

Security of Plasma Supply for Immunoglobulin

Briefing document for stakeholder engagement

Purpose

This document has been prepared to support stakeholders in providing their perspectives on securing Canada's plasma sufficiency for immunoglobulin. Written submissions from stakeholders on this topic are due to be sent to Dialogue Partners no later than December 17, 2021 and will support our preparation for a subsequent virtual stakeholder dialogue session on this important topic planned for January 2022.

Background and context

In 2016, a risk-based decision-making exercise was undertaken to assess the emerging risks related to the security of supply of immunoglobulins for Canadian patients. Canadian Blood Services is now undertaking a renewed risk-based decision-making analysis (RBDM) focusing on the security of Canada's supply of both plasma and immunoglobulin in our efforts to meet the needs of Canadian patients. The objectives of this latest RBDM are to project the next five-year risk scenario and to evaluate the options for mitigating the risks identified.

Plasma and the blood system supply chain

Canadian Blood Services operates the blood and plasma supply system in all provinces and territories except Québec, which has its own similar system and blood operator. We are accountable to provincial and territorial ministers of health, who are also our corporate members, and are regulated by Health Canada.

Our blood and plasma supply chain is a single, integrated system operated on behalf of provincial and territorial governments — and a vital connection between donors and patients across the country, in a national unified system.

What is “blood plasma”? What is it used for? Why is it essential for patients?

Plasma, also called “blood plasma,” is the protein-rich liquid in blood that helps other blood components circulate throughout the body. It supports your immune system and helps control excessive bleeding, which is why plasma donations are important to help treat bleeding disorders, liver diseases and many types of cancer.

Plasma is a vital treatment for patients with immune deficiencies, rare blood disorders, various cancers, certain infections, nervous system disorders, bleeding disorders, kidney and liver diseases, severe burns, surgeries, newborns with Rh disease and much more.

Plasma has two main applications:

- **Transfusion:** It can be transfused directly into patients in hospitals; or,

- **Plasma-derived products:** It can be manufactured into specialized medicines called plasma protein products (or plasma-derived products.) Immunoglobulins, albumin, and coagulating factors are examples of these products.

Globally and in Canada, the most widely used plasma protein products are immunoglobulins. Canadian Blood Services estimates that about half of the patients in Canada who use immunoglobulins must take these drugs to live, with no other treatment available for their conditions.

What is “plasma sufficiency” for immunoglobins?

“Plasma sufficiency” refers specifically to the percentage of plasma collected in Canada by the accountable blood operator to manufacture into immunoglobulins exclusively for patients in this country. Blood supply systems around the world track plasma sufficiency with a focus on immunoglobulins because they are such a universally used category of plasma protein products.

On behalf of the provinces and territories, Canadian Blood Services ensures plasma sufficiency and security of supply for immunoglobulins by doing two things:

- Collecting plasma to ship to fractionators who manufacture it on our behalf into plasma protein products for use exclusively in Canada. Once manufactured, these medications are licensed by Health Canada as biological drugs and returned to Canadian Blood Services for shipping to the hospitals and clinics we serve.
- Purchasing additional plasma protein products, including immunoglobulins, which are manufactured by the global biologics industry using plasma they have collected themselves. We supply these and other related products which we have also purchased on the global market, to hospitals for patients across the country.

Through these two activities, we meet 100 percent of the need for immunoglobulins for the hospitals we serve.

Because there is currently a global shortage of plasma to make immunoglobulins, it is essential that blood systems around the world increase their plasma collections. For Canada, this involves growing our collection activities until about half of the immunoglobulins required are made from plasma donated by people in this country.

Currently, Canadian Blood Services collects about 15 percent of the plasma needed to make enough immunoglobulins for the hospitals and clinics we serve. It is important to understand that this does not mean patients are going without treatment. Rather, it means that we purchase about 85 percent of the immunoglobulin required as finished products that do not include plasma collected by Canadian Blood Services. By substantially increasing the amount of plasma we collect, we will adjust this ratio, in keeping with global supply and demand pressures.

Historically, when supply was less pressured, purchasing a greater percentage of finished plasma protein products on the global market was an affordable way to source these products. More recently, however, many factors support the need to recalibrate sufficiency levels so that more plasma is collected within Canadian Blood Services' supply chain to manufacture into immunoglobulins for patients in Canada in a cost-effective and scalable manner. In the event of a disruptive event (e.g., new pathogen such as experienced by U.K. with variant Creutzfeldt-Jakob disease (vCJD) in the 1990s), we would still have access to essential medicines manufactured by the global plasma industry that do not include plasma collected in Canada. To ensure resilience and redundant sources of supply, a strategy of 100 percent self-sufficiency in plasma for immunoglobulins is not the objective.

To further diversify risk, we also engage in a range of other activities. An example of these is to maintain contracts with two separate plasma fractionators (specialized pharmaceutical companies) so that should one experience conditions that negatively affect its supply chain, there is another whose services we can continue to use.

Canadian Blood Services is increasing plasma collections to meet patients' needs

Canadian Blood Services has a mandate to manage sufficiency of immunoglobulins in jurisdictions we serve. We are working with governments to help ensure a robust domestic supply of plasma that supports patients in this country.

In recent years, three independent reports have recommended that Canadian Blood Services increase plasma collections, among other items. These include [Health Canada's expert panel on immune globulin product supply of 2018](#); PWC's [Collaborative Performance Review of Canadian Blood Services' operations in 2019](#); and the [Ontario Auditor General's Value-for-Money Audit on Blood Management and Safety](#) in 2020.

Globally, during the COVID-19 pandemic, [not-for-profit blood systems](#) and [commercial plasma collectors](#) have called for increased plasma collections as quickly as possible to relieve the current shortage of immunoglobulins and to help meet growing demand for plasma protein products.

In April of 2021, we were pleased to announce that, with funding from provincial and territorial governments, the next new plasma donor centres will open in Brampton and Ottawa, Ontario by spring 2022, and plans are underway for a third centre. These new locations will build on the success of the dedicated plasma donor centres that opened in 2020 in Sudbury, Ontario and Lethbridge, Alberta along with the Kelowna, B.C. location that opened in June of 2021. Through these centres, we can collect plasma in a cost-effective, efficient manner.

Also in April, the federal government announced support for Canadian Blood Services' increased plasma collection in the coming years. Discussions with the federal, provincial, and territorial governments are ongoing as we work toward increasing the plasma we collect inside our supply chain and recalibrating national sufficiency of immunoglobulins in keeping with

supply and demand pressures. This is not only essential for Canadian patients, but also important on a global scale, as well. As Canada becomes less reliant on the international plasma industry, more global plasma capacity will become available to support patients around the world.

A global shortage of immunoglobulins and COVID-19 pandemic dynamics

Use of immunoglobulins has been growing substantially in health systems around the world for many years. The growth in demand has been consistently strong for the last several years, and blood supply systems and the global commercial plasma industry are challenged with keeping pace to collect enough plasma to meet demand.

In August of 2019, the American Food and Drug Administration declared a [shortage of immunoglobulins](#). The U.S. supplies much of the world with plasma for plasma protein products, so an American shortage has serious ramifications globally. This shortage has been made more acute by the COVID-19 pandemic, which has disrupted supply chains around the world, keeping both donors and pharmaceutical industry workers at home. Patients in the U.S. and Europe continue to be affected by this shortage.

To date, Canadian Blood Services has been able to leverage our national supply chain and bulk buying expertise — as well as our utilization management capabilities and those of governments and hospitals across the country — so that patients in Canada have not gone without treatment.

Dynamic and evolving plasma industry in Canada

Like many peer blood operators internationally (including Australia, the U.K., and many others), Canadian Blood Services operates a not-for-profit, publicly funded system. Although we do not pay donors as commercial collectors do, we and our agents are exempt from legislation that prohibits payment in some provinces, and could do so, should the need arise.

Commercial plasma collection (where donors are paid) is a new dynamic in Canada. There are a small but growing number of commercial plasma collection sites emerging in the jurisdictions we serve. However, large-scale commercial growth — without appropriate controls — could encroach on the existing system for both blood and plasma collections.

Canadian Blood Services is having ongoing dialogue with governments to determine how, as a country, we should approach commercial plasma collection with respect to sufficiency needs and to mitigate any impact on national blood system operations and our mandate to meet the need of hospitals and patients in Canada.

Risk-Based Decision-Making Framework for Blood Safety (RBDM)

A comprehensive analysis is being undertaken using the Risk-Based Decision-Making Framework for Blood Safety, developed by the Alliance of Blood Operators – it can be found [online](https://allianceofbloodoperators.org) at allianceofbloodoperators.org.

The Framework's objectives are to:

- Optimize safety of the blood supply while recognizing that elimination of all risk is not possible
- Allocate resources in proportion to the magnitude and seriousness of the risk and the effectiveness of the interventions to reduce risk
- Assess and incorporate the social, economic, and ethical factors that may affect decisions about risk.

The 2021-2022 risk-based decision-making analysis is focused on Canada's plasma sufficiency for immunoglobulin security of supply, including risks across both collection and fractionation capacity. In 2016, a similar exercise was conducted assessing emerging risks related to the security of supply for immunoglobulins for Canada patients.

The objectives of the current analysis will be to project the next five-year scenario and to evaluate the options for mitigating the risks, with decision drivers focusing on:

- **Patient need:** To ensure an adequate supply of immunoglobulin for Canadian patients who rely on this therapeutic product; to create certainty and security of domestic supply.
- **Affordability:** To deliver an adequate supply of immunoglobulin for Canadian patients at an affordable cost to Canadian healthcare systems.
- **Sustainability of blood and plasma collection network in Canada:** To maintain donor engagement and access to a sustained supply of plasma necessary to serve the transfusion needs of all Canadian patients; to maintain donor well-being and trust; to maintain value proposition for workforce. This RBDM analysis includes assessments on security of supply, health economics and outcomes, operational impacts and contextual factors (e.g., social, legal and ethical), along with development of a participation strategy.

Stakeholder engagement

As noted above, the participation strategy is key input informing the 2021-2022 risk-based decision-making analysis, and stakeholder engagement is a crucial step in facilitating the opportunity to ensure stakeholder perspectives are heard and contribute to informing the overall analysis and decision-making in this process. The stakeholder engagement strategy has been designed as a three-part process. Stakeholders are asked to:

1. Review this **briefing document** to develop a clear understanding of the current situation regarding Canada's need to increase our security of plasma supply for immunoglobulins.

2. Complete the **written submission** using the template provided and return to natasha@dialoguepartners.ca by email no later than Friday December 17, 2021.
3. **Select a session to attend and RSVP** to one of the stakeholder dialogue sessions to attend in January 2022.

If you have any questions or require further information or assistance on this, please contact Stephanie Kelly at steph.kelly@blood.ca.

Appendix

Key terms and context related to blood and plasma sufficiency and Canada's blood system supply chain

Our blood and plasma supply chain is a single, integrated system operated on behalf of provincial and territorial governments — and a vital connection between donors and patients across the country.

The following terms and context are needed to build an understanding of the plasma and blood system supply chain in Canada:

- **Blood:** In the context of the blood supply system “blood” is an overarching term that means “whole blood and blood products, plasma and plasma products and their respective artificial and substitute products.” Since we opened our doors in 1998, Canadian Blood Services has been accountable for a “national blood supply system which assures access to a safe, secure and affordable supply of blood, blood products and their alternatives, supports their appropriate use and carries out such other functions” as designated by provincial and territorial governments.
- **Whole blood:** Whole blood is the unprocessed raw material Canadian Blood Services collects from donors at donor events across the country. After we collect whole blood, we process it into its different components at facilities we own and operate and then deliver these products to hospitals.
- **Fresh blood products:** Fresh blood products are components of whole blood used for transfusion therapies, in hospitals. They include products such as red blood cells, platelets, and plasma, and are manufactured by Canadian Blood Services from the whole blood we collect.
- **Plasma for transfusion:** Plasma for transfusion can be manufactured in two ways: it can be made from plasma recovered from whole blood donations (recovered plasma) or from plasma collected using an apheresis machine (apheresis plasma). An apheresis machine separates only the plasma from the rest of the donor’s blood and then returns the remaining blood to the donor in a single closed loop at the time of donation.
- **Plasma for fractionation:** Fractionation refers to the process used to manufacture plasma protein products. Plasma intended for fractionation is mainly collected using an apheresis machine, although some plasma recovered from whole blood donations may also be used. Because there is a global shortage of plasma for fractionation, Canadian Blood Services, like other blood operators globally, is increasing the amount of plasma it collects to ensure the needs of patients in Canada for immunoglobulins and other plasma protein products continue to be met.
- **Other related terms:** Within the supply chain, various technical terms are sometimes used to describe plasma and other blood components, often referring to the collection process. Some of these include:

- **Recovered plasma:** This term refers to plasma produced by separating whole blood into plasma and other cellular components. Recovered plasma volumes are limited to the amount of whole blood we collect.
- **Source plasma:** Source plasma is collected from donors using an apheresis machine. It is used exclusively to manufacture plasma protein products through a process called fractionation.
- **Apheresis plasma:** This term refers to plasma collected using an apheresis machine. Apheresis plasma can be used for transfusion or for fractionation. Donation using an apheresis machine can happen more frequently than whole blood donation because the body replaces the volume of donated plasma faster than that of other donated cellular components.
- **Apheresis platelets:** This term refers to platelets collected using an apheresis machine. Platelet donation using an apheresis machine can also happen more frequently than whole blood donation.
- **Plasma protein products:** Plasma protein products are medications manufactured (or fractionated) from the proteins found in human plasma. These products have an excellent safety profile — whether they are made from the plasma of donors that have been paid or those who have not — in part because the fractionation process itself includes multiple dedicated steps of pathogen removal or inactivation. Although there are multiple categories of these plasma-derived products, three main ones are widely used in patient care:
 - **Immunoglobulin**, which helps people living with primary and secondary immunodeficiency disorders, autoimmune disorders, and neurological disorders, among other medical conditions. **Immunoglobulins are the most widely used category of plasma protein products.**
 - **Albumin**, which helps patients with liver disease, and patients being treated for shock and serious burns among other medical conditions.
 - **Coagulation factors**, which help those living with congenital bleeding disorders, such as hemophilia A and B and von Willebrand's disease.
- **Utilization management:** This term refers to essential work across the broader blood system to identify, maintain and encourage evidence-based uses of blood products, including plasma protein and related products, to improve patient outcomes and reduce system costs. Utilization management also includes planning for potential shortages.
- **Risk mitigation:** As part of managing its supply chain, Canadian Blood Services engages in a range of risk mitigation activities. Examples include increasing our plasma collections, calling out potential supply shortages to funding governments and hospitals before they are imminent; holding an appropriate inventory of products, where possible, in light of global supply pressures; coordinating and updating national shortage plans for both blood and immunoglobulins; diversifying supply chain risk by maintaining contracts with more

than one plasma fractionator and with multiple drug suppliers; monitoring the emergence of potential new pathogens that could affect safety and security of supply, etc.

- **Risk-based decision-making framework:** Blood operators are often faced with complex, evolving situations in which they must make decisions to ensure the safety and security of the blood supply for patients.

Canadian Blood Services uses a robust risk-based decision-making framework for blood safety developed by the Alliance of Blood Operators, of which we are a member. It can be found [on-line](https://allianceofbloodoperators.org) at allianceofbloodoperators.org.

This framework involves environmental scanning, ethical and legal considerations, and stakeholder perspectives in its approach. It supports effective decision-making for the benefit of health systems and patients.

- **Integrated supply chain:** On behalf of provincial and territorial governments except Québec, Canadian Blood Services owns and operates an integrated national blood system supply chain. “Integrated,” in this context, refers to two main things:
 - That the supply chain collects whole blood, plasma, and platelets under a unified plan that considers many factors, including donor population, health, marketing, and relationships; geographic location of donor collection events and sites within the supply chain; best practices in keeping with a biologics manufacturer; efficiency and affordability of the publicly funded supply chain; etc.
 - That the blood system supply chain is integrated across multiple processes and platforms — with Canadian Blood Services acting as a health system partner for governments and hospitals, as well as the system operator and expert possessing specialized capabilities. These capabilities include recruitment, collection, manufacturing, testing, and shipping products to hospitals, as well as bulk purchasing of plasma protein and other related products, utilization management, and risk mitigation practices. They also include research and development initiatives, and specialized medical and supply chain expertise.