

Canadian Cancer Clinical Trials Network Portfolio Eligibility Criteria and Guidelines

1) Introduction

The Canadian Cancer Clinical Trials Network (3CTN) will support a portfolio of academic clinical trials reflecting the priorities of clinicians, researchers, patients, ministries of health and funders. Scientific oversight will be provided by the Portfolio Committee (PC) and operational management by the 3CTN Coordinating Centre (CC).

2) Purpose

This document will outline the trial portfolio eligibility criteria and the process for identifying and maintaining portfolio trials.

3) Trial Eligibility

To be eligible for inclusion into the Portfolio, a study must be:

- Interventional oncology trial;
- Academically sponsored (Clinical Trial Applications held by academic institution);
- Open to multiple Canadian sites;
- Funded independently of 3CTN;
- Peer reviewed by external reviewers.

See Appendix A for definitions. Additional eligibility criteria may be required for clinical trials with unique trial designs.

Automatically Eligible: A study will be automatically included into the Portfolio if the above criteria apply. Eligibility will be reviewed by the CC, Scientific Director, and by the PC twice annually.

Potentially Eligible: If trial eligibility is uncertain, for example, if the trial appears to meet the objectives or is of benefit to 3CTN and does not meet the above criteria, the study will undergo Portfolio eligibility review by the PC.

a) Considerations for Special Clinical Trial Designs:

i) Feasibility/Pilot/Vanguard Trials – A trial will be considered in this category if the primary endpoints relate to the feasibility of conducting a larger and more definitive trial (i.e. meeting accrual targets). To be eligible for the Portfolio, it must meet both of the following additional criteria:

1. There are patient-related/patient-relevant endpoints;
2. The patients enrolled in the feasibility study will be included in the major/full study's analysis.

ii) Cluster Design Trials – A trial will be considered in this category if the planned randomization for the trial is 'higher' than the level of the patient (i.e. randomization occurs at the level of the healthcare provider or institution). To be eligible for the Portfolio, it must meet both of the following additional criteria:

1. The intervention must change clinical management at the patient-level (i.e. ensure that the trial satisfies 3CTN's definition of "Intervention");
2. There must be informed consent and data collection activities at the individual patient level for at least some of the study subjects.

ii) Umbrella Trials – studies may need to be divided and assessed individually. Only the eligible part/sub study may be considered eligible for the Portfolio.



4) Trial Ineligibility:

A trial will be excluded from the Portfolio if the study does not meet the above criteria and/or is:

- An audit;
- A needs assessment study;
- A quality improvement and other local service evaluations;
- A routine banking of biological samples or data except where this activity is integral to a self-contained research project designed to test a clear hypothesis.

5) Process for Portfolio Status

Once a study has met the Portfolio eligibility criteria listed above, interested applicants must submit a completed Portfolio application form to be considered for Portfolio status. To reduce potential delays, it is recommended a study is submitted for Portfolio status at the time of research ethics submission.

The application form and the clinicaltrials.gov record will be reviewed by the CC to determine initial trial eligibility. The information listed on the clinicaltrials.gov record may not be accurate or up to date. The applicant can include additional information at the time of the application or the CC may request for additional details required for assessment.

If the study is automatically eligible, it will be added to the Portfolio database. If eligibility is uncertain, the study will undergo Portfolio eligibility review by the PC members. After a study has been added to the Portfolio, all 3CTN sites will be notified and the study will be eligible for 3CTN support until it exits the Portfolio.

6) Communication of the Network Trial Portfolio

Trials will be listed in the 3CTN trial database and assessable from the 3CTN website 3ctn.ca. Updates to the Portfolio will be communicated electronically to all members of the Network.

7) Scientific Oversight of the Portfolio

The PC is responsible for the scientific oversight of the Portfolio and reports to the 3CTN Management Committee. PC members will meet at least twice annually to: a) review the Portfolio for scientific merit, priority and performance; b) review/approve the trials that were automatically added since their last meeting; c) review the balance of Portfolio trials to ensure a wide range of trials of interest/relevance to Canadians and the Canadian health care system.

The committee may highlight important initiatives such as those in rare cancers, young adults, cancer survivors, personalized medicine that may lead to inclusion of trial into the Portfolio.

8) Exit Criteria/Change of Portfolio Status

It is important to direct limited resources to supporting priority trials and to ensure these trials are done efficiently. All trials that exit the Portfolio will continue to be tracked for Portfolio impact. Studies that meet the following criteria will exit the Portfolio:

- Closed to recruitment;
- Deemed not eligible by PC.

Appendix A: Definitions

Academic Sponsored Clinical Trial

As per the Canadian Cancer Research Alliance, "Academic trials are defined as those developed by and coordinated by academic investigators such as trials that are "sponsored" by academic organizations like universities or cooperative clinical trial groups. Trials that are supported by grants from peer-reviewed agencies, charitable funding or by contracts from the pharmaceutical industry may also be included if their conduct, analysis and publication lies in the hands of academic investigators."

Canadian Academic Sponsor

A trial that is sponsored by a Canadian academic group, for example Canadian Cancer Trials Group, Ontario Clinical Oncology Group etc.

Clinical Trial Application (CTA) (Health Canada)

Clinical Trial Application are required for human clinical trials using drugs not authorized for sale in Canada, including clinical trials in Phases I through III of drug development and comparative bioavailability studies; as well as trials involving marketed drugs, where the proposed use of the drug is outside the parameters of the NOC or DIN, e.g., one or more of the following is different:

- a. Indication(s) and clinical use;
- b. Target patient populations(s);
- c. Route(s) of administration; or
- d. Dosage regimen(s).

Industry sponsored trial

A trial that is sponsored by the pharmaceutical industry.

Funded independently of 3CTN

The study has external funding from other funding agencies and can be sustained without 3CTN incentive funding.

Interventional Study/Clinical Trial (clinicaltrials.gov)

A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.

Observational Study (clinicaltrials.gov)

A clinical study in which participants identified as belonging to study groups are assessed for biomedical or health outcomes. Participants may receive diagnostic, therapeutic, or other types of interventions, but the investigator does not assign participants to specific interventions (as in an interventional study). If an intervention was withheld, this may also be considered an interventional study.

Open to Multiple Canadian Sites

A trial that is open to recruitment in more than one participating Canadian centre. In order to be considered a multi-centered trial, at the time of the application, the sponsor must have the intention of opening the study to multiple Canadian sites. 3CTN may remove the trial from the Portfolio if after inclusion, the trials remains single centered.



Peer Reviewed by External Reviewers

Studies will be considered peer-reviewed if:

- They are supported by an agency (CIHR, CBCRF, etc) that uses a peer-review process to allocate funding or;
- They are trials undertaken by a cooperative clinical trials group (i.e., CCTG) or;
- *Neither 1 nor 2, they have been approved by two experts external to the project and the institution(s) supporting it.

**Must contact the 3CTN Coordinating Centre (info@3ctn.ca) for more information before locating external experts. See Appendix B for more information.*

Sponsor (Health Canada)

An individual, corporate body, institution or organization that conducts a clinical trial as per Division 5. The sponsor must comply with its obligations as set out in the *Regulations* (including C.05.010-C.05.015) in adhering to good clinical practices for the proper use of the drugs, drug labeling requirements, record keeping, submission of information, reporting of ADRs, and trial discontinuation reporting requirements.

Appendix B: 3CTN Peer Review Guidelines

Peer Review Definition (Webster):

Peer review is a process by which a scholarly work (such as a paper or a research proposal) is checked by a group of experts in the same field to make sure it meets the necessary standards before it is published or accepted.

Purpose:

The 3CTN peer review process for a research application submitted for consideration for inclusion in the 3CTN Portfolio is intended to promote a process whereby applications are evaluated on the basis of a process that is fair, equitable, timely, and free of bias.

Guideline:

1. Peer review should include:
 - Analyzing the content of each application, and check for completeness.
 - Documenting and managing conflicts of interest.
 - Conducted by qualified reviewers based on scientific and technical qualifications and other considerations, including:
 - a. Authority in their scientific field
 - b. Dedication to high quality, fair, and objective reviews
 - c. Experience in research grant review
 - d. Departmental review within an institution is not eligible
 - e. Balanced representation
2. Studies will be considered independent peer-reviewed if one of the following criteria is met:
 - a. Eligible independent reviews include those conducted by the review panels of funding agencies such as CIHR, CCSRI, CBCF, Prostate Canada. NCI, including NCI CTEP Steering Committees, individual cancer clinical trial groups may also have independent peer review panels and procedures such as the Clinical Trials Committee of CCTG that review scientific merit and feasibility of proposals. Trial groups and networks should describe their external peer review processes to determine eligibility. But may also include favourable reviews from external experts. Trials that have undergone the peer review process for funding and score an equivalent to CIHRs top two categories (outstanding or excellent) will be seen as meeting the external peer review criteria; others will be reviewed on a case by case basis.

NOTE: Review within an institution is **not** eligible. Review by pharmaceutical companies is **not** eligible
3. If an eligible external review as described has not taken place, the project will require independent peer review.
 - a. Trial lead investigators may initiate independent peer review by identifying a minimum of two independent reviewers with the required knowledge and without conflicts to report on the scientific merit and feasibility of the study prior to submission to 3CTN for Portfolio inclusion. If required, the 3CTN Coordinating Centre (info@3ctn.ca) should be contacted for more information before locating external experts.
 - b. 3CTN Coordinating Centre can facilitate an external peer review process for the purposes of trial inclusion in the Portfolio. Contact info@3ctn.ca for more information. The deadline to complete the facilitated peer review process (FPR) is 12 weeks. The application will be closed until Applicant notifies the CC that FPR can be reopened for assessment.

Document Revision History

Version	Date	Description	Approval
1.0	11/19/2014	New document	
2.0	10/9/2019	<ul style="list-style-type: none"> • Updated document for consistency with 3CTN Strategic Plan 2018-2022 and current internal Coordinating Centre processes • Added section 3a) Considerations for Special Trial Designs • Updated Appendix A: Definitions • Removed Appendix B: Metrics • Added Appendix B: Peer Review Guidelines 	Approved by the Portfolio Committee September 26, 2019