As part of a research project funded by a Stem Cell Network public policy impact grant, our research team has put together a “roadmap” document that guides researchers through the various stages and regulatory requirements involved in conducting clinical trials of stem cell-based therapies and ultimately using them in the clinic. It shows the steps that need to be followed, references to the key legal and policy documents (with hyperlinks to the documents, where available), and the major classifications that will determine what requirements apply. The main focus of this document is the Health Canada requirements under the Food and Drugs Act and related regulations. What we have prepared is an overview of the regulatory framework. For additional information, please read the Acts, Regulations, Guidelines, or contact Health Canada regarding specific products.

Our first complete draft of the roadmap document is attached. We hope you will find it to be a useful reference and welcome your feedback on any aspect of the document.

Please send any comments or questions to Thu.nguyen@mcgill.ca.
Is the product intended for **human application**?

**YES**

**Food and Drugs Act (F&D)(1985)**

Cell & tissue products/therapies can also fall under one or more regulations developed under the F & DA. (Regulations: CTO Regulations, Food and Drug Regulations, Medical Devices Regulations)

- **Health Canada**
  - Health Products and Food Branch (HPFB)
    - Biologics and Genetic Therapies Directorate (BGTD) (Biological drugs & radio-pharma-ceuticals, ex. blood, blood products, gene therapy products, tissues & organs, xenografts, viral & bacterial vaccines)
    - Health Products and Food Branch Inspectorate (responsible for inspecting CTO establishments)
    - Therapeutic Products Directorate (TPD) - (Drugs & Medical Devices)
    - Marketed Health Products Directorate (post-marketing surveillance)
    - Office of Regulatory and International Affairs (provides guidance on specific products, product classification, Clinical Trial Application process, etc.)
    - Etc.
Is the product for **allogeneic use** (i.e. donor and recipient not the same person)?

- **YES**
  - Does the product perform the same function after transplantation (i.e. is the product for **homologous use**)?
    - **YES**
      - Is the product “**minimally manipulated**”?  
        - **YES**
          - Does the product have a systemic effect or depend on their metabolic activity for its primary function?  
            - **NO**
              - Is the product combined with non-cell or non-tissue products? (e.g. in case of tissue engineering)
                - **NO**
        
    - **NO**

- **NO**

**CTO Regulations DO NOT apply**

**CTO Regulations**: (Registration/Attestation Requirements – No pre-market review)
- Ensures the protection of the health and safety of Canadian transplant recipients  
- Contain safety requirements with respect to processing, storage, record keeping, distribution, importation, error, accident and adverse reaction investigation and reporting  
- Since CTO regulations are based primarily on ensuring safety, they do not contain requirements for the evaluation of clinical efficacy or quality. Thus, they are considered only adequate for those cells, tissues that are “minimally manipulated” (or that are more likely to maintain their integrity and function during processing)  
- CTO regulations are based on national standards established by the Canadian Standards Association  
- CTO regulations are “stand-alone” – i.e. any product falling under the CTO regulations are not subject to any other Act or Regulation.

---

Minimally manipulated:
- a) in respect of a **structural tissue**, that the processing does not alter the original characteristics that are relevant to its claimed utility for reconstruction, repair or replacement; and  
- b) in respect of cells and **non-structural tissue**, that the processing does not alter the biological characteristics that are relevant to their claimed utility →must look at the manufacturing process and/or the clinical data to support their intended use  
→“processing” – ex. Cutting/sizing/shaping, disinfection/sterilization, freezing, cryopreservation, etc.

---

Safety of Human Cells, Tissues and Organs for Transplantation (CTO) Regulations (2007)

Biologics & Genetic Therapies Directorate (BGTD) & Health Products and Food Branch Inspectorate (inspects and monitors compliance with Regulations)

Does the investigator intend to sell or import the product for the purpose of a clinical trial?

NO

If Phase IV Clinical Trial

No registration with Health Canada (however, still subject to Good Clinical Practice Guidelines)

Does the study involve Phase I-III clinical trials?

YES

Is the product a:

DRUG/BIOLOGIC?

Drug: any substance or mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease or its symptoms, (b) restoring, correcting or modifying organic function [F&DA definition]

Biologic: a subset of therapeutic products that are made from biological starting material, including those obtained by recombinant DNA procedures.

Examples: blood and blood products, drugs obtained by recombinant DNA procedures, etc. [Complete list in F&DA, Schedule D] [Also see: Health Products and Food Branch, Access to Therapeutic Products: The Regulatory Process in Canada (2006)]

DEVICE?

Device: any article, instrument, apparatus or contrivance, including any component, part or accessory thereof, manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, or its symptoms, (b) restoring, correcting or modifying a body structure and includes a contraceptive device but does not include a drug [F&DA definition]

COMBINATION PRODUCT?

“combination product”: “a therapeutic product that combines a drug component and a device component (which by themselves would be classified as a drug or a device), such that the distinctive nature of the drug component and device component is integrated in a singular product”

1. where the principal mechanism of action by which the claimed effect or purpose is achieved by PHARMACOLOGICAL, IMMUNOLOGICAL, OR METABOLIC means

2. if action of the product is pharmacological, immunological or metabolic BUT ACTION OCCURS IN VITRO without reintroducing a modified cellular substance to the patient

File: Clinical Trial Application (CTA)

File: Investigational Testing Application (ITA)
Before any new drug, biologic, or medical device can be sold in Canada, it must successfully pass a review process to assess its safety, efficacy and quality.

The Health Products and Food Branch (HPFB) reviews the Clinical Trial Application (CTA) on a case-by-case basis to ensure that the trial is properly designed and participants are not exposed to undue risks.

Also see: Food and Drug Regulations – Part C, Division IA & 2: all facilities engaged in manufacturing a drug or biologic must obtain an establishment license. Licences are approved based on inspection and evidence that there is compliance with GMP.
Other useful links:

- **Assisted Human Reproduction Act (2004)** ([http://laws.justice.gc.ca/eng/acts/A-13.4/](http://laws.justice.gc.ca/eng/acts/A-13.4/)) – for research involving human embryos, includes acts that are prohibited and subject to criminal sanctions (e.g. ban on cloning, creation of embryos for research purposes, buying/selling of human embryos)

- **Updated Guidelines for Human Pluripotent Stem Cell Research (2010)** ([http://www.cihr-irsc.gc.ca/e/42071.html](http://www.cihr-irsc.gc.ca/e/42071.html)) - Establishes the Stem Cell Oversight Committee (SCOC) – national stem cell protocol review board) which reviews and approves publicly funded research involving human pluripotent stem cells


- **International Conference on Harmonization (ICH) – Guidance on Good Clinical Practice (GCP)** ([http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/e6-eng.pdf](http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/e6-eng.pdf)) - International ethical and scientific quality standards for designing, conducting, recording and reporting trials that involve human participants. Standards ensure that rights, safety and well-being of trial participants are protected in accordance with established ethical principles (e.g. Declaration of Helsinki).