# Emergence and Advancement of Technologies: Regulatory Challenges and Considerations

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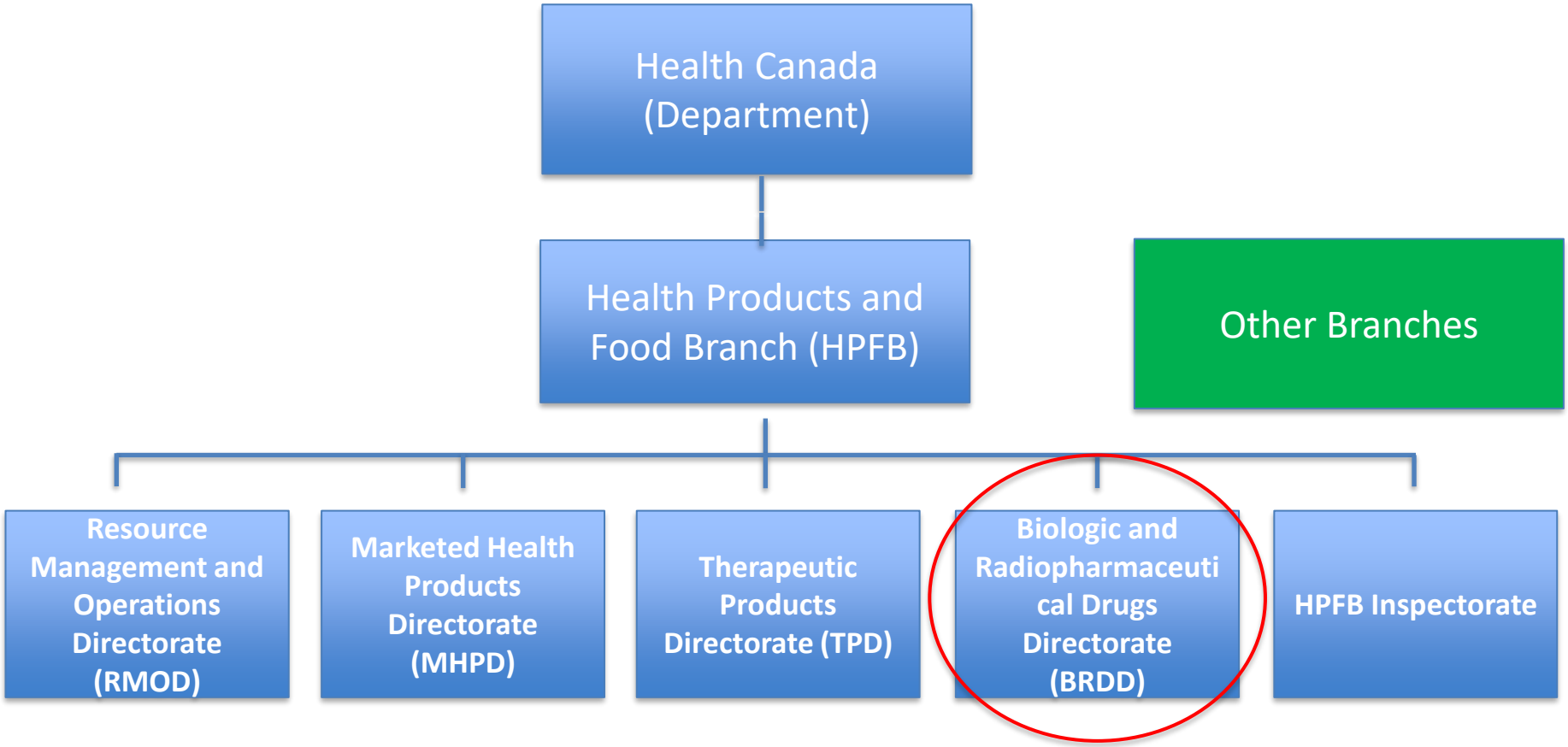
# Overview/Objectives

The presentation will elucidate on:

- Health Canada organization
- Existing Regulatory Frame work of Gene and Cell Therapy Products
- Health Canada's plans to enhance the agility of the health product regulatory framework: making regulations more adaptive to innovation while continuing to maintain our rigorous safety standards

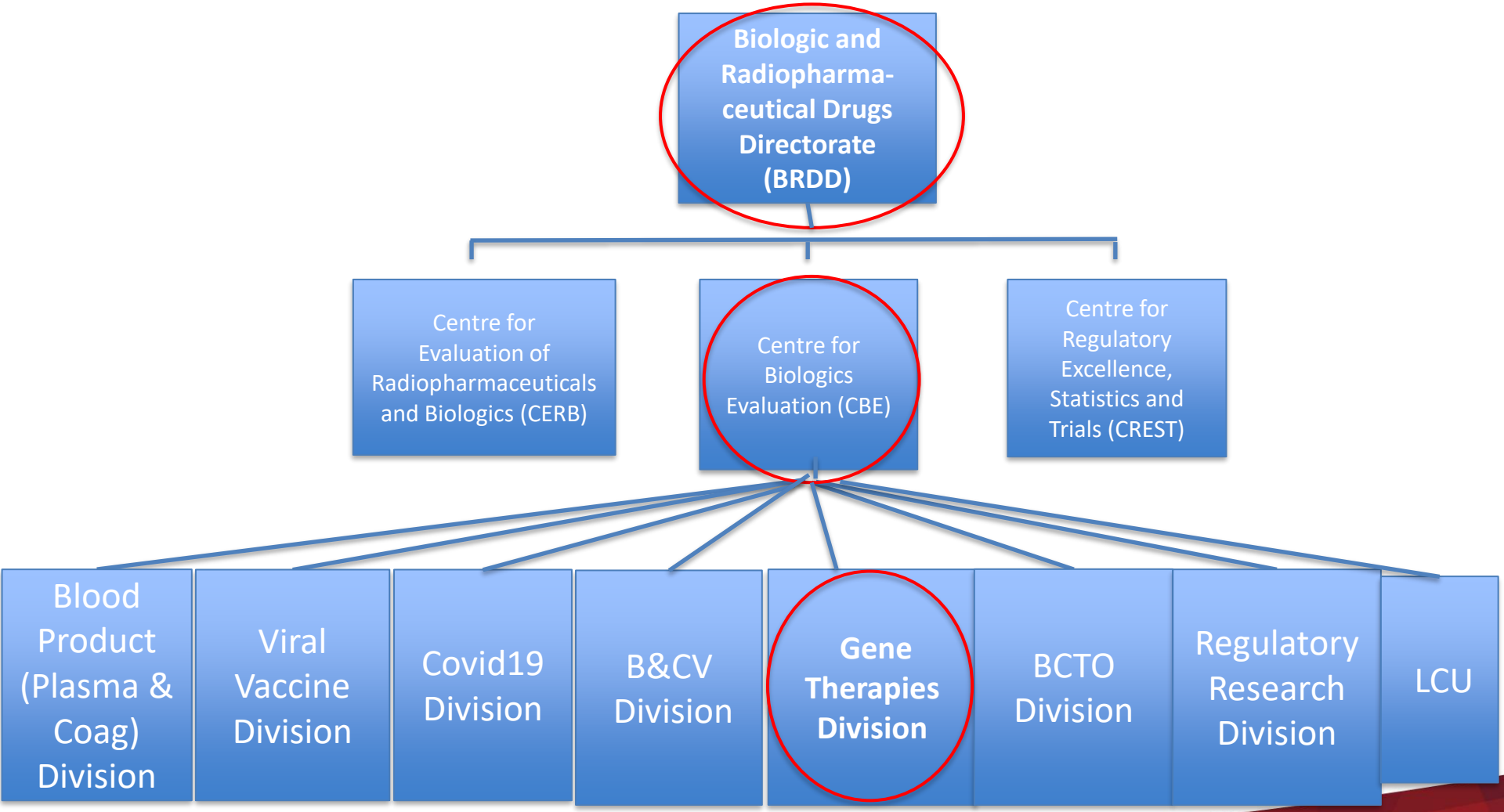
# Where does BRDD fit in?



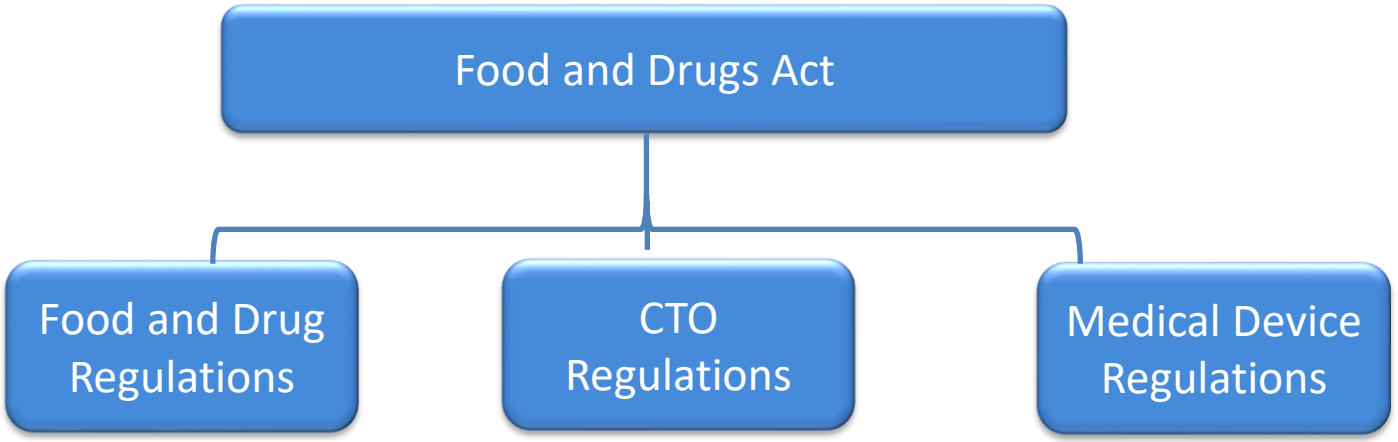

Mission:

BRDD works to maximize the quality, safety and efficacy of biological and radiopharmaceutical products in Canada.

# Where do Cell and Gene Therapies fit within BRDD (for Quality Review)?



# Regulatory Framework in Canada




- Unproven therapies
- Autologous (mostly)
- Allogeneic (except ones under CTO)
- Non-homologous use
- More than minimally manipulated
- Has systemic effect

- Proven therapies
- Allogeneic (except ones under FDR)
- Homologous use
- Minimally manipulated
- No systemic effect

- Devices containing or formed from human cells or tissues
- Devices used in manufacturing of cell therapy products

Regulations permit decision making that is based on:

**A) Risk-benefit analysis.**
**B) Sound scientific evidence.**
**C) Risk management plan post approval.**

Viral vectors, recombinant proteins, antibodies and vaccines are all regulated as biologics (schedule D) under the food and drug regulations.

# Regulation of Gene and Cell Therapy Products in Canada

- **Gene Therapy:**
  - Transfer and expression of an exogenous gene compensating for a missing or non-functional endogenous gene including by the following means:
    a) Nucleic acid (DNA or RNA) delivered directly or by viral vector resulting in expression of RNA (mRNA, miRNA or siRNA) and in some cases the translation of protein (directly *in vivo* or via *ex vivo* transduction and re-introduction of cells)
    b) Modification of genes (expression or repair) without transfer of genetic material

       -Direct treatment of cells in vivo or ex vivo with regulatory RNA or protein that bind DNA is not considered gene therapy but a therapeutic use of nucleic acids and proteins
    c) Oncolytic viruses for treatment of cancer

# Regulation of Gene and Cell Therapy Products in Canada (cont'd)

- **Cell and Gene Therapeutic Products**
  - Regulated as Biologics, in Schedule D (Biologic Drugs) of the Canadian Food and Drug Regulations
  - Gene therapies are better captured by Schedule D than cell therapies
  - Safety of Human Cells, Tissues, and Organs Regulations for Transplantation Regulations
  - Cell therapies meet the definition of a drug as defined by Food and Drugs Act
    - Food and Drugs regulations are widely applicable to Cell Therapies
    - Assisted Human Reproduction Act: embryonic stem cells

# Other Applicable Regulations…

- Canadian Environmental Protection Act
- New Substances Notification Regulations (Organisms/microorganisms)
  - An Environmental Assessment is required for new organisms not already on the “Domestic Substances List”
  - Includes viruses (ie. Gene therapy, oncolytic), but not plasmids
  - Sponsors of New Drug Submission (NDS) or Clinical Trial Applications (CTA) for a viral or bacterial vector should notify Environment Canada
  - Review conducted by Health Canada (HECS)

# ICH Quality Guidelines

- Although scope excludes CGT's, many of the principles can and should be applied
  - Eg. Comparability, stability, viral clearance etc.
- Relevant ICH Consideration Documents:
  - General Principles to Address Virus and Vector Shedding
  - Oncolytic Viruses
  - General Principles to Address the Risk of Inadvertent Germline Integration of Gene Therapy Vectors

# Other Guidance Documents Considered

- **FDA Cell and Gene Therapy Guidance Documents**
  - Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs) 2020
  - Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus During Product Manufacture and Patient Follow-up 2020

- **EMA Cell and Gene Therapy Guidance Documents**
  - EMA/CAT/80183/2014- Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products
  - EMA/CAT/GTWP/671639/2008 - Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells
  - CHMP/BWP/2458/03 - Guideline On Development And Manufacture Of Lentiviral Vectors

# The Food and Drug Regulations: CGT

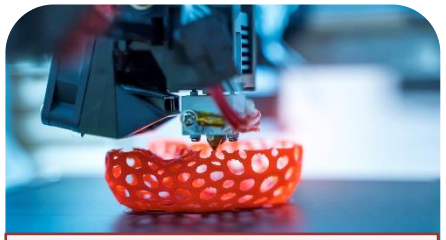
| Division in Part C | Key sections |
|---|---|
| Division 1 – General Section | -Drug Identification Number (DIN)<br>-Labelling requirements<br>-Adverse Drug Reaction Reporting |
| Division 1A – Establishment Licensing | -Activity-based (fabricate; package/label; GMP requirements; distribute; import; wholesale)<br>-Changes require EL amendment<br>-Annual renewal required |
| Division 2 – Good Manufacturing Practices | -Control of all manufacturing processes (including premises and cleaning, record keeping and training) |
| Division 5 – Clinical Trials (CT) | -CT Application (CTA) to test a drug in humans<br>-Verify the clinical efficacy, various pharmacological parameters, safety and look for any adverse events attributable to the drug |
| Division 8 – New Drugs | -Sufficient scientific evidence of safety, quality and effectiveness must be provided to Health Canada for market authorisation<br>-Preclinical, quality (Chemistry and manufacturing) and clinical, post market plan<br>-On site evaluation and lot release for biologics |

# Regulatory Challenges: The health context is changing

- Products are becoming increasingly complex and personalized (e.g., AI-enabled devices, advanced cell therapy, 3D-printed bio-products, Big Data, Novel Drug Delivery ).
- Growing range of innovative products accompanied by a wider spectrum of risk.
- Canadians demanding faster access to innovative products and greater engagement on decisions about their health.
- The COVID-19 pandemic has reinforced the need for agility and innovation to get high-demand products to Canadians quickly, without compromising safety.

**Artificial Intelligence**

**Advanced Cell Therapies**



**3D Bio-Printing**

# Responding to the need for regulatory agility

Since 2017, Health Canada has initiated a range of regulatory modernization initiatives. Progress has been made through initiatives such as the **Regulatory Review of Drugs and Devices** (R2D2), the **Self-Care Framework** and the **Medical Devices Action Plan**.


In 2018, the **Health and Bio-Sciences Economic Strategy Table** and **Advisory Council on Economic Growth** highlighted additional opportunities to enhance regulatory agility in support of innovation and economic growth.

Following a **targeted Regulatory Review** of the health and bio-sciences sector, Health Canada consulted a broad range of stakeholders as we developed an ambitious **Roadmap** to achieve greater regulatory agility.

**Budget 2019** announced funding ($120M/5 years) and **Bill C-97** provided the legislative powers to achieve this vision.

# Regulating for the future: The 5 pillars of our plan

1

## Modernizing clinical trial regulations

to encourage clinical trials by creating an environment that supports more innovative trials

2

## Enabling Advanced Therapeutic Products

to ensure a flexible approach for innovative products that do not fit in the current system

3

## Agile licensing for drugs

to make sure regulations align with the nature and lifecycle of health products

4

## Agile licensing for medical devices

to ensure appropriate oversight while better enabling innovation

5

## Information to Canadians: A mobile strategy

to help empower Canadians to maintain and improve their health

# Regulatory innovation objectives

## Modernizing clinical trial regulations

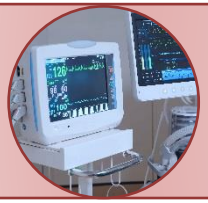
- Greater flexibility to oversee new trial types and designs
- Proportional oversight of clinical trials based on risk
- Better access to and transparency on information about trials

## Enabling Advanced Therapeutic Products

- Market access pathway for products that challenge existing regulations
- Use of “regulatory sandboxes” to develop tailored oversight requirements
- Concierge service to support innovators navigate new pathway

## Agile licensing for drugs

- Allow risk-based approval and oversight of products throughout their lifecycle
- Provide more agile regulatory tools to optimize oversight, e.g., Terms and Conditions (T&Cs)
- Support the use of decisions from trusted foreign regulators in specific situations



## Agile licensing for medical devices

- Use of foreign regulatory decisions
- Use of T&Cs
- Better classification for lower-risk devices

## Information for Canadians: A mobile strategy

- Develop a mobile platform that delivers credible and unbiased health product information
- Information and services tailored to consumers’ needs and expectations
- Serves as authoritative source of choice for health product information

# In 2020, COVID-19 required an unprecedented regulatory response to ensure Canadians had access to needed health products

## Our approach:

### Proactive engagement and collaboration

with stakeholders and health system partners to provide timely advice and guidance, as well as heightened collaboration with international regulators to ensure alignment.

### Emergency regulatory pathways and measures

to prioritize and expedite the review and licensing processes, including use of agile regulatory tools and approaches (e.g., T&Cs, rolling reviews).

### Enhanced post-market surveillance

of safety and effectiveness, including life-cycle oversight of approved products, adjusting T&Cs based on emerging information, real-time response to and information sharing of safety signals.

### Increased communications and transparency

including release of clinical data, to support high demand for information and data from broad range of stakeholders on regulatory requirements and decisions.

**5** vaccines

**2** treatments

**600+** medical devices

**4500+** sanitizers & disinfectants

# COVID-19 an opportunity to “test” agile ways of regulating

**…enhancing Health Canada’s pandemic response while informing our longer-term regulatory innovation plans.**

- COVID-19 reinforced importance of regulatory agility to enable timely access to needed health products.
- Regulatory response to pandemic provided an opportunity to “test” certain agile measures planned as part of the Regulatory Innovation Agenda (e.g., T&Cs).
- We’re currently implementing a transition approach for COVID-19-related products approved under these temporary measures, so that:
  - Canadians have uninterrupted access
  - Industry continues to benefit from similar flexibilities
- Early insights learned from the temporary measures are helping us continue to enhance the agility of Canada’s health product regulations, and will inform the Regulatory Innovation Agenda moving forward.

# By 2024, our efforts will have contributed to tangible results

- Encouraging clinical trials in Canada by creating an environment that supports more innovative trials.
- Enhancing patient access to new and innovative health products that do not fit in today's regulatory system.
- Advancing timely access to drugs and devices while more effectively overseeing their safety and effectiveness by:
    - Leveraging agile regulatory tools such as T&Cs;
    - Allowing the use of foreign decisions to help address unmet health needs; and,
    - Providing more transparency about the risks, benefits and uncertainties of drugs.
- Supporting innovation and economic growth by:
    - Creating a more modern regulatory system that removes outdated requirements and irritants;
    - Increasing harmonization and alignment with international regulators; and,
    - Enabling a low-cost market authorization pathway for low-risk drugs.

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