Backgrounder: Blueprint for greater security of immunoglobulins for patients in Canada

Overview

On Sept. 7, 2022, Canadian Blood Services announced that in response to a heightened risk environment, it is taking action to increase and protect the supply of plasma to make immunoglobulins for patients in Canada. To that end, we released a comprehensive risk analysis that provided five recommendations for collaborative action across the broader blood supply system, including recommendations to act with urgency and to leverage both not-for-profit and commercial sectors. We also announced a related agreement with Grifols, a global healthcare company and leader in producing plasma medicines.

Our priority is to ensure lifesaving immunoglobulins remain available for patients in Canada. Under the agreement, to reach a minimum target of 50 per cent plasma sufficiency in the quickest time possible, both Canadian Blood Services and Grifols will collect plasma which will be made into immunoglobulins for patients in Canada. Canadian Blood Services will then purchase the immunoglobulins from Grifols. Purchasing medications from the commercial plasma sector has been part of our practice for more than two decades.

The agreement will:

- Provide essential protections for the national blood system, including controls to prevent negative impacts on Canadian Blood Services' current and future network of blood and plasma donor centres;
- Ensure plasma donated in Canada is used to make immunoglobulins in Canada, exclusively for patients in Canada; and,
- Enable the country's first end-to-end supply chain to meet patients' critical needs for immunoglobulins — many of whom have no other treatment option available.

The agreement does not involve the sale of any aspect of the national blood system and in no way changes Canadian Blood Services' previously announced plans to collect more plasma. Canadian Blood Services will continue to increase the number of plasma donor centres it operates across the country.

These are responsible actions for the blood operator to take, in the best interest of patients, and in keeping with our mandate to ensure security of supply of needed blood and plasma products for the country.

The material below provides essential background on the environment informing these actions, the risk analysis and the agreement with Grifols.

Key Facts

- Plasma is a straw-coloured liquid that makes up most (55 per cent) of the body's blood volume. It is rich in proteins that protect the body from illness, infection and excessive bleeding.
- Immunoglobulins are the most widely used type of medications made from plasma. They are used to treat patients with primary and secondary immunodeficiency disorders, autoimmune disorders and neurological disorders, along with other medical conditions.
- Canadian Blood Services estimates that more than half (50–60 per cent) of patients in Canada prescribed immunoglobulins must use them to live, with no other treatment option available for care.
- Canadian Blood Services is Canada's national blood operator (except in Québec). As such, Canadian Blood Services is accountable for managing the integrated national blood system on behalf of provincial and territorial governments, including the supply of plasma and plasma medications, such as immunoglobulins.
- "Plasma sufficiency" refers specifically to the percentage of plasma collected in Canada by the accountable blood operator or its agents to manufacture into immunoglobulins exclusively for patients in this country.
- Currently, Canadian Blood Services collects enough plasma to manufacture 16 per cent of the immunoglobulins needed in Canada. The balance (~84 per cent) of immunoglobulins is purchased from the global biologics industry through competitive procurement processes and made from plasma collected by other sources (including paid donors).
- A plasma sufficiency target of 50 per cent was established in 2016 through a risk-based decision-making analysis to ensure patients' critical needs for immunoglobulins in Canada will continue to be met into the future.
- The risk analysis was repeated in 2021–2022. It confirmed this target remains appropriate, and that in Canada (excluding Québec), an estimated 50-60 per cent of immunoglobulins are used to treat life-threatening medical conditions for which no other therapy is available.
- Because demand for immunoglobulins is outpacing the plasma collections necessary to make them, there is currently a global shortage of immunoglobulins.
- The COVID-19 pandemic further disrupted global supply chains for many essential products including plasma-derived medications, and escalated supply and demand pressures.
- In response, and with governments' support, Canadian Blood Services continues to open new plasma donor centres and maximize its plasma collection capacity. Once fully operational, these activities will increase domestic plasma sufficiency for immunoglobulins to approximately 25 per cent.

- While Canadian Blood Services is moving in the right direction, there remains a significant gap to reach a minimum 50 per cent plasma sufficiency target with urgency, to secure the supply of immunoglobulins for patients who use them on a lifesaving basis.
- To help inform the risk analysis, Canadian Blood Services also conducted a comprehensive request for proposal (RFP) process to assess whether the commercial plasma sector could be leveraged while still maintaining protections for the national supply chain.
- Grifols was the successful proponent. In September 2022, 2e announced an agreement with Grifols that enables an end-to-end domestic supply chain for immunoglobulins, while achieving essential protections for the national blood system.
- Under this agreement, both Canadian Blood Services and Grifols will collect plasma in Canada to achieve a target of at least 50 per cent plasma sufficiency.
- Outside of this agreement, plasma collected by the commercial plasma industry does not contribute to Canada's plasma sufficiency. Rather, it contributes to the global market for patients around the world.
- **To be clear, Canadian Blood Services is not purchasing plasma in this agreement. Rather, we are purchasing finished medications, which has been our practice for more than two decades.**
- This agreement with Grifols is a responsible approach for Canada, both to ensure minimal impact of the commercial industry on Canadian Blood Services' operations and to ensure national system control of a domestic end-to-end supply chain of lifesaving immunoglobulins for the patients we serve. **Plasma collected in Canada under this agreement will be used to make immunoglobulins exclusively for patients in Canada, thereby increasing domestic sufficiency. None of the immunoglobulins can be sold offshore.**

Environment/Context

Constricted global supply: Use of immunoglobulins has been growing in health systems around the world for many years. Blood supply systems and the global commercial plasma sector are not currently able to collect enough plasma to meet demand.

In August of 2019, the American Food and Drug Administration declared a shortage of immunoglobulins that continues to affect patients today. The U.S. supplies much of the world with plasma to manufacture plasma-derived medications, collectively referred to as plasma protein products. Despite the large amount of plasma collected in the U.S., there continues to be an inadequate amount of plasma to meet the global need for a specific type of plasma protein product called immunoglobulins. This is why many countries are seeking to increase plasma collection to keep up with growing demand.

This shortage has been made more acute by the COVID-19 pandemic, which disrupted supply chains internationally. The pandemic caused countries to try to ensure that more vital medical therapies, such as vaccines and other products, are manufactured domestically.

Canadian Blood Services and plasma sufficiency: Part of Canadian Blood Services' role is maintaining Canada's plasma sufficiency to make immunoglobulins and other plasma-derived medications for use by hospitals and patients across the country. Key to this is regular monitoring of supply and demand to identify emerging risks and enable an appropriate, effective response.

Canadian Blood Services ensures security of supply for immunoglobulins by doing two things:

1. Collecting plasma we ship to pharmaceutical companies in the global biologics industry that manufacture medications, including immunoglobulins, on our behalf and exclusively for use in Canada. The medications are then licensed by Health Canada and returned to Canadian Blood Services for supply to the health centres we serve.
2. Bulk purchasing additional medications, 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 provincial and territorial health systems to ensure patients' needs are met in Canada.

These two activities meet 100 per cent of demand for immunoglobulins in Canada (excluding Quebec).

Why we must increase plasma sufficiency for immunoglobulins in Canada: Currently, Canadian Blood Services collects about 16 per cent of the plasma required to manufacture immunoglobulins for health centres we serve. This does not mean patients are going without treatment. Rather, it means that we purchase the balance (approximately 84 per cent) of the immunoglobulins as finished medications from the global biologics industry, which are made from plasma they collected themselves.

Because demand for immunoglobulins is outpacing plasma collections necessary to make them, there is currently a global shortage of immunoglobulins. It is essential for blood supply systems around the world to increase their plasma collection substantially, including here in Canada.

In recent years, third-party reports have validated the need to collect more plasma in Canada:

- The 2018 Health Canada Expert Panel on Immune Globulin Product Supply and Related Impacts in Canada recommended options "be carefully examined to ensure that all source plasma collected in Canada from Canadian donors (whether paid or volunteer) be made available for the needs of Canadian patients".
- The 2020 Ontario Auditor General audit related to blood and blood products recommended Canada achieve 50 per cent immunoglobulin sufficiency as soon as possible.

How Canadian Blood Services is growing Canada's plasma supply: With financial support from federal, provincial and territorial governments, Canadian Blood Services is growing its capacity to collect more plasma. Since 2020, we have opened seven dedicated plasma donor centres in Abbotsford and Kelowna, B.C.; Lethbridge, Alta.; and, in Ontario, Brampton, Ottawa, Sudbury and Vaughan; with two more centres planned to open in 2023 in St. Catharines and Windsor, Ont. Pending confirmation of financial support, another two centres will follow to bring the total to 11 dedicated plasma donor centres in Canada in 2024. We are also improving pre-existing plasma collection programs at our blood donor centres. Together, these enhancements are expected to achieve at least 25 per cent plasma sufficiency for immunoglobulins once the centres are fully operational.

While these efforts will improve plasma sufficiency in Canada, there remains a significant gap to meet a minimum target of 50 per cent plasma sufficiency urgently, to bring greater security to the supply of immunoglobulins for patients in Canada who use them on a lifesaving basis.

Risk Analysis

In 2021–2022, Canadian Blood Services applied the Alliance of Blood Operator's Risk-Based Decision-Making framework to refresh similar work conducted in 2016–2017 and to assess ongoing and emerging risks to plasma and immunoglobulin supplies. This framework was developed to facilitate blood-system decision-making in complex situations and is a best practice used by blood operators around the world.

The analysis included substantive input from experts and stakeholders, including governments, patients, clinicians, industry and market analysts, health economists, ethicists, legal specialists and international blood operators, among others. It includes qualitative and quantitative assessments, including horizon scans on supply and demand for immunoglobulins, reviews of emerging alternative treatments, jurisdictional scans, and a health economics study. It was also informed by stakeholder consultations.

Through the analysis, the following five key recommendations were generated, which provide a blueprint for collaborative action across the broader blood system to bring greater security to the supply of immunoglobulins in Canada:

1. Undertake additional risk-mitigation measures with urgency
2. Pursue a targeted range of approximately 50–60 per cent domestic plasma sufficiency to meet patients' most critical needs in Canada — which have no other treatment option.
3. Leverage both not-for-profit and commercial sectors
4. Continue working with the National Emergency Blood Management Committee, a pan-Canadian expert advisory body, to address short-term product shortages
5. Maintain active monitoring of supply and demand for immunoglobulins

The report from the analysis was completed and shared with governments in June 2022. Many of these recommendations are in various stages of implementation by Canadian Blood Services and governments.

A role for the commercial plasma sector

To help inform this risk analysis, and in alignment with the recommendations of Health Canada's expert panel, Canadian Blood Services conducted a comprehensive request for proposal (RFP) process to assess whether the commercial plasma sector could be leveraged while still maintaining protections for the national supply chain. With this caveat, our objectives were to secure a greater domestic supply of immunoglobulins in a timely and cost-effective way and achieve an end-to-end supply chain for immunoglobulins in Canada. Several potential proponents from within the plasma industry were invited to submit proposals. After completion of all stages of the procurement process, which was aligned with industry best practices and monitored by a fairness advisor, the successful proponent was Grifols.

Through this agreement, we will:

- Enable an end-to-end domestic supply chain for immunoglobulins where plasma is collected and manufactured in-country exclusively for patients in Canada
- Rapidly increase domestic plasma sufficiency to reach a minimum target of 50 per cent sufficiency for immunoglobulins (meaning that the critical needs of patients who require immunoglobulins to live will be met with plasma collected in Canada).
- Reach the optimal sufficiency target at a competitive price
- Offer greater predictability of cost than purchasing immunoglobulins from the global market and remove foreign exchange and high demand volatility
- Reduce direct competition with Canadian Blood Services' existing blood and plasma collection network built through investments by governments, and ensure that Grifols only collects the amount of plasma required to fulfill the needs of Canadian Blood Services

To be clear, Canadian Blood Services is not purchasing plasma in this agreement. Rather, we are purchasing finished medications, which has been our practice for more than two decades.

The difference, under this agreement, is that immunoglobulins purchased from Grifols will be made from plasma collected in Canada and manufactured in Canada, enabling the country's first end-to-end domestic supply chain for immunoglobulins.

This agreement with Grifols is a responsible approach for Canada, both to ensure minimal impact of the commercial industry on Canadian Blood Services' operations and to ensure national system control of a domestic end-to-end supply chain of lifesaving immunoglobulins for the patients we serve. **Plasma collected in Canada will be used to make immunoglobulins exclusively for patients in Canada, thereby increasing domestic sufficiency. None of the immunoglobulins can be sold offshore.**

The agreement also includes important measures to prevent negative impacts on Canadian Blood Services' plasma and blood collections, as well as clear benefits in terms of stable pricing of these medications for provinces and territories.

It is important to recognize that this agreement represents only part of the recommendations generated through the risk analysis. Canadian Blood Services will also continue to expand its own plasma collections network across the country. Further, we are engaged in a range of other system-level activities designed to mitigate risk to security of supply of plasma for immunoglobulins.

Key points of the agreement:

- **Preventing negative impacts on Canadian Blood Services' blood and plasma network:** Under the agreement, Canadian Blood Services has approval rights on where Grifols will open its new centres in Canada. Canadian Blood Services will only approve locations that reduce negative impacts on the national blood system. Our site selection criteria for plasma donor centres generally includes factors such as population size, proximity to shopping and post-secondary institutions and access to public transit. Grifols cannot operate plasma collection sites outside the agreement in Canada (i.e., all plasma collected by Grifols in the country will contribute to Canadian Blood Services' plasma sufficiency for immunoglobulins).
- **Plasma collected in Canada stays in Canada for patient care:** Grifols cannot ship or sell immunoglobulins they make in Canada to other countries (i.e., plasma collected by Grifols in Canada will be used to manufacture immunoglobulins on behalf of health systems in Canada via Canadian Blood Services, exclusively for patient care in Canada).
- **Operational independence:** Canadian Blood Services and Grifols operations will remain separate and autonomous; however, Grifols' consent forms will note that the plasma they collect will be used to make products for Canadian Blood Services to meet the needs of patients in Canada. Operational independence also means that Canadian Blood Services is not prohibited from purchasing medications from other vendors, as it currently does now, on the global market or sending plasma Canadian Blood Services collects to other manufacturers, to ensure essential diversification of supply.

- **Cost competitiveness:** Canadian Blood Services remains committed to delivering an adequate supply of immunoglobulins for patients in Canada at an affordable cost to Canadian health-care systems. Immunoglobulins acquired through this agreement will be purchased at a competitive rate to the international market, particularly in the context of the tightening global supply.

Canadian Blood Services' long-standing relationship with Grifols

Canadian Blood Services and the broader transfusion community in Canada have had a long and positive relationship with Grifols, a global healthcare company and leader in producing plasma medicines. The company has gained deep knowledge of Canada's plasma and health-care systems over the more than 30 years it has manufactured plasma collected in Canada at its facilities in the U.S. These contract manufacturing services have enabled Grifols to provide plasma-derived medications that have enhanced the lives of thousands of patients in Canada for decades.

In 2020, Grifols purchased manufacturing facilities in Montréal, which will be fully operational in 2026 and which will produce immunoglobulins for Canadian Blood Services, manufactured from plasma Grifols collects in Canada. This manufacturing capacity will provide an essential component in the domestic end-to-end supply chain and will reduce risk to Canada's supply of immunoglobulins.

Commercial plasma sector in Canada

Commercial plasma collection (where donors are remunerated) is a relatively new dynamic in Canada. We have always maintained that a small number of commercial collection sites would not have a negative effect on the national blood system supply chain. However, large-scale commercial growth — without appropriate controls such as those put in place through our agreement with Grifols — could have negative impacts on the existing system for both blood and plasma collections and threaten our ability to meet patient need. At the same time, Canadian Blood Services recognizes that governments continue to hold a range of views about commercial plasma collection. All governments agree, however, that Canada must increase plasma collection and immunoglobulin sufficiency with urgency.

This agreement solves these challenges by ensuring necessary domestic security of supply, with both Canadian Blood Services and Grifols collecting more plasma on behalf of patients in Canada and manufacturing that plasma into immunoglobulins on Canadian soil. It also provides essential protections from negative impacts of large commercial industry on national blood system operations, something we realized was not achievable legislatively in a timely manner across all jurisdictions where we operate

Looking ahead

Canadian Blood Services will continue discussions with governments to determine how, as a country, we should approach commercial plasma collection with respect to sufficiency needs and to further mitigate any impact on national blood supply system operations and our mandate to provide these lifesaving medications to hospitals for patients in Canada. Our agreement with Grifols does not negate the need for these ongoing discussions.

Canadian Blood Services continues to manage the blood and plasma supply system in all provinces and territories except Québec. This agreement with Grifols does not encroach upon or minimize our role. We will continue to ensure the supply of blood and plasma products for patients across the country.

Canadian Blood Services has no plans to remunerate donors. We will continue to collect plasma and blood, and to encourage registration for stem cell, organ and tissue donation in the same manner we always have. We do all our work with the overarching and ever-present priority of safety and security of supply for patients. The actions outlined in this document align with this priority and will help us achieve one of our essential objectives: to increase plasma sufficiency for immunoglobulins on behalf of the patients in Canada who depend on them.