This Guide is designed to be used in tandem with Nova Scotia Health Authority’s Clinical Trial Protocol Template. Please note that not all sections may apply; it will depend on the type of intervention and the complexity of your trial.

The World Health Organization (WHO) defines a clinical trial as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioral treatments, process-of care changes, preventive care, etc.

Designing and conducting a clinical trial is a complex undertaking requiring compliance with applicable scientific, ethical, regulatory and logistical standards. A clearly written protocol is the first step and ensures that the trial is conducted in a consistent, standardized fashion. Detail should be sufficient to allow the trial to be evaluated by a research ethics board (REB) and replicated at any research site.

Please note that protocol compliance is required. Any modification to the final version must be formally documented with a protocol amendment (description of a change or clarification) and/or amended protocol and must be approved by the sponsor and the REB prior to implementation unless immediate implementation is required for safety reasons.
COVER PAGE

Full Protocol Title:
The protocol title should clearly identify the design, population and intention of the trial, e.g., randomized, placebo-controlled, double-blind, clinical trial of X in the treatment of Z. For ease of reference, consider adding a shorter subtitle or protocol identifier.

Protocol Version:
Date and/or version number for identification and tracking purposes. Any amendment should also bear the amendment date and/or number.

Trial Registration Number:
Registry name and trial identifier. Registry must participate in the WHO International Clinical Trials Portal. See Registering Clinical Trials at NSHA’s guideline at: http://www.cdha.nshealth.ca/discovery-innovation/documents

Funder:
The names of the individuals or organizations providing financial, material, and/or other supports for the study. Funders may include corporations (e.g., a pharmaceutical company or device manufacturer providing financial support and/or investigational product), government, granting agencies and foundations.

Sponsor:
The name and contact information (including address) of the individual, company, institution, or organization that takes responsibility for the initiation, management and/or regulatory compliance (if applicable) of the clinical trial. The term “sponsor” is not synonymous with funder as the sponsor has many more responsibilities than providing fiscal and/or material support. There may be only one sponsor per study.

NOTE: An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a participant, is referred to as a “sponsor-investigator” The obligations of the sponsor-investigator include both those of the sponsor and those of an investigator. (ICH GCP 1.54).

Roles and Responsibilities:
These should be detailed here, elsewhere in the protocol or in a separate document (e.g., clinical trial agreement). The following are suggestions, as applicable:

- The role of the sponsor and funder, if any, in study design; collection; management; analysis and interpretation of the data; writing of the report; and the decision to submit the report for publication, including whether or not the sponsor or funder will have ultimate authority over any of these activities.
- Composition, roles and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, as applicable.
- The following roles may also apply, depending on the study. There may be overlap between one or more roles, especially if the investigator is also the sponsor. The name, title and
contact information (including address) for each individual should also be noted. Roles may include:

- principal investigator(s) / qualified investigator(s) at the clinical trial site(s) (note: site-specific information may be provided on a separate protocol page or addressed in a separate agreement)
- sponsor’s medical expert
- individual authorized to sign the protocol and any protocol amendments on behalf of the sponsor
- contract research organization or monitor, if different from the sponsor
- clinical laboratory (ies) and other medical and/or technical department(s) and/or institutions involved in the trial.
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APPENDICES
Typical appendix items are outcome scales, flowcharts and organizational charts.
SYNOPSIS
The following sections should provide a bare-bones outline of approximately one–two pages.

Study Title
Specify the full title (and subtitle, if applicable) of the study.

Objectives
Specify the primary and secondary objectives.

Design and Outcomes
Provide a very brief description of the study design (e.g., multi-centre, randomized, double-masked, Phase III), including the outcome variables for the primary and, if applicable, secondary objectives. Use a brief overview diagram here, if applicable. Complex diagrams may be included in Section 3, Study Design, instead.

Interventions and Duration
Briefly describe the interventions to be compared. Indicate the total length of time each participant will be on study (intervention period + additional follow-up off intervention, as applicable). A brief statement about the schedule and type of evaluations to be performed during the study may also be included.

Sample Size and Population
Briefly describe the number and type (population) of participants to be studied. If the randomization will be stratified, list the stratification factors. If there will be separate objectives and outcome variables for the strata, list these in the appropriate sections (above).
1 STUDY OBJECTIVES AND OUTCOMES

1.1 Primary Objective
The primary objective should always be to address a specific hypothesis. State the hypothesis in quantifiable terms; e.g., the experimental treatment will result in 12 months of additional survival compared to the control treatment. For statistical purposes, it may be worthwhile to state both the null and the alternative hypotheses. This primary objective must match the one used in Section 9, Statistical Considerations.

1.2 Secondary Objectives
Secondary objectives may or may not be hypothesis-driven, may include secondary outcomes, and more general non-experimental objectives (e.g., to develop a registry, to collect natural history data).

2 BACKGROUND

2.1 Rationale
- Describe the research question and justification for undertaking the trial.
- Describe the patient population to be studied and justify any restrictions on the population.
- Name and describe the intervention regimens, and justify why these particular interventions have been chosen.
- Describe and justify the route of administration, dosage regimen, intervention period, etc. Explain the choice of comparators (including placebo) if applicable.

2.2 Supporting Data
- Provide the scientific and/or medical data that justify the study, its design, and the intervention groups, including summary of relevant studies (published and unpublished).
- Summarize the known and potential risks of the interventions. For drug and natural health products, refer to the product monograph or package insert information.
- Justify any aspects of the study which are outside the defined parameters of use (e.g., different dosing schedule, new indication, new drug formulation).

3 STUDY DESIGN
- Briefly describe the study design and indicate, in general terms, how the design will fulfill the intent of the study.
- Include the type of trial (e.g., parallel group, crossover, single group, factorial), allocation ratio and framework (e.g., superiority, equivalence, non-inferiority, exploratory).
- Include a statement that the trial will be conducted in compliance with the protocol and any applicable research standards (e.g., regulatory requirements, ICH GCP).

4 SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1 Study Setting and Sample Size
A description of the study setting(s) (e.g., community clinic, academic hospital) and the estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.
4.2 Eligibility Criteria

List the inclusion and exclusion criteria to define and limit the kinds of patients that can participate in the trial. Eligibility criteria must be adhered to as written, so word them carefully and ensure they reflect your intention. Criteria that are too restrictive can:

- limit generalizability
- fail to mimic clinical practice
- increase study complexity and cost
- make it difficult to recruit

Criteria that are too open may result in:

- too many variables, making it difficult to attribute cause and effect
- safety concerns (increased risk of side effects in participants with severe health problems)

Keep the following tips in mind when creating criteria:

- include only those necessary to ensure scientific validity and patient safety
- ensure they are clearly defined and verifiable—they should not be open to interpretation (e.g., “current consumption of more than 10 units of alcohol per week” vs “alcohol abuse”; “myocardial infarction within 60 days of Baseline” vs “recent heart attack”)
- allow provision for investigator judgment where appropriate (e.g., “use of effective contraception, as judged by the principal investigator or designated associate”)
- criteria should be either inclusion or exclusion but not both (e.g., do not list “age 18 or over” as an inclusion criterion and “under 18” as an exclusion criterion)
- write in the affirmative.

4.2.1 Inclusion Criteria

Sample inclusion criteria:

- the disease or disorder under study, and how it is to be documented, i.e., diagnostic methods, criteria for classification, etc.
- clinical indicators of current status, as measured within XX days of randomization
- prior therapy, if any. Consider listing specific prior treatments and/or the allowable duration of prior therapy for the specific population to be studied (e.g., treatment-naïve, treatment-experienced or prior-treatment-failed “salvage” participants).
- demographic characteristics (e.g., gender, age) as applicable

4.2.2 Exclusion Criteria

Sample exclusion criteria:

- specific clinical contraindications. Specify grades of signs/symptoms.
- clinical/laboratory indicators of current status, obtained within XX days prior to randomization. List the specific tests to be performed and the narrowest acceptable range of laboratory values for exclusion, consistent with safety.
- any exclusion related to pregnancy, lactation, or plans to become pregnant. Specify methods for assessing current status and willingness to use contraception, if applicable.
- use of (excluded drugs, devices, etc.) within XX days prior to study entry
- for drug studies: allergy/sensitivity to study drugs or their formulations.
- any clinical (e.g., life expectancy, co-existing disease), demographic (e.g., age) or other
characteristic that precludes appropriate diagnosis, treatment or follow-up in the trial

- active drug or alcohol use or dependence that, in the opinion of the investigator, would interfere with adherence to study requirements
- serious illness (requiring systemic treatment and/or hospitalization) until participant either completes therapy or is clinically stable on therapy, in the opinion of the investigator, for at least XX days prior to study entry. List specific illnesses and acceptable times.
- inability or unwillingness of participant or legal guardian/representative to give written informed consent

4.3 Study Enrollment Procedures

4.3.1 Methods for identifying and recruiting candidates for the trial
Describe in detail.
Note: Please keep in mind that if personal health information is accessed for research purposes (e.g., identification of potential study participants), express consent is required from the participant before accessing the information unless certain criteria are met and the REB has agreed that consent is impracticable or is not required. Please review the REB Ethics Approval Submission Form for Clinical Trials, Section F Privacy and Confidentiality, for additional guidance and instruction. http://www.cdha.nshealth.ca/discovery-innovation/ethics

Describe procedures and any mandatory tools (e.g., a screening log at each clinical site) for documenting how participants learned about the trial, who referred them to the trial, reasons for ineligibility, and reasons for nonparticipation of eligible participants.

4.3.2 Consent procedures
Describe informed consent procedures; include instructions related to any special circumstances (e.g., obtaining assent from minors, use of substitute decision makers, and involvement of an impartial witness to the consent process if the participant is unable to read).

4.4. Randomization Procedures

If participants are to be randomized, describe the randomization procedure.

4.4.1 Sequence Generation
Detail the method of generating the allocation sequence (e.g., random number table, computer-generated sequencing). To reduce predictability of a random sequence, details of any planned restriction (e.g., blocking) should be provided in a separate document that is not accessible to those who assign interventions. Keep the following tips in mind for randomizing participants. Consider block randomization to keep numbers in the groups equal. Consider stratified randomization to account for baseline covariates (variable expected to influence outcome) to ensure group characteristics are similar; e.g., patients with covariate of diabetes are equally randomized to treatment arms.

4.4.2 Concealment Mechanism:
- Describe mechanism of implementing the allocation sequence (e.g., interactive voice randomization system, sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until the interventions are assigned.
• Identify who will generate the allocation sequence and who will assign participants to
groups (Note: individuals who generate codes should not typically randomize
participants to treatment).

4.5 Blinding
• Identify who will be blinded after assignment to interventions (e.g., participants, care
providers, outcome assessor, and data analysts). Consider the possibility of accidental
unblinding and how this would be addressed or prevented. For example, an unblinded
participant and a blinded assessor.
• Define circumstances under which unblinding is permissible and the procedure for
revealing a participant’s allocated intervention during the trial.

5 STUDY INTERVENTIONS

5.1 Interventions, Administration and Duration
• Indicate each study intervention, including how it is administered and the schedule, as
well as potential side effects. If applicable, describe the dosage form, packaging and
labeling of the intervention. Drugs, devices and natural health products must adhere to
regulatory requirements for labeling.
• Indicate where the participant will be treated (e.g., intensive care unit). Describe the
guidelines for use of appropriate supportive care medications or other treatment.
• Describe the criteria for discontinuing or modifying allocated interventions for a given trial
participant (e.g., treatment change in response to harms, participant request or
improving/worsening of symptoms).
Note: Standard of care does not need to be described. Standard of care refers to
procedures and interventions that will be administered to participants regardless of trial
participation.
All procedures and interventions that are administered as a direct result of trial participation
are not considered standard of care and need to be described in this section.

5.2 Handling of Study Interventions
• Describe how the interventions are to be acquired by the participating clinical site(s)
(e.g., the pharmaceutical company will distribute the drug in bulk to the site pharmacist),
and how they are to be stored, prepared and dispensed.
• If applicable, describe the disposition of unused study products (e.g., materials to be
returned to the pharmaceutical or device company supplying them or destroyed at site
and by whom).
• Describe procedures for documenting study product accountability (e.g., receipt,
assignment, preparation, dispensing, administration, return, destruction).
• If appropriate, develop and/or reference standard operating procedures (SOPs) for
detailed instructions on these issues. Capital Health’s pharmacy department has
developed medication-related SOPs for clinical trials for which they provide support.
Note mechanisms (if any) for masking (i.e., blinding) study intervention; e.g., if a placebo is
being used in a drug trial, note whether it has similar color, taste, etc., as the active drug.
5.3 Concomitant Interventions

Required, prohibited and precautionary interventions (e.g., medications) will depend upon the interventions used in the study and the outcomes of the study. Interventions not listed in sections 5.3.2 and 5.3.3 are permitted.

5.3.1 Required Interventions

5.3.2 Prohibited Interventions

Include drugs, devices, etc. from the exclusion criteria (Section 4.2.2) if they are also prohibited while the participant is on study.

5.3.3 Precautionary Interventions

Include instructions for modifications to the study interventions, if appropriate.

5.4 Adherence Assessment

Indicate whether compliance of participants with the study intervention is to be assessed. If so, provide details as to how this will be carried out (e.g., pill counts, electronic monitoring devices, adherence questionnaires), and in the section on Data Analyses (Section 9.4), describe how this information will be incorporated into the analysis of the study results.

6 CLINICAL AND LABORATORY EVALUATIONS

The Schedule of Evaluations in Section 6.1 should include all study evaluations. Use an ‘X’ in a cell to indicate that a particular evaluation is to be performed at a particular study visit. The definitions for the Schedule of Evaluations included in section 6.2 define the evaluations, provide timelines and include special considerations or instructions for evaluations. The evaluations listed and their order in the table are only examples! The evaluations should be specific for the particular protocol and should be arranged for clearest presentation. Additional columns may be needed to specify evaluations at intervention failure, at premature discontinuation of study interventions, or at other special time points that require a different set of evaluations. In complicated studies with multiple study steps or multiple randomization points, it may be useful to include in the table the time of each step and the time that study intervention is given to the participant.
6.1 Sample Schedule of Evaluations

<table>
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<tr>
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<th>Screening (XX days)</th>
<th>Baseline (XX days)</th>
<th>Intervention assignment and initiation</th>
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<th>8 wk</th>
<th>12 wk</th>
<th>16 wk</th>
<th>20 wk</th>
<th>24 wk</th>
<th>32 wk</th>
<th>40 wk</th>
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</table>
6.2 Timing of Evaluations

This section should include definitions of the column headings in the Schedule of Evaluations and any special instructions.

6.2.1 Pre-Intervention Evaluations

These evaluations occur prior to the participant receiving any study interventions. Also consider if a run-in or wash-out period is necessary and when that should occur.

6.2.1.1 Screening

The process and procedures required for evaluation of inclusion and exclusion criteria to determine if a participant is eligible to enter the study and receive the study intervention. Specify allowable range of time prior to intervention start during which all screening evaluations to determine eligibility must be completed. Indicate whether screening and baseline evaluations must be separated by a certain number of days or hours or whether screening and baseline evaluations may occur concurrently.

6.2.1.2 Baseline Evaluations

The process and procedures required to capture baseline measures before administration of the study intervention(s). Specify allowable windows for pre-entry evaluations relative to screening evaluations and intervention start. May occur as part of screening or may be conducted separately after screening is completed.

6.2.1.3 Intervention Assignment and/or Initiation

Specify time window for randomization (if applicable) and/or starting the study intervention relative to completion of screening and baseline evaluations.

6.2.2 On-Intervention Evaluations

Indicate schedule of evaluations occurring while the participant is on-intervention. Include the allowable time window in which evaluations may take place; e.g., study visits must be scheduled on the weeks indicated in the Schedule of Evaluations ± 7 days.

6.2.3 Intervention Discontinuation Evaluations

- Specify evaluations needed at the time of discontinuation of study intervention.
- Define “intervention discontinuation” if necessary.
- Also specify evaluations needed for participants who prematurely discontinue study intervention if these differ from those for participants who completed the full treatment course expected under the protocol. Note that for trials following an intention-to-treat design, participants who discontinue intervention should continue to be followed and evaluated as if they were receiving the intervention.

6.2.4 Post-intervention Follow-up Evaluations

Indicate the schedule for evaluations to be completed while the participant is no longer on study intervention but still being followed for outcomes, if applicable. Indicate evaluations needed for participants who complete scheduled study intervention and for participants who prematurely discontinue from study intervention, if applicable.

6.2.5 Final Evaluations

Indicate the schedule for procedures to be completed at the participant’s final study visit.
6.2.6 Post-Study Requirements
Specify any requirements for follow-up on participants once they have completed the study; e.g., it may be appropriate to ask the participant to return to the site two weeks or so after the participant goes off study in order to evaluate any adverse effects and to provide further information about options for future clinical care.

6.2.7 Pregnancy (Optional)
Specify instructions for women who become pregnant while on-study. If they are allowed to remain on study, specify whether they must sign a pregnancy consent form (refer to appropriate appendix) and whether additional evaluations are needed. Specify any requirements for men who father children while in the study, including any follow-up of pregnant partners and their offspring.

6.3 Special Instructions and Definitions of Evaluations
This section should explain the rows of the table of the Schedule of Evaluations from top to bottom. Specify the data items that must be included in the source documents.

6.3.1 Informed Consent
Describe the participant education and informed consent process; any plan for reviewing consent documents if changes are required; and how consent will be documented.

6.3.2 Documentation of [specify the disease/disorder under study]
Include clinical, laboratory, radiological or other recognized methods of documenting the disease or disorder.

6.3.3 Medical History

6.3.4 Treatment History

6.3.5 Concomitant Treatments

6.3.6 Study Intervention Modifications

6.3.7 Clinical Assessments
Define which clinical parameters are measured and when.

6.3.8 Laboratory Evaluations
Specify recording instructions.

6.3.9 Pharmacokinetic Studies
This section applies to drug trials when pharmacokinetics are performed. Pertinent additional information can be included in an appendix.

6.3.10 Other Laboratory Studies
Other laboratory studies (e.g., metabolic studies) and special tests should also be explained.

6.3.11 Additional Evaluations
6.3.12 Questionnaires
Include participant and caretaker interviews regarding quality of life, etc.

6.3.13 Adherence Assessments

7 ADVERSE EVENTS

- Specify safety parameters and the methods and timing for assessing, recording and analysis of same.
- Define adverse events, serious adverse events and any expedited reporting requirements. If there are serious adverse events that are known to be related to the disease under study and do not require reporting to the sponsor, list them here.
- Mention that local REB requirements and regulatory requirements (as applicable) for reporting adverse events must be followed, including expedited reporting of suspected unexpected serious adverse reactions.
- Indicate how adverse events are to be recorded and reported, and within what time-frame.
- Define the type and duration of the follow-up of participants after adverse events.
- Define the criteria for management or modification of treatment (if necessary)

For drug or natural health product trials, see ICH-GCP sections 4.11, 5.16 and 5.17 and ICH E8 for additional guidance.

Detailed definitions of adverse events, a table for grading their severity, and details of how clinical sites are to report them, may appear in a separate Manual of Operations, which may be referred to here.

If there are specific reactions that are not to be reported to the sponsor because they are expected please note and list the expected reactions for each study intervention. If the study intervention is a drug, natural health product or medical device, the sponsor may need to report certain events to Health Canada. Please review the applicable regulations and describe reportable events here.

Specify any events (e.g., suspected unexpected serious adverse reactions) to be communicated to the market authorization holder.

8 CRITERIA FOR DISCONTINUATION

List criteria (“stopping rules”) for discontinuing individual participants, parts of the trial or the entire trial and methods for determining when these criteria are met.

8.1 Study Withdrawal Procedures
- Describe when (e.g., unblinding, symptom worsening) and how participants must be withdrawn from the study and the scope of the withdrawal (study treatment and/or follow-up period).
- Describe the type and timing of the data to be collected from withdrawn participants.
- Describe whether and how participants are to be replaced.
- The follow-up (if any) for withdrawn participants (specify procedures and length of time).
8.2 Termination or Suspension of the Study

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues
It is recommended that a statistician be engaged to create a statistical plan and analysis. Describe general design issues including:
- primary and secondary objectives and how they relate to choice of primary and secondary outcome measures,
- the validity and reliability of the primary and secondary outcome measures,
- whether the documentation of an outcome will be reviewed and adjudicated by a committee, how quickly the committee will perform the adjudication, and whether the committee will be masked to the participant’s intervention group assignment,
- choice of study design (e.g., parallel groups, crossover, immediate versus deferred intervention, factorial, large simple trial, equivalency or non-inferiority trial),
- details of why certain design features were chosen (e.g., for a crossover trial, how the length of the washout period was chosen),
- what factors (if any) will be used to stratify the randomization,
If each participant is to be followed for a fixed follow-up period (e.g., to 24 months) rather than to a common closeout date (e.g., 24 months following enrollment of the last participant), clarify why the particular fixed time period was chosen.

9.2 Outcomes
Describe the primary, secondary and other outcomes, including the specific measurement variable (e.g., weight, lab value, analysis metric (e.g., change from baseline, final value, method of aggregation [e.g., median] and the time point for each outcome). Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

9.2.1 Primary outcome

9.2.2 Secondary outcomes

9.3 Sample Size and Accrual
- Describe the number of participants to be enrolled. In multicentre trials, specify the numbers for each trial site.
- Describe the statistical and clinical bases for the sample size calculation.
- State the assumptions made regarding accrual rate, event rate, noncompliance rate, loss-to-follow-up rate and Type I and II errors.
- Describe the plan for compensating for failures in these assumptions. Also describe what the power will be for assessing secondary outcomes.
- If the randomization will be stratified, indicate whether (and why) there is a sample size goal for each stratum.

9.4 Data Analyses
- List the statistical methods to be used to analyze the primary and secondary outcomes.
- Specify any confounding variables for which it is anticipated adjustment will be made.
- Indicate the timing of the analysis (e.g., interim, periodic, end-of-study).
- Specify the selection of participants to be included in the analysis (e.g., all randomized participants, all eligible participants, all participants who received study intervention as per protocol specifications, intention-to-treat analysis), and explain how missing data, outliers, noncompliance and losses to follow-up will be handled in the analyses.
- Describe any additional analyses (e.g., subgroup, adjusted analyses).

10 DATA COLLECTION, SITE MONITORING, AND ADVERSE EXPERIENCE REPORTING

10.1 Data Collection
- Describe the plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires) along with their reliability and validity, if known.
- Indicate data to be collected from participants who discontinue or deviate from the study protocol.

10.2 Study Records
Study records provide evidence that the investigator and team took good care of the participants, followed all the rules and produced valid results.
- Indicate what information will be retained for each participant and by whom.
- Describe methods for maintaining confidentiality of participant records. If the study intervention is a drug or natural health product, the records must be retained for 25 years. See: ICH-GCP Section 8: Essential Documents for required records.

Please keep in mind that sufficient source documentation must exist to permit complete reconstruction and evaluation of the trial. Source documentation is all information in original records and certified copies of original records of clinical findings, observations or other activities. Case Report Forms (CRFs) are frequently used in a clinical trial to record only the data required for statistical analysis. This data is captured/extrapolated from source documentation. CRFs that are sent offsite cannot contain any information that would identify the participant.

Identify any data to be recorded directly into the CRF (i.e., no prior written or electronic record of data) that will be considered source data. Keep in mind that source documentation is required and thus you cannot have an entire CRF that is not verified by source documentation. Direct entry into a CRF should be reserved for specific situations where it would be difficult to reproduce the source data (e.g., patient’s mark on a visual analogue scale).

10.2.1 Data Management
- Briefly describe clinical site responsibilities in data collection and management.
- Briefly describe sponsor responsibilities in data management; plans for data entry, coding, security and storage. If not included in the protocol, reference where the details of data management procedures can be found, (e.g., manual of operations/standard operating procedure).
10.3 Quality Assurance

- Briefly describe methods (e.g., site monitoring) for assuring protocol compliance, ethical standards, regulatory compliance and data quality at the clinical sites. A monitoring plan, separate from the protocol is recommended, as it can be revised without requiring REB approval for a protocol amendment. Reference the monitoring plan in this section. This section is mandatory for trials involving drugs and natural health products. Ensure that the protocol or other written agreement specifies that the investigator(s)/institution(s) must permit trial-related monitoring, audits and regulatory inspection(s), providing direct access to source data/documents.

11 SAFETY MONITORING

- If a Data and Safety Monitoring Board (DSMB) will be used, describe its composition, role, reporting structure and statement of whether it is independent from the sponsor and competing interests.
- Describe the interim monitoring plan, including the schedule of interim analyses and guidelines for stopping the study for reasons of efficacy, safety, futility or poor study performance (e.g., slow accrual, high losses-to-follow-up, and poor quality control).
- Note that interim monitoring (for safety and study performance) must be done at least annually following the randomization of the first participant.
- If the study includes stratification factors, indicate whether there are separate monitoring considerations for each stratum.
- Define who will have access to interim results and make the final decision to terminate the trial.
- If the trial is regulated by Health Canada and a DSMB is not to be used, explain why it is not needed.

12 ETHICAL CONSIDERATIONS RELATING TO THE TRIAL

12.1 Research Ethics Board (REB) Review and Informed Consent

This protocol and the informed consent document and any subsequent modifications must be reviewed and approved by the REB responsible for oversight of the study.

- Describe the plans for seeking REB approval and for communicating important protocol amendments to impacted parties (e.g., investigators, REBs)
- Describe who will obtain informed consent or assent from potential trial participants or their substitute decision makers. If you do not plan to enroll participants who cannot provide consent on their own mention this here. (not sure I understand the last sentence)

Sample text: A consent form will be signed by the participant. For participants who cannot consent for themselves, such as those below the legal age, a parent, legal guardian or substitute decision maker must sign the consent form and the participant's assent must also be obtained if he/she is able to understand the nature, significance and risks associated with the study. The consent form must describe the purpose of the study, the procedures to be followed and the risks and benefits of participation. A copy of the consent form is to be given to the participant, parent, legal guardian or substitute decision maker, and this fact will be documented.
12.2 Participant Confidentiality

- Describe how personal health information about potential and enrolled participants will be collected, shared and maintained in order to protect confidentiality before, during and after the trial.

Personal health information includes all information relating to health and health services that may (alone or in combination with other information) identify an individual, their family or their substitute decision maker. Use and disclosure of personal health information must comply with Capital Health policy and provincial legislation. See: REB Ethics Approval Submission form for Clinical Trials, Section F Privacy and Confidentiality. http://www.cdha.nshealth.ca/discovery-innovation/ethics.

- Describe plans for collection, evaluation and storage of biological specimens in the current trial and for future use in ancillary studies if applicable.

Sample text: All laboratory specimens, evaluation forms, reports, video recordings, and other records that leave the site will be identified only by a code number to maintain participant confidentiality. All records will be kept in a secure location. All computer entry and networking programs will contain on coded information. Personal health information will not be released without the participant’s documented permission.

12.3 Study Modification/Discontinuation

The study may be modified or discontinued at any time by the REB, the sponsor and/or by a regulatory authority (if applicable) to ensure that research participants are protected.

13 PUBLICATION OF RESEARCH FINDINGS

Include (if not addressed in a separate, written agreement) plans for investigator(s) and/or sponsor to communicate trial results to participants, professionals, the public and other relevant groups (e.g. via publication, data sharing) including any publication restrictions, authorship eligibility guidelines and intended use of professional writers.

14 REFERENCES

Provide the citations for all publications and presentations referenced in the text of the protocol.

APPENDICES (AS APPLICABLE)