Plasma and Immunoglobulin Security of Supply:

Risk-Based Decision-Making Analysis

June 2022
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1 Introduction

Blood operators in many countries, including Canada, are increasing the amount of plasma they collect to manufacture into life-saving immunoglobulin, in response to increasing rates of utilization and a challenging global market for the product.

Canadian Blood Services provides immunoglobulin (derived from blood plasma) through a not-for-profit supply system, as part of the mandate it delivers on behalf of all Canadian provinces and territories (except Québec). A biologics manufacturer, Canadian Blood Services is regulated by Health Canada.

Canadian Blood Services carries out two main activities to ensure a secure immunoglobulin supply (see text box for explanation of these key terms).

- Collection of plasma from donors in Canada to ship to global biopharmaceutical companies, which manufacture it into immunoglobulin (and other plasma protein products) through a process of fractionation, for use exclusively in Canada ("toll fractionation"). The manufactured products are licensed by Health Canada as biologic drugs and supplied to Canadian hospitals and clinics by Canadian Blood Services.

- Purchase of commercially available immunoglobulin manufactured by global biopharmaceutical companies, using plasma collected as part of their own supply chains. These products are also acquired and shipped by Canadian Blood Services to hospitals across the country for use by Canadian patients.

For several years, the strategy of collecting plasma for manufacture of immunoglobulin by offshore toll fractionators and purchasing additional immunoglobulin on global markets had enabled Canadian Blood Services to meet patient needs.

However, risks to the availability of adequate amounts of plasma and immunoglobulin began to emerge, and in 2016 a risk-based decision-making (RBDM) analysis was conducted to project growth in demand for immunoglobulin, global plasma market risks, immunoglobulin supply risks and shortages, and future costs. It also considered competitive challenges to ensuring a secure plasma supply for essential Canadian needs. That assessment led to the recommendation of a refreshed target of 50% domestic plasma sufficiency, and a strategy to increase Canadian Blood Services’ plasma collection capacity.

The current and projected risks to plasma sufficiency and immunoglobulin security of supply have proven to be at least as significant as had been projected in the 2016 RBDM assessment, as described in Section 2, Risk Horizon.
Key Terms and Definitions

PLASMA:
The straw-coloured liquid portion of human blood, containing several proteins with therapeutic benefits.

- Collected from human donors through two processes: “recovered” plasma is separated from whole blood collected through the blood donor program; “source” plasma is collected in a specialized procedure performed at plasma collection centres. As less whole blood is being collected, reflecting a decrease in the use of red cells, there may be a greater reliance on source plasma.
- Plasma may be used as a treatment in itself, but it is more often used as a raw material for other specialized products such as immunoglobulin.

FRACTIONATION:
The process by which components in plasma are manufactured into therapeutic products such as immunoglobulin.

- Canada does not currently have fractionation capacity and sends domestic plasma to facilities in the U.S or Switzerland for processing into plasma protein products, which are returned for use in Canada. This is referred to as “toll fractionation.”

IMMUNOGLOBULIN:
Also known as antibodies, glycoprotein molecules are produced by plasma cells (white blood cells). These act as a critical part of the immune response by specifically recognizing and binding to particular antigens, such as bacteria or viruses, and aiding in their destruction.

- Immunoglobulin is manufactured into “finished immunoglobulin” from plasma by fractionation in dedicated facilities. It may take two forms: IVIg is administered intravenously, while SCIg is administered by sub-cutaneous injection and may be used outside a hospital for some indications.
- Demand is growing worldwide as immunoglobulin is used for an increasing range of conditions.

PLASMA SUFFICIENCY:
Percentage of plasma collected by or on behalf of accountable blood operator (Canadian Blood Services) to manufacture into immunoglobulin exclusively for patients in Canada.

- A target of 50% plasma sufficiency for Canadian-sourced plasma was developed in the 2016 analysis, in order to protect immunoglobulin supply required to treat patients in the highest priority categories of indications, where there are no alternative treatments.
2 Risk horizon

2.1 Canadian immunoglobulin utilization

**Key trends:** Immunoglobulin remains a crucial therapy. For many indications, there is a risk to life without treatment and there is no alternative therapy. There is a projected 5-7% annual increase in use.

The growth rate of immunoglobulin in Canada has been 7-8% yearly since 2017, with some observed reduction over the fiscal year 2020–2021, with a growth rate in immunoglobulin use of only 1.1%, attributed to the pandemic. The growth rate of immunoglobulin is expected to return in future years to slightly below the previous baseline, with overall annual growth rates of 5-7% over the next five years.

Some developments may affect trends in usage of immunoglobulin. One is the possibility of new indications for immunoglobulin. Although some currently approved indications may increase in usage, it is considered unlikely that new indications with a major impact on immunoglobulin usage will emerge within the next five years. Another is that new therapies, such as neonatal Fc receptor (FcRn) antagonists, may be developed that will replace immunoglobulin use, reducing demand for certain indications, though these are unlikely to exceed 10% of immunoglobulin demand within seven to ten years.

2.2 Immunoglobulin supply and price impacts

**Key trends:** Several shortages of immunoglobulin products arose prior to 2020. Immunoglobulin has continued to be in a shortage situation globally as demand continues to outstrip supply. The pandemic further constrained production in several countries and caused supply chain disruptions, all with price implications. In addition, faced with a shortage situation, there is a risk that systems in other jurisdictions could require fractionation capacity to be preserved for domestic purposes, similar to protectionist policies taken for other essential products during the pandemic.

Since 2018–2019, immunoglobulin has been in a shortage situation globally, with shortages being officially declared by the U.S. Food and Drug Administration in 2019. The global immunoglobulin shortage has continued, with no indication as to how long the situation will last.

The COVID-19 pandemic further constrained production in several countries and caused supply chain disruptions. Canadian Blood Services was able to mitigate severe shortages of immunoglobulin products during the pandemic through pre-emptive purchases of additional inventory on the global market, though at significantly elevated price points. In addition, the impacts of the pandemic on acute care health service delivery reduced demand for immunoglobulin transiently. Even if plasma collections return to pre-COVID levels in the future, the continuing increase of global immunoglobulin demand, coupled with the long lead time from
plasma collection to immunoglobulin manufacturing, will mean that the sustained gap between supply and demand will continue for some time.

A lack of domestic fractionation capacity is another challenge, as it means that Canada currently does not manufacture immunoglobulin in the country. The risks associated with the absence of an end-to-end supply chain in Canada for critical products were exemplified during the pandemic. For example, the early inability to access adequate volumes of personal protective equipment, and more dramatically the significant delays of accessing sustained volumes of COVID-19 vaccines, exposed serious weakness within the Canadian health care system due to our heavy reliance on offshore manufacturing capacity. These examples – which Canada’s federal and provincial governments resolved through partnering with the commercial manufacturing industry – are somewhat comparable to the risks to the plasma fractionation industry. In the event of a global shortage of immunoglobulin, national governments or pan-government entities could declare that domestic fractionation capacity is to be prioritized or preserved for domestic purposes. A U.S. presidential order permits the president to retain biopharmaceutical products in the country, exclusively for domestic use, should the circumstances dictate.

Industry experts are predicting that rising immunoglobulin costs will continue post-pandemic and the market for immunoglobulin will remain highly competitive, as product shortages continue through the next several years. Market intelligence has also predicted that the price for collecting plasma for immunoglobulin will continue to increase; these increases are expected throughout the decade, driving sustained price increases for commercial product.

### 2.3 Plasma for immunoglobulin

**Key trends:** Currently at 15%, Canadian plasma sufficiency is projected to be at approximately 25% once the 11 planned Canadian Blood Services plasma donor centres are operational. Plasma collected by commercial plasma collectors operating in Canada is manufactured into products for markets outside the country (largely through vertically integrated arrangements).

Over 85% of Canada’s immunoglobulin is purchased by Canadian Blood Services from out-of-country commercial manufacturers who make the product using plasma collected in the U.S., from donors who are remunerated.

Plasma sufficiency in Canada remained at only 15% in late 2021. A total of 11 Canadian Blood Services plasma donor centres are planned. The plasma collected at those centres is projected to increase Canada’s domestic sufficiency to approximately 22% when they are all operating at capacity. Canadian Blood Services is also working toward increased plasma collections within its current network of blood centres to add additional volume, which will support an increase in sufficiency levels to 25%, leaving a significant gap from the original target of 50% plasma sufficiency.
Currently, plasma collected by commercial plasma collectors operating in Canada is manufactured into products for other markets (through integration arrangements with fractionators), enabling diversion of Canadian plasma away from production of immunoglobulin for patients in Canada. Continued expansion of commercial collection in Canada is expected, with few or no barriers at the present time. This poses a risk to the existing public sector blood and plasma collection network in Canada, through encroachment. Encroachment occurs as commercial plasma collectors draw donors away from the public system. There are, currently, no protections in place in Canadian jurisdictions to protect against these risks of diversion and encroachment. At present, commercial plasma collectors in Canada do not contribute to domestic plasma sufficiency, and there is no way to ensure that commercially collected Canadian plasma benefits patients in Canada. In addition, in the absence of protections, there is a continuing risk of the unknown impacts of encroachment on national blood system operations.

A further trend of note relating to the availability of plasma is that there is no viable, scalable plasma-for-purchase market due to ever-increasing vertical integration. Large fractionation companies either control their own collection sites or purchase recovered plasma. Historically, there were many independent plasma collectors in the U.S. and Europe selling plasma, but all have been acquired by the large-scale fractionation companies over the last decade. In Canada, Canadian Plasma Resources (CPR) began with two small plasma collection centres (in Moncton, New Brunswick and Saskatoon, Saskatchewan) and has opened two larger centres in Calgary and Edmonton, with more centres announced for imminent opening. CPR has recently entered into vertically integrated arrangements as well. In addition, Prometic (an Winnipeg-based collector, formerly known as Cangene) was acquired by Grifols, and this plasma now feeds Grifols' fractionation enterprise.
3 2021-2022 Risk-based decision-making analysis

In 2021, the risks described above motivated a return to further risk-based decision-making analysis, to project the next five-year risk scenario related to plasma sufficiency and immunoglobulin security of supply, encompassing both plasma collection and fractionation capacity.

As in 2016, the Alliance of Blood Operators (ABO) Risk-Based Decision-Making Framework for Safety was used as the methodology for the current analysis. This structured decision-making approach takes a system perspective, oriented towards the achievement of three key objectives:

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

The framework guides a decision-making process through the stages of preparation, problem formulation, participation strategy, assessments, evaluation, and decision. More detail on the ABO RBDM framework can be found at https://www.allianceofbloodoperators.org/abo-resources/risk-based-decision-making.aspx.

An analysis was conducted pursuant to the framework with two objectives in mind: first, to explore the security of Canada’s plasma and immunoglobulin supply, including risks across both collection and fractionation capacity; and second, to evaluate options for managing the risks that are on the horizon, with decision drivers focused on patient outcomes and affordability for the system. The goal is to support the development of a strategy that offers the greatest benefit for the future.

As part of the framework methodology and in order to guide the analysis, a set of decision drivers, risk assessment questions, and preliminary risk management options were developed.

3.1 Decision drivers

To frame the RBDM analysis the following decision drivers were identified:

1. **Patient safety**: To ensure an adequate supply of plasma and immunoglobulin for Canadian patients who rely on this therapeutic product; to create certainty and security of domestic supply.

2. **System costs**: To deliver an adequate supply of immunoglobulin for Canadian patients at an affordable cost to the Canadian health care system.
3. **Sustainability of blood and plasma collection network in Canada**: To maintain donor engagement necessary to serve the transfusion needs of all Canadian patients; to maintain donor well-being and trust; to maintain value proposition for workforce.

### 3.2 Assessment questions

Informed by assessment findings and the evaluation of risk management options in mitigating the articulated risks, the RBDM analysis sought to answer a set of overall assessment questions:

1. **If the status quo** is maintained, what risks to the availability of immunoglobulin for Canadian patients and its affordability will likely materialize in the next five years?

2. **What level of plasma collection** by Canadian Blood Services or its agents ("plasma sufficiency") is required to ensure immunoglobulin availability for clinically relevant needs?

3. **What risk management option** is recommended which achieves the best balance of domestic security of supply (e.g., plasma collection, production of licensed immunoglobulin, in-country inventory), reasonableness of finished product costs, and overall system sustainability for the benefit of Canadian patients?

4. **What mitigation measures** are recommended to manage immunoglobulin supply shortages that may arise even if the risk management option selected as part of question 3 is implemented?

5. **What monitoring processes** are required to understand the scenario risks and to trigger a re-evaluation of this risk assessment? What **risk indicators** should be monitored in order to track the onset and magnitude of these risks?

### 3.3 Risk management options

A set of five risk mitigation approaches were evaluated in the RBDM process:

1. **Increase Canadian Blood Services’ plasma collection capacity (beyond 11 sites)**

   Canadian Blood Services expands collection capacity within Canada, beyond that which is provided by the 11 sites currently planned. This could be through new infrastructure (i.e., building additional sites) or other means (e.g., plasma derived from mixed collection sites in the Canadian Blood Services’ blood and plasma network).

2. **Purchase additional plasma, if available, collected within Canada or elsewhere**

   Canadian Blood Services purchases additional plasma, if available, collected within Canada by commercial collectors, or from outside Canada, or a combination of both.
Purchase additional finished immunoglobulin fractionated within Canada or elsewhere

Canadian Blood Services purchases additional finished immunoglobulin, fractionated within Canada, when possible, or from outside Canada, or a combination of both. This is not a stockpile of immunoglobulin.

4. **Develop domestic immunoglobulin supply chain from collection to fractionation, through commercial contracts**

Canadian Blood Services collaborates with a commercial plasma collector and fractionator to establish a vertically integrated immunoglobulin supply chain from plasma collection to fractionation, under the auspices of the blood system operator.

5. **Partner to optimize utilization**

Canadian Blood Services collaborates with the provincial and territorial (P/Ts) health systems to determine and promote optimal immunoglobulin utilization. Two alternatives within option 5 have been considered:

a) **Best practices in utilization of immunoglobulin**

   This option involves allocating immunoglobulin for the treatment of those conditions for which there is evidence of the greatest benefit, and ensuring that patients receive the immunoglobulin product that is most effective for them. It would seek to reduce inappropriate uses of immunoglobulin, or those for which there is weak or no evidence of effectiveness.

b) **Gatekeeping for the use of immunoglobulin**

   Under this option, access to immunoglobulin would be restricted to use only by patients in the most critical diagnostic categories.
4 Participation

An important element of risk-based decision-making is the participation and input of those affected by the risks being assessed. Two sets of stakeholders have been engaged: (i) patients, clinicians, and health organizations and (ii) donors and members of the public.

4.1 Patient, clinician, and health organization stakeholders

The intent of the engagement was to understand the perspectives of patients living with primary and secondary immunodeficiency disorders, autoimmune disorders, and neurological and other disorders for which immunoglobulins are a vital part of treatment. Canadian Blood Services sought to understand the level of concern that patients and their treaters have, and their priorities in securing supply. The design included stakeholders making written submissions and/or attending a virtual engagement opportunity. Dialogue Partners Inc. facilitated the discussions, with Canadian Blood Services’ team members in attendance to present the issues and to answer any questions. Government representatives joined the sessions as observers.

A high value was placed by participants on the criticality of securing domestic immunoglobulin supply, ensuring safe and adequate supply of immunoglobulin and other blood products, and minimizing the impact of future supply disruptions. Participants noted that an insecure supply has high impact for patients.

While there was agreement on the need to collect greater immunoglobulin data to optimize utilization, clinicians referenced several evaluations of Canadian immunoglobulin utilization which confirm that the vast majority of immunoglobulin is prescribed for appropriate indications. It was expressed that “research initiatives to develop modern technology for the manufacture of plasma proteins by alternative, non-plasma-dependent processes, such as recombinant technology” would also support efforts to achieve longer-term plasma sustainability in Canada.

There were varying perspectives in terms of leveraging commercial collectors. A few stakeholders were opposed to commercialized collection models and would like to see capacity and investments in voluntary collection models only. However, others see greater balance being achieved through a mixed model that utilizes both public sector and commercial collection models, while still maintaining a connection to the global immunoglobulin supply chain. Those in support of a mixed approach believe that this approach is more likely to be capable of meeting supply targets and more cost-effective. While the issues of donation incentives and donor remuneration were areas of contention, many participants expressed the belief that such approaches play a key role in future sustainability.

Despite differing views, all stakeholders were in consensus that more Canadian plasma is needed and that the immunoglobulin security of supply risk is a high priority that should be addressed with urgency.
See Appendix 1: Securing Canada’s Plasma for Immunoglobulin Supply: What We Heard Report for further details.

4.2 Donors and public

The engagement with donors sought their viewpoints on plasma collection generally, on remuneration for plasma donation, and on commercial plasma collection in Canada. The design included virtual sessions with whole blood donors who had converted to plasma donation, and student leaders at universities across Canada who were involved in campus blood or stem cell clubs. As well, data were garnered from Ipsos surveys of members of the general public, new plasma donors, and whole blood donors.

Donors and the general public wanted Canadian Blood Services to be less reliant on plasma from paid donors in the U.S. Most source plasma donors are either opposed to payment for donation, or not interested in payment personally. Those opposed are concerned that payment could compromise the safety of the product, while others would be open to Canadian Blood Services paying donors for plasma if needed to increase sufficiency.

There is a lack of awareness and knowledge about commercial plasma collection centres operating in Canada and their potential impact on non-remunerated donation, as well as confusion with the relationship between Canadian Blood Services and commercial operators in Canada.

See Appendix 2: Donor and Public Consultation for further details.
5 Assessment

Informed by significant data gathering, a number of assessments were undertaken to support the evaluation and decision stages:

1. Canadian immunoglobulin utilization
2. Horizon scan: Neonatal Fc receptor (FcRn) antagonists
3. Security of supply
4. Jurisdictional assessment
5. Health economics and outcomes
6. Contextual assessment
7. Operational risk and impact.

These assessments are comprehensive and key findings are summarized below.

5.1 Canadian immunoglobulin utilization assessment

The immunoglobulin utilization assessment is a summary of the factors related to the demand for immunoglobulin and the major indications for which it is used. It considers Canadian usage in relation to international factors and usage categories.

Since 2017, the growth rate of immunoglobulin in Canada has been 7-8% yearly (with some rate reduction observed during the pandemic) and is expected to return to 5-7% over the next five years.

In Canada, secondary immune deficiency (SID) is expected to be the fastest growing area for immunoglobulin use in Canada (estimated growth approximately 15% over the next five years). Immunoglobulin usage in primary immune deficiency (PID) will continue to grow, but at a declining rate over time (estimated growth approximately 8%). The use of immunoglobulin overall is expected to increase, especially due to the availability of subcutaneous immunoglobulin (SCIg) therapies. New indications or new therapies may affect usage trends, but not over the next five years.

It is estimated that approximately 60-65% of Canadian immunoglobulin utilization is for conditions for which treatment is high priority (risk to life without treatment and no alternative therapy). These conditions include primary immune deficiency (PID) disorders, secondary immune deficiency (SID) states, immune thrombocytopenic purpura (ITP), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), Guillain-Barré syndrome (GBS), and multifocal motor neuropathy (MMN).
Canadian clinicians were further asked to consider the proportion of patients who would be critically dependent on immunoglobulin within these high priority diagnostic categories. The expert elicitation indicated that access to approximately 30% of Canadian immunoglobulin usage would ensure that all patients with a critical, acute need would receive immunoglobulin, but it would require the triaging of patients within a diagnostic category. It should be noted that in this scenario, within a relatively short period of time, the proportion of immunoglobulin use considered critical would move toward the higher percentage (60-65%) as patients would be required to delay therapy.

See Appendix 3: Immunoglobulin Utilization Assessment for further details.

### 5.2 Horizon scan: FcRn antagonists

A horizon scan was completed regarding the potential for new drugs called neonatal Fc receptor (FcRn) antagonists to affect the demand for immunoglobulin in Canada. There has been considerable activity in the clinical development of FcRn antagonists for treatment of immune-mediated conditions.

As there are many uncertainties on the indications for these drugs and the Canadian uptake of them, it is unlikely that these drugs will impact demand for immunoglobulin products by more than 10% within seven to nine years. While it is very important to monitor their progress, they are unlikely to have a substantial impact on the overall demand for immunoglobulin both at this time, and for the medium-term future.

See Appendix 4: FcRn Antagonists: A Centre for Innovation Horizon Scan for further details.

### 5.3 Security of supply

The Security of Supply Assessment is a qualitative review of conditions that contribute to the current challenges in accessing a sufficient and affordable supply of immunoglobulin for Canadian patients. There has been a global shortage of immunoglobulin since FY 2018–2019, and COVID-19 has had a significant impact on global immunoglobulin supply chains.

Forecasts indicate that:

- source plasma collections are expected to grow in the U.S. as well as in Canada and Europe in the coming years;
- global immunoglobulin usage is also predicted to continue to grow at a sustained pace of about 7% annually until at least 2027, when growth will slow to about 5%;
- prices for collecting plasma and purchasing commercial products are expected to increase through the decade.
Increased commercial plasma collection is expected to continue to compete with non-remunerated collection systems in North America and Europe. As noted above, there are currently no controls to ensure that plasma that is commercially collected in Canada stays in Canada or is used to produce products for Canadian patients.

While Canada has no fractionation capacity at this time, there will be domestic fractionation capacity in Canada in the next three years. Fractionators continue to add new plants and increase capacity, and new technologies may achieve higher immunoglobulin yields from a given plasma volume.

The pandemic has demonstrated that protectionist government actions and plant shutdowns are a real risk, as are more recent extreme weather events that affect plant operations and supply chains.

See Appendix 5: Security of Supply Assessment for further details.

### 5.4 Jurisdictional review

The jurisdictional assessment describes the strategies taken by countries to manage their plasma and immunoglobulin supply.

In Canada, alongside our own target of 50% plasma self-sufficiency, Héma-Québec is aiming to increase plasma self-sufficiency to 42%.

The following countries, which have a single blood operator supported by public funding and protected mandates (that preclude the presence of commercial collectors in the market), have established varying targets for sufficiency, using a non-remunerated model of plasma collection:

- United Kingdom (U.K.): began collecting source plasma in 2021, after removal of a plasma collection moratorium (in place due to Creutzfeldt-Jakob risk); targeting 20% of domestic plasma by 2025;
- Australia: supplying 53% of immunoglobulin demand with 76 collection sites; targeting 60% in 2025;
- Netherlands: aiming for 60% self-sufficiency with a model similar to Canadian Blood Services.

Other countries use mixed plasma collection models (both commercial for-profit and public programs):

- Austria, Czech Republic, Germany, and U.S.: 100% immunoglobulin sufficiency, with excess product offered on global market;
- Most of the source plasma is collected by the commercial companies.

Fractionation and manufacture of plasma-derived medical products (PDMPs) are carried out under different models:

- Australia, U.K., Netherlands, Austria, Germany and U.S.: privately owned fractionation plants;
- France: state-owned fractionation company;
• U.K.: seeking to identify a commercial fractionator.
See Appendix 6: Jurisdictional Assessment for further details.

5.5 Health economics and outcomes assessment

This assessment used a quantitative modelling exercise to analyze the impacts of a set of scenarios on each of the risk management options, in terms of cost and health outcomes.

The model simulates impacts on Canadian Blood Services’ ability to acquire plasma and immunoglobulin to meet the needs of Canadian patients across:

• **health outcomes** risk in quality-adjusted life years – QALYs (a population health metric in which one QALY is one year of perfect health for one individual);
• **cost-effectiveness**: a measure of the cost to save one QALY, expressed as the number of dollars (millions) per QALYs gained;
• **cost** of the risk management options, as they would accrue over the period of 2021–2040.

The modelling process focused primarily on the scenarios that are considered most likely: protectionist government policies, economic factors resulting in reduced plasma collection in the U.S. (both 24-month and 5-year recovery timeframes), challenges to plasma collection in Canada (competition), higher cost of plasma, demand fluctuations, and plant failures.

In terms of **health outcomes**, options 1 (increase Canadian plasma collection capacity), 4 (develop domestic immunoglobulin supply chain from collection to fractionation, through commercial contracts) and 5 (partner to optimize utilization) consistently show QALY gains – with option 4 having the greatest QALY gains. Options 2 (purchase additional plasma) and 3 (purchase additional immunoglobulin) have mixed outcomes with QALY losses estimated under scenarios that increase reliance on purchase of foreign sources of finished immunoglobulin.

Option 5 is the most **cost-effective** option and has the most cost saving across all scenarios; however, this option does not protect full demand for all current immunoglobulin indications, nor did the model assume any costs for a utilization management program.

In terms of **cost**, there may be additional cost associated with domestic fractionation in option 4. However, options 1, 4 and 5 provide protection against price increases in the future. Option 2 could provide cost protection if commercial plasma were available; but it is unlikely that fractionation could be achieved domestically. Option 5 has cost savings over all scenarios; however, as noted above, this is as a result of not addressing full demand (and costs were not assumed).

See Appendix 7: Exploration of Risk Management Options to Support the Security of IG Supply for further details.
5.6 Contextual assessment

The contextual assessment reviewed the legislative, social and ethical implications associated with plasma sufficiency and immunoglobulin security of supply.

There are currently Voluntary Blood Donation Acts in two provinces served by Canadian Blood Services (British Columbia and Ontario) which prohibit payment of blood donors. There is an exemption from this legislation for Canadian Blood Services and its agents; the exemption for agents is explicit in the B.C. legislation and implicit in the Ontario legislation.

An international legislative review indicates that various countries have legislation and/or other mechanisms (e.g., contractual) that they enact to: promote greater national (and community) sufficiency, control domestic use of plasma collected in-country, import/export plasma and immunoglobulin, restrict entities who may collect plasma in-country, consider plasma and/or immunoglobulin critical/essential medicines, and prohibit remuneration or encourage unpaid donation (e.g., Canada, the European Union, United Kingdom and Australia).

Approaches to protect domestic security of supply are evident. For example, in the U.S., there is an increased number of executive orders, memos, and policies related to medical products, vaccines, personal protective equipment, and related tariffs, etc. The United Kingdom is seeking to implement mechanisms to ensure U.K. plasma must be used for U.K. patients.

A review of ethical implications focuses on two domains: (1) patient well-being and (2) the values associated with voluntary blood donation. Based on the principles articulated in the RBDM framework, some of those ethical considerations include:

- From a distributive and social justice (fairness) perspective, it may be (increasingly) unfair for Canada to rely so heavily on the plasma donations and finished products from other countries without reducing dependence and overall demand on the global supply.

- Evidence from other countries indicates that some form of remuneration can lead to meeting sufficiency targets. This speaks to practicality and proportionality, especially in the changing global context.

- A move toward remuneration of plasma donation is something that could impact the level of trust or perceived trust that some stakeholders may have with regard to the national blood supply system. Significant attention to communication of any plan involving remuneration, including rationale, would be required. As well, the details regarding remuneration (how, in what way, to what degree, etc.) also matter.

See Appendix 8: Contextual Assessment for further details.
5.7 Operational assessment

This assessment considered the operational implications associated with the implementation of the risk management options.

Feasibility risks (i.e., funding and timing constraints) were found to be key operational risks associated with option 1 (increase Canadian plasma collection capacity). Organizational capacity risks were identified for option 1 and for option 4 (develop domestic immunoglobulin supply chain from collection to fractionation, through commercial contracts) in different ways, with the draw on internal capacity being significantly greater for option 1.

Labour relations risks were also identified in connection to option 4. As well, this option was found to introduce other risks such as risks to reputation and stakeholder relationships, due to association with remunerated collection. The risks connected to a long-term third-party transaction were also identified (e.g., length of the contract, costs, performance indicators, etc.), along with implications for operational considerations such as fractionation redundancy strategy.
6 Evaluation

Each risk management option was evaluated in terms of:

- Effectiveness in risk reduction (key risks include inability to meet plasma sufficiency of approximately 50% and immunoglobulin supply for user needs; uncertain costs to procure sufficient plasma and immunoglobulin, straining affordability for the Canadian health care system; and reduced sustainability of Canada’s not-for-profit blood and plasma collection network);
- Additional benefits it may provide;
- Ability to manage stakeholder concerns; and
- Operational feasibility of the option.

An important aspect of the evaluation stage is the assessment of risk tolerability of the options. Risk tolerability is a judgment that a risk is reasonable given the expected benefits of an activity and resources required to manage the risk. The following factors were considered in assessing risk tolerability:

- Individuals or groups at risk (inequitable risk burden; vulnerable risk bearers);
- Risk perception;
- Risk-benefit balance;
- Risk management rationale and appropriateness;
- Accountability; and
- Trust.

6.1 Option evaluation

The key factors considered during the evaluation process are summarized below:

<table>
<thead>
<tr>
<th>Option 1</th>
<th>Increase Canadian Blood Services’ plasma collection capacity (beyond 11 sites)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit</td>
<td>Residual risk</td>
</tr>
<tr>
<td></td>
<td>QALY impact</td>
</tr>
<tr>
<td></td>
<td>Risk tolerability</td>
</tr>
<tr>
<td>Offers domestic security of supply and supports sustainability of existing blood and plasma collection network.</td>
<td>Risks include unfunded upfront infrastructure costs, internal capacity constraints, and insufficient pace of implementation.</td>
</tr>
</tbody>
</table>
### Option 2
**Purchase additional plasma, collected within Canada or elsewhere**

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Residual risk</th>
<th>QALY impact</th>
<th>Risk tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Useful as a small-volume business continuity management tool, if plasma is available.</td>
<td>Little plasma available for purchase due to ongoing vertical integration of industry; no controls to protect existing blood and plasma collection network; not viable to solve overall immunoglobulin supply issue.</td>
<td>Has mixed results across QALY gains and loss. It generally provides a health benefit or equivalence to the status quo, with the exceptions being in the event of protectionist actions, economic factors and domestic plant failure if the plasma source is either domestic or foreign (but not when a combination of both sources is used).</td>
<td>Tolerable in exceptional circumstances.</td>
</tr>
</tbody>
</table>

### Option 3
**Purchase additional finished immunoglobulin fractionated within Canada or elsewhere**

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Residual risk</th>
<th>QALY impact</th>
<th>Risk tolerability</th>
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<tbody>
<tr>
<td>Useful as a business continuity management tool, if product is available.</td>
<td>Not viable to solve the overall immunoglobulin supply issue, due to global short supply conditions; little or no domestic security achieved.</td>
<td>Provides a QALY savings for reduced U.S. plasma collection with a 2-year recovery period and foreign plant failure; and equivalence or loss for all other scenarios. There is a QALY loss under scenarios with protectionist government policies or reduced U.S. plasma collection with a 5-year recovery time.</td>
<td>Tolerable in exceptional circumstances.</td>
</tr>
</tbody>
</table>
**Option 4**

**Develop domestic immunoglobulin supply chain from collection to fractionation, through commercial contracts**

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Residual risk</th>
<th>QALY impact</th>
<th>Risk tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leverages commercial sector to accelerate plasma sufficiency and ensure domestically secured immunoglobulin; offers some protection for blood and plasma collection network through control measures in long-term contractual agreement.</td>
<td>Transactional risks (long-term contract with third-party); stakeholder risks associated with donor remuneration.</td>
<td>Provides QALY savings or equivalence to status quo and estimated to provide the highest QALY gain across the options for all scenarios as described in the model except one (plant failure).</td>
<td>Tolerable if strongly managed, due to benefits gained.</td>
</tr>
</tbody>
</table>

**Option 5**

**Partner to optimize utilization (5a. Best practices in utilization of immunoglobulin; 5b. Gatekeeping for the use of immunoglobulin)**

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Residual risk</th>
<th>QALY impact</th>
<th>Risk tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valuable to support utilization practices in collaboration with provinces and territories.</td>
<td>Not viable to solve the overall immunoglobulin supply issues, as a stand-alone strategy.</td>
<td>Estimated to provide QALY saving or status quo equivalency.</td>
<td>5a tolerable; 5b tolerable only in exceptional circumstances.</td>
</tr>
</tbody>
</table>

### 6.2 Evaluation outcomes

None of the options evaluated is, on its own, the full solution to the risks on the horizon. Overall, the assessment findings and evaluation indicate that option 1 (*increase Canadian Blood Services plasma collection - beyond 11 sites*) and option 4 (*develop domestic immunoglobulin supply chain from collection to fractionation, through commercial contracts*) offer a balance of benefits and risks, but in different ways.

Option 1 provides greater risk control in terms of domestic security of supply and protection for the sustainability of the existing public sector blood and plasma collection network as a whole, but carries unfunded upfront infrastructure costs, internal capacity constraints, and an insufficient pace of implementation. Innovative funding strategies could potentially be pursued, however, with an impact on timing and capacity.

Option 4 is premised on domestic resilience through a vertically integrated supply chain composed of 1) remunerated plasma collection by a commercial collector; and 2) domestic fractionation, to achieve enhanced security of supply for immunoglobulin. This option would be applied in concert with Canadian Blood Services’ step-wise strategy to increase its (non-remunerated) plasma collections.
Associated with this option are the risks related to stakeholder reactions regarding the remunerated model utilized by the commercial collector. In addition, this option relies on commercial collaboration, and hence carries the risks of any long-term third-party transaction.

These risks were assessed to be tolerable if strongly managed and in view of the benefits gained. The option leverages the commercial sector to accelerate progress towards the plasma sufficiency objective, while ensuring plasma collected in Canada is directed to the manufacture of domestically secured product for Canadian patients. It also affords key controls to protect the sustainability of the existing public sector blood and plasma collection network in Canada (through non-encroachment provisions).

While option 4 offers the expediency to achieve the required increase in plasma collection, continued support for optimal immunoglobulin utilization practices (option 5a) remains important, in collaboration with provincial and territorial health systems. Option 5a will always be an adjunct to the primary strategy (and not a solution on its own); it will evolve as new innovations provide alternatives to immunoglobulin in the future.

Options 2 (purchase additional plasma) and 3 (purchase additional immunoglobulin) were not assessed to be viable as stand-alone strategies. Both strategies depend on plasma/product availability for purchase. Regarding option 2, today, there is very little commercial plasma available for purchase, as the vast majority of plasma, including that which is collected in Canada, is absorbed into vertically integrated arrangements for fractionation. With respect to option 3, experience has demonstrated that product is very difficult to access during shortage situations when other countries are equally seeking to increase inventory. However, if plasma and/or product are available, these options could function as useful business continuity management tools to supplement a primary strategy.
7 Decision

In this stage, a series of outputs of the RBDM process (characterization of the overall risk, possible risk management options, assessment findings, stakeholder input, and evaluation data) were considered and applied to develop recommendations.

7.1 Assessment responses and recommendations

The evidence and the evaluation outcomes were applied to the questions that have framed the overall analysis, and a series of recommendations were generated.

1. If the status quo is maintained, what risks to availability of immunoglobulin for Canadian patients and affordability will likely materialize in the next five years?

If no additional strategies are undertaken beyond that which is planned (i.e., Canadian Blood Services’ 11-centre plasma collection model currently in execution), a series of risks to immunoglobulin availability for Canadian patients and system affordability are projected as likely in the short to medium term.

Low plasma sufficiency levels heighten exposure to supply shortages and rising prices

**Sufficiency:** Once the 11 currently planned plasma collection centres are operating at capacity in Canada, it is projected that plasma sufficiency will increase to 22-25%, meaning reliance on international sources for at least 75% of needed plasma. If no measures beyond the status quo are pursued and immunoglobulin utilization continues to grow at the expected rate of 5-7%, Canada will experience declining plasma sufficiency, significant ongoing reliance on the U.S. for commercial product, and vulnerability to immunoglobulin supply shortages and price increases.

**Supply:** Over the last two years, the global pandemic has had several significant and concerning impacts on immunoglobulin supply. Over a period of just a few months in 2020, Canadian Blood Services was advised by multiple suppliers that the full amount of previously agreed volumes of immunoglobulin supply would no longer be available. Although formal supply contracts were in place to secure the supply, *force majeure* negated legal obligations for suppliers. This left Canadian Blood Services with a significant forward immunoglobulin supply gap, with minimal time to fill in an already severe seller’s market.

With plasma volumes down and manufacturing capacity planned years in advance, unused fractionation capacity was high through the pandemic and remains high.

**Price:** Industry experts are predicting that rising immunoglobulin costs will continue post-pandemic and the market for immunoglobulin will remain highly competitive, as product shortages continue through the next several years. Market intelligence has also predicted...
that the price for collecting plasma for immunoglobulin will continue to increase, and these increases are expected throughout the decade (driving sustained price increases for commercial product). Without adequate plasma collection capacity in Canada, and hence domestic sufficiency, the Canadian system will have to bear the increasing costs of purchasing commercial immunoglobulin on the open market.

Competitive domestic plasma market footprint
In a competitive global plasma market environment, commercial for-profit plasma collection companies have begun to establish operations in many jurisdictions. While domestic efforts to increase source plasma collections are continuing, the competition is anticipated to grow in North America and Europe, with commercial plasma collectors opening plasma collection centres in areas that have traditionally been dominated by blood operators collecting plasma from non-remunerated donors. This “crowding out” phenomenon is still evolving, and the full impact will likely be seen in the next five years.

Commercial plasma collection is still a relatively new dynamic for Canada, and uncontrolled expansion of the commercial market in jurisdictions where this is permitted will almost certainly negatively impact both the existing blood collection program and any existing or future plasma collection network. In terms of final product, commercial plasma collectors divert Canadian plasma through vertical integration, for use in immunoglobulin destined to other markets. In the absence of commercial and/or legislative controls and strategic participation in this market, commercial plasma collection will expand, in a way that is unrelated to the needs of Canadian patients and system accountability and affordability.

Vulnerability to supply chain disruptions related to fractionation capacity
The lack of Canadian fractionation capacity for immunoglobulin leaves Canada vulnerable to the implications of significant global shortages and/or supply chain disruptions. For instance, global immunoglobulin shortages could lead national governments or pan-government entities to declare that all or a portion of domestic fractionation capacity must be preserved for domestic purposes, with directions to deprioritize toll manufacturing contracts in favour of domestic fractionation, to ensure finished goods are available for citizens in the country in which the fractionation plant is situated. While globally, fractionators are increasing their capacity, the pandemic and other large-scale disruptive events have demonstrated that threats such as protectionist government actions and plant shutdowns are now higher risk factors.

Current risk landscape, without additional mitigation measures, leaves Canadian health care system in a reactive position
If no additional risk mitigation strategies are employed, the Canadian health care system remains vulnerable to the need to adopt extraordinary measures to address shortages when they occur, either in terms of attempting to secure short-supply, high-cost product or to arbitrarily triage available product across various patient needs, introducing other implications for patient outcomes and cost of care. A proactive approach is critical to ensure immunoglobulin products are available for Canadian patients, at a cost that is sustainable for the health system.
Recommendation 1

- It is recommended that additional risk mitigation measures be undertaken with urgency to secure availability of immunoglobulin for Canadian patients and affordability for the Canadian health system, based on the risk horizon that is projected over the next five years.

- While proactive and immediate measures must be pursued now, it is also recommended that long-term protections be pursued through the legislative and policy environment.

2. What level of plasma collection by Canadian Blood Services or its agents ("plasma sufficiency") is required to ensure immunoglobulin availability for clinically relevant needs?

Appropriateness of immunoglobulin utilization

In provinces that have collected data about immunoglobulin use by indication, the proportion of immunoglobulin utilization considered to be inappropriate or “not indicated” is generally less than 1%. It is assumed that these numbers reflect national use of immunoglobulin.

Utilization management activities, to date, have focused on optimizing utilization. In other words, the focus of the programs has been to ensure that the product is used at the correct doses (or lowest doses that will still give benefit) only in those patients for whom there is evidence that it will be beneficial. With these activities in place, although beneficial to patients and resulting in slight decreases in immunoglobulin usage, it is generally agreed that immunoglobulin use will continue to increase.

Plasma sufficiency

Recent immunoglobulin utilization data and forecasts further elucidate the system planning target for domestic plasma sufficiency. A target of 50% was developed in the 2016 RBDM analysis, with the rationale to protect, through domestic plasma security, that portion of immunoglobulin volume which is directed to the highest priority clinical indications. In Canada (excluding Québec), it is now estimated that 60-65% of immunoglobulin used (by volume) is directed to high-priority conditions. When asked about a shortage scenario, Canadian clinicians estimated that approximately 30% of immunoglobulin (by volume) would be required to meet the most acute needs within those high priority indications.

The higher value (estimated to be 60-65%) would ensure that all patients within the diagnostic categories identified as being high priority have access to immunoglobulin. Supplying the lower value would ensure that in a shortage situation, all patients with a critical, acute need would have access to immunoglobulin but this would require the triaging of patients within a diagnostic category. Within a relatively short period of time, the proportion of immunoglobulin use considered critical would move toward the higher number as patients would be required to delay therapy. Further, it is acknowledged that there are several indications falling outside the 60-65% in which patients gain clear benefit from immunoglobulin and in which morbidity is reduced, along with associated health care costs.
Recommendation 2

- It is recommended that a range of 50-60% be pursued as a target for domestic plasma sufficiency, in order to provide specific protection for the immunoglobulin supply needed for the highest priority indications.

- This target should be revisited over time as the utilization of immunoglobulin products is influenced by such factors as the development of new therapies, changing demographics, and evolving clinical practice.

- A level of 100% plasma sufficiency is not recommended, in order to ensure diversification of plasma supply, balancing risk between Canadian and international supply chains.

3. What risk management option is recommended which achieves the best balance of domestic security of supply, reasonableness of finished product costs, and overall system sustainability for the benefit of Canadian patients?

In moving beyond currently planned plasma collection capacity, option 1 (*increasing Canadian Blood Services’ plasma collection capacity*) offers important benefits and risk reduction, by enhancing domestic security of supply and supporting sustainability of the existing blood and plasma collection network. However, as a stand-alone solution, this option is undermined by challenges in funding, pace of development, and internal capacity limits.

The evaluation of risk management options suggests that it would be prudent to continue to increase Canadian Blood Services’ plasma collection while also pursuing a commercial collaboration to build a vertically integrated domestic supply chain from plasma collection to fractionation (option 4), under the auspices of the national blood operator. This option was found to offer acceleration toward the 50% sufficiency target in a shorter time period, without the need for upfront government investment in infrastructure. Additional market control (via a long-term agreement) would enable Canadian Blood Services to secure Canadian plasma to be manufactured into immunoglobulin for Canadian patients. In addition, a domestic fractionation solution would reduce risks of limited access to supply manufactured in other jurisdictions in the event of major disruptive events and protectionist actions (as seen during the early stages of the pandemic with personal protective equipment and vaccine access challenges).

Option 2 (*purchase of additional plasma*) and/or option 3 (*purchase additional finished immunoglobulin*) do not on their own offer viable solutions but may be prudently deployed when needed as business continuity management tools to supplement the primary strategy, subject to plasma/product availability.

It also remains important to continue to support option 5a (*partner to optimize immunoglobulin utilization practices*), in collaboration with provincial/territorial health systems. This option will always be an adjunct to the primary strategy (and not a solution on its own). It will evolve as new innovations provide alternatives to immunoglobulin in the future.
Plasma and Immunoglobulin Security of Supply:
Risk-Based Decision-Making Analysis

Recommendation 3

- It is recommended that both the not-for-profit and private sectors work together for the mitigation of the plasma and immunoglobulin security of supply risk.

- Continued innovation is required to advance, and resource, Canadian Blood Services’ plasma collection capacity and to extract the highest value from the current and future blood and plasma collection network.

- At the same time, it is recommended that the commercial sector be leveraged through a collaboration to create a vertically integrated domestic supply chain from plasma collection to fractionation (option 4). A long-term transaction between Canadian Blood Services and a commercial entity is recommended to accelerate plasma sufficiency and to ensure that plasma collected in Canada is directed to the manufacture of domestically secured product for Canadian patients. The collaboration should also include key controls to protect the sustainability of the existing not-for-profit integrated blood and plasma collection network in Canada (protections such as non-encroachment and non-competition).

- As the overall risk is complex and the approach to risk mitigation is multi-faceted, it is also recommended that Canadian Blood Services, in concert with provincial and territorial governments, develop a comprehensive communications and stakeholder engagement plan which considers anticipated stakeholder concerns, conflicting perspectives, and reputational risk, as well as opportunities for engagement and support.

4. What mitigation measures are recommended to manage immunoglobulin supply shortages that may arise even if the risk management option selected as part of question 3 is implemented?

The National Plan for Management of Shortages of Immunoglobulin Products (Ig) – Interim Guidance seeks to maximize the effectiveness of a response to a crisis which impacts the adequacy of the overall immunoglobulin supply in Canada, and assumes that all efforts to increase the available supply of immunoglobulin have been exhausted. This interim plan is intended as an acute response to potential supply impacts on the near horizon and to remain in place until a full plan is developed.

Recommendation 4

- It is recommended that Canadian Blood Services continue to work with the National Emergency Blood Management Committee (NEBMC) to address any immunoglobulin shortages and to support the further development and enhancement of the National Plan for Management of Shortages of Immunoglobulin Products (Ig).
5. What monitoring processes are required to understand the scenario risks and to trigger a re-evaluation of this risk assessment? What risk indicators should be monitored in order to track the onset and magnitude of these risks?

Recommendation 5

- It is recommended that Canadian Blood Services continue its regular horizon scans of all key supply and demand factors to ensure that prompt actions can be taken to respond to changing conditions or to mitigate any emerging risks.

- To monitor plasma sufficiency and immunoglobulin security of supply risks, several indicators and triggers should be monitored, including approvals of new indications for immunoglobulin, innovations in alternatives to immunoglobulin, notable shifts in demand, consolidation of commercial entities and other market developments, business disruptions across plasma collection and fractionation industry, supply chain performance, and changes in the legislative and/or policy environment.

7.2 Conclusion

The findings of the 2021–2022 risk-based decision-making exercise regarding plasma sufficiency and immunoglobulin security of supply are consistent with and build on the findings and projections of the 2016–2017 analysis. Risk trends were further escalated by the global pandemic, as domestic resiliency emerged as a fundamental risk mitigation. In the 2021–2022 exercise, the risk horizon related to plasma and immunoglobulin was depicted and analyzed with the engagement and input of relevant stakeholders; the collaboration and expertise of clinicians, industry and market analysts, health economists, operations leaders, specialists in ethics and law; as well as the experience of international blood operators across a varied set of models and approaches. Taking a system perspective, the analysis reviewed risks and solutions from a variety of vantage points (e.g., patient, clinician, donor, operator, funder, regulator, industry). The above recommendations represent the outcomes which emerged to achieve patient safety, system affordability, and sustainability of the integrated blood and plasma collection network in Canada, when viewed through the lens of a complex set of competing risks described in this report.
Plasma and Immunoglobulin
Security of Supply:

Risk-Based Decision-Making Analysis

Appendix 1:
Securing Canada’s Plasma for Immunoglobulin Supply:
What We Heard Report

Prepared by Dialogue Partners
SECURING CANADA’S PLASMA
FOR IMMUNOGLOBIN SUPPLY

WHAT WE HEARD REPORT

For Canadian Blood Services

February 24, 2022
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Abiding by the Code of Ethics of the International Association of Public Participation (IAP2), the Dialogue Partners team has aimed to reflect the themes and summary of participant input from the stakeholder engagement activities in a manner that captures the essence of what was shared. Any errors or omissions made in this summary report are based solely on our interpretation and analysis of that input.

Dialogue Partners Team

WHY THIS, WHY NOW?

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. The organization is regulated by Health Canada and funded primarily by provincial and territorial ministers of health, who are also its corporate members.

Background: A global shortage of immunoglobulins and COVID-19 pandemic dynamics

Use of immunoglobulins has been growing 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 its national supply chain and bulk buying practices — as well as its national emergency planning measures alongside governments and hospitals across the country — so that patients in Canada have not gone without immunoglobulin, although some have been required to switch between product brands and vial sizes.

Risk-Based Decision-Making Framework

As part of Canadian Blood Services’ responsibility to manage plasma sufficiency for immunoglobulin (Ig), the organization is undertaking a comprehensive analysis using the Risk-Based Decision-Making
Framework for Blood Safety, developed by the Alliance of Blood Operators – it can be found on-line 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.

2021-2022 Risk-Based Decision-Making – Canada’s plasma sufficiency for immunoglobulin security of supply

A risk-based decision-making analysis was initiated to focus 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 risk-based decision-making analysis requires, and is informed by, a robust stakeholder engagement process. Within this context, Canadian Blood Services contracted Dialogue Partners to conduct stakeholder engagement activities on the issue of securing Canada’s plasma sufficiency for immunoglobulin (Ig). Engagement activities provided stakeholders with opportunities to share their views on risk mitigation pertaining to securing a more robust domestic supply of Ig. In a continued effort to reduce the spread of COVID-19, Canadian Blood Services hosted virtual engagement opportunities, providing a virtual engagement platform to provide input in both written submissions and virtual dialogue formats.

The engagement process was designed to better understand the perspectives of patients living with primary and secondary immunodeficiency disorders, autoimmune disorders, neurological and other disorders for which immunoglobulins are a vital part of treatment. Canadian Blood Services sought to understand the level of concern patients and their treaters have and understand their priorities in securing supply. This patient community bears the greatest burden of risk brought about by any supply challenge.

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.
This report summarizes participant input shared through written submissions received and notes taken at the virtual engagement sessions hosted on January 19th and 20th, 2022 and represents Dialogue Partners’ professional summary of what was heard. Comments on this report can be directed to info@dialoguepartners.ca.

**HOW WE ENGAGED AND WHAT WE ASKED**

Stakeholder participation is crucial to ensuring various perspectives are heard and contribute to informing the overall analysis and decision-making in this process.

Seventy-nine invitations to participate in virtual engagement sessions were extended (a list of which is provided in Appendix A). To support designing and planning the dialogue sessions, Dialogue Partners invited stakeholders to provide their thoughts on the topics to be discussed as part of the ensuing sessions. Twelve written submissions were received and themes arising from these written submissions supported the introduction of views from many stakeholder perspectives. Of those stakeholders invited to participate, a total of 24 attended virtual engagement sessions hosted on January 19th (17 participants) and January 20th (7 participants). A list of engagement participants who attended the virtual engagement sessions can be found in Appendix B.

Participants joined the sessions via Zoom. A facilitator from Dialogue Partners guided the sessions while Canadian Blood Services’ senior leaders walked participants through background on the status of plasma collection globally and domestically, the impacts of COVID-19 on Ig sufficiency, and the need to expand plasma collection to secure immunoglobulin (Ig) sufficiency. They also introduced the Risk-Based Decision-Making framework and steps in the process to define, assess and propose recommendations on how to mitigate risks related to plasma sufficiency and security of Ig supply.

Following these presentations, participants were engaged in facilitated discussion on the following questions:

1. In a post-pandemic world, what value do you place on domestic security of supply of immunoglobulin?
2. How does security of domestic supply of immunoglobulin directly impact the patient population you represent?
3. What should be considered when determining an “adequate supply of immunoglobulin”?
   a. From your patient population’s perspective?
   b. From a system-wide perspective?
4. What should be considered when determining “sustainability”?  
   a. From your patient population’s perspective?
   b. From a system-wide perspective?
5. What considerations should be kept in mind as these ideas are pursued on their own or in combination?
On January 19th, stakeholder dialogue occurred in small break-out groups to provide all participants the opportunity to express their thoughts. Dialogue Partners facilitators guided the break-out conversations and a dedicated notetaker captured participant input. Representatives from provincial and territorial governments attended as observers. Representatives from Canadian Blood Services also attended to present the issues and answer questions.

On January 20th, due to a smaller number of participants, the discussion was held in plenary format. Again, participants were supported by a Dialogue Partners facilitator and a dedicated notetaker. Representatives from provincial and territorial government and Canadian Blood Services also attended this discussion.

Both sessions’ plenary formats were recorded to assist with preparing this report.

Participants were encouraged to utilize the Zoom chat function to share ideas, opinions, and thoughts throughout both sessions.

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**WHAT WE HEARD**

The views outlined in the section below represent those from patient groups, advocacy groups, and clinicians who prescribe Ig products and support patients across Canada. Participants shared their thoughts through written submission and virtual engagement opportunities helping to address key questions related to Ig sufficiency and the need to expand plasma collection to secure Ig.

A diversity of participant views and thoughts were shared around key questions, almost all participants placed a high value on domestic security of supply. Through discussion, key patient-perspective insights emerged around adequate supply and the importance of guaranteed supply and access to preferred products. Guaranteed access to preferred products was considered essential, as disruptions often impact patients’ standards of care and overall wellbeing. When considering a systems perspective, participants brought forward key considerations around understanding need and demand, how to better forecast demand of Ig products by tracking and assessing Ig utilization factors, and building partnerships and coordinating policy approaches to achieve greater security of the product. Other key themes included sustainability costs, donor incentives, and plasma collection and production methods. While there was a recognized need to increase efforts to grow and develop a pool of plasma donors to support efforts to increase supply, opinions diverged when considering the potential role commercial collection plays in achieving this overall increase. Despite differences in some approaches, there was seen to be value in creating opportunities for greater collaboration between system partners and driving security through new and innovative solutions.

Input gathered will be used by Canadian Blood Services to inform its analysis of the key risks discussed and continue to inform and influence ongoing deliberations and policy discussions with governments on domestic security of immunoglobulin supply to meet patient needs in Canada.
Q1: In a post-pandemic world, what value do you place on domestic security of supply of immunoglobulin?

Participants placed a high value on domestic security of supply of immunoglobulin (Ig). As per participant written submissions and views shared during the dialogue sessions, there was consensus that Canada must adopt strategies quickly to ensure greater security of the domestic supply of Ig through increased plasma collection. Participants shared views that security of supply was an ongoing concern prior to the pandemic, with some noting they have been working with Canadian Blood Services on domestic security of Ig issues for many years. Participants shared their thoughts on current and future barriers, challenges, and considerations that will impact domestic security of supply.

**Key Themes**

**Patient Care**
Participants shared that insecure supply of Ig directly impacts patients who require the treatment. Supply shortages can result in patients and their clinicians needing to switch Ig products and treatment plans, which could potentially impact their health condition and quality of care. Clinicians and patients who participated in the conversation shared that supply shortages may have high social, emotional, physical and mental health impacts on patients who rely on Ig.

**Demand, Supply and Production**
One participant suggested that the pandemic has caused delayed diagnoses of new patients, and that once health systems begin to recover, these patients may be diagnosed, leading to increasing demand for—and therefore a more restricted supply of—Ig.

Supply was seen to be deeply connected not only to the collection of plasma, but also to the production cycle of plasma-based products such as Ig. Some participants noted that a lack of domestic fractionators in Canada limits the country’s ability to manufacture Ig products.

**Affordability**
Participants viewed the notion of affordability from a personal lens and shared that patient access to second-line or long-term therapies can be hindered due to cost barriers stemming from limited insurance and formulary coverage. This, in turn, can induce a heavier reliance on first-line therapies like Ig, which are more easily prescribed and accessible across all health systems.

**Sector Innovation and Funding**
Other suggestions offered by participants included monitoring potential opportunities for innovative therapies in the sector that could reduce dependence on Ig. While innovations are welcomed by participants, there was recognition that the sector is years away from realizing the benefits of novel therapies. Participants shared insights on how current resource allocation strategies may deter innovations that could reduce future reliance on Ig products, citing the need for a review of current practices to create more efficient investments.
Tensions
There was recognition that Ig products currently available to patients are safe. One participant expressed concerns regarding the safety of plasma collected through commercialized remunerated models, particularly those located outside of Canada. However, the majority of participants, in particular those representing patients receiving Ig and other plasma product treatments, offered counterpoints on this point and noted there being no difference in the level of safety if the product is collected through not-for-profit or commercialized models. Patient organizations also provided that they have not experienced any safety concerns of manufactured plasma products for many years.

Q2: How does security of domestic supply of immunoglobulin directly impact the patient population you represent?

Participants had a range of direct and indirect connections to the supply and use of Ig in Canada. Patient groups, advocacy groups, and clinicians who prescribe Ig products and support patients were represented. Some participants noted that, while they do not directly serve patients that rely on immunoglobulin therapies themselves, the domestic collection of plasma helps secure other plasma-derived products of interest to them. Some also noted that broadening plasma product fractionation to include other plasma-derived products could potentially lower or leverage Ig production costs overall.

Key Themes
Participants noted the following implications for patients when faced with product insecurity. These included:

- Product availability anxiety and increased stress leading to impacts on mental health
- Anxiety and stress can also negatively impact a patient’s condition
- Inconvenient infusion mechanisms
- Adverse side effects when required to repeatedly change Ig products
- Reduced quality of life, work attendance, family support, social interaction and potentially death

In addition to the above implications, Ig prescribers (i.e., clinicians) shared that insecurity of products can negatively impact the ability of prescribers and clinical staff to provide appropriate care to their patients.

Overall, there was repeated recognition that Ig shortages and insecurity of supply pose significant emotional, physical, and mental health impacts for those who rely on Ig products, especially those without alternative treatment pathways.

Tensions
No tensions were noted.

Q3: What should be considered when determining “adequate supply of immunoglobulin”?

Anything is possible with a little dialogue.
A. From your patient population’s perspective?
B. From a system-wide perspective?

Key Themes - Patient Perspective

Guaranteed Supply
There was agreement that patients should have access to a guaranteed supply of Ig products. Access to prescribed treatments was consistently discussed as a fundamental consideration around envisioning an adequate supply.

Preferred Product and Accessibility
While access to Ig products that meet the needs of patients was critically important, participants viewed patient access to their preferred product as equally important. This means ensuring that patients and their providers have access to Ig products in the size and modality that matches patient treatment plans, as well adequate access to a variety of product brands, as some patients may potentially respond well to some brands and not others.

Overall, participants shared that adequate supply not only means patients and providers have access to Ig products they need, but that they have access to the preferred products that support optimal treatment outcomes.

Key Themes - Systems Perspective

Defining Need and Demand
Participants expressed in determining what adequate supply looks like, the sector needs to better understand what Ig usage, patient need, and demand look like across Canada.

In written submissions, “need” and “demand” were cited as unique in their own definition, with “need” being more aligned to patient’s treatment requirements, as determined by a clinician. Where “demand” was aligned with how the supply is managed and monitored across health systems. Participants noted the importance of prioritizing supply according to patient need rather than market demands.

Collection and Production
Throughout stakeholder engagement activities, participants acknowledged that there is growing demand for Ig nationally and globally. There was recognition that it is important to ensure Canada remains competitive in securing an adequate supply of Ig. Participants’ comments indicated a need not only to bolster efforts around the collection of plasma, but to consider how the sector can increase its ability to manufacture Ig products domestically.

Ig Utilization Factors
Participants called on health systems to pursue opportunities to improve demand forecasting for Ig products to more accurately predict and plan for adequate supply. Participants noted that this will require the sector to better assess, track and monitor need, demand, and supply, which may require more coordinated approaches to collecting data on drivers of Ig usage locally and nationally – across
all health systems. Those who submitted written feedback indicated that to achieve this, it would be important to:

- Establish mechanisms to identify, monitor and measure real-time trends in usage
- Evaluate and understand if, how, and to what degree misuse and lack of adherence to standards drives demand and supply issues for Ig products
- Evaluate the usage needed in contingency conditions to sustain patient needs in the event of a shortage.

**Managing Shortages and Establishing a Management Framework**

Written submissions noted that it may be helpful to establish a framework to support standardized management and usage of Ig, particularly one that prioritizes patients whose health is dependent on Ig-based therapies. Other feedback called for protocols for managing supply shortages while building the needed infrastructure to enhance capacity. This was also viewed as an opportunity to reduce supply risks associated with over-reliance on global supplies.

**Building Partnerships and Coordinated Policy Approaches**

Participants highlighted the need for more coordinated policy approaches to achieve greater security of plasma supply and the current system managed by Canadian Blood Services. Provincial and territorial governments recognized a "lack of policy overseeing the engagement with commercial plasma collectors", and that future national policy should "address the existing, and future, commercial plasma collection sector" in Canada. Alternatively, those against the use of commercial collectors shared that increasing capacity through not-for-profit collection would be needed to address current gaps.

**Healthcare Funding**

Clinician participants noted that Ig usage can sometimes be driven by formulary funding, siloed healthcare funding, and costs and reimbursement strategies. Limiting funding of alternative therapies was also seen to stifle innovation. Other participants noted that health system partners in general must find a better way to coordinate and collaborate on issues like siloed funding to reduce the barriers faced by patients and clinicians in finding optimal treatments and therapies.

**Donors**

Participants noted that donor input is an essential consideration when determining how to increase plasma collection in Canada to ensure an adequate supply of Ig. Participants raised the need to gather and understand donor views on increasing plasma collection, remunerated vs non-remunerated collection models, and commercially operated vs health funded national blood system operated. There was also interest in better understanding donor reaction on ethics and health considerations of plasma donors to support an adequate supply of plasma to ensure Ig security.

**Tensions**

Sustainability concepts pivoted on how stakeholders defined Ig “need” and “demand.” Some stakeholders noted that patient needs must always be prioritized over market demand. It is unclear if there is a collective sense of agreement regarding how competing needs are or should be prioritized in relation to the use of Ig products.
Additionally, while all participants agree that securing an adequate supply of Ig is important, differences of opinion remained regarding how this should be achieved. A couple of participants maintained strong opposition to using commercialized collection models to secure an adequate supply of Ig, however current Ig product users, other patient group representatives and some clinicians expressed support for utilizing both commercial and not-for-profit collection models to increase supply.

Some participants indicated that to achieve adequate supply, there is a need to enhance sector capacity through commercial and voluntary collection models, as well as global supplies.

Q4: What should be considered when determining “sustainability”?

A. From your patient population’s perspective?
B. From a system-wide perspective?

Key Themes – Patient Perspective
When discussing what should be considered when determining sustainability, participants again noted the importance of patients having access to Ig products when they are needed and ensuring that supply keeps pace with the projected growth of need. Participants also shared that the following factors should be considered when framing sustainability from a patient perspective:

- Patients must have continued undisturbed access to treatment and therapy as prescribed
- Innovative therapies are monitored and invested in to support future needs
- A greater diversity of Ig suppliers should be engaged and supported by longer contracts with sufficient flexibility to be able to change to newer/innovative therapies as they become available
- Patients value a sustainable and secure supply of Ig, whether it be achieved through not-for-profit, commercialized, or public/private partnership collection models.

Confidence in the safety of the product provided to patients was also seen as critical.

Key Themes – Systems Perspective
Supply, Demand and Costs
Participants expressed the view that patient need, and product demand should be better understood. This includes better understanding what products are being used and are requested by patients and clinicians and how patients respond to varying treatments and therapies. In addition to understanding need and demand, participants noted that plasma collection efforts should be cost-effective, which will require health systems to look at affordable collection models that achieve the best value.

Donor Incentives
While donation incentivization was not framed as a core discussion issue (specifically related to the Risk-Based Decision-Making process), many participants noted that, for them, it plays a key role in determining future sustainability. In general, participants expressed a desire to further explore if and
what role donor incentivization could play in increasing plasma donations. Participants raised various perspectives on this topic, noting that stakeholders sought further discussion on this topic.

**Plasma Collection and Product Development Factors**

Participants noted that collection of plasma and production of finished Ig products are deeply connected. Given this, there was discussion around the need for taking steps towards vertical integration between collection and production. If sustainability of supply is to be achieved, increasing collection efforts, such as the development of supporting collection infrastructure, should be coupled with increasing the development of domestic fractionization capacity within Canada.

Participants also expressed a need to increase efforts to grow and develop a pool of plasma donors, which includes increasing citizen education, donor awareness and engagement, and outreach to promote the purpose of plasma in treating patients and value of donating plasma. There was collective recognition that this would require significant public investment. Provincial and territorial governments, as stewards of public dollars, indicated that collection models must be cost-effective and sustainable.

**Integrity of Collection Practices and Processes**

Participant submissions noted that it is important to uphold and secure “the integrity of our system.” For some, this means ensuring that Canadian Blood Services and health systems are not collecting plasma from vulnerable groups (e.g., those who are impoverished). For others, it means protecting the donor base of not-for-profit collection systems from commercial remunerated collection models that were seen to commodify plasma and jeopardize the sustainability of supply in Canada.

**Need for Greater Collaboration**

Throughout the discussions, participants stated that current approaches to managing Ig issues are disjointed. Participants pointed to the need for greater coordination and collaboration between federal, provincial, and territorial governments, health authorities, non-for-profits (e.g., Canadian Blood Services), patients, and clinicians to fully understand current dynamics surrounding insecurity of supply while planning future sustainability.

**Other**

Some participants noted that Canadian Blood Services can play an advocacy role to communicate patient and hospital needs. A consideration expressed by a participant was the concept of revisiting formulary reimbursement for products and investment in the patient care side of Ig usage and management – this related back to discussion among patient organizations on the need for a comprehensive care model.

Participants reiterated the need for health systems to remain open to innovation (e.g., develop innovative technology in manufacturing of plasma protein products or in using alternative non-plasma-dependent processes).

Lastly, patient advocate participants emphasized the significant role comprehensive care plays in developing the sustainability of Ig supply. Comprehensive care benefits both patients and systems by decreasing product waste, improving service and system-level budgetary efficiency, and enhancing the quality of care provided to Ig patients. Noting that all costs associated (a comprehensive view) with assessing, delivering, and administering products to patients must be considered.
Tensions
As in other sections, there is a clear divide in how respondents envision the potential role of commercial collection. Some submissions indicated that commercial collection models where donors are paid creates instability for not-for-profit collection models. Others indicated that sustainability and affordability go together. Overall, participants acknowledged that to develop a more secure and sustainable supply of Ig, the models in which the sector procures these limited products must be cost-effective and deliver value overall. For some, this means leveraging both commercial and not-for-profit collection models, while others oppose the utilization of commercial collection models and pushed to increase and expand capacity within the public system.

Within written feedback, some participants expressed support for greater use of utilization management approaches to conserve plasma-derived supplies and products. However, during virtual engagement sessions, those closest to current utilization management approaches pointed to there being is no evidence to suggest that Ig is being misused. Resulting in diverging opinions among participants on how much value any additional utilization management approaches could have in conserving and managing Ig within the sector.

Q5: What considerations should be kept in mind as these ideas are pursued on their own or in combination?

Key Themes
Increase Plasma Collection and Purchase More Ig
Participants agree that increasing plasma collection is critical to securing a greater domestic supply of Ig in Canada. Themes resulting from group discussions included:

- Both the commercial and not-for-profit sectors must establish a steady base of plasma donors to build an adequate supply of Ig. It will be important that Canadian Blood Services continues to engage and educate the public on the growing need for plasma donations in Canada, as well as creating hassle-free and accessible plasma collection experiences.
- Several participants acknowledged that not-for-profit collection models have not yet been able to meet their collection/supply targets independently. Noting that establishing a sustainable supply may require looking at use of a mix of not-for-profit, commercial, and public/private partnerships to expand domestic collection capacity.
- Several participants also pointed to the need to explore donor incentives to quickly securing and sustaining an expanded plasma donor base. Participants proposed exploring alternative donor incentive solutions such as: charitable tax receipts, tax credits, etc.

Optimizing Use and Utilization Practices
In written submissions, participants noted concerns around Ig being overused in Canada. In the virtual sessions, clinicians noted that there is not much evidence of inappropriate use and perceived efforts to restrict clinicians’ ability to prescribe Ig were not productive and created tensions. Additionally,
some noted that the screening requirements were onerous and limited clinicians’ time spent on patient care.

Some participants indicated support for using evidence-based utilization approaches to better manage the supply and demand for Ig in Canada. Provincial and territorial governments indicated a commitment to pursuing optimized, evidence-based utilization as a management strategy to address potential scarcity in supply and growing demands. In virtual sessions, some participants indicated that additional practices, increased monitoring, or management efforts around optimizing use and utilization of Ig would not likely yield significant reduction in overall usage.

Data Collection to Plan Supply
Participants explored the establishment of a systems-level approach to tracking, monitoring and reporting the use of Ig to inform planning around adequate supply. Participants noted that a broader priority for better data collection and analysis could help understand drivers of usage while streamlining communication actions to address Ig needs between system and service level actors. Some participants pointed to the need for greater transparency in reporting product usage and inventory data.

Donor Compensation/Incentives
While some participants expressed opposition to use of commercialized renumerated collection models, other participants supported it. As in other discussion questions, participants noted the need to find ways to encourage individuals to donate plasma, which includes understanding if and how different compensation methods can help increase plasma collection efforts. One written submission noted that Canadian Blood Services could consider pursuing non-cash compensation models to incentivize donations, which may address the concerns of those who object to direct cash remuneration. These included:

- Credits to offset the cost of post-secondary education for students who donate plasma
- Non-refundable tax credits for people who donate plasma
- “Points” to augment pensions through the Canada Pension Plan who donate plasma

Some participants who identified as Ig patients, patient advocates, and clinicians expressed their support for donors to be compensated. Some acknowledged that legislation would need to be amended if donor compensation practices were considered desirable.

Plasma Safety
In written submissions, several participants pointed to the need to ensure the ongoing safety and quality of plasma-derived products. Those opposed to procuring plasma from commercial suppliers shared concerns related to the robustness of screening measures and processes to control infection risks among these operators. Patient organizations representing long-standing users of plasma products shared a different view about the safety of plasma products provided to Canadian patients, explaining that there have not been concerns related to the safety of these plasma products among patients for many years.

Sustainability Through Innovation
Several written submission responses indicated that “research initiatives to develop modern technology for the manufacture of plasma proteins by alternative, non-plasma-dependent processes,
such as recombinant technology” would also support efforts to achieve longer-term plasma sustainability in Canada.

**Tensions**

As indicated in previous sections describing diverging views opinions among participants, or tensions, there were mixed views on how to achieve an adequate and sustainable supply of immunoglobin in Canada.

Prior to group discussions, facilitators shared key insights from written submissions. One key theme that emerged was the perceived need for greater monitoring, assessment, and management of Ig products within Canada. This included the potential need to establish mechanisms to better track and measure real-time trends in usage, as well as to better evaluate if, how, and to what degree misuse or over-prescription of Ig drives demand and supply issues. During group discussions, participants noted that there is significant misinformation regarding the misuse of Ig in Canada and that discussions on optimizing use have limited benefit, given that minimal misuse is occurring. Participants called for sharing more detailed information and data on usage.

As noted in previous sections, there continue to be diverging perspectives about the use of donor incentives and commercial suppliers in the collection of plasma in Canada. Some participants were opposed to providing incentives/compensation to donors. Reasons shared by these participants included concerns that incentive-based models pose risks for vulnerable populations who may donate too frequently for their health, for financial incentives. Additionally, these participants felt strongly against using commercial collection models to secure Ig, citing concerns around product safety and the belief that not-for-profit models could meet supply targets with government funding. Other participants saw greater balance being achieved through a mixed approach model that utilizes both commercial and not-for-profit collection models while still maintaining a connection to the global Ig supply chain. Those in support of a mixed approach believe this approach is more likely to be able to meet supply targets, in a timely manner, and that it will be more cost-effective.

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**WHAT’S NEXT**

Canadian Blood Services has informed Dialogue Partners that stakeholder input gathered will inform its analysis of the key risks discussed.

We have also been advised that stakeholder input will continue to inform and influence ongoing deliberations and policy discussions with governments on domestic security of immunoglobin supply to meet patient needs in Canada. Canadian Blood Services will be reporting to stakeholders on these developments, and how they are shaped by the input provided through this engagement process.
APPENDIX A – INVITATION LIST

<table>
<thead>
<tr>
<th>Organization / Affiliation</th>
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<tbody>
<tr>
<td>Alpha-1 Canada</td>
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<tr>
<td>Answering TTP Foundation</td>
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<tr>
<td>Aplastic Anemia and Myelodysplasia Association of Canada (AAMAC)</td>
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<td>Association of Hemophilia Clinic Directors of Canada (AHCDC)</td>
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<td>Atypical Hemolytic Uremic Syndrome (aHUS)</td>
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<td>BloodWatch</td>
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<td>Canadian Apheresis Group</td>
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<td>Canadian Association of Nurses in Hemophilia Care (CANHC)</td>
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<td>Canadian Fanconi Anemia Research Fund</td>
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<td>Canadian MPN Network (Myeloproliferative neoplasms)</td>
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<td>Canadian Neurological Society (CNS)</td>
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<td>Canadian Organization for Rare Disorders (CORD)</td>
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<td>Canadian Rheumatology Association</td>
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<td>Canadian Society of Allergy and Clinical Immunology (CSACI)</td>
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<td>Canadian Society of Transfusion Medicine</td>
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<td>Friends of Medicare</td>
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<td>GBS/CIDP/MMN Foundation of Canada</td>
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<td>Immunodeficiency (IG) Working Group</td>
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<td>Myasthenia Gravis Society of Canada</td>
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<td>Myeloma Canada</td>
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<tr>
<td>Network of Rare Blood Disorders Organization (NRBDO)</td>
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<td>Platelet Disorder Support Association (immune thrombocytopenia)</td>
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<tr>
<td>Provincial and Territorial Ministry Representatives &amp; Observers</td>
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<td>British Columbia</td>
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<td>Saskatchewan</td>
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<tr>
<th>National Advisory Committee on Blood and Blood Products</th>
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<tbody>
<tr>
<td>Dr. Alan Tinmouth</td>
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<tr>
<td>Dr. Andrew Shih</td>
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<td>Dr. Charles Musuka</td>
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<tr>
<td>Dr. Jason Quinna</td>
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<tr>
<td>Dr. Jennifer Fesser</td>
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<tr>
<td>Dr. Katerina Pavenski</td>
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<td>Dr. Lakshmi Rajappanair</td>
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<td>Dr. Lucinda Whitman</td>
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<tr>
<td>Dr. Oksana Prokopchuk-Gau</td>
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<td>Dr. Robert Coupland</td>
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<td>Dr. Robert Liwski</td>
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<td>Dr. Ryan Lett</td>
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<tr>
<td>Dr. Shabani-Rad Meer-Taher</td>
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<tr>
<td>Dr. Susan Nahirniak</td>
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<td>Dr. Vincent Laroche</td>
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# APPENDIX B – LIST OF ENGAGEMENT PARTICIPANTS

## January 19, 2022, Session

<table>
<thead>
<tr>
<th>Participant Name</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Angela Diano</td>
<td>Alpha-1 Canada</td>
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<tr>
<td>Kat Lanteigne</td>
<td>Blood Watch</td>
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<tr>
<td>Dr. Gail Rock</td>
<td>Canadian Apheresis Group</td>
</tr>
<tr>
<td>Dr. Michele Bril-Edwards</td>
<td>Canadian Health Coalition - Board Member</td>
</tr>
<tr>
<td>Pauline Worsfold</td>
<td>Canadian Health Coalition - Chair of Board</td>
</tr>
<tr>
<td>David Page</td>
<td>Canadian Hemophilia Society (CHS)</td>
</tr>
<tr>
<td>Whitney Goulstone</td>
<td>Canadian Immunodeficiencies Patient Organization (CIPO)</td>
</tr>
<tr>
<td>Dr. Bruce Ritchie</td>
<td>Canadian Immunodeficiency Patient Organization Medical Science Advisory Committee</td>
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<tr>
<td>Dr. Steven Peters</td>
<td>Canadian Neurological Society (CNS)</td>
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<tr>
<td>Dr. Durhane Wong-Rieger</td>
<td>Canadian Organization for Rare Disorders (CORD)</td>
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<tr>
<td>Dr. Ophir Vinik</td>
<td>Canadian Rheumatology Association (CRA)</td>
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<tr>
<td>Chris Gallaway</td>
<td>Friends of Medicare</td>
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<tr>
<td>Steven Staples</td>
<td>Canadian Heath Coalition</td>
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<tr>
<td>Dr. Katerina Pavenski</td>
<td>National Advisory Committee on Blood Products</td>
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<td>Dr. Charles Musuka</td>
<td>National Advisory Committee on Blood Products</td>
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<tr>
<td>Dr. Alan Tinmouth</td>
<td>National Advisory Committee on Blood Products</td>
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<tr>
<td>Dr. Oksana Prokopchuk-Gauk</td>
<td>National Advisory Committee on Blood Products</td>
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## January 20, 2022, Session

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<tr>
<th>Participant Name</th>
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<tr>
<td>Dr. Hans Katzberg</td>
<td>GBS/CIDP/MMN Foundation of Canada Medical Advisor</td>
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<tr>
<td>Caroline Herzberg</td>
<td>Canadian Dermatology Association</td>
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<tr>
<td>Donna Hartlen</td>
<td>GBS/CIDP/MMN Foundation of Canada</td>
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<tr>
<td>Dr. Vera Bril</td>
<td>Immunodeficiency (IG) Working Group</td>
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<tr>
<td>Dr. Susan Nahirniak</td>
<td>National Advisory Committee for Blood and Blood Products</td>
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<tr>
<td>Jennifer van Gennip</td>
<td>Network of Rare Blood Disorders Organization (NRBDO)</td>
</tr>
<tr>
<td>Jennifer DiRaimo</td>
<td>Platelet Disorder Support Association (immune thrombocytopenia)</td>
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References

1 One participant shared a link to a report on plasma collection during one of the dialogues. The resource was not discussed further and the link is included in this report as part of the engagement record. Dialogue Partners cannot comment on the report’s accuracy. https://www.europeanbloodalliance.eu/wp-content/uploads/2013/04/eba_online.pdf