Outline

• Regenerative Medicine Landscape in Canada

• Overview of the relevant legislation and regulations concerning cell and gene therapies
  – *Food and Drugs Act*;
  – *Safety of Human Cells, Tissues, and Organs for Transplantation Regulations*; and
  – *Food and Drug Regulations*

• Equipment used to manufacture cell and gene therapies

• Resources to help navigate regulations
  – Guidance for cell therapies
  – Early access mechanisms
Realizing the Promise of Regenerative Medicine

- Supports for infrastructure
- Regulatory Oversight
- Research
- Pharmaceutical Policy
Access to Regenerative Medicine

Minister of Health mandate letter (2015)
“...improve access to necessary prescription medicines”

HPFB priorities – new Strategic Plan

Research & development

Health Canada review / authorization

Patented Medicine Prices Review Board (PMPRB)

Health Technology Assessment

Provincial/Territorial Drug Plans

Hospitals

Private Plans

pan-Canadian Pharmaceutical Alliance (pCPA)

Innovation and access to drugs - What role does the regulator play?
Federal Oversight of Cell and Gene Therapies

Food and Drugs Act

“Drug” Definition:

includes any substance or mixture of substances manufactured, sold or represented for use in:

• the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state, or its symptoms, in human beings,
• restoring, correcting or modifying organic functions in human beings
Regulatory Framework for Gene Therapies

Gene Therapy Definition (informal):

Products, including cells that have been genetically manipulated such that the therapeutic function of the product is afforded by the introduced gene(s).
Cell Therapy Definition (Informal):

Includes human cells of somatic (fetal, neonatal and adult) or embryonic origin that are used for therapeutic purposes. This includes both cells derived from the individual undergoing treatment (autologous) as well as from donated tissues (allogeneic) and encompasses induced pluripotent stem cells or other cells in which the differentiation potential has been altered or enhanced.
“Advanced Cell Therapy” vs CTO for Transplantation

Food and Drugs Act

Food and Drug Regulations

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

Cells considered “drugs”
- Requirement of pre-market approval; Establishment License; Good Manufacturing Practices; Lot Release testing; and Supporting Evidence of Safety, Quality, and Efficacy

Investigational Cells
- Requirement of authorization to perform clinical trial

Cells for transplantation
- Requirement to certify the establishment is in compliance and that the cell is safe for transplantation

New Drug Submission
Clinical Trial Application
Establishment Registration
Overview of CTO Regulations
Safety of Human Cells, Tissues and Organs for Transplantation Regulations (CTO Regulations)

- No pre-market review since efficacy established
- Based on safety - mitigating risks of transmissible diseases

Excludes Cells and Tissues that are
- More than Minimally Manipulated
- Not for Homologous use
- Autologous use
- Reliant on their systemic effect or rely on metabolic activity for the primary mechanism of action (with the exception of lymphohematopoietic cells from cord blood, peripheral blood or bone marrow, or islet cells)
- Subject of clinical investigations (device or drug)
Overview of Food and Drug Regulations
Food and Drug Regulations

- Part C - Drugs
  - Division 1 – General
  - Division 1A – Establishment Licenses
  - Division 2 – Good Manufacturing Practices
  - Division 4 - Schedule D Drugs (Biologics)
  - Division 5 – Drugs for Clinical Trials Involving Human Subjects
  - Division 8 – New Drugs

http://laws-lois.justice.gc.ca/eng/regulations/c.r.c.,_c._870/index.html
Division 5 – Clinical Trials

Stipulates what criteria must be met to sell or import a drug for the purpose of a clinical trial.

- Requirement for an application for CT authorization or amendment
- Sponsor’s obligation to Good Clinical Practices, labelling and records
- Adverse Drug Reaction reporting, trial discontinuance, and suspension and cancellation
Clinical Trial Application

Clinical Trial Applications should contain:

- Detailed information about the clinical trial protocol
- Manufacturing/Clinical information about all unapproved components & components not approved for that use
- REB status and Good Laboratory/Clinical/Manufacturing Practices (GLP, GCP, GMP), compliance

Ultimately, authorization requires evidence to establish that the clinical trial does not endanger/does not run contrary to the interests of the participants

*30 day default authorization of submission*
Policy themes

Leverage existing policies
- “Drug” approach / classification policies apply
- ICH principles / CTD format encouraged

Flexibility in approach
- Early/late stage approach vs Phase I,II,III trials
- Increasingly stringent controls/evidence

Consistent with other regulated human derived materials
- Infectious disease testing/screening (as appropriate)

Consistent with other regulated (biologic) products
- TSE risks
- Adventitious agents

Aware of unique ethical concerns
- Use of animals
- Human donors
- Human subjects (& potential long-term issues)
Division 8 – New Drugs

• Sufficient information and material is required for Health Canada to assess safety and effectiveness is required for authorization of a “new drug”
  – chemistry & manufacturing data
  – non-clinical data
  – clinical data

• Data Protection & Market Exclusivity
Equipment Used to Manufacture Cell and Gene Therapies
Device Definition:

Includes an instrument, apparatus, contrivance or other similar article, or an in vitro reagent, including a component, part or accessory of any of them, that is manufactured, sold or represented for use in treatment or mitigation of disease.

- It does not include equipment that achieves its therapeutic function solely by pharmacological, immunological or metabolic means or solely by chemical means.
Accelerators available to Cell Therapies
Pre-sub meetings as a tool to accelerate development

• Health Canada provides advice, at no cost, to clinical trial sponsors and recommends early consultation

• Experts at the Health Products and Food Branch are available to assist sponsors at any stage of development. If beneficial to the sponsor more than one pre-meeting can be arranged to provide ongoing support and advice

Types of Meetings:

• Pre-Clinical Trial Application (CTA) Consultation Meeting
• Pre-submission meetings
• Early parallel scientific advice
Pre-sub meetings as a tool to accelerate development

• Pre-CTA and pre-NDS discussions have been used to discuss sponsor proposals for unique regulatory approaches to promising drug products for unmet / insufficiently met medical needs

• Discussions include
  – Priority review process / eligibility
  – NOC/c eligibility
  – Early regulator input on submission approach / plan (non-binding)
Priority review as a tool to accelerate development

- Applies to NDSs and SNDSs for serious, life-threatening or severely debilitating disease for which there is substantial evidence of clinical effectiveness that the drug provides:
  - effective treatment of a disease for which no drug is available; OR
  - Offers a significant increase in efficacy and/or significant decrease in risk over existing therapies for a disease that is currently not adequately managed.

- Manufacturer submits a written request (Clinical Assessment Package) including
  - Generic name and brand name; indication; synopsis of data; description of disease condition and role of product

- HC gives a response in 30 days.
- Company then has 60 days to submit.
NOC/c as a tool to accelerate development

- NOC/c clinical eligibility criteria are in line with Priority Review criteria, but applies to products with promising evidence of clinical efficacy.

- Sponsor indicates request for conditional approval as part of the NDS submission.

- Health Canada’s first cell therapy authorization (Prochymal) relied on NOC/c conditional authorization. The authorization was granted with the sponsor agreeing in a letter of undertaking to complete confirmatory clinical trials.
Continual Improvement Future Alternative Pathways/Tools in Development

- Early/parallel scientific advice with Health Technology Assessment bodies

- Alignment of the HC review with the Health Technology Assessment bodies

- Expansion of priority review pathways to address healthcare system need

- Enhanced use of foreign reviews/decisions
Appendix – Links to applicable guidance

• Guidance Document For Clinical Trial Sponsors: Clinical Trial Applications

• Guidance Document: Preparation of Clinical Trial Applications for use of Cell Therapy Products in Humans

• Guidance for Industry: Management of Drug Submissions

• Guidance for Industry - Priority Review of Drug Submissions