

Virtual Tour of Canadian Blood Services

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Blood Transfusion Boot Camp

Relevant Disclosures & Acknowledgements



Employee of CBS



Receive research funding from CBS



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Objectives

- Recognize the history and importance of precautionary strategy
- Understand and describe how blood products are manufactured at Canadian Blood Services (CBS)
- Consider resources and cost in blood transfusion policy and patient care decision-making
- Improve participation in maintenance of blood supply safety through adverse events reporting, recipient notification for retrievals, and lookback / traceback events

Tragedy

After being transfused blood between late 1970s and 1980s

- **1,200 infected with HIV**
- **60,000 infected with hepatitis C**

“Arguably the largest public health catastrophe in the country’s history”

-Picard, A. The Gift of Death 1995

The Krever Inquiry

- The Commission of Inquiry on the Blood System in Canada (known as the Krever Inquiry) was commissioned by the Federal Government in October 1993
- Headed by Mr Justice ...
 - ~Four years
 - Final report
 - Legal battles those who ha
- Redefined the regulatory framework that
- One of its most inquiry, almost \$10 billion in legal claims and a criminal investigation

In retrospect, the findings of the Krever Commission could perhaps be considered the most influential report on public health in Canadian history. The report and the success of the reformed blood system provide important lessons related to public health.
-Wilson CMAJ 2007

Krever Recommendations

1. Compensate victims
2. Safe, Free, Sufficient, Accessible
3. Single, public, open, independent operator
4. Promote appropriate use of blood products
5. Funded by hospitals
6. Creation of a national database
7. 10% of funding for research
8. Mandatory reporting of adverse events

“...action to reduce risk should not await scientific certainty. When there was reasonable evidence that serious infectious diseases could be transmitted by blood, the principal actors in the blood supply system in Canada refrained from taking essential preventive measures until causation had been proved with scientific certainty. The result was a national public health disaster.”

Estimated numbers of persons with haemophilia alive in 2007 and infected with HCV, HIV and related compensation

Country (number of persons with haemophilia)	Number of persons with haemophilia alive today with HCV or HIV		Year of publication of report from official public inquiry into viral contamination of the blood supply		Approximate average award from national compensation fund (year compensation fund established)	
	HCV	HIV ^a	HCV	HIV	HCV	HIV
USA (14 886)	4456	1698	None	1995	None	\$125 000 (1995)
UK (6109)	2829	405	Scotland only (2000)	None	\$36 000 (2004)	\$37 000 (1988)
Italy (5319)	4361	534	None	None	None ^b	None ^b
Japan (4683)	2436	871	None	None	None	\$375 000 (1996)
France (4000)	2600	1250	None	1991	None	\$150 000 to \$400 000 (1991)
Canada (2772)	1100	251	1997	1997	\$50 000 (1989)	\$160 000 (1991)
Australia (1070)	534	84	2004	None	Some assistance with medical care	\$39 000 (1989)
Ireland (545)	157	37	1997, 2002	2002	\$36 000 (1997)	\$46 000 (2002)

^aActual number of persons with haemophilia infected with HIV is larger than the numbers living today, but many have since died of AIDS-related complications.

^bCompensation was recommended but not paid.



A NEW Beginning: Rebuilding Broken Trust

From reactive to proactive
With emphasis on safety, efficacy,
accessibility, innovation, education

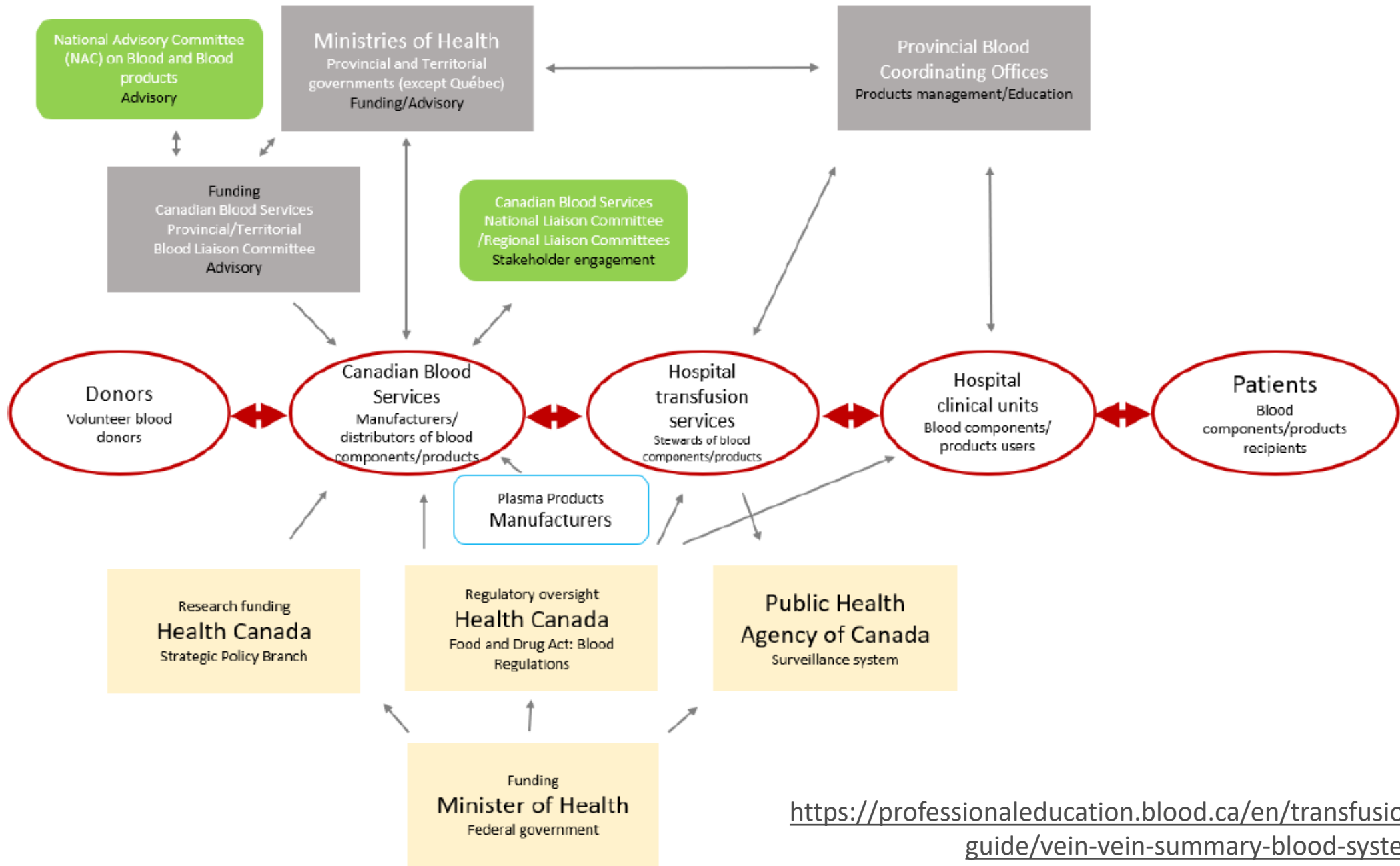
Precautionary Principle

- “Rio” definition:
 - *“where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation”*
 - (United Nations Environmental Programme [UNEP] 1992)
- “Wingspread” definition:
 - *“when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically”*
 - (SEHN 1998)

The Blood Services Landscape in Canada



- **Canadian Blood Services and Hema-Quebec**
- Highly structured, organized, not-for-profit biologic manufacturers
- Health Canada regulated as a drug



Our business by the numbers

Fiscal 2022–2023



767,000* whole blood collections



91,000* total plasma collections



396,000* active blood, plasma and platelet donors



1,908,000* appointments booked



37 permanent donor centres



573 hospitals served



3,700 employees



3,500 active volunteers



\$1.5 billion annual budget**

CBS: Celebrating 25 Years

- Blood supply in provinces and territories outside of Quebec
- Trusted, respected and valued leader in Canadian health care extended beyond blood and blood products:
 - *One of the safest blood systems in the world*
 - *Stem cell registry*
 - *National public umbilical cord blood bank*
 - *Renewed focus in education, research and innovation*
- Focused on rigorously maintaining the safety and effectiveness of products and services while improving productivity and efficiency

Implementation Measures

- Donor selection/deferral criteria
 - <https://www.blood.ca/en/blood/am-i-eligible-donate-blood?>
 - <https://www.blood.ca/en/blood/donating-blood/donor-questionnaire>
- Donor testing
- Post Donation Information
- Look back
- Trace back
- Assessing Risk of Emerging Threat; Pathogen Inactivation**

Adverse Transfusion Reactions

RISK OF EVENT	EVENT
1 in 13	Red cell sensitization, increasing risk of hemolytic transfusion reaction and hemolytic disease of the fetus and newborn ⁷⁹
1 in 100	Febrile non-hemolytic transfusion reaction per pool of platelets ^{80,81,82}
1 in 100	Transfusion-associated circulatory overload per transfusion episode ⁸³
1 in 100	Minor allergic reactions (urticaria)
1 in 300	Febrile non-hemolytic transfusion reaction per unit of RBC
1 in 2,500	Delayed hemolytic transfusion reaction per patient transfused ⁸⁴
1 in 10,000	Transfusion-related acute lung injury (TRALI)
1 in 10,000	Symptomatic bacterial sepsis per pool of non-pathogen reduced platelets ⁸⁵
1 in 40,000	Serious allergic reaction per unit of component
1 in 100,000	Post-transfusion purpura
1 in 200,000	Death from bacterial sepsis per pool of non-pathogen reduced platelets
1 in 250,000	Symptomatic bacterial sepsis per unit of RBC
1 in 354,000	ABO-incompatible transfusion per RBC transfusion episode ⁸⁶
1 in 500,000	Death from bacterial sepsis per unit of RBC
<1 in 1,000,000	Transmission of West Nile Virus
1 in 2,000,000	Residual risk of hepatitis B per unit ⁸⁷
1 in 4,000,000	Transmission of Chagas disease per unit
1 in 12,900,000	Residual risk of human immunodeficiency virus (HIV) per unit ⁸⁷
1 in 27,100,000	Residual risk of hepatitis C per unit ⁸⁷
<1 in 1,000,000,000	Transmission of HTLV per unit ⁸⁸

* All of these risk frequencies are likely to have quite wide confidence intervals.
Refer to HQ Circular of Information for residual risk for transfusion-transmitted infections in Quebec not in chart.

Total Budget FY 2022/2023 (\$ million)

Total Budget	\$1.4 Billion
Fresh Blood Products	\$450.3
Plasma Protein and Related Products	\$864.4
Plasma Proof of Concept and PDCs	\$20.6
Stem Cells (including HLA and Cord)	\$32.2
Organs and Tissues	\$8.7
Diagnostic Services	\$17.5

Figures shown above represent total expenditure budgets



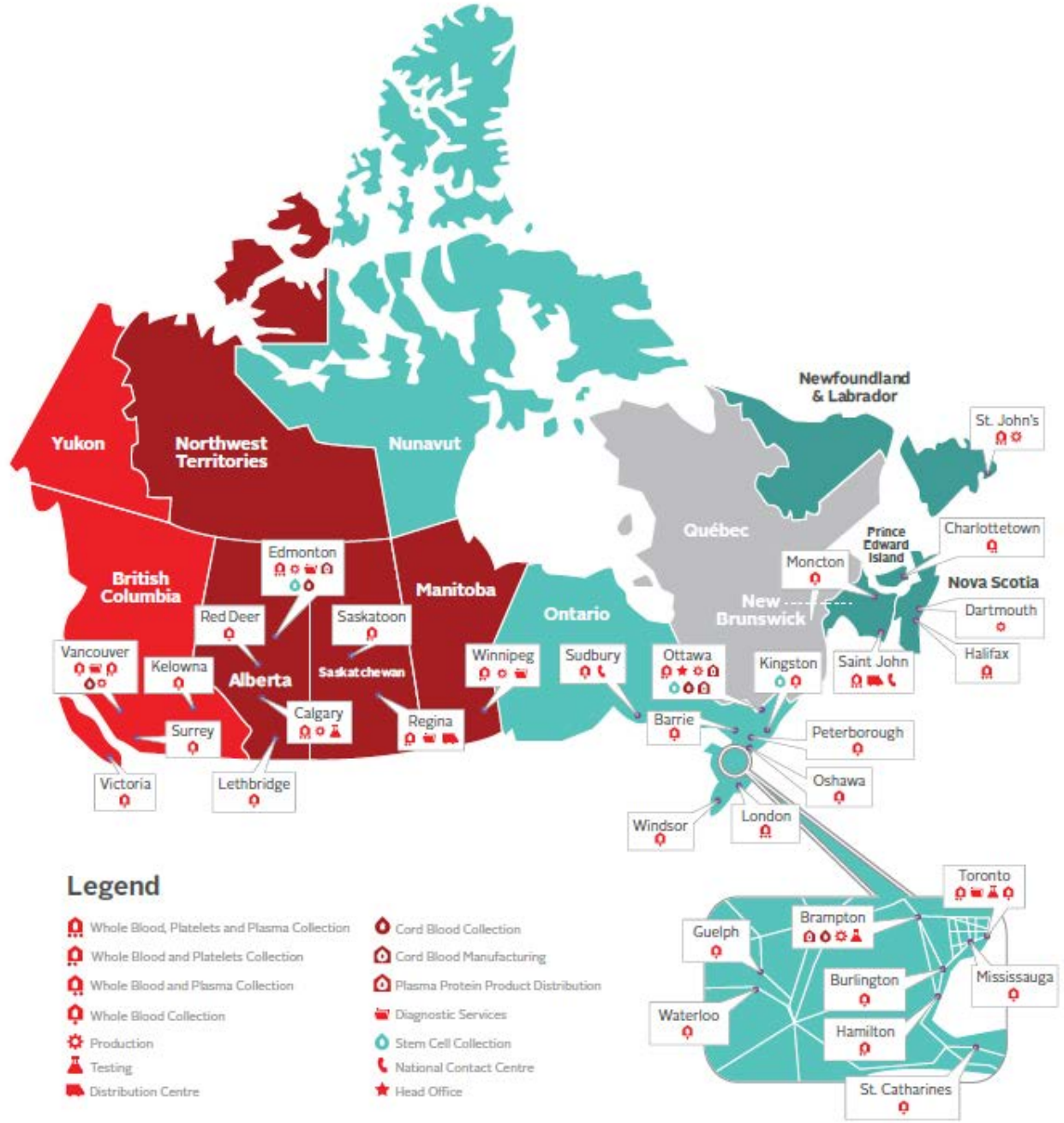
Blood Component Distribution & Cost

Product	Units FY 21/22	Cost / Unit FY 21/22
Red Cells	720,225	\$421
Total Platelets	120,275	
Apheresis	32,093	\$480
Buffy Coat Pool	88,182	\$192
Plasma for Transfusion	102,010	*\$126
Plasma for Fractionation	579,156	NA

Question

Which is true regarding the cost of blood in Canada

- A. The majority of the budget for Canadian Blood Services goes to producing components intended for direct transfusion
- B. Canadian Blood Services produces products for free
- C. Buffy coat platelets are significantly more expensive to produce than are apheresis platelets
- D. The majority of plasma collected by Canadian Blood Services goes for production of plasma-based drugs rather than for transfusion



Canadian Blood Services National System



Whole Blood

Red Blood Cells

Platelets

Plasma

What about the White Blood Cells?



Apheresis

Platelets + Plasma

Plasma

Universal Leukoreduction



Filled Whole Blood Collection Pack



This Photo by Unknown Author is licensed under [CC BY-ND](https://creativecommons.org/licenses/by-nd/4.0/)

In Canada

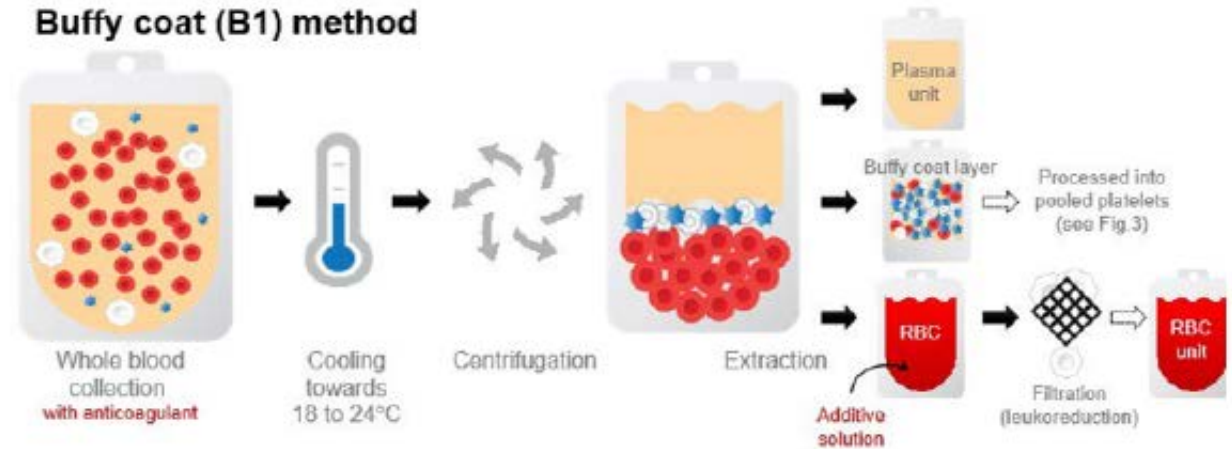
- Donor plasma
 - Platelets
 - Frozen plasma
 - Plasma protein products
- Pathogen inactivation technology is now available in all parts of Canada
 - Platelets
 - Plasma
- Whole Blood for use in the Canadian Military

<https://professionaleducation.blood.ca/en>

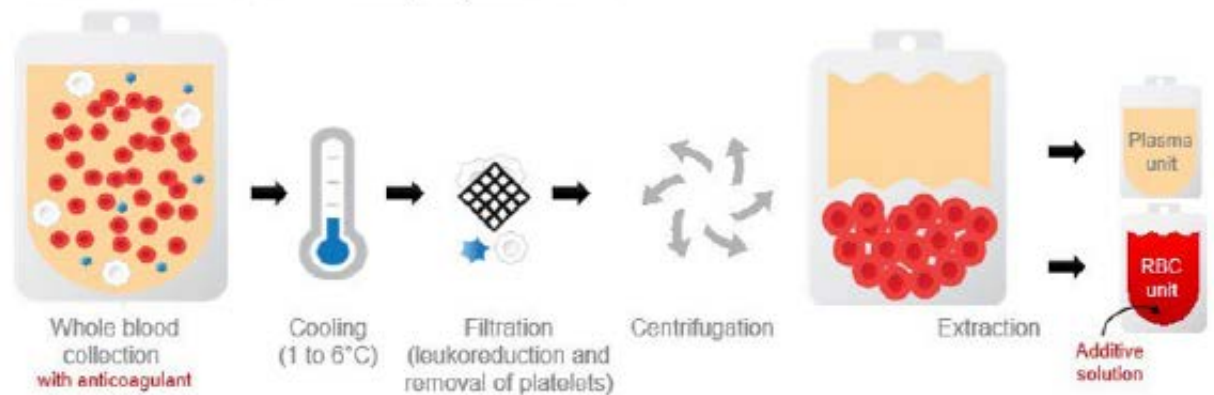
CLINICAL GUIDE TO TRANSFUSION




Chapter 2: Blood Components

Buffy coat (B1) method



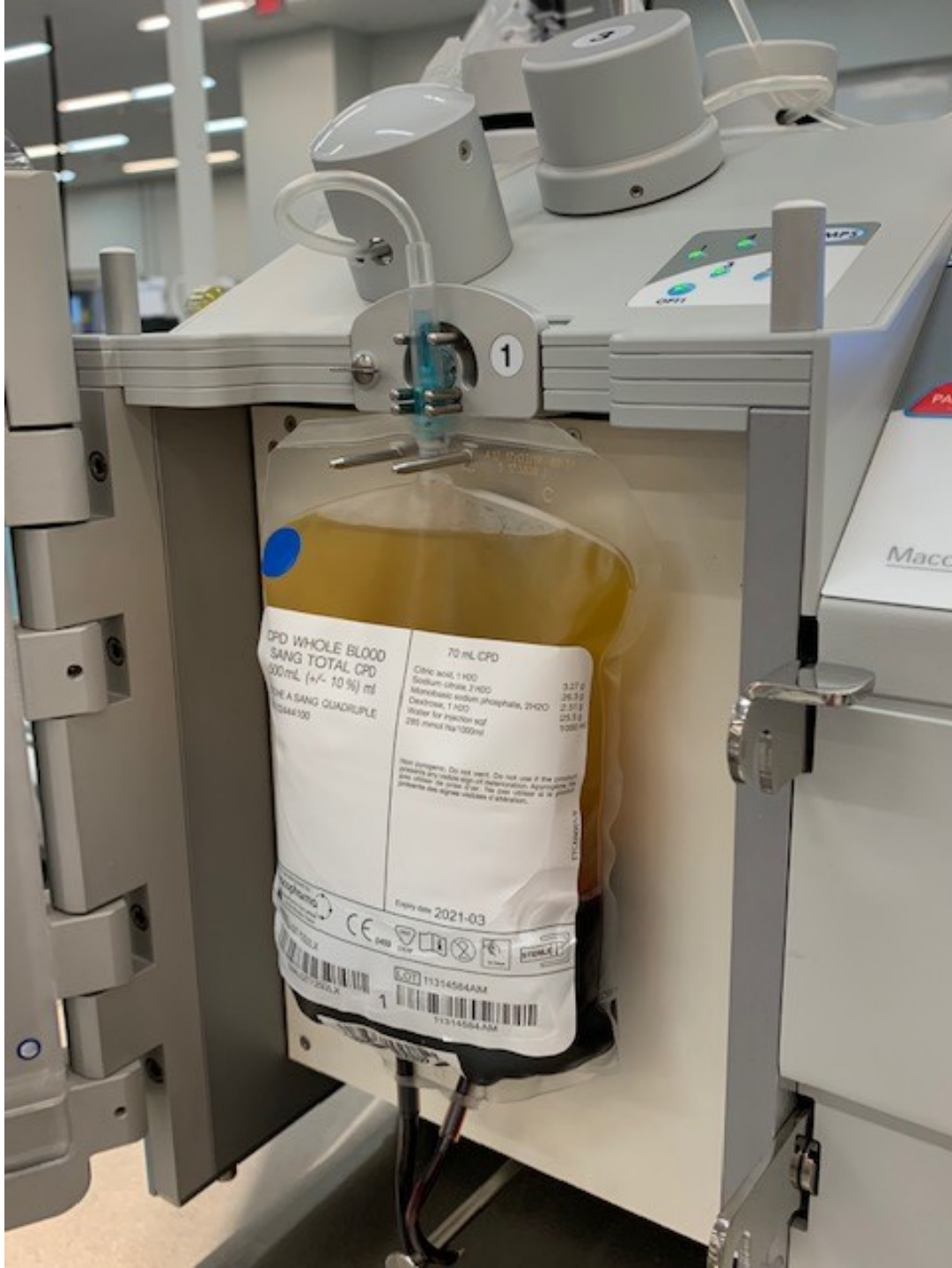
Whole blood filtration (B2) method



 Platelets  White blood cells  Red blood cells



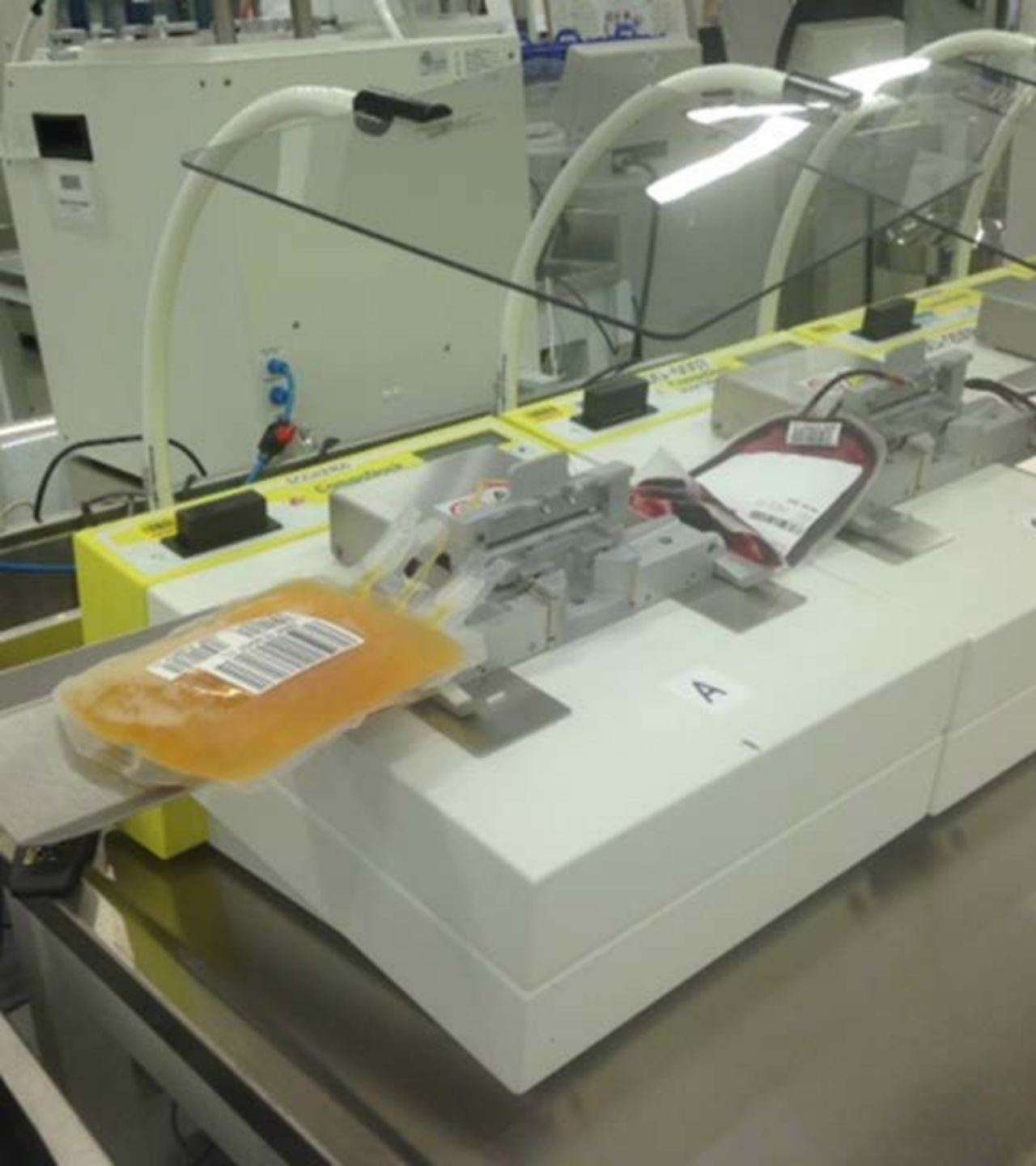
Whole Blood Leukoreduction by Gravity



Whole Blood Component Separation



Component Separation



**Buffy Coat Units
from 4 Donors
Connected in Series**



**Buffy Coat Units
Pooled by Gravity**



**Pooled buffy coats
re-spun then
platelets decanted
with plasma**

Transfusion-Transmissible Disease Testing

Pathogens	Screen Tests	Confirmatory/Supplemental Tests
HIV 1/2 (Human immunodeficiency virus, types 1 and 2)	<ul style="list-style-type: none"> • Combination Anti-HIV-1/2 and HIV-1 p24 (4th generation) ElectroChemiluminescence assay • HIV NAT 	<ul style="list-style-type: none"> • Geenius™ HIV-1/2 confirmatory testing
HBV (Hepatitis B virus)	<ul style="list-style-type: none"> • Hepatitis B surface antigen (HBsAg) ElectroChemiluminescence assay • Antibody to hepatitis B core antigen (HBcore) ElectroChemiluminescence assay • HBV NAT 	<ul style="list-style-type: none"> • HBsAg confirmatory testing (ElectroChemiluminescence assay) • There is no confirmatory testing for HBcore
HCV (Hepatitis C virus)	<ul style="list-style-type: none"> • Anti-HCV ElectroChemiluminescence assay • HCV NAT 	<ul style="list-style-type: none"> • HCV Line testing (LIA)
HTLV-I/II (Human T-cell lymphotropic viruses, types I and II)	<ul style="list-style-type: none"> • Anti-HTLV I/II ElectroChemiluminescence assay 	<ul style="list-style-type: none"> • HTLV Western Blot Assay testing
<i>Treponema pallidum</i> (pathogen for syphilis)	<ul style="list-style-type: none"> • Micro-hemagglutination assay for <i>Treponema pallidum</i> (MHATP)* 	<ul style="list-style-type: none"> • Algorithms may vary depending on reference laboratory site and initial/follow-up results • <i>Treponema pallidum</i> Particle Agglutination (TPPA) Test • Rapid Plasma Reagin (RPR) • Fluorescent treponema antibody absorption (FTA-ABS)
WNV (West Nile virus)	<ul style="list-style-type: none"> • WNV NAT 	<ul style="list-style-type: none"> • Sequencing or alternate NAT may be done at reference laboratory on WNV NAT-positive specimens when history suggests a potential exposure to another member of Japanese encephalitis virus serocomplex
<i>Trypanosoma cruzi</i> (pathogen for Chagas)	<ul style="list-style-type: none"> • Anti-<i>Trypanosoma cruzi</i> ElectroChemiluminescence assay 	<ul style="list-style-type: none"> • Enzyme-linked immunosorbent assay (ELISA) • Immunoblot • Polymerase chain reaction (PCR)
CMV (cytomegalovirus)	<ul style="list-style-type: none"> • Anti-CMV particle agglutination assay 	<ul style="list-style-type: none"> • None available

* chicken erythrocytes which have been fixed and then sensitized with components of sonicated *T. pallidum* (Nichols strain)
performed on at-risk donors
performed on a subset of donations for components required for intrauterine transfusion

Fractionation

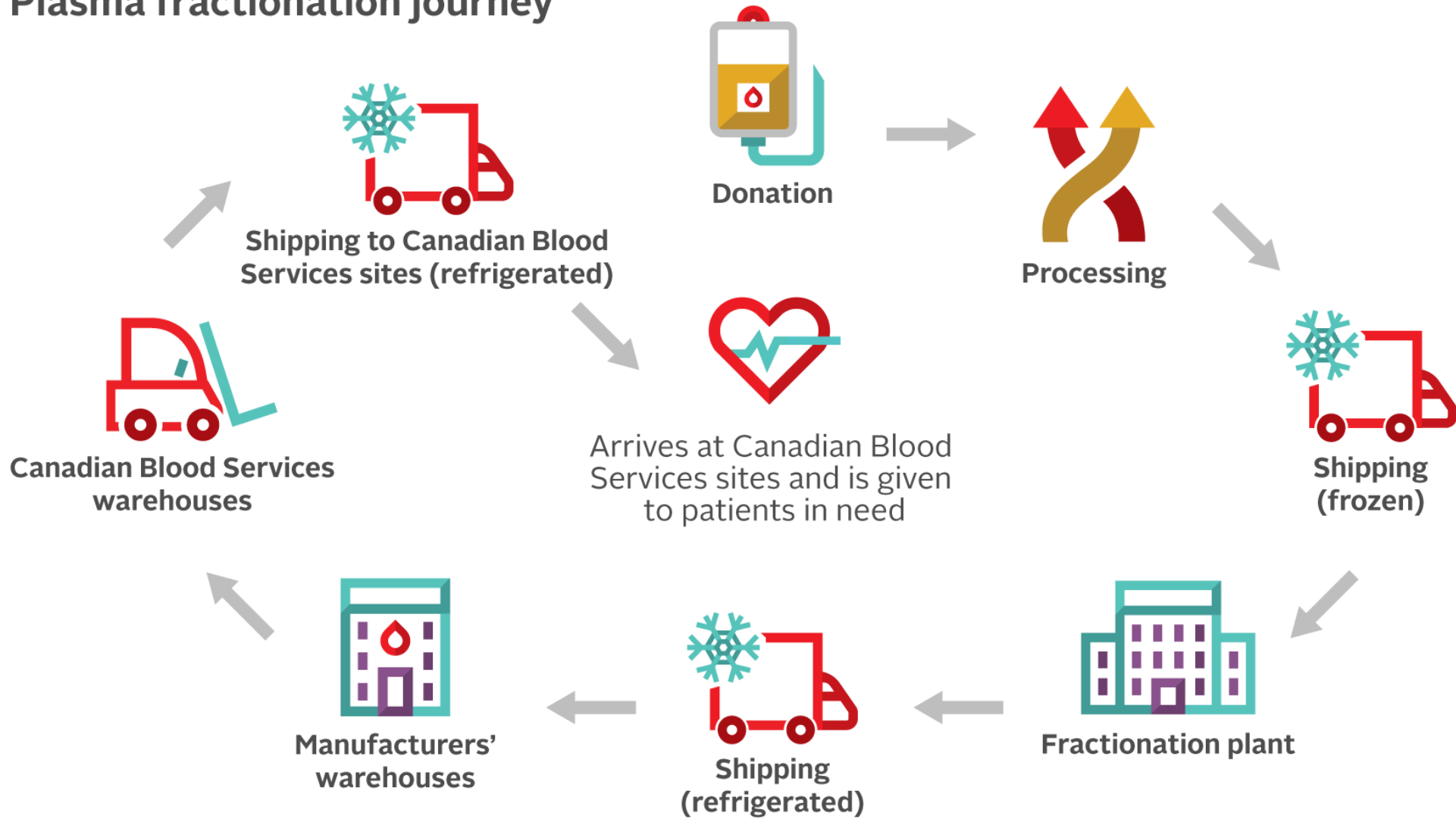


Photo from <https://montco.today/2017/06/csl-acquires-majority-interest-chinese-plasma-business/>

Plasma Protein Product manufacturing occurs outside of Canadian Blood Services.

This picture is an example of fractionation available on the web and may not represent products distributed by CBS

Plasma fractionation journey



Canadian Plasma for Protein Drugs

- Canadian plasma provides:
 - *Less than 50% of the demand for albumin in Canada*
 - *Less than 15% of the demand for IVIg in Canada*
 - *Remainder purchased off the open market*
 - *Health Canada approved with excellent safety profiles*

Question

Why is it important to report adverse transfusion reactions to Canadian Blood Services?

- A. To inform patient management at bed side*
- B. To guide management of donors and co-components*
- C. To obtain a refund for the hospital*

Post Donation Information

- We instruct donors to call if health status changes after donation
- Donors call National Contact Center
- New information on screening that pertains to previous donations
- If new information suggest donor was not eligible previously, or if there is a risk to recipients, we will retrieve blood components
- Notification to blood bank whose medical director may reach out to transfusing physician to discuss possible recipient notification

Lookback / Traceback

- Lookback: Donor with new risk information leading to recall of previously donated products
- Traceback: Patient with new illness after transfusion leading to investigation of all donors from whom patient received blood products

Adverse Events / Transfusion Reaction

- Reactions where a feature of the product appears to be the cause should be reported to the blood center
 - *Septic reaction from bacterial contamination, TRALI*
 - *Not TACO, febrile non-hemolytic transfusion reaction*
- Will retrieve in-date co-components
- Can defer donors that represent a risk to recipients

Circular of Information



Canadian
Blood
Services

BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

▼ Blood

Plasma

▼ Stem Cells

← Component types

Circular of Information

What is the Circular of Information?

The *Circular of Information* is an extension of the component label and provides information regarding component composition, packaging, storage and handling, indications, warnings and precautions, adverse events, dose and administration etc. The *Circular* conforms to the applicable regulations issued by Health Products and Food Branch, Health Canada.

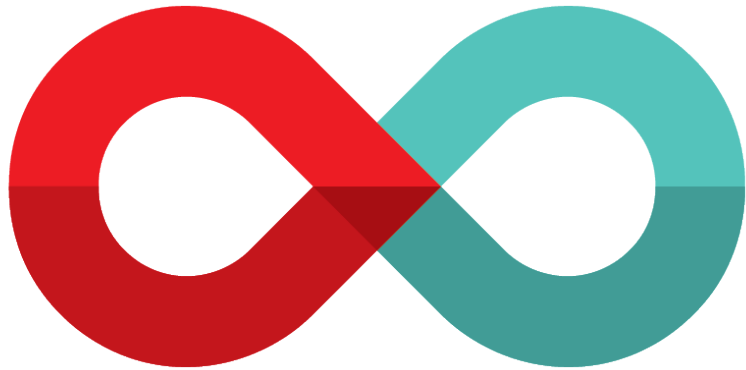
Summary

- Transfusions carry risk - adverse events should be reported so appropriate steps can be taken with products and donors
- Out of a dark period in the history of Transfusion Medicine in Canada came the establishment of CBS & HQ
- Through rigorous emphasis on safety, efficacy, accessibility, innovation, education and research Canada has one of the safest blood supplies in the world
- It is incumbent on all of us to ensure judicious use of blood
 - *Precious*
 - *Limited*
 - *Life altering – hopefully for good...*



Thank you!

Questions & Comments Welcome



Canadian Blood Services

BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

Blood for Life

You can save lives and change many more.

1 888 2 DONATE (1-888-236-6283) or <https://www.blood.ca/>

Extra Slide: Decisions & Non-Decisions

- Early in the AIDS epidemic, failure to screen out high-risk donors
- Importation of plasma collected in US prisons and in high-risk areas like San Francisco at the height of the AIDS epidemic
- Delays in purchasing safer, heat-treated blood products for hemophiliacs prompted by a desire to use up inventory of contaminated products
- Delays in implementation of testing for the AIDS virus due to spending restrictions
- Failed attempt by provinces to build a network of blood manufacturing plants hence requiring high-risk plasma to be imported from the US

Extra Slide: Decisions & Non-Decisions cont.

- Refusal to use a test that would have identified ~ 90% HCV
- Once tragedy became known, a failure to track down those who had received tainted blood so they could receive treatment and avoid passing on the viruses to others
- Destruction of key documents of the Canadian Blood Committee
- Denial of compensation to infected claimants by provincial health ministers
- Refusal of the Red Cross and provincial and federal ministers to apologize for their failings