Upcoming *Blood Regulations:* Error/Accident, and Adverse Reaction Investigation and Reporting

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Canada

Objectives

- Overview of the Inspectorate
- Overview of the Biologics and Genetic Therapies Directorate
- Regulated activities and oversight under the Blood Regulations
- Error and Accident Investigation & Reporting
- Adverse Reaction Investigation & Reporting

Organizational Structure

Health Canada

Various Branches

e.g., Regions and Programs Branch (RAPB)

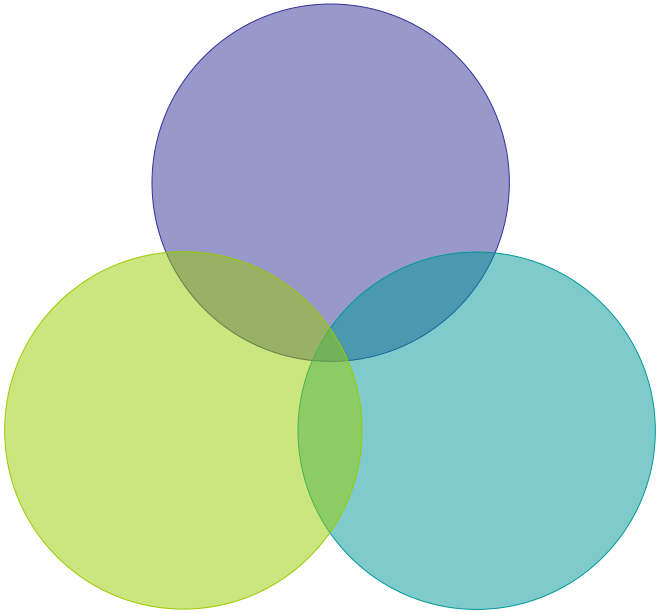
Health Products and Food Branch (HPFB)

- Therapeutic Products
- **Biologics & Genetic Therapies**
- Natural Health Products
- Veterinary Drugs
- Marketed Health Products
- **Inspectorate**

Collaboration within Product Lifecycle

Inspectorate

- National office - Ottawa
- Regional Operations



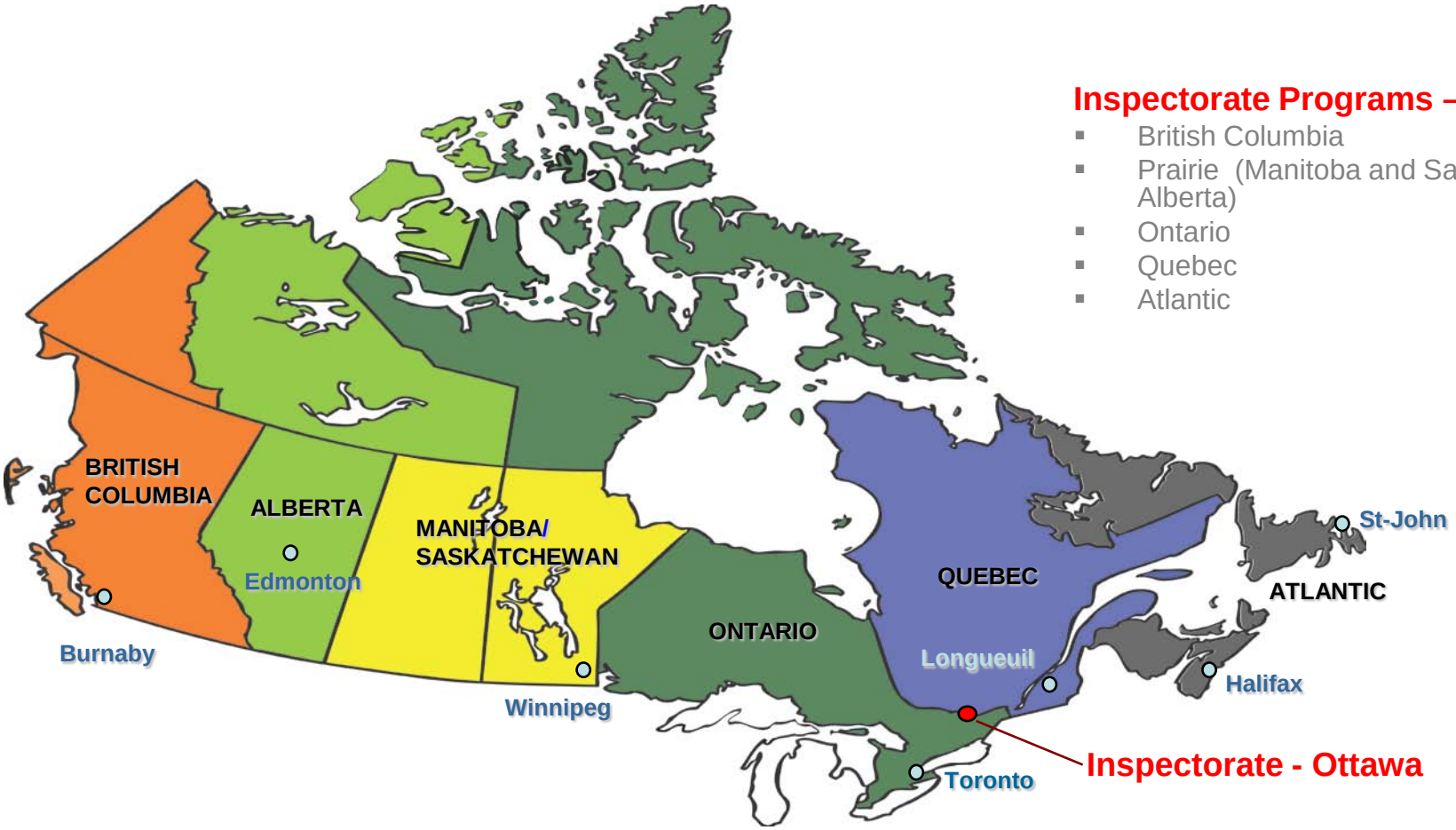
Pre-market Review

- Therapeutic Products Directorate (TPD)
- Biologics and Genetic Therapies Directorate (BGTD)
- Veterinary Drugs Directorate (VDD)
- Natural Health Products Directorate (NHPD)

Post-market Review

- Marketed Health Products Directorate (MHPD)

Inspectorate Overview



Inspectorate Programs – Regions

- British Columbia
- Prairie (Manitoba and Saskatchewan, Alberta)
- Ontario
- Quebec
- Atlantic

Inspectorate Overview cont'd

To deliver a national compliance and enforcement program for the following products:

Veterinary Drugs

Natural Health Products

Human Drugs & Medical Devices

Biologics & Genetic Therapies

Blood, tissues, organs, cells, donor semen, vaccines, genetic therapeutic products, radiopharmaceuticals

Spectrum of Activities

Compliance Promotion

Compliance Monitoring *(proactive inspection)*

Compliance Verification *(reactive inspection)*

Investigation

Prosecution

Biologics and Genetic Therapies Directorate – Regulatory Oversight

- Centre for Vaccine Evaluation
- Centre for Evaluation of Radiopharmaceuticals and Biotherapeutics
- Centre for Blood and Tissues Evaluation
- Office of Policy and International Collaboration
- Office of Regulatory Affairs
- Director General's Office
  - Office of Quality and Information Management
  - Office of Business Integration and Risk Management
  - Administrative Services Unit

Biologics and Genetic Therapies Directorate – Regulatory Oversight

Products

- Blood [components]
- Haemostatic agents [blood derived and recombinant]
- Cells, tissues and organs, including xenografts (living cells, tissues and organs from animal sources)
- Gene and cell therapies
- Viral and bacterial vaccines
- Therapeutic products produced through biotechnology [biotherapeutics]

Risk Based Regulated Activity Oversight

Activities: ▪ Allogeneic blood processing **Requirements** ▪ Authorization ▪ Establishment Licence Blood Operators	**Activities** ▪ Autologous blood processing, ▪ Transformation (pooling, irradiating, washing) ▪ Pre-Assessed Donor (Walking donor) Programs **Requirements** ▪ Registration Blood Operators & some Hospitals	**Activities** ▪ Storage and ▪ Transportation of already released blood **Requirements** ▪ Comply with appropriate sections of the *BR* All Establishments

All establishments are subject to compliance and enforcement activities which may include: compliance promotion, routine inspections, compliance verification for cause.

Error and Accident Investigation & Reporting
Regulatory Requirements

Blood Regulatory Framework

Definitions

- "**Error**" means a deviation from the operating procedures or applicable laws that could compromise the safety of a donor or recipient or the safety, quality or efficacy of blood.
- "**Accident**" means an unexpected event that is not attributable to a deviation from the operating procedures or applicable laws and that could compromise the safety of a donor or recipient or the safety, quality or efficacy of blood.

Errors & Accidents (E/A)

Establishments must have:

- Documentation of any E/A
  - Investigation and reports
  - Corrective action taken
- Copies of all notices sent out and notices received

Errors & Accidents (E/A) cont'd

Under the *Blood Regulations*:

Actions are required when the safety of blood is suspected to be compromised

- **E/A of another establishment**
  - An establishment has reasonable grounds to believe that an E/A occurred during an activity conducted by another establishment
- **Establishment's own E/A**
  - An establishment receives a notice that the safety of blood may have been compromised
  - An establishment suspects that an E/A occurred during an activity that it conducted

Required Actions

When reasonable grounds to believe that E/A occurred during activity by another establishment:

- Determine donation codes of the implicated blood
- Identify & quarantine implicated blood in its possession
- Notify:
  - The establishment that collected the implicated blood
  - The establishment from which it received the implicated blood, if different
  - Any establishment to which it distributed blood

Notice and Actions on Receipt of Notice

- **Notice includes**
  - The donation codes of implicated blood
  - Whether is whole blood or blood components
  - Reason for belief that safety of blood may be compromised

- **An establishment that is notified, must:**
  - Immediately notify every establishment to which it distributed implicated blood
  - Quarantine all implicated blood in its possession

Further Actions Required

When an establishment receives a notice or suspects that an E/A occurred during an activity it conducted:

- Determine donation codes of implicated blood
- Identify & quarantine implicated blood in its possession
- Determine whether there is sufficient evidence to warrant proceeding to an investigation
  - **If not warranted**, the establishment must notify the establishment that sent it the notice that it will not be conducting an investigation & provide reasons for that decision
  - An establishment that is notified must immediately notify every establishment to which it distributed implicated blood

Investigation is Warranted

An establishment:

- Must investigate
- Notify every establishment & other person to which it distributed implicated blood
- Include in the notice:
  - The donation codes of all implicated blood
  - A description of the suspected E/A
  - An explanation of how the safety of blood may have been compromised
- An establishment that is notified, must notify every establishment to which it distributed implicated blood and quarantine all implicated blood in its possession

Cooperation & Communication

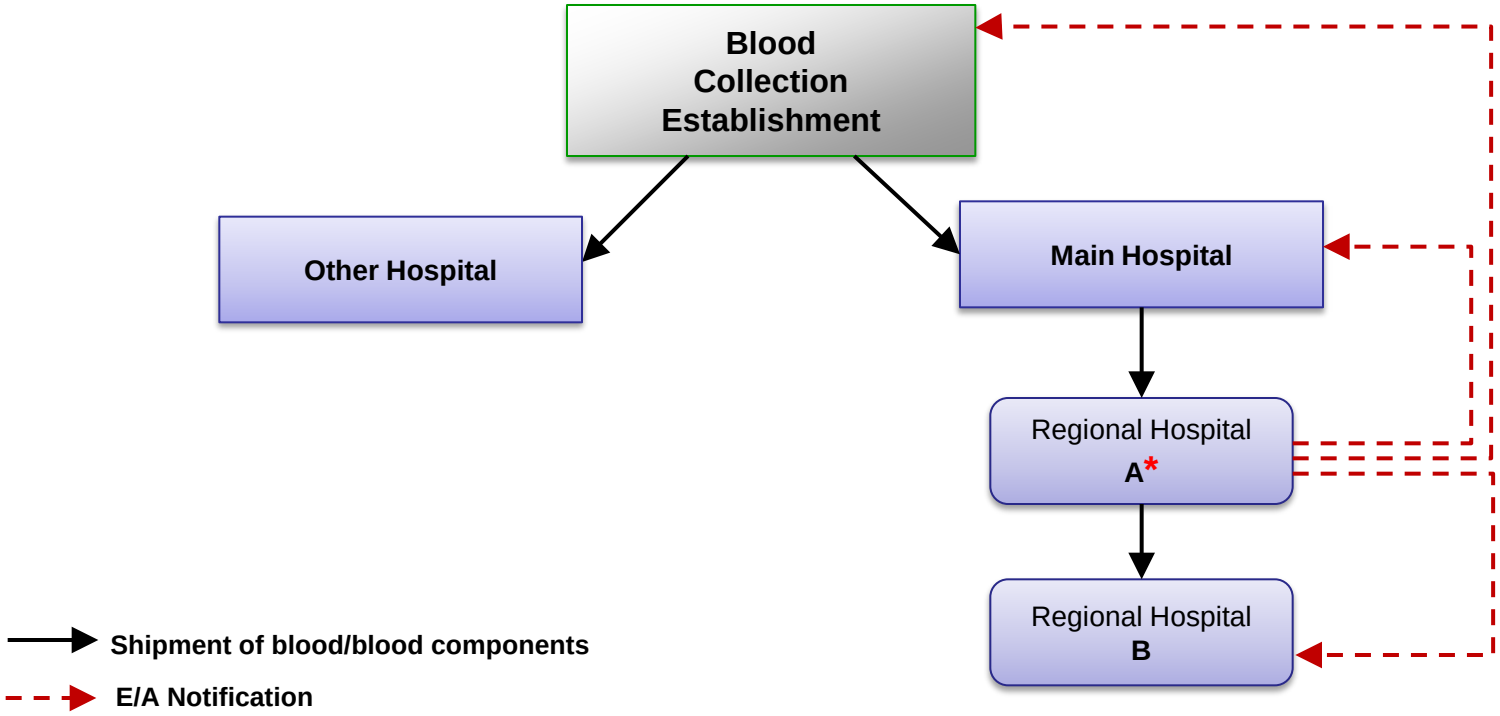
- An establishment must, on request, provide any establishment conducting an investigation with any relevant information in its possession in respect of blood that is distributed or transfused

- When more than one establishment is affected, each establishment must ensure that every other establishment that is involved is kept informed of all relevant information and of all developments and issues

Investigation Results

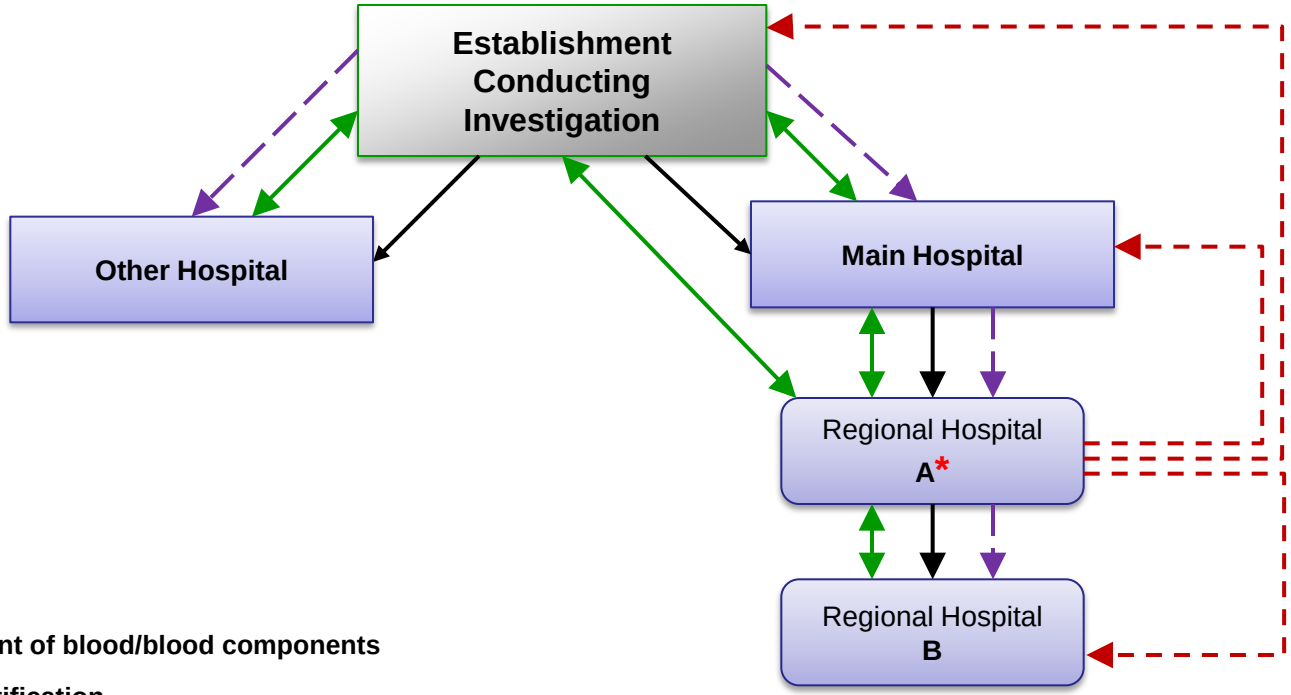
- An establishment that is conducting an investigation must notify in writing every establishment and other person to which it distributed implicated blood of the results of the investigation and any action required to be taken
- An establishment that is notified must send a copy of the notice to every establishment to which it distributed implicated blood

Errors & Accidents Notification Upon Discovery



* Hospital that discovered suspected E/A

Cooperation, Communication & Investigation Results



Shipment of blood/blood components

E/A Notification

Relevant information, developments & issues

Investigation results and required actions

* Hospital that discovered suspected E/A

Reporting to Health Canada

An establishment that is conducting an investigation into a suspected E/A that is thought to have occurred during an activity that it conducted and that is identified after the blood is distributed or transfused must file reports with the Minister if there is a reasonable probability that the E/A could lead to a serious adverse reaction.

Reporting to Health Canada cont'd

Reports to the Minister:

- Preliminary report within 24 hours that includes all relevant information
- A written update on any new information, on progress made in the investigation and on steps taken to mitigate further risks:
  - Within 15 days after start of investigation
  - Upon request of the Minister
- On completion of an investigation:
  - The results of the investigation
  - The final disposition of the blood and the reasons for that disposition
  - Any corrective actions taken and any other recommended changes

Annual Report

- An establishment must prepare an annual report that summarizes all E/A investigations conducted in the previous 12 months, including a concise and critical analysis, and file it with the Minister upon request
- If the analysis reveals a previously unidentified risk to the safety of blood, notify the Minister immediately
- Additional reports upon Minister's request

Adverse Reaction Investigation & Reporting
Regulatory Requirements

Adverse Reactions

Definitions

- Adverse Reactions is an undesirable response that is associated with the collection of blood (donor); or the safety of the transfused blood (recipient)
- Serious if the reaction results in:
  - hospitalization or its prolongation
  - persistent or significant disability or incapacity
  - medical or surgical intervention to preclude disability or incapacity
  - life-threatening condition
  - death
- Unexpected if the reaction is not identified in the circular of information.

Adverse Reactions & Transfusion Context

Prohibitions

An establishment must not distribute or transfuse blood in either of the following circumstances:

(a) while the blood is in quarantine; or

(b) when the results of an investigation into a suspected error or accident or an *unexpected adverse reaction or serious adverse reaction* are inconclusive or indicate that there has been a compromise to the safety of the blood.

Labelling

An establishment that collects blood for transfusion must ensure that the following information appears on the label of the blood:

- in the case of allogeneic blood for transfusion, a direction to refer to the *circular of information* for indications, *contraindications, warnings and a list of possible adverse reactions*.

Adverse Reaction Reporting - 1

Suspected Adverse Reaction

An establishment that has *reasonable grounds to believe* that a recipient has experienced an unexpected adverse reaction or a serious adverse reaction must immediately take all of the following actions:

- (a) determine the *donation codes* of all implicated blood;
- (b) *identify & quarantine* any implicated blood in its possession;
- (c) notify all of the following establishments:
  - (i) the establishment that collected the implicated blood,
  - (ii) the establishment from which it received the implicated blood, if different from the establishment mentioned in subparagraph (i),

    …if a preliminary inquiry indicates that the cause of the adverse reaction is attributable to an *activity carried out by the establishment from which it received the implicated blood*

Adverse Reaction Reporting - 2

… Suspected Adverse Reaction

- (c) …notify
  - (iii) any establishment to which it distributed implicated blood.

    … and it conducts an **investigation** into the adverse reaction, if a preliminary inquiry indicates that the cause of the adverse reaction is attributable to an activity that *it carried out*.

Adverse Reaction Reporting - 3

… Suspected Adverse Reaction

The notice required

- (a) a *description* of the adverse *reaction*;
- (b) an explanation of how the safety, quality or efficacy of the implicated blood may have been compromised, if known;
- (c) the *donation codes* of all implicated blood;

  …indicating whether the implicated blood is *whole blood* or *a blood component*

- (d) the name of any *suspected* transmissible *disease or disease agent*, if known.

Adverse Reaction Reporting - 4

… Suspected Adverse Reaction

Actions after receipt of the notice:

- immediately notify to the same effect every establishment and other person to which it distributed implicated blood, and
- quarantine all implicated blood in its possession.

… if a preliminary inquiry indicates that there are reasonable grounds to believe that the cause of the adverse reaction is attributable to an *activity that the establishment carried out*, it conducts an **investigation** into the adverse reaction and the implicated blood.

Adverse Reaction Reporting - 5

Adverse Reaction Investigation & Reporting

- An establishment must, on request, provide every establishment that is conducting an investigation with any relevant information in its possession in respect of blood that it distributed or transfused (i.e., cooperate).

- An establishment that is conducting an **investigation** must notify the ***Minister*** of the adverse reaction within 24 hours after it learns of the death of a recipient or within 15 days after it learns of any other unexpected adverse reaction or serious adverse reaction.

Adverse Reaction Reporting - 6

Results of investigation

- The establishment that is conducting an investigation must *notify in writing every establishment and other person to which it distributed* implicated blood of the results of the investigation and of any action that is required to be taken.
- On completion of the investigation, the establishment must file a final report with the ***Minister*** that contains all of the following information:
  - (a) the results of the investigation;
  - (b) the final disposition of the blood that was the subject of the investigation and the reasons for that disposition; and
  - (c) any corrective actions taken and any other changes that are recommended to be made to processes or procedures.

Adverse Reaction Reporting - 7

Annual Report

At the end of each year, an establishment must *prepare* an annual report that *summarizes all of the final reports* that it filed in the year, including a *concise critical analysis* of the investigations that were the subjects of those reports

… and *file* it with the ***Minister*** *on request*.

Thank You

Questions?

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