), give the list of the Canadian sites authorized to import the study product(s).

Appendix 2: Template authorization for a Third Party to Sign/File a Drug Submission Application on Behalf of the Manufacturer/Sponsor

☐ "Not applicable" if the University of Calgary is the sponsor.

Appendix 3 – Clinical Trial Application Information

☐ Information in box #82 is accurate. There are two options for a protocol number:

- If the study was submitted to CHREB prior to CTA, you may use the REB ID,
- If you do not have an REB number, an independent protocol ID must be created. (An example could be the study acronym and year VITdALIZ-Kids-2020).

☐ Information in box #84 is accurate (verify drug supply – information in the protocol or from the study team).

☐ Information in box #85 is accurate (see protocol for inclusion/exclusion criteria, population, age, etc.).

Information in box #86 is accurate. Note: If the initial CTA was for a pilot study and this CTA is based on a larger study from Phase II, a Quality of Overall Summary will need to be completed if moving to a Phase III.

☐ Links to Quality of Overall Summary forms are found here:

- Quality Overall Summary - Chemical Entities Clinical Trial Application - Phase I (QOS-CE (CTA - Phase I))
- Quality Overall Summary - Chemical Entities Clinical Trial Application - Phase II (QOS-CE (CTA - Phase II))
- Quality Overall Summary - Chemical Entities Clinical Trial Applications Phase III (QOS-CE (CTA - Phase III)

☐ Information in boxes #87- 88 is accurate and complete.

Signature boxes #89 - 96 are completed.

- **Note**: List QI's Department Head as Senior Medical Officer or Scientific Officer in Canada. List Dr. Marcello Tonelli, Associate Vice President (Research – Health) as the Senior Executive Officer. Signatures can be electronic.

☐

89. Senior Medical Officer or Scientific Officer in Canada	90. Tel. No. and Address	91. Signature	92. Date
QI Department Head's Name	403-123-4567 Address	Signature	YYYY MM DD
93. Senior Executive Officer	94. Tel. No.	95. Signature	96. Date
Dr. Marcello Tonelli, Associate VP - Research(Health)	403-220-7833	Signature	YYYY MM DD

Appendix 4 - Drug Product Formulation Information – animal and/or Human Sourced Ingredients/materials:

*If you have checked "No" for **all** the questions listed in sections 56, 57, and 58, thereby indicating that there are no animal and/or human-sourced ingredients, then do not complete appendix 4.*

☐ If applicable, all human and/or animal-sourced ingredients and/or materials used are properly identified and named.

- **Note**: Matching placebo often contains animal sources – check with the supplier to confirm if anhydrous lactose is a bovine milk product.

☐ Information in box #97 -102 is accurate and complete.

For each individual ingredient/material, a separate Appendix 4 is accurately completed.

☐

- **Note**: Please complete a separate Appendix 4 for *each* individual ingredient and/or material used at any stage in the manufacture of the drug product that was identified as animal and/or human-sourced in 'Part 2- Drug Product Formulation Information' of the Drug Submission Application form. Attach separate sheets (same format) if necessary. Indicated the number of pages attached.

Appendix 5 – Schedule A Form for Non-prescription Products (excluding NHPs).

Note: that this form is only to be completed for non-prescription products that have associated Schedule A claims.

☐ If applicable, drug identification information provided is accurate (manufacturer, product name, DIN if issued).

☐ All diseases and disorders that apply to claims made are accurate.

☐ All Schedule A Claims/Indications associated with the product are correctly identified and listed.

Supporting Documentation: Complete

☐ The cover letter with a list of all the documents submitted to Health Canada is provided (with dates of versions submitted. E.g., Protocol May 2019, Informed Consent May 2019, etc.).

- *Refer to Appendix C for template*

Cover letter must include the following:

- Type of submission (CTA or CTA-A)
- Reference to correspondence with HC prior to filing if applicable (e.g., Pre-CTA meeting information etc.)
- Name of sponsor (CHEO RI/QI), manufacturer, DIN owner or agent
- Brand name
- Reason for application (e.g., new indication/route/importing drug)
- Control number if known
- Information re: drug supply
- The cover letter must be signed by the QI

Note: a signed copy of the cover letter must be included in electronic format. A hard copy of the cover letter must also be submitted with the USB/CD/zipped file when the CTA/CTA-A is sent to Health Canada.

☐ It is recommended that the cover letter is signed by the QI. Note: an electronic signature can be used.

☐ The QA cover letter template that includes the 3011-summary table is used.

☐ In the case of a CTA-A, the cover letter refers to previous submissions (initial and amendments). Reference to previous submissions/control numbers is included in the summary table in the QA cover letter template.

CTA(-A)'s may be submitted to the TPD via the following email (oct.smd-dgp.bec@hc-sc.gc.ca). Sponsors may use this email until further notice by the TPD. Please note the following email restrictions:

- The maximum email size accepted by the corporate mail server is 20 megabytes,
- The regulatory transaction must be provided as a zipped file, in accordance with the *Guidance Document: Preparation of Regulatory Activities in the "Non-eCTD Electronic-Only" Format,*
  - **Note**: The University of Calgary server does not allow zipped filed to be sent or received from University email addresses. Health Canada will allow you to send the file in separate parts. You may also use an alternate email address (e.g., AHS) to submit a zipped file
  - 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 email should state: "CTA(-A), [Product Name], [Protocol Number], [Part 1 of X](if applicable)"
- Emails received after 3:00pm EST will be considered received the following day,
- Health Canada will send an acknowledgement of receipt within 7 business days.

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).

Electronic Signatures

As per U.S. Code of Federal Regulations (CRF) Title 21 Part 11 (21CFR11), the definition of an electronic signature (e-signature) is “a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual’s handwritten signature.”

Health Canada, as per GUI-0100, considers e-signatures acceptable only if the electronic system is fully validated, the proper controls are in place to assure that the signature belongs to the user who applied it, and limited access or passwords should be used. The individuals using electronic signature must understand that an e-signature is equivalent to a handwritten wet ink signature.

All electronic sign-offs on a given document should be obtained using the same e-signature application to maintain the sign-off audit trail. If the audit trail is broken (e.g., either by use of another method of sign-off or the document is converted to a different format), all collected e-signatures are no longer valid.

The QA and Regulatory Compliance Office will coordinate the signatures using the University of Calgary e-signature platform, Adobe® Sign, once the application has been reviewed and approved.

Click to download the completed form.

APPENDIX A – GCP Required Protocol Elements

GCP 6.1 General Introduction

6.1.1 Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).

6.1.2 Name and address of the sponsor and monitor (if other than the sponsor).

6.1.3 Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor.

6.1.4 Name, title, address, and telephone number(s) of the sponsor's medical expert (or dentist when appropriate) for the trial.

6.1.5 Name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s)

6.1.6 Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable), who is responsible for all trial-site related medical (or dental) decisions (if other than investigator).

6.1.7 Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

GCP 6.2 Background Information

6.2.1 Name and description of the investigational product(s).

- Describe the dosing and administration, route, starting dose, dose escalation schedule and detailed procedures about dose adjustments, duration of therapy, and potential side effects in this section).
- Describe the control product (placebo) that will be used in the study, and if there might be allergies to any of the excipient products, etc.
- Describe the accountability procedures for the investigational product(s), including the placebo.
- Include all the risks associated with the Drug/NHP from the Product Monograph (PM) both known and potential risks ***in both the consent form and the protocol***.
- Describe the formulation, packaging and labeling of the investigational product and the placebo (i.e., the formulation of the medication, manufacturer, strength, etc. Indicate how the medication will be labelled (according to the Drug/NHP regulations), packaged and numbered (if applicable).
- Describe the accountability procedures and storage of the investigational product. Describe the study product receipt procedures, handling and storage, retrieval of unused product, destruction procedures after verification by monitor, and how the study product will be tracked for accountability (e.g., medication dispensing logs, etc.). **Consult with the pharmacy,** if necessary, on these points.
- Describe the concomitant medications and prohibited co-therapies (if any). Describe those that are permitted or not during the trial. Indicate which concomitant medications/natural remedies/foods are to be recorded on the CRF's. (E.g., OTC medications, prescription medications, vitamins, herbal remedies, certain foods/juices, etc.).

6.2.2 A summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.

6.2.3 Summary of the known and potential risks and benefits, if any, to human subjects.

6.2.4 Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).

6.2.5 A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).

- The protocol should have a signature page after the front cover page where the QI signs to ensure he will conduct the trial according to GCP and Health Canada NHP and Division 5 Regulations (See attached Protocol template). Each site investigator should also sign off on a similar agreement page to confirm they will follow the NHP regulations and GCP guidelines at their site (see protocol template). Each time the study protocol is amended the site investigators are required to sign the protocol again. The QI must retain these signature pages in the regulatory study file.

6.2.6 Description of the population to be studied.

6.2.7 References to literature and data that are relevant to the trial, and that provide background for the trial.

GCP 6.3 Trial Objectives and Purpose

- A detailed description of the objectives and the purpose of the trial.

GCP 6.4 Trial Design

6.4.1 A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.

6.4.2 A description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures, and stages.

6.4.3 A description of the measures taken to minimize/avoid bias, including: (a) Randomization. (b) Blinding.

6.4.4 A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s).

6.4.5 The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.

6.4.6 A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

6.4.7 Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.

- Description of accountability procedures for the IP, including placebo or comparators. 7 Please elaborate on the following: how the investigational product (IP) is received and inventoried in the CHEO pharmacy, how will drug accountability work for the subjects, labeling of the drug according to the regulations, preparation and handling of the investigational product in pharmacy, documentation, unused IP and supply.

6.4.8 Maintenance of trial treatment randomization codes and procedures for breaking codes.

6.4.9 The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.

- Identify any data to be recorded directly on the CRF (i.e., no prior written or electronic data) and to be considered to be source data. Please clarify if the case report form will be electronic (i.e., REDCap) or paper CRF and documentation of source documentation into the electronic CRF i.e. "The study data will be transcribed by study personnel from the paper source documents/files into the eCRF. The investigator will verify that all data entries in the paper and eCRF are accurate and correct ……. etc." Describe the identification of any data to be recorded directly on the paper CRFs

(i.e., no prior written or electronic record of data), and to be considered to be source data. Indicate when QI will sign off on paper source data and electronic data entry.

GCP 6.5 Selection and Withdrawal of Subjects

6.5.1 Subject inclusion criteria.

6.5.2 Subject exclusion criteria.

- Subject exclusion criteria should specify all groups for whom the study medication is contraindicated (see page __ of the Product Monograph) as well as all potential drug interactions

6.5.3 Subject withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying:

a. When and how to withdraw subjects from the trial/ investigational product treatment.
b. The type and timing of the data to be collected for withdrawn subjects.
c. Whether and how subjects are to be replaced.
d. The follow-up for subjects withdrawn

6.6 Treatment of Subjects

6.6.1 The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.

6.6.2 Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

6.6.3 Procedures for monitoring subject compliance.

6.7 Assessment of Efficacy

6.7.1 Specification of the efficacy parameters.

6.7.2 Methods and timing for assessing, recording, and analyzing of efficacy parameters.

6.8 Assessment of Safety

6.8.2 Specification of the safety parameters

6.8.2 Methods and timing for assessing, recording and analyzing safety parameters

6.8.3 Procedures for eliciting reports of and for recording and reporting adverse events and intercurrent illness.

6.8.4 The type and duration of the follow-up of subjects after adverse events.

- Please define unexpected adverse events and when serious unexpected ADR's will be reported to Health Canada and the timelines (See Health Canada Division 5 regulations and GCP5.17. Describe the procedures for eliciting reports of, recording and reporting adverse event and inter-current illnesses. The protocol refers to the CCCTG SOP on SAE reporting but does not define adverse events (AE) or outline how AEs will be captured at the sites defining severity, causality and oversight and monitoring by the QI/PI at each site, along with follow up. Adverse events must be graded, assessed by severity and causality and reviewed by the site investigator or designee for medical oversight on the delegation log (see protocol template).

6.8.4 The type and duration of the f/up of subjects after adverse events

6.9.1 A description of the statistical methods to be employed, including timing of any planned interim analysis(ses).

6.9.2 The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.

6.9.3 The level of significance to be used.

6.9.4 Criteria for the termination of the trial.

6.9.5 Procedure for accounting for missing, unused, and spurious data.

6.9.6 Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).

6.9.7 The selection of subjects to be included in the analyses (e.g. all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).

6.9.7

- Please define unexpected adverse events and when serious unexpected ADR's will be reported to Health Canada and the timelines (See Health Canada Division 5 regulations and GCP5.17. Describe the procedures for eliciting reports of, recording and reporting adverse event and inter-current illnesses. The protocol refers to the CCCTG SOP on SAE reporting but does not define adverse events (AE) or outline how AEs will be captured at the sites defining severity, causality and oversight and monitoring by the QI/PI at each site, along with follow up. Adverse events must be graded, assessed by severity and causality and reviewed by the site investigator or designee for medical oversight on the delegation log (see protocol template).

6.9 Statistics

6.10 Direct Access to Source Data/Documents

The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

- Describe the direct access to source data/documents. The sponsor should ensure that it is specified in the protocol or other written agreement that the site /institution will permit trial related monitoring, audits, REB review, and regulatory inspections providing direct access to source data /documents

6.11 Quality Control and Quality Assurance Procedures

- Please describe how the trial will be monitored which is a GCP requirement by the Sponsor-Investigator GCP 5.18 Outline the monitoring plan for the study, develop systems and procedures to ensure the quality of every aspect of the clinical trial. Items such as quality assurance (Procedure manual, standard operating procedures, staff training, etc.) and quality control systems (maintenance records, calibration records, process validation, certificates, etc.) around both the investigational product and the Qualigen POCT used in the trial would be required.

- Quality Control and Quality Assurance - Monitoring of a regulated trial is a GCP requirement. Describe how you will ensure that this study is conducted and that data are generated, documented (recorded), and reported in compliance with this protocol, with GCP, and the NHP regulatory requirements. Describe the monitoring plan for the study. Elaborate on the type of monitoring that will be done (i.e., risk-based monitoring) and the timelines around the on-site and remote monitoring of the study at the multiple sites.) Describe further how queries in REDCap will be verified against the source documents and health records. See the protocol template and contact QA personnel for more information on a Monitoring plan.
- Provide the QA monitoring plan template and recommend the monitor plan be developed according to risk. As per section 5.0.4 Risk Control: Risk reduction activities may be incorporated in protocol design and implementation, monitoring plans, agreements between parties defining roles and responsibilities, systematic safeguards to ensure adherence to standard operating procedures, and training in processes and procedures.
- Predefined quality tolerance limits should be established, taking into consideration the medical and statistical characteristics of the variables as well as the statistical design of the trial, to identify systematic issues that can impact subject safety or reliability of trial results. Detection of deviations from the predefined quality tolerance limits should trigger an evaluation to determine if action is needed.

6.12 Ethics

Description of ethical considerations relating to the trial.

- Describe in detail procedures that will be utilized to maintain subject confidentiality, i.e., information about study subjects will be kept confidential and personal health information (PHI) is able to flow freely between members of the circle of care in responding to a patient's clinical needs. Within a hospital setting, the circle of care includes the attending physician and the health care team (i.e., residents, nurses, technicians, clinical clerks and other employees assigned to the patient) who have direct responsibilities for providing care to the individual.

6.13 Data Handling and Record Keeping

- Describe how the source documents and lab reports will be reviewed by the clinical team and data entry staff, who will ensure that they are accurate and complete. Describe how adverse events will be graded, assessed by severity and causality and reviewed by the site investigator or designee to ensure medical oversight. Describe the medical oversight over eligibility criteria, i.e., eligibility is considered medical oversight in a trial and will be verified and signed off by a physician investigator who is delegated this task.
- Record retention- Describe how records, files etc. will be retained and for the appropriate length of time. (25 years).

6.14 Financing and Insurance

Financing and insurance if not addressed in a separate agreement.

- Financing and insurance if not addressed in a separate agreement. This section should describe how the study will be funded, but should not contain specific dollar amounts

6.15 Publication Policy

Publication policy, if not addressed in a separate agreement.

- This section should include the requirements any publication policies of the Hospital, Research institute

etc. If, in addition to the sponsor-investigator, other investigators are involved in the study, identify who holds the primary responsibility for publication of any results of the study. Also define the need to first obtain approval from the primary responsible party before any information can be used or passed on to a third party.

6.16 Supplements

NOTE: Since the protocol and the clinical trial/study report are closely related, further relevant information can be found in the ICH Guideline for Structure and Content of Clinical Study Reports.

APPENDIX B – GCP Required Elements of Consent

Consent Review

4.8.10 Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

a. That the trial involves research.
b. The purpose of the trial.
c. The trial treatment(s) and the probability for random assignment to each treatment.
d. The trial procedures to be followed, including all invasive procedures.
e. The subject's responsibilities.
f. Those aspects of the trial that are experimental.
g. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
h. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
i. The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
j. The compensation and/or treatment available to the subject in the event of trial-related injury.
k. The anticipated prorated payment, if any, to the subject for participating in the trial.
l. The anticipated expenses, if any, to the subject for participating in the trial.
m. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
n. That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
o. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
p. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
q. The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
r. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
s. The expected duration of the subject's participation in the trial.
t. The approximate number of subjects involved in the trial.

APPENDIX C – Cover Letter Template

[Date]

Office of Clinical Trials
Therapeutic Products Directorate
5th Floor, Holland Cross, Tower B
Address Locator: 3105A
1600 Scott Street
Ottawa, Ontario
K1A 0K9

Dear Office of Clinical Trials Directorate,

Please find here enclosed the completed [**Clinical Trials Application (CTA) or Clinical Trial Application – Amendment (CTA-A)**] for the study entitled: [**Insert Protocol Title**].

This study is sponsored by the Governors of the University of Calgary and intends to utilize **[brand name].**

The reason for this application is a [**new indication/route/importing drug**].

The drug supply is manufactured by [**Company name**].

The proposed study is [**provide a brief description**].

I am happy to provide any additional information, as required.

Table: Information from the HC-SC3011 Form

Regulatory Activity Type	[box 5]
Brand Name	[box 8]
Common Name	[box 9]
Stakeholder Name	[box 11]
Stakeholder Legal Address	[boxes 12-16]
Dosage Form	[box 60]
Route of Administration	[box 63]
Drug Product	[box 64]
Proposed Indication/Use	[box 67]
Phase of Clinical Trial	[box 86]
Medicinal Active Ingredients	[box 56]

Sincerely,

[QI Signature Block]