GEORGE & FAY YEE
Centre for Healthcare Innovation

The Manitoba Clinical Research Manual

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Clinical Trials Platform, George & Fay Yee Centre for Healthcare Innovation

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Foreword

Welcome to the Clinical Trials Platform's Clinical Research Manual,

Conducting clinical research is becoming increasingly complex. In addition to subject matter knowledge and technical expertise in study design, data analysis and interpretation, nowadays a clinical investigator needs to know how to navigate the regulatory approval process, meet all ethical and regulatory obligations, engage patients and other stakeholders, and secure and effectively manage resources to implement the study plan.

The purpose of this manual is to provide practical information to clinical investigators and research project coordinators, managers and associates on how to effectively conduct clinical research studies in Manitoba. The main audience is clinicians (including students, interns and residents), graduate students and others new to clinical research or experienced researchers new to doing research in Manitoba. The manual is intended to provide a quick overview of the research process and a focused catalog of the resources and services available to support Manitoba researchers.

The manual consists of three sections:

1. **Overview of clinical research methods**
   A high-level and necessarily superficial description of the most commonly used clinical research approaches and study designs. There are many excellent courses, books and websites providing introductions to clinical research methods. The objective of this section is to complement these more in-depth sources with an overview that introduces new and aspiring researchers to the topic.

2. **Research practice**
   This part provides an overview of the practical steps of conducting clinical research projects from developing a research protocol and applying for funding to publishing the findings and 'closing' the project. We outline all the important steps in implementing research projects and alert the reader to important administrative procedures, such as obtaining research approvals, providing links to websites and other sources of additional information on every step along the way.

3. **Legal, Ethical and Organizational Considerations**
   This part provides a high-level discussion of the international, federal and provincial laws and regulations, as well as institutional, provincial and national policies governing the conduct of clinical researchers in Manitoba.

I would like to thank current and past members of the Clinical Trials Platform who contributed to researching, writing and developing this manual. Dr. Xibiao Ye and Ms. Connie Feschuk, with assistance from Brendan Foot and Tarpan Mankand, put together the manual whereas Mr. Barret Monchka developed the Website. I am also grateful for the contributions made by many CHI staff and other colleagues. For a list, please see the credits page.

I hope you find this manual informative and useful and wish you the best in all research adventures,

Salaheddin Mahmud, MD, PhD, FRCPC
Director, Clinical Trials Platform

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Copyright

Legal Disclaimer

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The information contained in this manual is intended solely to provide general guidance on matters of interest for the personal use of the reader, who accepts full responsibility for its use. In particular, this manual is not intended as a substitute for research training or to advice from research experts, clinicians and legal experts. It is also not intended as a replacement for the various research funding, ethics, site approval and data access and privacy committees and agencies. The reader should check with the appropriate agency before initiating a research study or significantly altering its objectives or methods.

Citation

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Chapter 1

Introduction: An Overview of Clinical Research Processes

According to the United States National Institutes of Health, clinical research is research with human subjects that is:

1. Patient-oriented research. This is research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator directly interacts with human subjects. This research includes: (a) mechanisms of human disease, (b), therapeutic interventions, (c) clinical trials, or (d) development of new technologies. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual
2. Epidemiological and behavioral studies
3. Outcomes research and health services research.

1.1 Identify the Research Question

> On the meaning of life, "Forty-two!" yelled Loonquawl. "Is that all you've got to show for seven and a half million years' work?"
>
> "I checked it very thoroughly," said the computer, "and that quite definitely is the answer. I think the problem, to be quite honest with you, is that you've never actually known what the question is."
>
> -Douglas Adams "The Hitchhiker's Guide to the Galaxy"

While it is difficult to determine if a research question is "good" or "bad", the most important point is to clearly define a specific research question. The question will often be relevant to clinical practice and patient care. Like priority-setting or question-forming processes in other areas, there are certain criteria that are useful to help researchers form a clinical research question. Here are some examples of issues to consider when forming a clinical research question:

- Importance and relevance
- Originality
- Feasibility (both technical and financial)
- Ethical considerations

Go to the Feasibility section to learn more about feasibility assessment

1.2 Develop a Research plan

A detailed research plan should include the research goal(s) and objectives, research strategy (population, data sources, study design, patient enrollment, intervention(s), and analytical plan), and how knowledge will be translated and disseminated.

A single study method cannot be applied to all clinical research questions. Choosing the right research design and method is one of the most important steps in planning and developing a clinical study. Check the overview of clinical research designs for information on different clinical research methods and the most appropriate method for your research question.

Go to the Proposal Development section to learn more about research proposal development

1.3 Seek Research Funds

Public (both governmental and non-governmental) funding organizations (e.g.,: CIHR, NSERC, SSHRC, NIH, Research Manitoba, and MMSF) and industry (i.e., pharmaceutical or medical device company) are the two main clinical research funding sources.

Go to the Funding section to find out funding opportunities

1.4 Obtain Approvals to Conduct the Research

Researchers must obtain approvals prior to conducting research involving humans. Reviews and approvals of research can come in many forms. You may be first required to have your proposed research reviewed through a peer-review or departmental review and approval process. Some studies, particularly data intensive research projects, may require a "feasibility review" to ensure the data exists and objectives are sound and practical. At minimum, most studies require ethical review and approval from a recognized Research Ethics Board (REB). You may also be required to submit your proposed research for institutional impact review at the institution where the research is being conducted. Research using patient data will often require privacy review and approval and studies being conducted under a contract (i.e. industry sponsored clinical trials) will require legal review of contracts and data user/sharing agreements. Finally, for research involving vulnerable populations, such as First Nations or Indigenous populations, further approvals may be required.

Go to the Approvals section to learn more about obtaining research approvals

1.5 Conduct the Research

Researchers may encounter many technical and administrative issues in conducting a research project. On this website, we list resources for supporting the conduct of your research involving humans.

Go to the Conduct Research section to learn more about the resources and tools

1.6 Report Research Findings

Writing and publishing a research article may be challenging, but there are many valuable and useful resources, including statistical consulting services, writing guidelines, scientific writing assistance, etc.

Go to the Publish section to learn more about the reporting of research findings

Part I

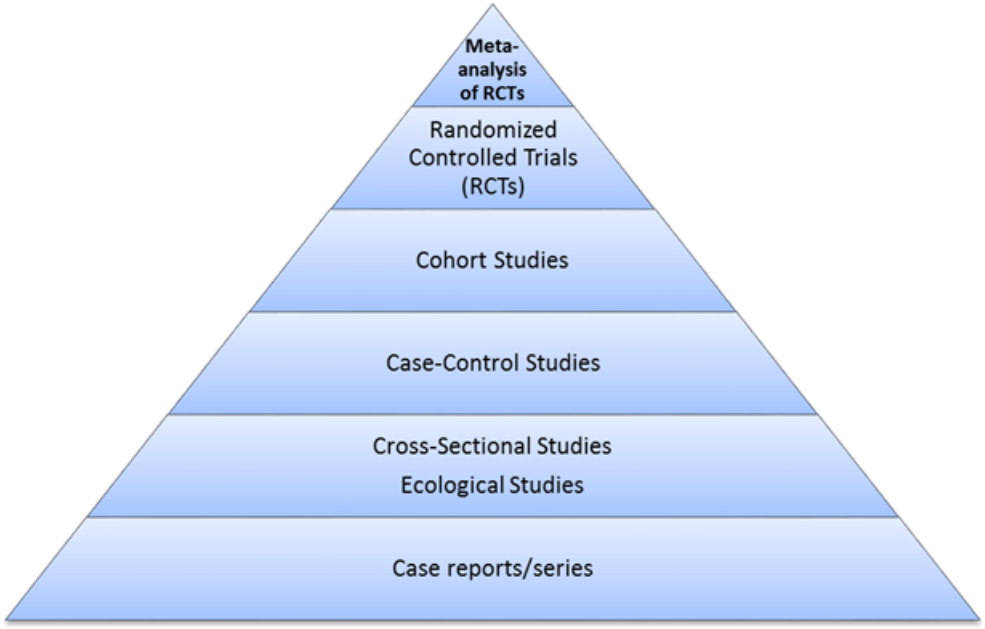
Choose the Right Study Method

Chapter 2

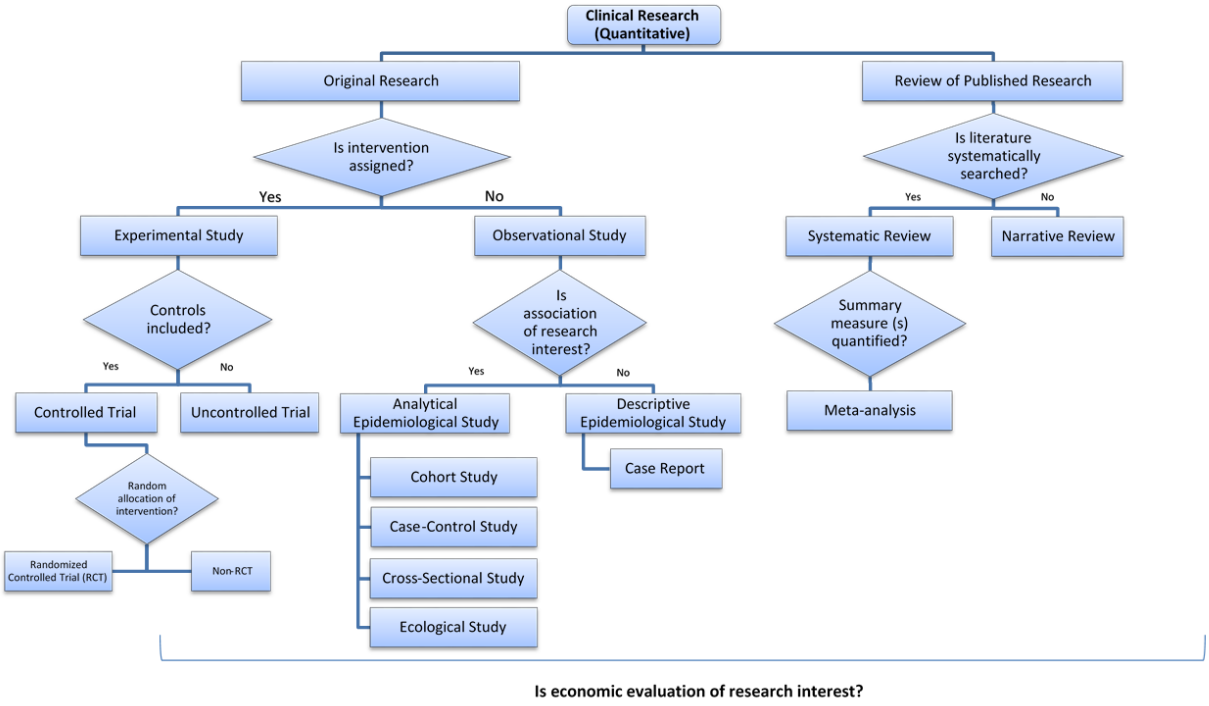
Overview of Clinical Research Designs

Clinical researchers may use either interventional studies or observational studies. Clinicians may also conduct other types of clinical research including case reports, economic evaluations (as an independent research or an integrated part of observational studies or clinical trials), and systematic reviews and meta-analyses. Qualitative research is increasingly conducted within or alongside these clinical studies.

Each study design has advantages and disadvantages, but generally speaking some designs provide more reliable evidence than others. The following hierarchy is often used to indicate the strength of evidence provided by different clinical research designs.



The chart below provides guidance on thinking about the most appropriate research design.



2.1 Clinical Trials

The World Health Organization defines a clinical trial as any study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials can be non-randomized or randomized. In randomized trials, researchers randomly assign participants to different intervention groups and compare patient outcomes according to the intervention status. Go to the Clinical Trials section to learn more.

2.2 Observational Studies

In observational studies, researchers do not assign any interventions, but observe what participants have received or were exposed to. Case-control studies and cohort studies are two commonly used observational study designs, but ecological studies and cross-sectional studies may also be used. Go to the Observational Studies section to learn more

Learn more about Differences Between Randomized Clinical Trials and Observational Studies

2.3 Other Types of Clinical Research Designs

There are several other types of clinical research designs that can be considered.

2.3.1 Case Reports

Case reports provide a detailed description of a limited number of patients, often without a comparison group. It is useful for hypothesis generation but not for hypothesis testing.

2.3.2 Economic Evaluations

The study of the economic cost associated with a disease itself (e.g., direct medical cost of type 2 diabetes) and with interventions to treat the disease (e.g., cost-effectiveness of a new drug for managing type 2 diabetes). Go to the Economic Evaluations section to learn more.

2.3.3 Systematic Reviews and Meta-analyses

The review systematically identifies relevant studies that answer a well-defined question and then synthesizes the evidence qualitatively or quantitatively. A meta-analysis will use statistical techniques to combine the synthesized data. Go to the Systematic Reviews and Meta-analyses section to learn more.

2.3.4 Qualitative Research

Qualitative research explores such things as ideas, opinions or problems in their natural setting to better understand them. It is increasingly used within or along with observational studies and clinical trials. Learn more about qualitative research.

Chapter 3

Clinical Trials

3.1 Trials by Phase

- Phase I trials focus on safety, dosage range and side effects of the new drug or treatment and involve a small number (20 to 100) of healthy participants or participants with the disease/condition.
- Phase II trials focus on efficacy, but also further test safety. Participants (up to several hundred) who have the disease are enrolled and often randomly allocated to control and treatment groups.
- Phase III trials often test efficacy and safety of an intervention on a large number of participants (300 to 3,000).
- Phase IV trials are observational studies conducted to gather information on the effectiveness and safety of the drug or intervention in routine practice (post-marketing). They complement pre-marketing efficacy trials and can identify adverse (and occasionally desirable) effects of the treatment.

3.2 Trials by Design

3.2.1 Explanatory Trials

Trials conducted in well-controlled conditions, in order to evaluate the efficacy and safety of an intervention, often employing one of the following designs:

- Parallel trial: A design in which participants are randomized to only one of the treatment or placebo groups and remain in that group throughout the duration of the trial. Differences in the occurrence of the study outcome provide the information needed to estimate the efficacy of the intervention.
- Crossover trial: A design in which all participants receive the treatment but in a different order. For instance, participants receiving treatment A may cross over to receiving treatment B later on during the same trial and vice versa.
- Delayed-Start trial (also known as randomized-start and one-way crossover trial): A design in which participants are randomized to receive either active treatment or placebo. But then, after a pre-specified period, the placebo group are switched to receive the active treatment. Often used in Parkinson's disease and dementia trials to determine whether the treatment can change the course of illness (disease-modifying effects) rather than just improve the symptoms.
- Stepped wedge trial: a generalization of the delayed-start design where the active treatment is sequentially rolled-out to all participants over time. Participants are randomized with respect to the order of receiving the treatment.
- Factorial trial: A design that tests the effects of more than one treatment focusing on possible interactions between them, permitting the simultaneous test of two or more different hypotheses. For instance, a

study a 2X2 factorial trial can be used to assess the effects of receiving Drug A, Drug B, both drugs compared to receiving neither drug.

3.2.2 Cluster Randomized Controlled Trials

Trials in which groups of subjects (clusters such as household, health units, villages etc) rather than subjects are randomized to receiving the intervention. All members of a cluster receive the same intervention. Often used to study the efficacy of interventions where the effects of treatment cannot be limited to a single subject (e.g., effect of healthcare provider training on their patient outcomes) or if the effect is at least partially mediated through group effects (e.g., "herd immunity" effects in vaccine trials).

3.2.3 Adaptive trials

A flexible design that allows planned modifications to the clinical trial procedures (e.g., drug dose) or statistical procedures in order to improve the chance of detecting a treatment effect or reduce potential harms.

3.2.4 Historical control trial

A design in which outcomes observed prior to the introduction of a new treatment are compared to that with the new treatment in similar participants. This is typically conducted when no parallel controls are available.

3.2.5 Pragmatic Trials

Trials conducted in "real-life" routine clinical practice conditions, in order to evaluate the effectiveness of an intervention.

Chapter 4

Observational Studies

Observational studies are studies where the effect of a risk factor or intervention is observed without changing who is or isn't exposed to the risk factor.

4.1 Case-control Studies

A case-control study compares exposure histories (e.g., medication use, vaccination, or surgical procedure) between participants who have the disease or condition under study (cases) and participants who do not have the disease or condition (controls) and is particularly useful in investigating relatively rare diseases (e.g., cancer).

4.2 Cohort Studies

A cohort study compares the incidence of outcomes (e.g., disease and mortality) between patients with different exposure status (with/without exposure or exposed at different levels). Depending on the frequency of the outcome, it may require a large number of participants and a long-term follow-up (e.g., for cancer). However, if information on exposure and outcome is already known (e.g., from existing records or databases), the analysis can be conducted retrospectively with significant saving in time and money.

Several variants of cohort and case-control designs (nested case-control, self-controlled case series and case-crossover designs) exist and might be more appropriate in studying a specific hypothesis.

4.3 Cross-sectional Studies

A cross-sectional study examines the relationship between the exposure (or intervention/treatment) of interest and the outcome (e.g., diabetes) in a defined population at a particular time. Researchers may not know whether the exposure occurred before or after the outcome. These studies measure prevalence of the outcome.

4.4 Ecological Studies

In ecological studies, both outcome and exposure are measured for groups of people rather than individuals. Therefore the conclusions, while applicable at the group level, may not not be applicable to the individuals (the "ecologic fallacy").

Learn more about the advantages and disadvantages of observational studies.

Chapter 5

Case Reports

Case reports provide detailed description of a limited number of patients, without a comparison group. It is useful for hypothesis generation but not for hypothesis testing.

Chapter 6

Systematic Reviews and Meta-analyses

Systematic reviews involve a systematic search of literature, a criterion-based identification of relevant studies, a critical appraisal of studies, and synthesis of evidence for a specific research question. A **meta-analysis** is a statistical analysis to quantify a summary measure (e.g., pooled odds ratio) of results from separate studies while considering the sources of difference and is often performed in a systematic review. Systematic reviews are different from narrative reviews, which do not involve a systematic search of literature or meta-analysis.

Learn more about reviews and services offered by CHI's Knowledge Synthesis Platform

Learn more: Cochrane Handbook for Systematic Reviews of Interventions.

Chapter 7

Economic Evaluations

Economic evaluations are increasingly being conducted alongside clinical trials in an effort to better inform decision makers of the economic value (i.e., return on investment) of the clinical intervention(s).The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) has developed Good Research Practices guidelines on cost-effectiveness analysis alongside clinical trials. Visit ISPOR website to learn more about the guidelines.

Cost of illness, cost-effectiveness/utility/benefit, and budget impact analysis are the main types of economic evaluation. Cost-effectiveness/utility analysis is particularly of interest to regulators, drug review committees, and drug/medical device companies as this type of data is increasingly used in decision-making.

7.1 Cost-Minimization Analysis

A study method to compare costs of alternative clinical interventions and is used if cost is the dominant determinant in a choice or if the health outcomes from each intervention are the same.

7.2 Cost-Effectiveness Analysis

A study method to compare the opportunity costs of various alternative clinical interventions in terms of obtaining desired clinical outcomes. Effectiveness is often measured specific to interventions (e.g., number of lives saved, number of re-admissions prevented).

7.3 Cost-Utility Analysis

A special type of cost-effectiveness analysis where generic outcome measures are used (e.g., quality of life [QOL] and quality-adjusted life-years [QALY]).

7.4 Cost-Benefit Analysis

A method to compare the opportunity costs of various alternative clinical interventions in terms of money-value benefit. Monetizing lives and health outcomes is often very challenging and controversial.

7.5 Budget Impact Analysis

An estimation of the budget impact of a change in clinical practice (e.g., use of a new drug or device). It is often conducted in accompaniment with cost-effectiveness/utility/benefit analysis and used for drug formulary or healthcare policy decision-making.

Chapter 8

Secondary Use of Data

Clinical studies can be based on data newly collected by researchers themselves (primary data collection) or based on data previously collected for another purpose such as for another research project, for health care or for education (secondary use of data). A major advantage of primary data collection is that researchers have full control of participant selection/enrollment and data elements, but this may require more research effort and funding. Secondary use of existing data may save time and cost, however, researchers have no or little control of the data, particularly the quality or format of the data. This means assessment of the data quality is critical before any analysis. Researchers may also be challenged with the absence of important information (e.g., lifestyle).

Researchers are increasingly using data collected in previous studies or data from existing studies collected for other purposes. For example, The Manitoba Follow-Up Study was originally developed for cardiovascular disease research, but has been used for supporting studies on diabetes, aging, and other health issues. This open data concept is gaining popularity and researchers are now able to access data from many studies developed by others, particularly some international consortium studies.

Find data sources

Line-level health data (e.g., cancer registry, hospital discharge abstracts) are important sources of data for clinical research. In Manitoba, The Manitoba Centre for Health Policy houses data on health, education, and justice that are linkable via a unique personal identity. Similar administrative data repositories are available in British Columbia (Population Data BC), Ontario (Institute for Clinical Evaluative Sciences), Nova Scotia (Health Data Nova Scotia), and Quebec (Quebec Health Data Banks). With appropriate approvals, researchers can gain access to these data via a virtual research environment.

Part II

Conducting Clinical Research in Manitoba

Chapter 9

Looking for Research Training?

The different training requirements for researchers are listed below in this section. In addition, the Community Health Sciences (CHS), the George and Fay Yee Centre for Healthcare Innovation (CHI) and the University of Manitoba (UM) conduct trainings and workshops on an ongoing basis on many relevant research topics. Researchers are welcome to attend them based on their interest.

9.1 (Possibly) Required Training

Prior to conducting research, an investigator/researcher may be required to complete privacy and human protection training. Below are links to training requirements. Researchers should not assume that the training they receive from one facility is recognized by another. Occasionally, researchers may be required to complete training on the same topic from differing agencies to ensure regulatory compliance.

9.1.1 Privacy Training

Privacy training to support the Personal Health Information Act (PHIA) and the Freedom of Information and Protection of Privacy Act (FIPPA) can be found at Manitoba Health, Seniors and Active Living - PHIA Online Training Program; at the University of Manitoba - PHIA/Privacy Training; and at Winnipeg Regional Health Authority - PHIA/Privacy Training.

9.1.2 Human Participants' Protection Training

Human participant protection training is required to be completed by all principal investigators (PI) submitting research to any of the University of Manitoba Research Ethics Boards (REB) for ethical review. The REB requires that the PI complete the Tri-Council Policy Statement Course on Research Ethics (TCPS2 CORE) prior to the awarding of the Certificate of Approval.

TCPS2 CORE is an online modular tutorial providing training on the safe and ethical conduct of research with humans and takes approximately 3 - 5 hours to complete. A certificate of completion is provided at the end of the course. This certificate will be requested by the REB before the Certificate of Final Approval is awarded.

Please Note: All members of your research team, including research nurses, research associates, and assistants are strongly encouraged to complete TCPS2 CORE training.

For more information:

- University of Manitoba Research Ethics Board Research Ethics Education and Training Modules
- The TCPS 2 Tutorial - Course on Research Ethics (CORE)

Key personnel of your research team may also be required to complete the National Institutes of Health (NIH) Online Tutorial - *"Human Participants Protection for Research Teams"*. This is a free tutorial offered to Researchers under a US federal funding (e.g. NIH) and takes approximately 3 hours to complete. For more information: Protecting Human Research Participants - NIH Office of Extramural Research

9.1.3 Sex and Gender Training

CIHR and Tri-Council stress the importance of incorporating sex (biological attributes) and gender (socially constructed roles, behaviours and identities) into health research when appropriate. CIHR Institute of Gender and Health offers online Sex and Gender training courses

9.1.4 Workplace Hazardous Materials Information System (WHMIS)

WHMIS is Canada's hazard communication system that was developed to provide workers with information on the safe use, storage, production, and handling of hazardous materials in the workplace. WHMIS Training can be accessed through the University of Manitoba

9.1.5 Biosafety

The UM Environmental Health and Safety Department provides information for Principal Investigator labs and biosafety training for research personnel. Generic Biosafety is currently a one-time requirement for all new laboratory personnel with subsequent refresher training as needed. Biological Safety can be accessed here

9.1.6 CITI Training

Researchers may also consider obtaining online training from the Collaborative Institutional Training Initiative (CITI Program). This non-profit organization, in partnership with the Network of Networks (N2), provides Canadian researchers with training in:

- Good Clinical Practice (GCP) and Refresher Courses
- Responsible Conduct of Research
- Health Canada Division 5 - Drugs for Clinical Trials Involving Humans
- Privacy in Research
- Biomedical Research Ethics
- Social and Behavioral Ethics
- Transportation of Dangerous Goods/International Air Transport Association.

For more information visit the CITI Program Course Offerings or contact the Centre for Healthcare Innovation for access to this free training.

9.1.7 Other Educational & Training Resources

- CHIMB Regulatory Documents Templates
- Clinical Research Educational and Training Calendar
- Network of Networks (N2)
- CIHR courses on integrating sex and gender in health research
- University of Manitoba (Learning & Organizational Development Services)
- Making Evidence Matter

Chapter 10

Assessing the Feasibility of your Research Idea

It is a good idea to determine the feasibility of your research project before committing your or someone else's resources to it. Often this assessment is optional and can be done informally, for instance via peer-review. Occasionally, the review is compulsory and is conducted by your employer (e.g., an academic department), by a data trustee like the WRHA Research Access and Approval Committee (WRHA-RAAC) or by a data steward like Manitoba Centre for Health Policy (MCHP). A feasibility review addresses questions such as, does the data or desired research population exist, can the data be obtained from existing data sets, who is interested in funding or collaborating in the project etc.

10.1 Clinical Trials Feasibility Assessment

If you are developing a clinical trial, there are templates for trial feasibility assessment. A sample form is available from the University of California San Francisco

10.2 Observational Studies Feasibility Assessment

If you plan to use administrative databases in Manitoba, MCHP requires an application for feasibility evaluation. The application form and submission information can be accessed at the MCHP website.

Chapter 11

Identify Funding Opportunities

- Advice on Applying for a Grant, Writing Papers, Setting up a Research Team and Managing Your Time CIHR guidebook for new principal investigators
- University of Manitoba Office of Research Service weekly newsletter
- CIHR research opportunities
- InfoEd Global SPIN funding alerts

Chapter 12

Clinical Research Sites and Services

- Health Sciences Centre: The largest WRHA-affiliated health care facility and one of the largest research and clinical trial centres in Manitoba. This tertiary care facility is a designated teaching hospital affiliated with the University of Manitoba. A wide spectrum of adult and pediatric research is conducted at the Centre annually. Researchers can access a variety of services for research through
  - the HSC Department of Research.
  - Children's Hospital Research Institute of Manitoba (CHRIM) by the Clinical Research Unit.

- St. Boniface Hospital: One of the largest tertiary health care facilities in Manitoba. The facility is a designated teaching hospital affiliated with the University of Manitoba. Researchers can access a variety of support services through
  - the Office of Clinical Research (OCR).
  - the St. Boniface Hospital Albrechtsen Research Centre:
    - Canadian Centre for Agri-Food Research in Health and Medicine (CCARM)
    - the Institute of Cardiovascular Sciences (ICS)
    - the Division of Neurodegenerative Disorders (DND).
  - the I.H. Asper Clinical Research Institute:
    - the WRHA Cardiac Sciences Program and Vascular Research.
- CancerCare Manitoba: Provides diagnostic services, treatment, supportive and palliative care to cancer patients in Manitoba. There are two locations in Winnipeg, one on the grounds of the Health Sciences Centre and the other on the grounds of St. Boniface General Hospital, and one centre located in Brandon, Manitoba. All centres conduct and support oncology research and clinical trials. The facility is a designated teaching hospital affiliated with the University of Manitoba. CancerCare Manitoba has several disease site research groups and provides support for research through the Research Institute of Oncology and Hematology (RIOH):
  - the Clinical Trials Unit, which facilitates and coordinates clinical research
  - the Manitoba Institute of Cell Biology, is dedicated to basic cell research to advance the understanding of cancer and blood disorders
  - the Department of Epidemiology and Cancer Registry, which provides cancer data and consultation for cancer epidemiological studies
- Seven Oaks General Hospital (SOGH): A community hospital located in Northwest Winnipeg and a major provider of Emergency Medicine and home of the Chronic Disease Innovation Centre and Wellness Institute. The institution has a focus on kidney research.
- Victoria General Hospital (VGH): A community hospital located in South Winnipeg and one of two community hospitals in Winnipeg to partner with its geographic area community services to facilitate improved patient flow. The hospital is home to the Victoria Hospital Institute of Clinical Research and Evaluation

- Grace General Hospital (GGH): A community hospital located in West Winnipeg. Patient care programs are organized into four major categories: Medicine Program, Surgery Program, Emergency Services Program and the Specialty Services Program.
- Concordia General Hospital (CGH): A community hospital in Northeast Winnipeg. Concordia Hospital specializes in orthopedics involving joint replacements and is home to the Hip and Knee Institute.
- The Deer Lodge Centre (DLC): A long-term care and rehabilitation facility located in West Winnipeg.
- Misericordia Health Centre: Provides specialized and long-term care, including unique programs, such as the Buhler Eye Care Centre, Provincial Health Contact Centre, Sleep Disorder Centre, and Urgent Care Centre.
- Manitoba Adolescent Treatment Centre (MATC): Provides a range of mental health services to children and adolescents who experience psychiatric and/or emotional disorders.
- St. Amant: A care facility for children with developmental disabilities and autism.
- Riverview Health Centre (RHC): A rehabilitation, palliative and long-term care facility.
- Panam Clinic: A facility focusing on athletes and sports-related injuries.
- Diagnostic Services Manitoba (DSM): Provides medical laboratory and medical imaging services to the province of Manitoba.

12.1 Health Research Institutes/Centres

- Centre on Aging
- Centre for Global Public Health
- Centre for the Research and Treatment of Atherosclerosis
- George and Fay Yee Centre for Healthcare Innovation
- IBD Clinic and Research Centre
- Manitoba Centre for Nursing and Health Research (MCNHR)
- Manitoba Centre for Proteomics and Systems Biology
- Manitoba Palliative Care Research Unit
- Manitoba Research Data Centre
- Manitoba Centre for Health Policy
- Richardson Centre For Functional Foods and Nutraceuticals
- University of Manitoba Vaccine and Drug Evaluation Centre

12.2 Regional Health Authorities (RHA)

- Winnipeg
- Prairie Mountain

- Southern
- Interlake-Eastern
- Northern

12.3 Looking for collaborators and experts

- University of Manitoba My Research Tools: A searchable database allows researchers to find collaborators using research expertise keywords. Researchers can also post project summaries to seek collaborators within the University.
- University of Winnipeg Experts Guide: This tool is primarily for connecting University of Winnipeg researchers to media. The directory lists experts by name and topic (area of research expertise).
- University of Brandon Research at BU: Researchers are encouraged to visit the individual faculty and school websites or to contact the Research Office when looking for a specific researcher or research area.
- Canadian Clinical Trials Asset Map: A searchable, web-based database of Canadian clinical research assets (i.e., hospitals, institutes, investigators). Researchers are encouraged to register and complete a profile and description of their research.

12.4 Looking for Research Data Sources

- Manitoba Population Health Research Data Repository: The data repository housed at the Manitoba Centre for Health Policy (MCHP) contains administrative data on health, education and justice and survey and census data primarily relating to residents of Manitoba. Line-level data can be linked to different data sets via a unique scrambled personal health information number.
- Manitoba Research Data Centre: The Centre is located on the grounds of the Bannatyne Campus of the University of Manitoba. The Centre is a secure Statistics Canada office that provides researchers with approved projects access to micro data from Statistics Canada's longitudinal surveys and other household surveys.
- the Department of Epidemiology and Cancer Registry, which maintains the Manitoba Cancer Registry and other cancer-related databases.

Chapter 13

Research Proposal Development

13.1 Tools and Resources for Grant Writing and Proposal Development

13.1.1 Literature Search Sources

- **Librarian services:** University of Manitoba Health Sciences Libraries offer service and support to health sciences researchers affiliated with the University and/or regional health authorities. The portal provides quick links to PubMed, ClinicalKey, UpToDate, and eJournals. Learn more about Health Sciences library services or find literature sources and all UM Libraries and services here.
- **Knowledge Synthesis Services:** The Knowledge Synthesis Platform of CHI can help researchers review research background and scientific evidence in a specific field. Learn more about Knowledge Synthesis services and submit a request

13.1.2 Research Protocol Development

Protocol Development Guidelines and Templates can be found at:

- SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials)
- TransCelerate Biopharma Inc. Common Protocol Template. TransCelerate is a non-profit organizations established by the world's leading biopharma companies
- Health Canada clinical trial protocol synopsis
- Clinical Research Portal protocol planning templates
- Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) provides a minimum set of items for reporting in systematic reviews and meta-analyses
- Information on randomization methods can be found at An overview of randomization techniques: An unbiased assessment of outcome in clinical research
- An overview of blinding in clinical trials can be found at Blinding in clinical trials and other studies
- A discussion of placebos in clinical trials can be found at Placebo in clinical trials

13.1.3 Patient Engagement

Requests for consults on how to authentically engage patients or involve people with lived experience as part of the research team can be submitted to the Knowledge Translation (KT) Platform. Patient engagement

should be considered as early in the research process as possible. There are multiple ways that patients can be involved throughout a project, including in the dissemination of results. The KT Platform can provide guidance on various engagement methods, budget considerations, and evaluation approaches.

13.1.4 Case Report Forms

Case report forms are developed to collect information from each participant as defined in the protocol. These forms may be electronic or paper. Development of the forms should begin early in the planning phase of the trial and should collect only information required by the protocol. Case report form design information can be found at Case Report Form (CRF) Design Tips - Slideshare. Case Report form templates can be found in the MB Clinical Research Portal's Research Tools

13.1.5 Informed Consent Guidelines, Templates and Example

- University of Manitoba forms and templates
- Informed consent requirements and templates by Health Canada and Public Health Agency of Canada.
- FDA's informed consent Information sheet

13.1.6 Online Sample Size and Statistical Power Calculation Tools

- Episheet Spreadsheets for analysis of epidemiologic data, developed by Kenneth Rothman. Sample size and power calculation for case-control and cohort studies.
- OpenEpi Open source software for epidemiological data analysis. Sample size and power calculation for case-control, cohort, cross-sectional studies and clinical trials.
- The Data Science Platform at CHI can assist researchers with the design, data collection, analysis and interpretation of their research.

13.1.7 Knowledge Translation

Knowledge translation (KT) includes the synthesis, exchange, application and dissemination of knowledge to improve health, the healthcare system and health service delivery. CHI's KT platform provides guidance and support related to both the practice and science of KT, including end-of-grant knowledge translation, integrated knowledge translation, and implementation science. A variety of KT training opportunities are also available. Learn more about Knowledge Translation Services and submit a request

KT Guidance and Resources

Guide to Knowledge Translation Planning at CIHR: Integrated and End-of-Grant Approaches are defined by CIHR as:

- Integrated knowledge translation (iKT) requires that knowledge users be members of the research team and participate in many stages of the research process. Research using an iKT approach still requires an end-of-grant KT plan.
- End-of-grant KT requires applicants to submit a plan for how they will translate their findings when the research is completed

SickKids Knowledge Translation Planning Template

Knowledge Translation in Health Care: Moving from Evidence to Practice

13.1.8 Budgeting Tools

- Budgeting for Clinical Trials at MB Clinical Research Portal, Research Tools, Templates, Budgeting
- University of Manitoba General Guidelines for Conducting Fee-For-Service Activities

13.1.9 Institutional Requirements for Grant Submissions

- University of Manitoba Funding Application Approval Form (FAAF): This form is mandatory for all grant applications to ensure compliance with the policies and requirements of the University of Manitoba and must be submitted to Office of Research Service prior to proceeding with the funding submission.
- University of Manitoba CIHR Grant Internal Reviews: Investigators are encouraged to submit their CIHR grants for internal panel review.
- University of Manitoba Policies and Guidelines on Research: This site contains the University of Manitoba policies on conduct of research, contract research and technical service activities, fund management and administration, appointment and employment, intellectual property, and other miscellaneous guidelines.
- University of Winnipeg
- Brandon University External Research Application Cover Sheet

13.1.10 Institutional Support

- University of Manitoba Medical and Health Sciences Research Facilitator: The Research Facilitator offers helps at all stages of research development, including grant application, editing support, and connection to other individuals, teams, offices, and organizations.

Chapter 14

Obtaining Approvals for Research

Researchers must obtain approvals prior to conducting their research (i.e. before a participant is enrolled or before data is obtained). Ethics, research impact, and privacy are the three essential reviews required for almost all clinical research projects conducted in Manitoba. For some research projects, additional reviews (e.g., feasibility, legal, other Types of reviews) may be required.

14.1 Research Ethics Review

The majority of research being conducted on humans or research involving access and analysis of health or personal health information data require ethical review and approval PRIOR to the commencement of the study. This means that study participants cannot be approached, recruited or enrolled prior to ethical review and approval. For data intensive research, this means that data cannot be obtained or accessed until a Research Ethics Board (REB) has reviewed the study and has granted approval to conduct the study.

REBs review research projects to ensure that the proposed research considers and safeguards the rights, safety and well-being of study participants. Research Ethics Board review and approval prior to study conduct is a legal requirement found in Canadian legislation, such as the Food and Drugs Act and Regulations (Health Canada) and in the Good Clinical Practice Guidelines (ICH-GCP).

Researchers affiliated with the University of Manitoba or the WRHA are required to submit their proposed research for ethical review to the University of Manitoba REB. Rural Researchers affiliated with the Brandon University are to submit their research projects to the Brandon University REB. Regional Health Authority (RHA) Researchers outside of the WRHA who are not affiliated with the University of Manitoba or Brandon University may be required to submit to a Canadian Central Research Ethics Board (e.g. Western IRB, Central IRB Services). For more information, contact the RHA where the research will occur.

Apply for REB Review:

- University of Manitoba
- University of Winnipeg
- Brandon University

14.2 Institutional Impact Review

If you are conducting your research from or within a health institution, such as a hospital or community health access centre, your proposed research may require impact review prior to commencement. Impact reviews and approval are required for all WRHA operated and affiliated institutions. Most institutions have a formal submission, review and approval process. Researchers should check with their respective institutions to determine whether an impact review is necessary prior to commencement of their research.

Impact reviews consider what impact the proposed research will have on institutional resources. Impact reviews by data trustees (i.e. Manitoba Family Services, Manitoba Justice, Vital Statistics etc.) also consider

how the data is being represented, used, and analyzed and the potential impact operationally, socially and politically of the outcomes of the research.

Impact review by Diagnostic Services of Manitoba (DSM) may be required for research involving human specimen sampling, processing or analysis.

Apply for Institutional Research Impact Review:

- WRHA Research Review Committees for all facilities.
- CancerCare Manitoba Research Resource Impact Committee (RRIC)
- HSC Research Impact Committee (Note: submission requirements are different for adult studies and pediatric studies)
- St. Boniface Hospital Research Review Committee

If the research will be conducted in a WRHA facility that does not have a Research Review Committee or if the research will be conducted in the community, the researcher must seek and receive approval from the WRHA Research Review Committee.

If the research will be conducted in a facility or community of another health authority, the researcher must seek approval from the appropriate authority as listed below:

- Prairie Mountain RHA
- Interlake-Eastern RHA
- Southern RHA
- Northern RHA

14.3 Privacy Review

Privacy review to meet PHIA requirements involving personal health information in relation to research is conducted by the UM REB during review of the study. The REB reviews the study's recruitment process, data security plans and the content of the consent form. Further information can be found at the Application of PHIA in a Research Ethics Context. In some cases an institutional Impact Committee may also review the research project to ensure privacy requirements are being met.

Researchers who are accessing data through the Manitoba Centre for Health Policy (MCHP) are required to obtain approval from the Province of Manitoba via the Health Information Privacy Committee (HIPC). Apply for HIPC privacy review at Health Information Privacy Committee (HIPC)

Researchers desiring access to health or personal health data from medical charts (paper or electronic) or from a WRHA database may require privacy review from either the Institutional Impact Committee where the medical charts are held or the WRHA Research Access and Approval Committee.

For research being conducted in other RHAs in Manitoba, Researchers may be required to submit to a data access granting committee or submit to HIPC.

14.4 Legal Review

Legal review may occur as part of an impact review or may be conducted independently by the institution or the university. Legal reviews typically involve the review and execution of agreements and contracts such as

confidentiality disclosure agreements, researcher data use and sharing agreements, and research contractual agreements between the researcher and the industry sponsor or funding agency.

Legal reviews typically address contractual projections for the participants, the researchers, and for the institutions where the research is being conducted. Legal reviews consider indemnification clauses, data ownership, intellectual property protections, and jurisdiction governance should the matter go to court.

In limited circumstances, legal review may also be required of the Participant Information And Consent Form, specifically for studies requiring high risk procedures or interventions or studies involving persons who are vulnerable or at high risk.

In Manitoba, legal review is typically conducted by the Director of Research, the institution's legal department, or the Office of Research Services (University of Manitoba). Depending on who will be a party within the contract, the Impact Review Committee may also review the contract.

For data researchers, data user and sharing agreements may also require legal review, particularly for those studies that are collaborating with institutions outside of Manitoba. User and sharing agreements provide the boundaries and scope of the data accessed for the purpose of the research, define who will access and review the data, the length of time the data will be accessed, and how the data will be shared and disseminated.

Further information can be obtained from:

- University of Manitoba Research Grant & Contract Forms
- University of Winnipeg Research Office
- Brandon University Office of Research Services

14.5 Protocol Review

Protocol review is performed to determine the feasibility of the proposed research. The review may be performed via peer-review, departmental review or by a data trustee like the WRHA Research Access and Approval Committee (WRHA-RAAC) or by a data steward like Manitoba Centre for Health Policy (MCHP).

14.6 Feasibility Review

Feasibility review is performed to determine the feasibility of the proposed research and typically occurs prior to other reviews and may or may not be compulsory (i.e. WRHA-RAAC's feasibility review is not compulsory prior to any other review where MCHP's feasibility review is). See Feasibility Assessment for more information.

14.7 Other Types of Reviews

Depending on the population under study, other reviews may be required.

- For studies involving **cancer patients**, review and approval from a CancerCare Manitoba Disease Site Group (CCMB-DSG) may be required prior to commencement.

- Studies involving **vulnerable populations** such as children, those who are physically or mentally infirm or those who are incarcerated may also require additional ethical or impact review prior to conduct.

- For projects involving **First Nations or Indigenous populations** including the Inuit or Metis, review and approval may be required from such organizations as the Assembly of Manitoba Chiefs or the Manitoba Metis Federation.

Researchers conducting research on the above populations should inquire with the Research Ethics Board or the institution where the research is being conducted (i.e. CancerCare MB, St. Amant Centre, Manitoba Justice etc.) as to whether additional reviews and approvals are required.

Research involving a **drug or device** may require approval from Health Canada through a Clinical Trial Application or Investigational Testing Authorization.

Chapter 15

Conduct Research

15.1 Register Your Study

The International Committee of Medical Journal Editors (ICMJE) requires that clinical trials, expecting to be considered for publication, be registered with a public registry prior to enrolling participants. ICMJE defines a clinical trial as research that prospectively assigns human participants to a health-related intervention. The Bannatyne REB provides information about registering a study at Guidelines for Registering in a Clinical Trial Registry

Clinical trial registries can be found at:

15.1.1 Original research

- Clinicaltrials.gov
- International Clinical Trials Registry Platform (ICTRP) ICTRP provides access to a central database containing the trial registration data sets provided by the registries in USA, Europe, China, UK, Australia and New Zealand.
- Health Canada's Clinical Trials Database
- Canadian Cancer Trials, including active cancer trials in Manitoba and other provinces.

Some of these registries are originally developed for clinical trials, but over the years the scope has been widened to include observational studies.

15.1.2 Systematic review and meta-analysis

The International Prospective Register of Systematic Reviews (PROSPERO) is a rapidly growing registry of systematic reviews. Some journals now require a registration with PROSPERO before manuscript submission.

15.1.3 Standard Operating Procedures (SOPs)

SOPs in research are written instructions to assure research processes are conducted to meet Good Clinical Practices and regulatory requirements. All staff participating in a research trial should be trained on the appropriate SOPs according to their function in the trial. Auditors will expect to see SOPs for the trial, evidence of staff training on the appropriate SOPs, and adherence to the SOPs by the study team.

The Network of Networks (N2) a national organization aiming to enhance clinical research capability and capacity in Canada has developed a set of clinical research SOPs. The George and Fay Yee Centre for Healthcare Innovation (CHI) and the University of Manitoba are N2 members. Contact CHI to learn more about N2 SOPs.

15.2 Data Collection Instruments

- Research Electronic Data Capture (REDCap)
- Questionnaires in clinical trials: guidelines for optimal design and administration by Phil Edwards.
- Selecting, designing, and developing your questionnaire by Petra M Boynton.
- Apple ResearchKit: An open source that allows clinical researchers to create a mobile app for informed consent, questionnaires, and biometric monitoring.

15.3 Research Support

- **Clinical Trial Design:** The Clinical Trials Platform of the George and Fay Yee Centre for Healthcare Innovation (CHI) offers trial design consulting services and monitoring services for investigator initiated trials conducted under a Health Canada application.
- **Collaboration Opportunities:** For assistance with identifying research collaboration opportunities involving the CHI platforms and external partners, contact Dr. Alanna Baldwin
- **Biostatistical Support:** The CHI Data Science Platform provides a range of statistical services and linkages to data resources.

15.3.1 Useful online resources for statistical analysis:

- Choosing the Correct Statistical Test: A table helping researchers to choose the right statistical method, originally developed by James D. Leeper. Sample SAS/STATA/SPSS/R code is provided.
- UCLA Statistical Computing: A collection of books, videos, SAS/STATA/SPSS/R example code for various statistical analysis methods.
- Episheet: Spreadsheets for analysis of epidemiologic data, developed by Kenneth Rothman.

- **Data Management:** REDCap (Research Electronic Data Capture) is a secure web application designed to support data capture for research studies. It provides users with multiple features such as multi-site data entry, real-time data entry validation, audit trails, and a calendar to schedule and track critical study events. CHI has implemented REDCap at the University of Manitoba to provide researchers with the ability to store, manage and analyze their research data. For more information visit the CHI REDCap webpage
- **Scientific Writing:** Researchers may contact a UM facilitator for assistance in identifying internal and external funding sources, reviewing proposals, facilitating the submission of large interdisciplinary team grant applications and assisting with knowledge translation, community engagement and exchange activities. University of Manitoba Research Facilitators
- **Customized IT Applications for Clinical Research:** Clinical Trials Platform IT Specialist offers customized IT and mobile solutions to researchers.
- **Educational events:** can be found on the Clinical Research Educational and Training Calendar hosted by CHI

15.4 Research Management

15.4.1 Regulatory Binder

The Regulatory Binder is a tool to organize essential documents that offer easy access to reference information by trial member and others (including trial monitor, auditor, REB, or regulatory authorities such as Health Canada).

According to the ICH-GCP, "Essential Documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of GCP and with all applicable regulatory requirements. Learn more about essential document contents before, during, and after the conduct of trials.

A Regulatory Binder (Trial Master File) Table of Contents for Canadian trials can be found here

An FDA Regulatory Binder developed by Harvard University can be found here

15.4.2 Managing Study Drugs, Devices, and Biologics

During the design and set-up phases of a trial, the investigator should develop a detailed plan regarding the receipt, storage, dispensing, and return or final disposition of investigational products (drugs, devices, and biologics).

15.4.3 Managing Trial Data

Management of trial data is an important consideration in clinical research to ensure the data collected is of high-quality and reliable. The collected data can then be statistically analyzed to support the outcomes of the research. Data management guidelines can be found at the sites below:

- Good Clinical Practice by the International Conference on Harmonization (ICH)
- Health Canada Guidance for Records Related to Clinical Trials (GUIDE-0068)
- FDA Guidance on Electronic Records; Electronic Signatures (21 CFR Part 11)
- Good Clinical Data Management Practices by The Society for Clinical Data Management

15.4.4 Retention of Trial Records

All records created during the conduct of a clinical trial must be retained. The length of time records need to be retained will depend on the relevant regulations, guidelines and any other regional, institutional or local requirements. However clinical trials conducted under a Health Canada Clinical Trial Application must be maintained for **25 years**. Further information from Health Canada can be found at Guidance for Records Related to Clinical Trials

Chapter 16

Participant Safety

16.1 Monitoring

There are two types of monitoring of clinical trials:

1. **To assess compliance**

   As per ICH E6 Guideline for Good Clinical Practice (GCP) for trials that involve human participants, trails should be monitored to protect participants, verify data integrity, and ensure compliance with GCP and regulatory requirements. The sponsor of the trial appoints a monitor who conducts monitoring in accordance with the site SOPs and the trial specific monitoring plan developed from the protocol in consideration of the risk to participants.

   For Health Canada approved Investigator Initiated Clinical Trials, the sponsor may be either the Principal Investigator or the University, and as such take on all the responsibilities of an industry sponsor. For more information on ICH Guidelines for monitoring see section 5.18

2. **Data and safety monitoring**

   A Data and Safety Monitoring Board (DSMB) is an independent group of experts who monitor the trial for participant safety, data quality and study performance. The DSMB makes recommendations concerning the continuation, modification, or termination of the trial. The number of DSMB members and meeting frequency are determined by the size and complexity of the trial, but a meeting may be called at any time if there is a concern regarding patient safety. The National Institute of Aging of the National Institutes of Health has developed a set of tools for data and safety monitoring, including:

   - Data and Safety Monitoring Plan (DSMP) Template and Guidelines
   - DSMP Checklist
   - Sample Data and Safety Monitoring Board (DSMB) Charter
   - Guideline for Budgeting for Data and Safety Monitoring
   - DSMB Conflict of Interest and Confidentiality Statement
   - DSMB Report Templates

16.2 Research Reporting

16.2.1 Adverse Events

Adverse event and unanticipated problems reporting is required for all research studies regardless of whether it is a clinical or non-clinical trial, or sponsor or investigator initiated. Adverse event collection should document unfavourable changes in current health status of the research participant or any incident, experience or outcome that suggests that the research may place participants or others at a greater risk of harm (including physical, psychological, economic or social harm).

The investigator must ensure the protocol outlines how adverse events will be defined, documented and monitored at the site and subsequently reported to the sponsor(s), Health Canada, applicable regulatory authorities (e.g. FDA, US Department of Health and Human Services) and the Research Ethics Board (REB).

Information about U of Manitoba adverse event reporting can be found here and the Adverse Events Report Form can be found here

Adverse events guidelines and templates developed by the National Institute of Aging of the National Institutes of Health:

- Adverse events and serious adverse events definitions and guidelines
- Adverse events form
- Serious adverse events form
- Adverse events and serious adverse events process flow

16.2.2 Protocol Deviations/Violations

Protocol deviations are activities that diverge from the Institutional Review Board approved protocol, whether deliberate or unintended. Deviations are classified as either "minor" or "major" and can be classified as a "deviation" or "violation".

Examples of minor protocol deviations, such as a minor deviation in testing time or a wording adjustment on a questionnaire may not require immediate reporting to the institutional ethics board (e.g. these are typically reported annually or on the final study status report) whereas the reporting of major protocol violations should occur in a timely manner.

According to the NIH, major protocol deviations (also called violations) occur when the divergence, whether deliberate or not, materially "(a) reduces the quality or completeness of the data, (b) makes the Informed Consent Form inaccurate, or (c) impacts a subject's safety, rights, or welfare."

Examples of major protocol deviations or violations include the following:

- Inadequate or poor informed consent or consenting procedures
- Enrolling a participant that does not meet eligibility (i.e. Inclusion/exclusion criteria not met)
- Unreported serious adverse events
- Improper breaking of the blind
- Use of prohibited or restricted medication or misuse of the study medication
- Incorrect or missing assessments or tests
- Mishandled biological samples
- Multiple visits missed or outside permissible windows
- Intentional deviation from protocol, Good Clinical Practice, or regulations by study personnel
- Subject repeated non-compliance with study requirements

(Source: Goldfarb, N, Journal of Clinical Research Best Practices Nov. 2005)

According to section 4.5.2 of ICH-GCP (E6 R2), "no deviations from, or change of, the protocol should be initiated without the prior written IRB/IEC approval/favorable opinion of an appropriate amendment, except when necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the trial" (e.g. changes in telephone #'s). Section 6.15 of the Tri-Council Policy Statement 2 (TCPS2), states that Researchers are obligated to report to their institutional ethics review board (REB)"any unanticipated issue or event that may increase the level of risk to participants, or has ethical implications that may affect the participant's welfare."

For more information on the required reporting of protocol deviations, visit University of Manitoba Ethics Medicine

16.2.3 Privacy Breaches

Any persons associated with the WRHA or WRHA Health Care Facility who have received a complaint or who have knowledge of a privacy breach of personal health information or reasonable suspicion of a privacy breach, shall immediately notify their manager or Privacy Officer at their site or the WRHA Chief Privacy Officer. More information can be found in the WRHA Privacy Policy.

Privacy breaches should also be reported to the University of Manitoba Research Ethics Board as a protocol deviation on the Major Protocol Deviation Form.

16.2.4 Participant Complaints or Questions

Provide the phone number of the University of Manitoba Bannatyne Campus Research Ethics Board (204 789-3389) to any participant that has complaints about the research or questions about his or her rights when participating in research.

Chapter 17

Analyze, Communicate, Publish and Close Clinical Research

17.1 Trial Completion and Close-out Documents

A close-out plan should be developed at the set-up phase of the study. Close-out should not happen before data queries and analyses are completed, documentation is stored, and the trial is closed with REB.

For University of Manitoba researchers, a Final Study Status Report is required.

17.2 Analyze and Interpret Trial Data

For analysis of trial data, Health Canada and USA FDA adopt the ICH Guidance: E9 Statistical Principles for Clinical Trials.

17.3 Reporting Guidelines

The EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network is an international initiative that seeks to improve the reliability and value of published health research literature by promoting transparent and accurate reporting and wider use of robust reporting guidelines. Reporting guidelines for the following main clinical study types can be found on the website of EQUATOR and the websites of individual guidelines (randomized trials, observational studies, systematic reviews, case reports, qualitative research, diagnostic / prognostic studies, quality improvement studies, economic evaluations, animal pre-clinical studies, and study protocols).

Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals can be found at the The International Committee of Medical Journal Editors'

17.4 Communicating Findings to Study Participants and Public

Below are links to sites that offer guidelines for providing clinical trail results:

- Creating a Standard Practice for Communicating Lay Language Trial Results to Study Volunteers. (by Ken Getz and Zach Hallinan, The Centre for Information and Study on Clinical Research Participation)
- Communications Handbook for Clinical Trials: Strategies, Tips, and Tools to Manage Controversy, Convey Your Message, and Disseminate Results. (by Elizabeth T. Robinson, Deborah Baron, Lori L. Heise, Jill Moffett, Sarah V. Harlan, Family Health International)

17.5 Knowledge Translation

The Canadian Institutes of Health Research (CIHR) defines knowledge translation (KT) as "raising knowledge users' awareness of research findings and facilitating the use of those findings." CIHR offers a Guide to Knowledge Translation Planning at CIHR: Integrated and End-of-Grant Approaches

Knowledge translation planning should begin early, ideally in the protocol development phase. During the protocol development phase, the CHI Knowledge Translation Platform can consult on how to develop a knowledge translation plan, provide guidance to ensure the budget is sufficient to support your plan, and provide advice on methods to evaluate knowledge translation efforts. More information can be found at the CHI Knowledge Translation Platform site or visit the CHI KT platform blog

Part III

Legal, Ethical and Organizational Considerations

Chapter 18

Understanding Regulations Governing Research: Legislation

18.1 Personal Health Information (PHI) and the Personal Health Information Act (PHIA)

The Personal Health Information Act was proclaimed into law in Manitoba in 1997. The law grants rights to individuals in accessing their personal health information while protecting the privacy of the individuals.

According to the Act, Personal Health Information is recorded information that can be linked to a specific person that relates to that person's health or health care history, including genetic information; the provision of health care to that person; and payment for the health care provided to that person. The law provides a mechanism to allow individuals to examine or receive information about themselves from their medical records held by a trustee (such as WRHA or Manitoba Health).

A Trustee is any person (such as a health care professional) or organization (such as a health care facility) that collects and/or holds personal health information. PHIA outlines the obligations of trustees as it pertains to the collection, use, disclosure, retention and destruction of personal health information.

Section 24 of the Act provides the obligations to trustees and researchers as it applies to health research.

Further information about PHIA can be found at:

- Personal Health Information Act (PHIA) of Manitoba
- Personal Health Information Act (PHIA) of Manitoba - Frequently Asked Questions
- Manitoba Ombudsman, Access and Privacy Division - PHIA FAQ
- Personal Health Information Act (PHIA) of Manitoba - Information for Trustees - Health Researchers

For more information/consultation on PHIA, contact

- **Provincial Government** Legislative Unit, Manitoba Health, Seniors and Active Living 300 Carlton Street Winnipeg MB R3B 3M9 Phone: 204-788-6612 Email: PHIAinfo@gov.mb.ca
- **Winnipeg Regional Health Authority (WRHA)** WRHA Chief Privacy Officer 4th Floor, 650 Main Street Winnipeg MB R3B 1E2 Phone: 204-926-7049 WRHA Affiliated Institutional Privacy Officers
- **University of Manitoba** 233 Elizabeth Dafoe Library Winnipeg, Manitoba R3T 2N2 Phone: 204-474-9462
- **Brandon University** FIPPA Access and Privacy Coordinator Brandon University Brandon, MB R7A 6A9 Phone: (204) 727-9707

18.2 Freedom of Information and Protection of Privacy Act (FIPPA)

The Freedom of Information and Protection of Privacy Act provides Manitobans with the right of access to records held by public bodies. To learn more about FIPPA visit

- Government of Manitoba - Freedom of Information and Protection of Privacy Act
- Government of Manitoba - FIPPA - Summary for Health Researchers - Trustees

Chapter 19

Understanding Regulations Governing Research: Regulations

19.1 Health Canada Regulations

Research involving a drug, medical device, nutraceutical, natural health product, biologic or radiopharmaceutical may require a Clinical Trial Application or an Investigational Testing Authorization Application to Health Canada and may require authorization from the applicable division of Health Canada **PRIOR** to conduct of the proposed research.

Please Note: that **drug trials** (Investigational or otherwise) are to be conducted under "Division 5" regulations of the Therapeutic Products Directorate. For more information on Division 5 visit Health Canada - Part C, Division 5 - Drugs for Clinical Trials Involving Human Subjects

To learn more about your obligations under Health Canada regulations visit:

Clinical Trials - Drug Trials

- Health Canada - Overview of Regulation of Clinical Trials in Canada
- Health Canada - Clinical Trials Manual
- Health Canada - Overview of Clinical Trial Application Process
- Health Canada - Clinical Trial Applications
- Health Canada - Institution/Investigator Initiated Clinical Trials
- Health Canada - Clinical Trial Applications - Sponsor Guidelines
- Health Canada - Efficacy
- Health Canada - ICH E6 - Good Clinical Practice Consolidated Guidelines

Clinical Trials - Medical Devices

- Health Canada - Medical Devices Acts and Legislation
- Health Canada - Preparation of an Application for Investigational Testing - Medical Devices
- Health Canada - Application for Investigational Testing Authorization

Clinical Trials - Natural Health Products/Nutraceuticals (NHP)

- Health Canada - Natural Health Products Directorate - NHP Regulations
- Health Canada - Guidance Documents on NHPs

19.2 Food and Drug Administration (FDA) Regulations - USA

Research involving a drug, medical device, nutraceutical, or natural health product with the intention of having the data recognized for a potential future marketing application in the United States, may be required to submit an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) application to the FDA and may require authorization from them **PRIOR** to conduct of the proposed research.

To learn more about FDA regulations visit:

- FDA - Investigational New Drug (IND) Application - 21 CFR Part 312
- FDA - Investigational New Drug (IND) Application
- FDA - Investigational Device Exemption (IDE) Application - 21 CRF 812
- FDA - Investigational Device Exemption (IDE) Application

19.3 Clinical Trials in the European Union (European Commission)

Collaborators with European partners in a clinical trial should become familiar with the Medicinal Products for Human Use - Clinical Trials Regulations EU No. 536/2014

To learn more about EU regulations visit:

- European Commission Medicinal Products for Human Use EU 536/2014

Chapter 20

Understanding Regulations Governing Research: Policies & Guidelines

Tri-Council Policy Statement (TCPS)

The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans is a research ethics policy statement established by three of Canada's federal research agencies (Canadian Institute of Health Research [CIHR], Natural Sciences and Engineering Research Council of Canada [NSERC] and Social Sciences and Humanities Research Council [SSHRC]) and was published in 1998. A revision of the policy statement (TCPS2) was published in December of 2010 and revised again in December of 2014.

The policy statement applies to all institutions eligible to receive or administer funding from one or more of the Agencies and to members of those institutions - faculty, staff and students. Requirement to adhere to this research ethics policy statement is a condition of funding. All universities in Manitoba are currently aligned with the policy statement and obligate researchers who receive Agencies' funding to comply with the obligations outlined therein.

Although Researchers who are under other types of funding are not mandated to comply with TCPS2, as good research practice, it is strongly recommended that all research comply with TCPS2. Researchers are strongly encouraged to familiarize themselves with this research ethics policy statement which can be found at Panel on Research Ethics - TCPS2 - December 2014

Training on the TCPS2 Course on Research Ethics (CORE) as required by the University of Manitoba Research Ethics Board can be accessed at TCPS2 CORE

International Council for Harmonization - Good Clinical Practice (ICH-GCP)

ICH-GCP provides technical requirements for human pharmaceutical research and is widely adopted by regulatory authorities throughout the world, including Health Canada and the US Food and Drug Administration. The ICH website offers a wealth of information on quality guidelines (such as good manufacturing guidelines), safety guidelines, efficacy guidelines (such as Good Clinical Practice Guidelines) and multidisciplinary guidelines. To learn more on ICH Guidelines visit the International Council for Harmonization (ICH)

Chapter 21

Working with Industry and Grant Funding Agencies

- **University of Manitoba** All research **grant applications** must be reviewed by the Office of Research Services (ORS) prior to submission to ensure compliance with the policies and requirements of the University and the sponsors.

  Research contracts may also be required to be reviewed by ORS, particularly if it involves an agreement between a UM affiliated faculty member or researcher where UM resources will be used or when research funds will be administered by University of Manitoba Finance. Contracts are negotiated by ORS staff in consultation with the researcher(s) on behalf of the university.

  Further information about contracts and research grants and templates can be found at University of Manitoba Research Grant and Contract Forms or ORS can be contacted directly at Funding Application Information: 204-474-7437 or Contract/Agreement information:204-474-6681.

  The University of Manitoba will enter into a research agreement with a sponsor if the Principal Investigator is performing research activities on behalf of the University and is receiving payment, or if a company is providing materials for research activities. Further information about research contracts can be found at:

  - Research Agreements Policy

- **WRHA and affiliated institutions** If the researcher is being engaged as a facility affiliated researcher (i.e. WRHA, HSC, SBGH) and not specifically a U of M Researcher, the contract and study agreement may be reviewed by the institution's respective research department. If the contract involves a fee for service and study funds are to be administered by the institution, then a "Specific Purpose Account" may be required to be opened with that institution.

  - Health Sciences Centre - If the study is to be administered at the HSC a Specific Purpose Account must be opened for each study. For further information about contracts, contact the HSC Department of Research

- **Brandon University** All research grant applications (e.g. CIHR, NSERC or NPO) and contracts for Brandon University affiliated researchers, unless otherwise agreed, must be reviewed by the Brandon University, Office of Vice-President (Academic & Provost). For more information read the Research Contract and Overhead Policy or contact the Office of Research Services at Brandon University directly at:204-727-7445.

- **Technology Transfer and Intellectual Property** The UM Technology Transfer Office's (TTO) role is to increase knowledge mobilization between UM and commercial partners. TTO promotes collaboration between industry and academia and oversees and guides intellectual property development. Further information about TTO can be found here. The UM Intellectual Property Policy can be found here.

21.1 Manitoba Funding Agencies

- **Research Manitoba** provides funds for research in the health, natural and social sciences, engineering and the humanities in Manitoba through a number of grants and awards programs from moneys received from the Province.
- **Manitoba Medical Service Foundation (MMSF)** provides funds for the establishment or furtherance of projects promoting scientific, research, educational and other activities in the maintenance and improvement of the health and well-being of the residents of Manitoba.
- **Health Sciences Centre Foundation** funds research, education, advanced technology and infrastructure enhancements.

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