Transfusion-Transmitted Malaria

Risk-Based Decision-Making Analysis

May 2024

Canadian Blood Services

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Executive summary

Malaria is a bloodborne illness caused by parasites that are transmitted mainly through the bite of infected mosquitoes. It can also be transmitted through blood during transfusion and through organ and stem cell transplantation. While malaria may cause only mild illness in some people, it can cause severe illness and even death in others.

In 2022, there were about 249 million cases of malaria in 85 countries and areas where malaria regularly occurs — an increase of five million cases compared with 2021. Worldwide, the malaria case incidence rate[1] was 58 per 1,000 people at risk, and about 608,000 people died of the disease.

As part of Canadian Blood Services' continuous improvement efforts, we started a process in the fall of 2022 to review how we are currently managing the risk of malaria in the blood supply. Continuously assessing our processes to ensure a safe supply of blood and blood products while adapting to developments in our environment and infectious diseases is key to everything we do.

Following our decision to conduct this review, a probable case of transfusion-transmitted malaria was reported in Canada in 2022 for the first time since 1997. While the risk of transfusion-transmitted malaria in Canada remains very low at about one in 9.4 million units of red blood cells transfused, this probable case confirmed the time was right to take a closer look.

Climate change is also expected to increase the spread of malaria and the number of people who get it. Higher temperatures, humidity and rain have already meant more mosquitoes that transmit the disease in various parts of the world. For example, several locally acquired cases of malaria were recorded in the U.S. in 2023 for the first time since the public health eradication of malaria in the 1950s. At the same time, technologies have emerged that can help us mitigate the risk of malaria in the blood supply. Pathogen inactivation technology, which inactivates malaria and other parasites, is being implemented at Canadian Blood Services for platelets and plasma. Specific technologies have been developed that can test for the presence of malaria antibodies and malaria parasites in donated blood. However, the availability of these tests (and lack of experience with them) poses some challenges for implementation in Canada.

As we consider our context and opportunities for change, we recognize the decisions we make to mitigate the risk of transfusion-transmitted malaria may affect people differently: people who rely on blood products to treat their health conditions, particularly those who need regular blood

[1] The malaria case incidence rate is the number of new cases of malaria as a proportion of the number of people at risk of getting malaria.

transfusions, such as people with sickle cell disease with rare blood groups; and potential donors, particularly Black, African, Caribbean and South Asian donors.

Safely managing the risk of transfusion-transmitted malaria is complex, and it is important that we continue to follow the science and listen and learn from all perspectives as we strive to meet the needs of patients while being as minimally restrictive as possible.

Approach

We used the Alliance of Blood Operators' *Risk-Based Decision-Making Framework for Blood Safety* (Alliance of Blood Operators, 2015) to conduct this analysis. This structured decision-making approach recognizes that it is impossible to eliminate all risk. It balances risks against benefits, acknowledging that some trade-offs will need to be made.

Five decision drivers helped guide our evaluation of a series of risk management options and our decision-making. Two of the decision drivers — maintaining the safety of the blood supply and striving to increase the availability of phenotype-matched blood — provided the central focus of the evaluation and recommendations, with safety of the blood supply being the main driver. Taken together, these decision drivers help us achieve our vision: to help every patient, match every need, and serve every Canadian.

We conducted four assessments to give us the most current and reliable information possible to evaluate the risk management options:

- **Blood safety review:** We reviewed the risk of transfusion-transmitted malaria to the blood supply in Canada. We considered the current prevalence of malaria around the world, the impacts of anti-malarial drugs and vaccines, changing environmental conditions, and the impacts of donor eligibility criteria for patients and donors, particularly Black donors.
- **Contextual assessment:** We looked at the current legal and regulatory context for the risk management options. We considered Canadian Blood Services' responsibility for safety, and the requirements associated with updating the donor eligibility criteria and implementing new testing technologies.
- **Ethical analysis:** We reviewed the implications of key ethical values and principles. We recognized the different perspectives, including those of stakeholders, on the relative importance of some values and principles over others.
- **Operational review:** We looked at what would be involved in implementing the risk management options. We assessed the feasibility of each option and the requirements for new processes both within and outside of the organization.

The key findings from these assessments informed our recommended actions.

Recommendations

Based on the information gathered throughout the risk-based decision-making process, we made the following recommendations:

- Recommendation 1: Implement nucleic acid testing for malaria in a subset of donors and change the related eligibility criteria for all donors except those donating source plasma.
- Recommendation 2: Maintain the current donor eligibility criteria related to malaria.
- Recommendation 3: Develop stakeholder communication and education plans.
- Recommendation 4: Continue surveillance and monitoring.
- Recommendation 5: Consider other changes to the donor eligibility criteria if Recommendation 1 cannot be implemented in a timely way due to external barriers. Consider:
    a. Updating the donor eligibility criteria related to malaria for people donating apheresis plasma and platelets to align with the current eligibility criteria for donating source plasma when pathogen inactivation technology is fully implemented for platelets and plasma for transfusion.
    b. Updating the donor eligibility criteria related to malaria for people donating whole blood when pathogen inactivation technology is fully implemented for platelets and plasma for transfusion.

While several of the risk management options we evaluated had benefits, introducing malaria nucleic acid testing is the best option to mitigate the risk of transfusion-transmitted malaria. Adopting this recommended approach would address all five decision drivers, and as we have learned from affected communities, would represent a meaningful change for the blood system in Canada.

The introduction of malaria nucleic acid testing and the other recommended approaches to mitigating the risk of transfusion-transmitted malaria are recommendations only; Canadian Blood Services may not implement them all. These recommendations provide a clear path forward; we will draw on the results of this analysis and continue to engage with and learn from stakeholders as we work to get there.

1. Malaria and blood transfusion in Canada

Malaria is a bloodborne illness caused by parasites that are transmitted mainly through the bite of infected mosquitoes. It can also be transmitted through blood during transfusion and through organ and stem cell transplantation.

The parasites that cause malaria can remain in a person's body for decades without causing illness. Just one malaria parasite in donated blood can lead to malaria being transmitted to a blood recipient. While malaria may cause only mild illness in some people, it can cause severe illness and even death in others if unrecognized and untreated.

Data from the United States Centers for Disease Control shows that malaria is mainly found in sub-Saharan Africa, South Asia, Central and South America, and Oceana. All recent cases of transfusion-transmitted malaria in North America have been linked to people who lived in or travelled to areas where malaria is endemic — areas where malaria regularly occurs. These cases of transfusion-transmitted malaria are associated mainly with donors who are semi-immune, likely from previous infections. Semi-immune donors are less likely to have symptoms of malaria because they have anti-malaria antibodies suppressing the malaria parasites in their body. Since they may not have symptoms, they may not know they have malaria parasites when they are being assessed for their eligibility to donate blood. There is no Canadian data on people who are semi-immune to malaria.

Canada's blood supply is recognized as one of the safest in the world. Between 1994 and 1997, Canada had three confirmed cases of transfusion-transmitted malaria. As a result, in 1997 Health Canada approved a proposal by the Canadian Red Cross Society (Canada's former blood operator) to change the three-year waiting period for people with a history of malaria to an indefinite ineligibility. In 2022, there was one reported probable case of transfusion-transmitted malaria. Based on these case reports, the risk of transfusion-transmitted malaria in Canada is about one in 9.4 million units of red blood cells transfused.

The risk of transfusion-transmitted malaria is expected to change, especially as climate change affects how malaria is spread and how many people get it. The development and adoption of vaccines, targeted for roll-out to children, is also expected to have a positive impact on global cases of malaria. People migrating from malaria-endemic areas may still carry malaria. Immigration from malaria-endemic areas is expected to increase, which could increase the number of people exposed to malaria within a given population. The impacts of these shifts must be continuously monitored to help us understand the evolution of malaria infections and its impact on blood safety in Canada.

1.1 Current eligibility criteria related to malaria

Today, people who know they have had malaria are ineligible to donate whole blood, platelets or plasma for transfusion. People who have had malaria and recovered more than six months ago may be eligible to donate source plasma if they meet all other donor eligibility criteria. Source plasma is used to make lifesaving medications, such as immunoglobin therapies, and undergoes a pathogen inactivation process before being used for patient care.

Those who have lived in a malaria-endemic area are ineligible to donate for three years. Short-term travellers who visit malaria-endemic areas may not be eligible to donate whole blood, platelets or plasma for transfusion for a certain amount of time. Whether and when they are eligible to donate depends on where they travelled to and for how long. Those who are ineligible to donate whole blood, platelets or plasma for transfusion for a certain amount of time may still be eligible to donate source plasma.

People visiting a Canadian Blood Services donor centre are asked a series of questions[2] to determine their risk of exposure to malaria and eligibility to donate. The answers to these questions are reviewed against the eligibility criteria to determine the donor's eligibility to donate.

The current donor eligibility criteria related to malaria are summarized in Table 1.

Table 1. Donor eligibility criteria related to malaria

Potential donor	Eligibility to donate source plasma	Eligibility to donate whole blood, platelets or plasma for transfusion
Person with a history of malaria	Eligible to donate six months after recovery date	Indefinitely ineligible to donate
Person who has spent more than six consecutive months in a malaria-endemic area	Eligible to donate	Eligible to donate three years from the date they left the malaria-endemic area
Person who has spent less than six months in a malaria-endemic area[3]	Eligible to donate	Eligible to donate three months from the date they left the malaria-endemic area

[2] These questions are current as of December 2023: 1. In the last three months, did you return from a stay of less than six months outside Canada and the U.S.? 2. In the last three and a half years, have you spent more than six months in a continuous period outside Canada or the U.S? 3. Have you ever had malaria?

[3] People who visit malaria-endemic areas for less than 24 hours in Mexico, Central America and the Caribbean are eligible to donate. People who travel in or through a malaria-endemic area in any other

Each year, about 200 to 225 people with a history of malaria who attend a Canadian Blood Services donor event are determined to be indefinitely ineligible to donate. Donor ineligibility related to malaria disproportionately impact African, Caribbean and Black communities, Southeast Asian communities, and others who have lived in or travelled to malaria-endemic areas. About 15 to 21 per cent of first-time Black donors are ineligible to donate due to a history of malaria. Many others (eligible or not) may self-defer. Black donors currently make up about 0.6 per cent of all whole blood donors, but 32 per cent of all blood donors with a rare blood group. These donors are important as we strive to meet the needs of people with high transfusion needs, such as people with sickle cell disease with rare blood groups.

For many people who need regular blood transfusions, a close blood type match is essential. Red blood cells have proteins on their surfaces called antigens. There are more than 600 known antigens, with more being found each year. A person's unique combination of antigens is called their "phenotype." Since a person's detailed blood type (beyond ABO blood group) is linked to their ancestry, a close match is more likely to be found in donors of the same race or similar ethnicity. Blood that has been phenotyped has been assessed for its profile of antigens. A donor base that reflects the population it serves helps to ensure these phenotype-matched products are available for the people who need it.

Canadian Blood Services provides a safe blood supply to meet the needs of patients. We also aim to be as minimally restrictive as possible in the donor eligibility criteria while maintaining safety. This approach is particularly important in ensuring that we can meet the changing needs of the diverse population of patients in Canada.

1.2 About this report

As part of our continuous improvement efforts, Canadian Blood Services started a process in the fall of 2022 to review current strategies and alternative options to manage the risk of transfusion-transmitted malaria to patients in Canada. This report presents the results of this analysis, including:

- the risk management options considered
- what we learned from stakeholders
- an overview of the assessments conducted
- how we evaluated the options and what we found
- recommendations for continuing to ensure a safe blood supply to meet the needs of people with complex transfusion requirements

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part of the world, for any length of time, are ineligible to donate, except for trips directly to and from airports in enclosed motor vehicles. Time spent in these areas is not cumulative; people may visit each destination for up to 24 hours.

Detailed feedback from stakeholders is included in the *What We Heard Report* (Canadian Blood Services, 2023).

1.3 Risk-based decision-making framework for blood safety

The Alliance of Blood Operators' *Risk-Based Decision-Making Framework for Blood Safety* (Alliance of Blood Operators, 2015) was used to conduct the current analysis.

This risk-based decision-making framework provides blood operators with an approach for making decisions about blood safety in the context of emerging risks, evolving technology, societal issues and economic realities. It recognizes it is not possible to eliminate all risk. It balances risks against benefits, acknowledging that some level of risk may be tolerable to achieve the anticipated benefits.

Through this structured decision-making approach, Canadian Blood Services aimed to:

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

The risk-based decision-making framework provided a thorough and analytical approach to guide our decision-making through six stages: preparation, problem formulation, participation strategy, assessments, evaluation, and decision.

2. Defining the risk

Determining the best approach to mitigate the risk of transfusion-transmitted malaria starts with clearly understanding the risk. Information was gathered about the risk to determine what options might be feasible and what assessments we would need.

2.1 Decision drivers

Decision drivers support our analysis by helping to define the issue, ensure we are conducting the appropriate assessments and, most importantly, guide decision-making.

The following decision drivers were identified for this analysis. The first two provided the central focus for the evaluation and recommendations, with safety of the blood supply being the primary driver:

- **Safety of blood supply:** To safeguard and provide effective, reliable products that meet safety and quality standards.

- **Patient requirements:** To ensure that patients with complex transfusion requirements have product available (i.e., rare red blood cell antigens).
- **Continuous improvement:** To inform and facilitate ongoing evaluation and improvement of our approach to addressing transfusion-transmitted malaria risks and their impacts on patients and donors.
- **Enhanced donor inclusion:** To support recruitment of a diverse donor base through policies that are minimally restrictive and uphold the safety and sufficiency of the blood supply (particularly Black, African, Caribbean and South Asian donors who are impacted by transfusion-transmitted malaria mitigations).
- **Trust and relationship:** To support effective risk communication and maintain or enhance relationships between stakeholders.

These decision drivers were used as criteria in the rating of the risk management options.

2.2 Risk management options

Along with maintaining the status quo, seven other risk management options were evaluated, recognizing that they are not mutually exclusive in addressing the risk of transfusion-transmitted malaria.

Risk Management Option 1: Maintain status quo

In this risk management option:

- No changes would be made to the current risk mitigation approaches for transfusion-transmitted malaria. We would continue to use the current donor screening questions without putting any new donor testing in place.
- No additional research would be conducted.

Risk Management Option 2: Define and implement a research agenda to assess the level of malaria parasitemia in donors and potential donors

In this risk management option:

- A research agenda would be implemented to define research priorities for assessing the level of malaria parasites in the blood of donors and potential donors in Canada. The research agenda would focus on epidemiological research that could inform a risk model for transfusion-transmitted malaria scenarios in Canada given the current lack of data.
- No changes would be made to the current donor eligibility criteria.

Risk Management Option 3: Update eligibility criteria related to malaria for people donating apheresis plasma (for transfusion) and apheresis platelets that would be pathogen reduced[4]

In this risk management option:

- The eligibility criteria related to malaria for people donating apheresis plasma (for transfusion) and apheresis platelets, which would be pathogen reduced, would be updated to match the current criteria for people donating source plasma:
  - A person with a history of malaria can donate six months after recovering from malaria.
  - A person who travels in or through a malaria-endemic area for any length of time can donate.
- No changes would be made to the current eligibility criteria for donating whole blood.
- Post-implementation monitoring activities would be put in place.

For people donating apheresis plasma (for transfusion) or apheresis platelets, this means:

- Those who were temporarily ineligible to donate because they travelled to or lived in a malaria-endemic area may be eligible to donate if they meet all other donor eligibility criteria.
- Those who were indefinitely ineligible to donate because they had a history of malaria may be eligible to donate six months after they recover from malaria if they meet all other donor eligibility criteria.

For people donating whole blood, there would be no change to their eligibility to donate.

Risk Management Option 4: Update eligibility criteria related to malaria for people donating whole blood; platelets and plasma for transfusion would be pathogen reduced and red blood cells would not be used for patient care

In this risk management option:

- The eligibility criteria related to malaria for people donating whole blood would be updated. Donors who have lived in a malaria-endemic area or who have had malaria may be eligible to donate whole blood in locations where pathogen inactivation technology is in place for platelets and plasma if they meet all other donor eligibility criteria.

[4] Pathogen inactivation technology is being implemented at Canadian Blood Services for platelets and plasma. We expect to distribute pathogen-reduced platelets across the country by summer 2024. Pathogen-reduced plasma is under development with implementation in the coming year.

- Red blood cells donated by people who have lived in a malaria-endemic area or who have had malaria would not be used for patient care. The red blood cells would either be discarded or used in limited quantities for other purposes. For example, the red blood cells could be used for quality assurance; evaluating the blood supply; process and product improvement testing; making reagents for testing; or teaching or research purposes.
- Post-implementation monitoring activities would be put in place.

For people donating whole blood, this means:

- Donors donating in locations where pathogen reduction is available may be able to donate whole blood even with a risk of exposure to malaria if they meet all other donor eligibility criteria. They would still be asked the current donor screening questions for malaria to determine how their donation would be used.
  - For donors without a risk of exposure to malaria, the donation would proceed through the regular manufacturing process for transfusable products.
  - For donors with a risk of exposure to malaria, the donated plasma or platelet components may undergo pathogen inactivation and be used to treat patients (platelets).
  - The donated red blood cells would not be used for patient care.
  - Depending on inventory levels, the donated plasma may also be directed to further manufacturing for fractionation into medications, such as immunoglobin therapies.

Risk Management Option 5: Ask potential donors with a risk of exposure to malaria to engage with a physician or other health-care provider to undergo malaria testing outside of Canadian Blood Services before donating

In this risk management option:

- Some potential donors who have lived in a malaria-endemic area or who have had malaria may be asked to consult a physician or other health-care provider, request testing for malaria, and discuss their results with the provider before making an appointment to donate blood, depending on when they lived in the malaria-endemic area or recovered from malaria.
- Potential donors who test negative for malaria may be eligible to donate whole blood if they meet all other donor eligibility criteria.
- Potential donors who test positive for malaria would be ineligible to donate whole blood.

Risk Management Option 6: Allow people with a history of malaria to donate after a certain amount of time, with no other mitigations.

In this risk management option:

- The eligibility criteria for donating whole blood, platelets and plasma for transfusion would be updated to allow people who have had malaria and were indefinitely ineligible to donate after a certain amount of time.
- No other mitigations for transfusion-transmitted malaria would be required, such as donor testing or the use of pathogen inactivation technology.
- Post-implementation monitoring activities could be put in place, depending on regulatory requirements.

For people who have had malaria, this means:

- They would still be asked the donor screening questions for malaria.
- They may no longer be indefinitely ineligible to donate. Instead, they may be eligible to donate after a certain amount of time if they meet all other donor eligibility criteria.

For people who have travelled to or lived in a malaria-endemic area, there would be no change.

Risk Management Option 7: Introduce malaria antibody testing for donors with a risk of exposure to malaria

In this risk management option:

- Malaria antibody testing would be used to test the immunological response (i.e., presence of antibodies) in the blood, rather than the infectiousness (i.e., the presence of parasites) of the blood.
- If the blood tests positive for malaria antibodies, the donation would not be used for patient care. The donation would be discarded, and a sample might be stored for future testing.

For people donating whole blood, this means:

- They would still be asked the donor screening questions for malaria.
- Some people who have lived in a malaria-endemic area or who have had malaria may have their donation tested for antibodies to malaria parasites before it is used for patient care, depending on when they lived in the malaria-endemic area or recovered from malaria.
- Potential donors who test negative for malaria antibodies may be eligible to donate if they meet all other donor eligibility criteria.
- Potential donors who test positive for malaria antibodies would be informed of their positive test results and would not be eligible to donate. Positive test results may be reportable to the public health authority depending on the jurisdiction.

Risk Management Option 8: Introduce malaria nucleic acid testing for donors with a risk of exposure to malaria

In this risk management option:

- Malaria nucleic acid testing would be used to test the infectiousness (i.e., presence of parasites) of the blood, rather than the immunological response (i.e., presence of antibodies) in the blood.

For people donating whole blood, this means:

- They would still be asked the donor screening questions for malaria.
- People who have had malaria or lived in a malaria-endemic area would have their donation tested to detect malaria parasites before it is used for patient care.[5]
- Potential donors who test negative for malaria may be eligible to donate if they meet all other donor eligibility criteria.
- Potential donors who test positive for malaria would be informed of their positive test results and would not be eligible to donate whole blood. Positive test results may be reportable to the public health authority depending on the jurisdiction.

Risk management options not further assessed

Two risk management options were identified but did not proceed to evaluation:

A) Collect red blood cells from donors with a risk of exposure to malaria for people who consent to receive products that could contain malaria parasites

In this risk management option:

- Donors who qualify for Canadian Blood Services' Rare Blood Program[6] and have a risk of exposure to malaria may be eligible to donate if they meet all other donor eligibility criteria.
- Blood components collected from these donors would not be required to undergo additional risk mitigation approaches for transfusion-transmitted malaria such as testing or the use of pathogen inactivation technology before being used for patient care.
- Recipients of these products would need to consent to receive products that could contain malaria parasites.

This risk management option does not meet the safety and quality standards for mitigating the risk of malaria and creates a two-tier blood supply system. Consistent quality standards for all products and all patients are the basis of a safe blood supply system and cannot be compromised. This option does not address the primary decision driver of the risk-based decision-making process, safety of the blood supply.

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[5] A malaria nucleic acid testing assay is under development by commercial vendors.
[6] The Rare Blood Program includes donors who have an antigen profile found in less than 0.1 per cent of the population.

B) Remove all current risk mitigation approaches for transfusion-transmitted malaria

In this risk management option:

- Donor screening questions and eligibility criteria related to transfusion-transmitted malaria[7] would be removed.
- Blood components would not be required to undergo additional risk mitigation approaches for transfusion-transmitted malaria such as testing or the use of pathogen inactivation technology before being used for patient care.

This option does not meet quality and safety standards for any non-endemic country reviewed. Removing all risk mitigation approaches would increase the risk of transfusion-transmitted malaria. This option does not address the primary decision driver of the risk-based decision-making framework, safety of the blood supply.

3. Learning from stakeholders

Engaging with stakeholders is a vital step in the risk-based decision-making process. It ensures that diverse perspectives are heard, considered and contribute to the evaluation of options to support decision-making.

Canadian Blood Services worked with an external organization to gather feedback from stakeholders on the risk management options. While the methodology was limited by sample size, time constraints, representation and scope, participants provided important insights for consideration.

Interviews were conducted with 14 stakeholders. Participants included representatives from patient product user groups and advocacy organizations, specialized researchers, and medical professionals who prescribe blood components to treat people with rare blood diseases. More than half of interview participants were members of African, Caribbean or Black communities or had direct connections to malaria-endemic areas. Significantly, half of participants had a good understanding of malaria, either through personal or professional encounters with the disease or by relying on blood products due to their health conditions.

In addition to providing valuable feedback on current and potential risk mitigation approaches for transfusion-transmitted malaria, stakeholders shared their perspectives on topics unrelated to the current analysis. Canadian Blood Services is working with stakeholders to address their valued input on these topics through other initiatives; the following section focuses on feedback related to transfusion-transmitted malaria alone.

[7]The donor screening questions as of December 2023 are as follows: In the last three months, did you return from a stay of less than six months outside Canada and the U.S.? In the last three and a half years, have you spent more than six months in a continuous period outside Canada or the U.S? Have you ever had malaria?

3.1 What we heard

Stakeholders supported transparent and evidence-informed changes to the current risk mitigation approaches for transfusion-transmitted malaria that balance safety and availability of blood components to meet patient needs. They were interested in changes that would increase and diversify the donor pool, increase the supply of phenotype-matched blood products for patient use, and enhance donor inclusion. Stakeholders also supported greater alignment of Canadian Blood Services' risk measures with those in other jurisdictions.

Stakeholder feedback on the proposed risk management options is summarized below:

- **Risk Management Option 1: Maintain status quo —** Stakeholders saw maintaining the status quo as out of date and too restrictive to meet the needs of an increasingly diverse population in Canada. Some stakeholders were concerned about the availability of phenotype-matched blood, especially components used to treat people with sickle cell disease.
- **Risk Management Option 2: Define and implement a research agenda to assess the level of malaria parasitemia in donors and potential donors —** Stakeholders supported the development of a research approach to better identify malaria parasites in donors' blood. They emphasized the need to conduct research with Black communities in Canada with great care, and in a respectful and collaborative way to build acceptance, trust and support.
- **Risk Management Option 3: Update eligibility criteria related to malaria for people donating apheresis plasma (for transfusion) and apheresis platelets that would be pathogen reduced —** Stakeholders supported the idea of inviting people who may have been previously ineligible to donate whole blood to donate apheresis plasma (for transfusion) and apheresis platelets once pathogen inactivation technology is in place. They emphasized the need to ensure front-line and donor centre staff are trained and able to communicate the change well and answer donors' questions.
- **Risk Management Option 4: Update eligibility criteria related to malaria for people donating whole blood; platelets and plasma for transfusion would be pathogen reduced and red blood cells would not be used for patient care —** Some stakeholders supported this option as a way to increase and diversify the donor pool. However, some stakeholders had ethical concerns and were uneasy about not using or discarding red blood cells when some people with sickle cell disease could potentially benefit from those unused red blood cells in their care. This option may have been more widely supported if it had included using the red blood cells for research.
- **Risk Management Option 5: Ask potential donors with risk of exposure to malaria to engage with a physician or other health-care provider to undergo malaria testing outside of Canadian Blood Services before donating —** This option was not supported. Asking some potential donors to take steps others are not asked to take was seen as exclusionary.

- **Risk Management Option 6: Allow people with a history of malaria to donate after a certain amount of time, with no other mitigations —** Stakeholders were open to changing the current donor eligibility criteria. While safety is still a priority for patients, stakeholders felt it is less of a concern than it was a couple of decades ago, especially if it means supply may not be available. Stakeholders noted that if a new temporary waiting period is introduced for patients with a history of malaria, the change must be supported by evidence.
- **Risk Management Option 7: Introduce malaria antibody testing for donors with risk of exposure to malaria or Risk Management Option 8: Introduce malaria nucleic acid testing for donors with a risk of exposure to malaria —** Stakeholders supported the idea of introducing testing for malaria. Some stakeholders wanted to better understand the real and theoretical differences between the testing options and levels of perceived risk. Several stakeholders saw testing alone (without donor screening questions) as the best way to mitigate the risk of transfusion-transmitted malaria, while others preferred to keep the donor screening questions for malaria along with the introduction of any testing.

More detailed information on the input shared by stakeholders is included in the *What We Heard Report* (Canadian Blood Services, 2023).

4. Assessments

Canadian Blood Services conducted the following assessments to support the evaluation of the risk management options:

- blood safety review
- contextual assessment (legal considerations and jurisdictional review)
- ethical analysis
- operational review

Key findings from these assessments are summarized below.

4.1 Blood safety review

This review considered the risk of transfusion-transmitted malaria.

Key findings

- The 2023 annual malaria report from the World Health Organization highlights the growing impact of climate change on the spread of malaria around the world. Changes in temperature, humidity and rainfall patterns directly affect the behaviour and lifespan of *Anopheles* (marsh) mosquitoes, the mosquitoes that transmit malaria. Extreme weather conditions like heatwaves and floods also have a serious effect on the spread of the disease and its overall impact. A notable example of this was seen in Pakistan in 2022, where catastrophic floods resulted in five times more cases of malaria (World Health Organization, 2023).
- The emergence of genetic polymorphisms (genetic variations) associated with resistance to anti-malarial drugs (e.g., pfhrp2 gene deletions) is a significant risk to the global effort to reduce the burden of malaria.

- Malaria vaccines are available and under continued development, with implementation programs prioritizing children in African countries who are at the highest risk of dying from malaria. If effective vaccines are distributed widely, they may alter the epidemiology of malaria in the coming years by providing protection against the disease.
- In 2022, there were about 249 million cases of malaria in 85 malaria-endemic countries and areas, an increase of five million cases compared with 2021. The malaria case incidence was 58 per 1,000 people at risk.
- About 608,000 people died of malaria around the world in 2022.
- In Canada, there have been four probable or confirmed cases of transfusion-transmitted malaria since 1994.
  - Two of these cases (1994 and 1995) involved donors who had a remote history of malaria, which means they had malaria more than three years before they donated. These donors were eligible at the time they donated but would be ineligible to donate under the current eligibility criteria. As a result of these cases, in 1997 Health Canada approved a proposal by the Canadian Red Cross Society to change the three-year waiting period for people with a history of malaria to an indefinite ineligibility.
  - The probable case of transfusion-transmitted malaria in 2022 involved a donor who met the eligibility criteria; the donor did not have a history of malaria and had not recently lived in or travelled to a malaria-endemic area. This donor is believed to have been semi-immune, meaning they might not have had symptoms of malaria, but they still carried malaria parasites in their red blood cells (asymptomatic donor).
  - Based on these case reports, the risk of transfusion-transmitted malaria in Canada is about one in 9.4 million units of red blood cells transfused (i.e., one potential case of transfusion-transmitted malaria over 13 years based on historical data and the current number of red blood cell units transfused in Canada).
- In Canada, just under 500 people who lived in or travelled to malaria-endemic areas are reported to have malaria each year.
- The prevalence of malaria among asymptomatic potential blood donors in Canada is unknown. A 2019 study reported that some African countries report the percentage of asymptomatic blood donors as more than 10 per cent.
- Studies conducted in the U.K. and Australia estimate that 0.1 to 0.5 per cent of donors who had a history of malaria three or more years before trying to donate likely have malaria parasites in their blood (parasitemia).
- Each year, about 200 to 225 people with a history of malaria who attend a Canadian Blood Services donor event are determined to be indefinitely ineligible to donate.

- If the donors currently ineligible to donate due to a history of malaria (n=200) were eligible to donate after three years (with no other implemented mitigations), it is estimated that over five years, one to five units of red blood cells could contain malaria parasites. There is a risk that these units could lead to malaria being transmitted to a blood recipient. This means that implementing a temporary waiting period for people with a history of malaria similar to the one adopted by the U.S. Food and Drug Administration could result in a conservative estimate of one to five cases of transfusion-transmitted malaria over five years. This estimate does not account for the fact that a whole blood donation from an asymptomatic donor carrying malaria parasites can be manufactured into two potentially infectious blood components (red blood cells and platelets), both of which have been associated with transfusion-transmitted malaria. It also does not account for a potential increase in new donors with a history of malaria who may be self-deferring today.

- The ineligibility of donors with a history of malaria to donate disproportionately affects Black donors. About 15 to 21 per cent of first-time Black donors are ineligible to donate due to a history of malaria. Others (eligible or not) may self-defer.
- Malaria is usually acquired outside of non-endemic countries, with rare exceptions.
- According to the U.S. Centers for Disease Control and Prevention, between May and August 2023 the U.S. reported nine cases of locally acquired malaria. These were the first cases of locally transmitted malaria reported in the U.S. in 20 years (Centers for Disease Control and Prevention, 2023).

4.2 Contextual assessment (legal considerations and jurisdictional review)

This assessment reviewed the legal and regulatory context for the risk management options within Canada as well as the laws and standards of other jurisdictions.

Key findings

- Canadian Blood Services is responsible for ensuring blood is safe and of high quality for transfusion in accordance with the *Blood Regulations*, which fall under the *Food and Drugs Act*.
- Blood will always carry some residual safety risk. Therefore, potential donors must be assessed as eligible to donate according to authorized criteria. Since there is no blood donor screening test approved by Health Canada that can detect malaria, eligibility to donate is currently determined based on criteria related to potential donors' medical and social histories. Any change to the current donor eligibility criteria related to malaria requires an amendment to Canadian Blood Services' authorization under the *Blood Regulations*.
- If malaria testing were to be implemented as part of a risk management approach, Canadian Blood Services may be required to report cases of malaria infection to public health authorities depending on the jurisdiction.
- There is no uniform approach to malaria screening around the world. Canada's indefinite ineligibility of people with a history of malaria to donate is the most stringent requirement among non-endemic countries in the world. For people who lived in or travelled to a malaria-

endemic area, Canada's eligibility criteria are similar to those of the other non-endemic countries reviewed.

4.3 Ethical analysis

This assessment explored the implications of the following key ethical values and principles: consistency and comparability; diversity, equity and inclusion; evidence-informed approach; justice; innovation and excellence; responsiveness; and safety and trust.

Key findings

- Many of the key ethical values and principles considered are part of and already reflected in the overall risk-based decision-making process. For example, they are integrated in the decision drivers related to the safety of the blood supply, donor diversity and inclusion, and trust and relationships.
- Considering the ethical implications of the risk management options is challenging given the different perspectives on the relative importance of some values and principles over others. For example, feedback described in the *What We Heard Report* (Canadian Blood Services, 2023) illustrated the complexity of balancing the expectation of a safe blood supply with the desire for a more diverse donor pool. Rather than seeing safety and diversity as competing values, the assessment integrated and reflected what each value and principle offers in relation to the proposed risk management options.

4.4 Operational review

This assessment reviewed the implications for Canadian Blood Services' operations associated with implementing the risk management options. The complexity and feasibility of each risk management option was assessed. Given that Risk Management Option 1 is our current practice (status quo), an operational review was not conducted for this risk management option.

Key findings

The following risk management options were found to be unfeasible or highly complex to implement:

- Introducing malaria nucleic acid testing for donors with a risk of exposure to malaria (Risk Management Option 8), should a malaria nucleic acid test become available, would require several new processes both within and outside of Canadian Blood Services. For example, processes would need to be developed within the broader health systems to manage asymptomatic people who test positive for malaria and report cases to public health authorities.
- Introducing malaria antibody testing for donors with a risk of exposure to malaria (Risk Management Option 7) would not be feasible given there is no licensed antibody test for blood donor screening approved by Health Canada and commercial vendors have shown no interest in obtaining licensure for use in Canada. There may also be external challenges given

the lack of experience in North American microbiology, infectious diseases, and public health communities with managing people who test positive for malaria.

- Engaging physicians and other health-care providers and requiring testing outside of Canadian Blood Services (Risk Management Option 5) was deemed unfeasible given the onus it puts on the potential donor and their physician. This risk management option would also rely on the use of a diagnostic test for malaria that is not approved or licensed by Health Canada as a blood donor screening test for malaria. Each testing facility would be required to have an establishment licence under the *Blood Regulations*. Canadian Blood Services would need to track every testing facility and test kit being used. The lack of access to physicians may also be another issue to be considered.

The following risk management options were found to be moderately complex to implement:

- Both updating the eligibility criteria for people donating apheresis plasma (for transfusion) and apheresis platelets (Risk Management Option 3) and updating the eligibility criteria for people donating whole blood with components for transfusion being pathogen reduced and red blood cells not being used for patient care (Risk Management Option 4) would require changes to several Canadian Blood Services processes.
- While the organization is experienced in conducting research studies, defining and implementing a research agenda to assess the level of malaria parasitemia in donors and potential donors (Risk Management Option 2) would require an extensive planning phase, a research ethics approval process, and a new donor consent process and materials. Most importantly, it might be difficult to recruit non-blood-donor participants across Canada.
- Changing the indefinite ineligibility of donors with a history of malaria to a temporary waiting period with no additional mitigations (Risk Management Option 6) is not feasible given the lack of data available to support a submission to Health Canada for a change to the eligibility criteria.

5. Evaluation

Each risk management option was evaluated using the following criteria:

- **Alignment with decision drivers:** Each risk management option was evaluated against the decision drivers. Maintaining the safety of the blood supply and striving to increase the availability of phenotype-matched blood provided the central focus for the evaluation and recommendations, with safety of the blood supply being the primary driver.
- **Additional considerations:** The evaluation also considered the following:
  - **Benefits** not already captured through the decision drivers, such as increased supply of some blood products and advances in science.
  - **Contextual factors**, including stakeholder concerns.
  - **Operational feasibility** of Canadian Blood Services implementing the risk management option and the level of complexity in doing so.

The key findings from the evaluation are summarized in the following table. The table indicates how each risk management option aligns with the decision drivers, along with some additional considerations.

Risk management option	Evaluation against the decision drivers	Additional considerations Benefits, contextual factors, operational feasibility
Risk Management Option 1 Maintain status quo	• **Safety of blood supply:** Would maintain the safety of the blood supply in our current context. • **Patient requirements:** Would not increase the inventory of red blood cells or the availability of phenotype-matched blood. • **Continuous improvement:** Would not support continuous improvement of Canadian Blood Services' approach to transfusion-transmitted malaria. • **Donor diversity and inclusion:** Would not contribute to donor diversity and inclusion; donors with a history of malaria would remain ineligible to donate, which disproportionately affects Black donors. • **Trust and relationships:** Would not be supported by some communities.	• Would be less effective if the epidemiology of malaria changes, which is more likely with climate change and changes in population diversity.
Risk Management Option 2 Define and implement a research agenda to assess the level of malaria parasitemia in donors and potential donors	• **Safety of blood supply:** Would not directly impact the safety of the blood supply. • **Patient requirements:** Would not increase the inventory of red blood cells or the availability of phenotype-matched blood. • **Continuous improvement:** Would provide data to evaluate Canadian Blood Services' approach to transfusion-transmitted malaria. • **Donor diversity and inclusion:** Would demonstrate Canadian Blood Services' commitment to donor diversity and inclusion. • **Trust and relationships:** Could be perceived by some stakeholders as delaying change.	• Could inform other blood operators' risk mitigation approaches through research and scientific advances. • Would require new Canadian Blood Services processes for overseeing research with the general population (versus with donors). • Would not promptly respond to the changing context given climate change and the potential increase in locally acquired malaria, as well as higher levels of immigration from malaria-endemic areas.

Risk management option	Evaluation against the decision drivers	Additional considerations Benefits, contextual factors, operational feasibility
Risk Management Option 3 Update eligibility criteria related to malaria for people donating apheresis plasma (for transfusion) and apheresis platelets that would be pathogen reduced	• **Safety of blood supply:** Would maintain the safety of the blood supply as pathogen inactivation technology inactivates malaria parasites in plasma and platelets. • **Patient requirements:** Would not increase the inventory of red blood cells or the availability of phenotype-matched blood. • **Continuous improvement:** Would provide data through post-implementation monitoring to understand the malaria rate in donors; would result in changes to eligibility criteria to allow more donations through apheresis. • **Donor diversity and inclusion:** May allow previously ineligible people to donate at select donor centres that collect donations through apheresis. • **Trust and relationships:** Would not address concerns raised by clinicians and people in the sickle cell community about the availability of red blood cells; may not support positive relationships with stakeholders.	• Would redirect donors and may increase the supply of plasma and platelets.

Risk management option	Evaluation against the decision drivers	Additional considerations Benefits, contextual factors, operational feasibility
Risk Management Option 4 Update eligibility criteria related to malaria for people donating whole blood; platelets and plasma for transfusion would be pathogen reduced and red blood cells would not be used for patient care	• **Safety of blood supply:** Would maintain the safety of the blood supply as pathogen inactivation technology inactivates malaria parasites in plasma and platelets. • **Patient requirements:** Would not increase the inventory of red blood cells or the availability of phenotype-matched blood. • **Continuous improvement:** Would provide data through post-implementation monitoring to understand the malaria rate in donors; would result in changes to eligibility criteria to allow more whole blood donations. • **Donor diversity and inclusion:** May allow previously ineligible people to donate. • **Trust and relationships:** Would not address concerns raised by clinicians and people in the sickle cell community about product availability; would not support positive relationships with stakeholders.	• May increase the supply of plasma and platelets. • Would carry operational challenges (e.g. increased potential for product discards, modifications to supply planning processes). • May have ethical considerations for donors related to iron depletion associated with the current donation process if donated red blood cells are not for patient use.
Risk Management Option 5 Ask potential donors with a risk of exposure to malaria to engage with a physician or other health-care provider to undergo malaria testing outside of Canadian Blood Services before donating	• **Safety of blood supply:** Would change Canadian Blood Services' standardized approach and internal controls for maintaining the safety of the blood supply. • **Patient requirements:** May only minimally increase the inventory of red blood cells and availability of phenotype-matched blood given the anticipated low number of potential new donors due to barriers to accessing health-care providers. • **Continuous improvement**: Would represent a change but would not significantly improve the approach to transfusion-transmitted malaria. • **Donor diversity and inclusion:** Would minimally address concerns related to exclusion given the associated barriers (e.g., access to health-care provider, cost impact on laboratories). • **Trust and relationships:** Would place burden on the donor and so would not support positive relationships with stakeholders.	• Would help asymptomatic people with malaria be diagnosed and receive treatment, if required. • Would carry operational challenges for the external laboratories requiring Health Canada oversight under the *Blood Regulations* (e.g., testing facilities would need an establishment licence and to comply with the regulations). • Would require that Canadian Blood Services add the testing to its Health Canada authorization and be informed of every testing facility and test kit being used; it is unknown whether Health Canada would approve the use of a diagnostic test for malaria that has not been licensed as a blood donor screening test for malaria.

Risk management option	Evaluation against the decision drivers	Additional considerations Benefits, contextual factors, operational feasibility
Risk Management Option 6 Allow people with a history of malaria to donate after a certain amount of time, with no other mitigations	• **Safety of blood supply:** Would increase the risk of transfusion-transmitted malaria associated with the increase of potentially infectious units in the blood supply. • **Patient requirements:** May reduce the number of people ineligible to donate, which could increase the inventory of red blood cells and availability of phenotype-matched blood. • **Continuous improvement:** Would represent a minor improvement to the approach to transfusion-transmitted malaria but presents further challenges. • **Donor diversity and inclusion:** Could enhance inclusion among members of African, Caribbean and Black communities, and Southeast Asian communities, including some who may have previously self-deferred. • **Trust and relationships:** Would have mixed support from stakeholders; some stakeholders are only open to change if it is informed by evidence; others are open to a wider range of changes for phenotype-matched blood because malaria is a treatable infection.	• Could be challenging to receive Health Canada approval without Canadian data to support changing eligibility criteria.

Risk management option	Evaluation against the decision drivers	Additional considerations Benefits, contextual factors, operational feasibility
Risk Management Option 7 Introduce malaria antibody testing for donors with a risk of exposure to malaria	• **Safety of blood supply:** Could increase the safety of the blood supply as it provides testing for donors who have lived in malaria-endemic areas who are currently eligible to donate. • **Patient requirements:** Would not affect the inventory of red blood cells or the availability of phenotype-matched blood because the anticipated donation gains (from previously ineligible donors with a history of malaria who would become eligible to donate) would be balanced out by losses (donors who were previously eligible to donate but who might not be anymore depending on their test results). • **Continuous improvement:** Would contribute to a better understanding of the malaria immunity rates in Canada; this data could be beneficial nationally. • **Donor diversity and inclusion:** Could encourage more people who have lived in malaria-endemic areas to donate. • **Trust and relationships:** Would be supported by stakeholders.	• Could help asymptomatic people with malaria be identified and receive treatment, if required. • Would require a Health Canada–approved test, which is not yet available. • Would carry challenges given the lack of experience in North American microbiology and public health communities with managing people who test positive. • Could negatively impact public health authorities and clinicians given reporting requirements for cases of malaria.

Risk management option	Evaluation against the decision drivers	Additional considerations Benefits, contextual factors, operational feasibility
Risk Management Option 8 Introduce malaria nucleic acid testing for donors with a risk of exposure to malaria	• **Safety of blood supply:** Could decrease the risk of transfusion-transmitted malaria by identifying people who are semi-immune, asymptomatic or both. • **Patient requirements:** May reduce the number of people ineligible to donate, which would increase the inventory of red blood cells and availability of phenotype-matched blood. • **Continuous improvement:** Would contribute to a better understanding of the malaria rate in Canada; this data could be beneficial nationally. • **Donor diversity and inclusion:** Would address concerns related to exclusion for donors with a history of malaria. • **Trust and relationships:** Would be supported by stakeholders.	• Could help asymptomatic people with malaria be identified and receive treatment, if required. • Would require a Health Canada–approved test, which is not yet available. • Would involve unknown process flows and cost implications, which would impact the timelines and specifics of implementation. • Would carry challenges given the lack of experience in North American microbiology and public health communities with managing people who test positive. • Would require resources and education for people who test positive and for clinicians who care for these potential patients. • Could negatively impact public health and clinicians given reporting requirements for cases of malaria.

6. Recommendations

Canadian Blood Services used the information gathered throughout the risk-based decision-making process to develop recommendations to mitigate the risk of transfusion-transmitted malaria. While each risk management option was evaluated on its own, the following recommendations combine parts of several risk management options to increase their impact.

Recommendation 1: Implement nucleic acid testing for malaria in a subset of donors and change the related eligibility criteria for all donors except those donating source plasma[8]

It is recommended that Canadian Blood Services:

a. Continue to collaborate with developers of testing assays on a Health Canada–approved malaria nucleic acid testing assay.
b. Once the malaria nucleic acid testing assay is approved for use in Canada, implement it as a safety measure for donors with a history of malaria and donors who have lived in or travelled to malaria-endemic areas.
c. Update the related donor screening questions and eligibility criteria as supported by scientific evidence and approved by Health Canada.
d. Monitor the use of the malaria nucleic acid testing assay to evaluate its impacts.

Recommendation 2: Maintain the current donor eligibility criteria related to malaria

It is recommended that Canadian Blood Services:

a. Maintain the current donor eligibility criteria related to malaria (see Table 1) while implementing Recommendation 1. This approach ensures that blood products are safe and meet high quality standards.

[8] Due to the pathogen inactivation steps used to manufacture plasma into plasma protein products (e.g., immunoglobulin therapies), nucleic acid testing is not needed for donors who are donating source plasma. All donors at risk of exposure to malaria can donate source plasma except those with a history of malaria, and donors with a history of malaria can donate six months after they are treated and recover from malaria without undergoing other screening tests.

Recommendation 3: Develop stakeholder communication and education plans

It is recommended that Canadian Blood Services:

a. Develop and implement communication and engagement plans to clearly describe to stakeholders how we are continuing to evolve our approach to transfusion-transmitted malaria while maintaining the safety of the blood supply. These plans should include what we will do and why, and how and when we will do it. They should also explain how we will continue to communicate and engage with all stakeholders, including affected communities.
b. Ensure physicians and public health offices have access to educational materials on the implementation of malaria nucleic acid testing and the related changes to the donor screening questions and eligibility criteria.

Recommendation 4: Continue surveillance and monitoring

We must continue our surveillance activities to safeguard the blood supply and ensure that we can respond promptly to changing conditions or mitigate emerging risks.

It is recommended that Canadian Blood Services:

a. Continue to track the epidemiology of malaria in the general public, especially developments in the U.S.
b. Re-evaluate risk mitigation approaches for transfusion-transmitted malaria if the epidemiology of malaria in Canada changes (e.g., local transmission).

Recommendation 5: Consider other changes to the donor eligibility criteria if Recommendation 1 cannot be implemented in a timely way due to external barriers

It is recommended that Canadian Blood Services consider:

a. Updating the donor eligibility criteria related to malaria for people donating apheresis plasma and platelets to align with the current eligibility criteria for donating source plasma (see Table 1) when pathogen inactivation technology is fully implemented for platelets and plasma for transfusion.

   This change would provide another layer of safety for pathogen-reduced transfusible plasma and platelets. Current risk mitigation approaches for transfusion-transmitted malaria would stay the same for red blood cells collected through whole blood donations. Donors with a risk of exposure to malaria would only be eligible to donate at select donor centres that collect donations through apheresis.

b. Updating the donor eligibility criteria related to malaria for people donating whole blood when pathogen inactivation technology is fully implemented for platelets and plasma for transfusion.

   The red blood cells collected using this approach would not be used for patient care since pathogen inactivation technology is not yet available. They would either be discarded or used in limited quantities for other purposes. For example, the red blood cells could be used for quality assurance, evaluating the blood supply, process and product improvement testing, making reagents for testing, or teaching or research purposes. Consent requirements for collecting red cells for non-clinical use would also need to be considered.

6.1 Rationale and considerations

Introducing malaria nucleic acid testing (Recommendation 1) is the best option for Canadian Blood Services to mitigate the risk of transfusion-transmitted malaria. Adopting this recommended approach would address all five decision drivers, and as we have learned from affected communities, would be considered a meaningful change. Being able to detect the presence of parasites directly reduces the risk of transfusion-transmitted malaria in the blood supply.

In addition to the blood safety benefits, introducing malaria nucleic acid testing could increase the inventory of red blood cells and availability of phenotype-matched blood for people with complex transfusion requirements by allowing previously ineligible people to donate. Unlike malaria antibody testing, malaria nucleic acid testing alone would not exclude donors who might carry malaria antibodies in their blood due to past exposure but whose donations might not actually contain the parasite. Increasing the participation of African, Caribbean and Black communities in whole blood donation contributes to the diversity of the donor base to support people with complex transfusion requirements, who are often from these communities (e.g., people with sickle cell disease).

To implement and fully benefit from malaria nucleic acid testing, we first need a licensed testing assay. Although a licensed assay is not yet available in Canada, commercial vendors have expressed interest in bringing their malaria nucleic acid donor screening test kits to the Canadian market.

Given that malaria nucleic acid testing would be new to Canada (and the world), implementing this new technology would require many changes and new processes both within and outside of Canadian Blood Services. It would also mean changes for donors, people who test positive for malaria with a malaria nucleic acid testing assay, physicians and public health colleagues. Engaging and clearly communicating with stakeholders early and often will be essential to ensure positive experiences for everyone involved in the change.

Canadian Blood Services must maintain the current malaria eligibility criteria while implementing malaria nucleic acid testing (Recommendation 2). To be approved by Health Canada, a submission to change the eligibility criteria would require Canadian data or a test to maintain the safety of the blood supply, neither of which is currently available in Canada. If we were to change the indefinite ineligibility to a temporary waiting period like the one adopted by the U.S. Food and Drug Administration, it could result in a conservative estimate of one to five cases of transfusion-transmitted malaria over five years versus the current risk of one potential case over 13 years based on historical data and the current number of red blood cell units transfused. We recognize that keeping the eligibility criteria as they are for now may not be aligned with our decision drivers to strive to increase the availability of phenotype-matched blood or enhance donor inclusion. However, we can continue to advance these goals through other approaches unrelated to transfusion-transmitted malaria. There are no other options that maintain the safety of the blood supply — our number one priority as a blood operator.

Ultimately, Canadian Blood Services is responsible for maintaining a safe blood supply. We also aim to be as minimally restrictive as possible in the donor eligibility criteria. Introducing pathogen inactivation technology for platelets and plasma gives us an opportunity to seek approval from Health Canada to change the eligibility criteria related to malaria, allowing previously ineligible people to donate. Although adjusting the eligibility criteria related to malaria when pathogen inactivation technology is implemented for platelets and plasma is a safe option, our chance to make the greatest impact in striving to increase the availability of phenotype-matched blood — a key decision driver — lies in malaria nucleic acid testing.

7. Toward continuous improvement

This risk-based decision-making analysis marks an important step in continuously improving the work we do to deliver lifesaving products and services for patients in Canada. With the recent probable case of transfusion-transmitted malaria in Canada, the impacts of climate change, and new technologies on the horizon, the time was right to review our approach to mitigating this risk to the Canadian blood supply.

This analysis gave us the chance to review several risk management options, drawing on the results of our assessments to find ways to improve. It also gave us the opportunity to learn from stakeholders about their priorities for a way forward.

The above recommendations reflect our current thinking on this complex issue. While implementing malaria nucleic acid testing and updating the donor eligibility related to malaria would take time and has its challenges, it is the appropriate path forward for us to ensure the safety of the blood supply while being as minimally restrictive as possible .

Looking ahead, we will continue to watch for changes to our current context and for ways to improve our approach to mitigating this risk and its impacts on patients and donors. The results

of this valuable risk-based decision-making analysis and our continuing review of the issue will give us the guidance we need to continue to ensure the safety of Canada’s blood supply.

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Appendix A: Key terms

Blood and blood products

Blood: In the context of the blood supply system, “blood” is an overarching term that means whole blood and blood products, plasma and plasma products, and their respective alternative products. Since Canadian Blood Services opened its doors in 1998, we have been responsible for a national blood supply system that ensures access to a safe, secure and affordable supply of blood, blood products and their alternatives. We support the appropriate use of these products and carry out other functions as designated by our corporate members, the provincial and territorial ministers of health, excluding Quebec.

Whole blood: Whole blood is blood that contains red blood cells, white blood cells, platelets and plasma. A whole blood donation is divided into components, such as red blood cells and platelets that are used to treat patients with different needs. Whole blood is collected from donors at fixed and mobile donor centres across the country. After Canadian Blood Services collects whole blood, it is processed at facilities we own and operate and then delivered to our customers.

Plasma: Plasma is the protein-rich liquid in blood that helps other blood components (red blood cells, white blood cells and platelets) circulate throughout the body. It supports the immune system and helps control excessive bleeding.

Apheresis plasma: Apheresis plasma is plasma collected using an apheresis machine. During an apheresis plasma donation, the equipment we use separates some of the plasma from the rest of the donor’s blood and then returns the remaining blood to the donor. People can donate apheresis plasma more often than whole blood because the body replaces the volume of donated plasma faster than it can replace red blood cells. Apheresis plasma can be used for transfusion or to manufacture plasma protein products through a process called fractionation.

Source plasma: Source plasma is a type of apheresis plasma. It refers to plasma collected from donors using an apheresis machine that is used exclusively to manufacture plasma protein products through a process called fractionation.

Platelets: Platelets are the component of blood that helps with clotting.

Apheresis platelets: Apheresis platelets are platelets collected using an apheresis machine. People can donate apheresis platelets more often than whole blood because the body replaces the volume of donated platelets faster than it can replace red blood cells.

Testing and other technology

Antibody testing: The parasites that cause malaria can lie dormant for decades. This means that no matter how much time has passed, there is still a small chance that someone who has had a malaria infection at some point in their lives may carry malaria parasites in their blood. There is a low-throughput serology assay at the National Centre for Parasitology located within the Research Institute of the McGill University Health Centre, but this assay is a specialized reference test. Serology assays are not broadly used in clinical microbiology or public health laboratories in North America because they are not useful for acute diagnosis. However, serology assays may be used by some blood operators to test subsets of donors with a risk of exposure to malaria. A variety of serologic assays have been used by blood operators in non-endemic countries around the world to identify donors with a history of malaria (Mangano et al, 2019).

Nucleic acid testing: Nucleic acid testing is a highly sensitive method of testing blood. Most traditional screening tests require the presence of antibodies to trigger a positive test reaction. The amount of time between initial infection and detection of antibodies is called the “window period.” Nucleic acid testing reduces the window period by detecting low levels of viral genetic materials that are present soon after infection but before the body has had a chance to start producing antibodies.

Pathogen inactivation technology: Technology that inactivates pathogens. Pathogen-reduced platelets are Canadian Blood Services’ first pathogen-reduced blood product. Platelets treated with pathogen inactivation technology are considered pathogen reduced because the process inactivates viruses, bacteria or parasites that remain despite other safety measures.

Donor eligibility

Self-deferral: People may not attempt to donate if they consider themselves ineligible to donate based on current eligibility criteria, accessibility issues or other factors.

Malaria

Malaria: Malaria is a bloodborne illness caused in humans by a parasite that is transmitted mainly through the bite of *Anopheles* (marsh) mosquitoes. In humans, the malaria parasite travels to the liver. Malaria parasites grow first within the liver and then invade the red blood cells and rapidly multiply. It is the blood stage of the malaria lifecycle that causes the symptoms and complications of malaria.

Malaria-endemic area: A malaria-endemic area is an area where malaria regularly occurs. Malaria-endemic areas are specific regions of countries where public health agencies recommend that travellers take medication (anti-malarial chemoprophylaxis) to prevent malaria

transmission. A disease outbreak is endemic when it is consistently present but limited to a particular region. This makes the spread of the disease and the rates of infection predictable.

Parasitemia: The presence of parasites in the blood. The level of parasitemia, or the quantity of parasites present in the bloodstream, can vary widely and is often used as an indicator of the severity of the infection.

Decision-making

Risk-based decision-making framework: Blood operators manage complex, evolving situations in which they must make decisions to ensure the safety and security of the blood supply for patients. Canadian Blood Services uses a robust risk-based decision-making framework for blood safety developed by the Alliance of Blood Operators (Alliance of Blood Operators, 2015). This framework involves environmental scanning, ethical and legal considerations, and stakeholder perspectives in its approach. It supports effective decision-making for the benefit of health systems and patients.